

Antigen Binding Proteins that Bind CXCR5

Technical Field

The present disclosure provides compositions and methods relating to or derived from anti-CXCR5 antibodies. More specifically, the present disclosure provides human antibodies
5 that bind CXCR5, CXCR5-binding fragments and derivatives of such antibodies, and CXCR5-binding polypeptides comprising such fragments. Further still, the present disclosure provides nucleic acids encoding such antibodies, antibody fragments and derivatives and polypeptides, cells comprising such polynucleotides, methods of making such antibodies, antibody fragments
10 and derivatives and polypeptides, and methods of using such antibodies, antibody fragments and derivatives and polypeptides, including methods of treating or diagnosing subjects having CXCR5 related disorders or conditions, including various inflammatory disorders and various cancers.

Background

CXCR5, also known as Burkitt lymphoma receptor (BLR1), CD185, MDR15 and
15 MGC117347, is a G protein-coupled receptor which is a member of the CXC chemokine receptor family. A ligand is BLC, also known as CXCL13, which is a B cell chemoattractant. The unprocessed CXCR5 precursor is 372 amino acids in length with a molecular weight of 42 KD- CXCR5 has a role in B cell migration and localization within particular anatomic compartments. Knockout mice lack peripheral lymph nodes, have fewer Peyer's patches and
20 have decreased B cell levels.

Summary

The present disclosure provides a recombinant fully human anti-CXC chemokine receptor 5 (CXCR5) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising complementarity determining regions (CDRs) as set forth in
25 a heavy chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174; and comprising a light chain variable domain comprising CDRs as set forth in a light chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO.: 137, SEQ ID NO. 139, SEQ ID NO. 150, and SEQ ID NO. 175.

30 The present disclosure provides a pharmaceutical composition comprising the recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, as described herein, and a pharmaceutically acceptable excipient.

The present disclosure provides a fully human antibody of an IgG class that binds to an CXCR5 epitope with a binding affinity of at least 10^{-6} M, which has a heavy chain variable
35 domain sequence that is at least 95% identical to the amino acid sequences selected from the

group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7,
SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID
NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29,
SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID
5 NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO.50, SEQ ID NO. 52,
SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID
NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74,
SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID
NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98,
10 SEQ ID

NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully human antibody has both a heavy chain and a light chain wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2 (called 52A9 herein), SEQ ID NO. 3/SEQ ID NO. 4 (called 52A10 herein), SEQ ID NO. 5/SEQ ID NO. 6 (called 52B10 herein), SEQ ID NO. 7/SEQ ID NO. 8 (called 52C6 herein),

SEQ ID NO. 9/SEQ ID NO. 10 (called 52D6 herein), SEQ ID NO. 11/SEQ ID NO. 12 (called 52D7 herein), SEQ ID NO. 13/SEQ ID NO. 14 (called 52D11 herein), SEQ ID NO. 15/SEQ ID NO. 16 (called 52E1 herein), SEQ ID NO. 17/SEQ ID NO. 18 (called 52E10 herein), SEQ ID NO. 19/SEQ ID NO. 20 (called 52H9 herein), SEQ ID NO. 21/SEQ ID NO. 22 (called PC12 herein), SEQ ID NO. 23/SEQ ID NO. 24 (called PD10 herein), SEQ ID NO. 25/SEQ ID NO. 26 (called D3-4 herein), SEQ ID NO. 27/SEQ ID NO. 28 (called E2-1 herein), SEQ ID NO. 29/SEQ ID NO. 30 (called A4 or 7A7 herein), SEQ ID NO. 31/SEQ ID NO. 32 (called A8 herein), SEQ ID NO. 33/SEQ ID NO. 34 (called A12 herein), SEQ ID NO. 35/SEQ ID NO. 36 (called B3 herein), SEQ ID NO. 37/SEQ ID NO. 38 (called C8 herein), SEQ ID NO. 39/SEQ ID NO. 40 (called F8 or 10G9 herein), SEQ ID NO. 41/SEQ ID NO. 42 (called G11 herein), SEQ ID NO. 43/SEQ ID NO. 44 (called H3 herein), SEQ ID NO. 45/SEQ ID NO. 46 (called H5 herein), SEQ ID NO. 47/SEQ ID NO. 48 (called H6 herein), SEQ ID NO. 49 (called 2D3 herein), SEQ ID NO. 50/SEQ ID NO. 51 (called 3A11 herein), SEQ ID NO. 52/SEQ ID NO. 53 (called 3B9 herein), SEQ ID NO. 54/SEQ ID NO. 55 (called 3D11 herein), SEQ ID NO. 56/SEQ ID NO. 57 (called 3D12 or 4E12 herein), SEQ ID NO. 58/SEQ ID NO. 59 (called 3E7 herein), SEQ ID NO. 60/SEQ ID NO. 61 (called 3E12 herein), SEQ ID NO. 62/SEQ ID NO. 63 (called 3F7 herein), SEQ ID NO. 64/SEQ ID NO. 65 (called 3G2 herein), SEQ ID NO. 66/SEQ ID NO. 67 (called 3G7 herein), SEQ ID NO. 68/SEQ ID NO. 69 (called 4A5 herein), SEQ ID NO. 70/SEQ ID NO. 71 (called 4E9 herein), SEQ ID NO. 72/SEQ ID NO. 73 (called 4F1 herein), SEQ ID NO. 74/SEQ ID NO. 75 (called 4F4 herein), SEQ ID NO. 76/SEQ ID NO. 77 (called 4H2 herein), SEQ ID NO. 78/SEQ ID NO. 79 (called 5A8 herein), SEQ ID NO. 80/SEQ ID NO. 81 (called 5F1 herein), SEQ ID NO. 82/SEQ ID NO. 83 (called 6A4 herein), SEQ ID NO. 84/SEQ ID NO. 85 (called 6F9 herein), SEQ ID NO. 86 (called 6G5 herein), SEQ ID NO. 87/SEQ ID NO. 88 (called 7B11 or 8B2 herein), SEQ ID NO. 89/SEQ ID NO. 90 (called 7H10 herein), SEQ ID NO. 91 (called 8D12 herein), SEQ ID NO. 92/SEQ ID NO. 93 (called 8H5 herein), SEQ ID NO. 94/SEQ ID NO. 95 (called 9A10 herein), SEQ ID NO. 96/SEQ ID NO. 97 (called 10A12 herein), SEQ ID NO. 98/SEQ ID NO. 99 (called 10B2 herein), SEQ ID NO. 100/SEQ ID NO. 101 (called 10C3 herein), SEQ ID NO. 102/SEQ ID NO. 103 (called 10C7 herein), SEQ ID NO. 104/SEQ ID NO. 105 (called 11E3 herein), SEQ ID NO. 106/SEQ ID NO. 107 (called 11A12 herein), SEQ ID NO. 108/SEQ ID NO. 109 (called 11A7 herein), SEQ ID NO. 110/SEQ ID NO. 111 (called 11C3 herein), SEQ ID NO. 112/SEQ ID NO. 113 (called 11D3 herein), SEQ ID NO. 114/SEQ ID NO. 115 (called 11D4 herein), SEQ ID NO. 116/SEQ ID NO. 117 (called 11D7 herein), SEQ ID NO. 118/SEQ ID NO. 119 (called 11F3 herein), SEQ ID NO. 120/SEQ ID NO. 121

(called 11G3 herein), SEQ ID NO. 122/SEQ ID NO. 123 (called 12A4 herein), SEQ ID NO. 124/SEQ ID NO. 125 (called 12B11 or 14E10 herein), SEQ ID NO. 126/SEQ ID NO. 127 (called 12B4 herein), SEQ ID NO. 128/SEQ ID NO. 129 (called 12C1 herein), SEQ ID NO. 130/SEQ ID NO. 131 (called 12C6 herein), SEQ ID NO. 132/SEQ ID NO. 133 (called 12D11
5 herein), SEQ ID NO. 134/SEQ ID NO. 135 (called 12D3 herein), SEQ ID NO. 136/SEQ ID NO. 137 (called 12G10 herein), SEQ ID NO. 138/SEQ ID NO. 139 (called 13E10 herein), SEQ ID NO. 114/SEQ ID NO. 140 (called 13E4 herein), SEQ ID NO. 141/SEQ ID NO. 142 (called 13A3 herein), SEQ ID NO. 143/SEQ ID NO. 144 (called 13F8 herein), SEQ ID NO. 145/SEQ ID NO. 146 (called 13F9 herein), SEQ ID NO. 147/SEQ ID NO. 148 (called 13G9
10 herein), SEQ ID NO. 149/SEQ ID NO. 150 (called 14E5 herein), SEQ ID NO. 151/SEQ ID NO. 152 (called 14B11 herein), SEQ ID NO. 153/SEQ ID NO. 154 (called 14B4 herein), SEQ ID NO. 155/SEQ ID NO. 156 (called 14C10 herein), SEQ ID NO. 157 (called 14C11 herein), SEQ ID NO. 158/SEQ ID NO. 159 (called 14C3 herein), SEQ ID NO. 160/SEQ ID NO. 161 (called 14D7 herein), SEQ ID NO. 162/SEQ ID NO. 163 (called 14F11
15 herein), SEQ ID NO. 164/SEQ ID NO. 165 (called 14F8 herein), SEQ ID NO. 166/SEQ ID NO. 167 (called 15C9 herein), SEQ ID NO. 168/SEQ ID NO. 169 (called 15D7 herein), SEQ ID NO. 170/SEQ ID NO. 171 (called 14D9 herein), SEQ ID NO. 172/SEQ ID NO. 173 (called 15F9 herein), SEQ ID NO. 174/SEQ ID NO. 175 (called 15G11 herein), SEQ ID NO. 176/SEQ ID NO. 177 (called 15G7 herein), SEQ ID NO. 178/SEQ ID NO. 179 (called 15G9
20 herein), SEQ ID NO. 180/SEQ ID NO. 181 (called 15H10 herein), SEQ ID NO. 182/SEQ ID NO. 183 (called 15H12 herein), SEQ ID NO. 184/SEQ ID NO. 185 (called 16E3 herein), SEQ ID NO. 186/SEQ ID NO. 187 (called 16A6 herein), SEQ ID NO. 188/SEQ ID NO. 189 (called 16A8 herein), SEQ ID NO. 190/SEQ ID NO. 191 (called 16B1 herein), SEQ ID NO. 192/SEQ ID NO. 193 (called 16B7 herein), SEQ ID NO. 194/SEQ ID NO. 195 (called 16F9 herein), and combinations thereof.
25

The present disclosure provides a fully human antibody Fab fragment, having a variable domain region from a heavy chain and a variable domain region from a light chain, wherein the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID
30 NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60,

SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully human antibody Fab fragment has both a heavy chain variable domain region and a light chain

variable domain region wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 49/SEQ ID NO. 50, SEQ ID NO. 51/SEQ ID NO. 52, SEQ ID NO. 53/SEQ ID NO. 54, SEQ ID NO. 55/SEQ ID NO. 56, SEQ ID NO. 57/SEQ ID NO. 58, SEQ ID NO. 59/SEQ ID NO. 60, SEQ ID NO. 61/SEQ ID NO. 62, SEQ ID NO. 63/SEQ ID NO. 64, SEQ ID NO. 65/SEQ ID NO. 66, SEQ ID NO. 67/SEQ ID NO. 68, SEQ ID NO. 69/SEQ ID NO. 70, SEQ ID NO. 71/SEQ ID NO. 72, SEQ ID NO. 73/SEQ ID NO. 74, SEQ ID NO. 75/SEQ ID NO. 76, SEQ ID NO. 77/SEQ ID NO. 78, SEQ ID NO. 79/SEQ ID NO. 80, SEQ ID NO. 81/SEQ ID NO. 82, SEQ ID NO. 83/SEQ ID NO. 84, SEQ ID NO. 85/SEQ ID NO. 86, SEQ ID NO. 87/SEQ ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 91/SEQ ID NO. 92, SEQ ID NO. 93/SEQ ID NO. 94, SEQ ID NO. 95/SEQ ID NO. 96, SEQ ID NO. 97/SEQ ID NO. 98, SEQ ID NO. 99/SEQ ID NO. 100, SEQ ID NO. 101/SEQ ID NO. 102, SEQ ID NO. 103/SEQ ID NO. 104, SEQ ID NO. 105/SEQ ID NO. 106, SEQ ID NO. 107/SEQ ID NO. 108, SEQ ID NO. 109/SEQ ID NO. 110, SEQ ID NO. 111/SEQ ID NO. 112, SEQ ID NO. 113/SEQ ID NO. 114, SEQ ID NO. 115/SEQ ID NO. 116, SEQ ID NO. 117/SEQ ID NO. 118, SEQ ID NO. 119/SEQ ID NO. 120, SEQ ID NO. 121/SEQ ID NO. 122, SEQ ID NO. 123/SEQ ID NO. 124, SEQ ID NO. 125/SEQ ID NO. 126, SEQ ID NO. 127/SEQ ID NO. 128, SEQ ID NO. 129/SEQ ID NO. 130, SEQ ID NO. 131/SEQ ID NO. 132, SEQ ID NO. 133/SEQ ID NO. 134, SEQ ID NO. 135/SEQ ID NO. 136, SEQ ID NO. 137/SEQ ID NO. 138, SEQ ID NO. 139/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 153/SEQ ID NO. 154, SEQ ID NO. 155/SEQ ID NO. 156, SEQ ID NO. 157/SEQ ID NO. 158, SEQ ID NO. 159/SEQ ID NO. 160, SEQ ID NO. 161/SEQ ID NO. 162, SEQ ID NO. 163/SEQ ID NO. 164, SEQ ID NO. 165/SEQ ID NO. 166, SEQ ID NO. 167/SEQ ID NO. 168, SEQ ID NO. 169, SEQ ID NO.

170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175,
 SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ
 ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID
 NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO.
 5 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO.
 195/SEQ ID NO. 196, and combinations thereof.

The present disclosure provides a single chain human antibody, having a variable
 domain region from a heavy chain and a variable domain region from a light chain and a
 peptide linker connection the heavy chain and light chain variable domain regions, wherein the
 10 heavy chain variable domain sequence that is at least 95% identical to the amino acid
 sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO.
 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID
 NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27,
 SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID
 15 NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50,
 SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID
 NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72,
 SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID
 NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96,
 20 SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106,
 SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116,
 SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126,
 SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136,
 SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147,
 25 SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158,
 SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179,
 SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189,
 SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has
 a light chain variable domain sequence that is at least 95% identical to the amino acid
 30 sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO.
 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID
 NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28,
 SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID
 NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49,

SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully human single chain antibody has both a heavy chain variable domain region and a light chain variable domain region, wherein the single chain fully human antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 49/SEQ ID NO. 50, SEQ ID NO. 51/SEQ ID NO. 52, SEQ ID NO. 53/SEQ ID NO. 54, SEQ ID NO. 55/SEQ ID NO. 56, SEQ ID NO. 57/SEQ ID NO. 58, SEQ ID NO. 59/SEQ ID NO. 60, SEQ ID NO. 61/SEQ ID NO. 62, SEQ ID NO. 63/SEQ ID NO. 64, SEQ ID NO. 65/SEQ ID NO. 66, SEQ ID NO. 67/SEQ ID NO. 68, SEQ ID NO. 69/SEQ ID NO. 70, SEQ ID NO. 71/SEQ ID NO. 72, SEQ ID NO. 73/SEQ ID NO. 74, SEQ ID NO. 75/SEQ ID NO. 76, SEQ ID NO. 77/SEQ ID NO. 78, SEQ ID NO. 79/SEQ ID NO. 80, SEQ ID NO. 81/SEQ ID NO. 82, SEQ ID NO. 83/SEQ ID NO. 84, SEQ ID NO. 85/SEQ ID NO. 86, SEQ ID NO. 87/SEQ ID NO. 88, SEQ

ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 15/SEQ ID NO. 91, SEQ ID NO. 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO. 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117, SEQ ID NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ ID NO. 139, SEQ ID NO. 114/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 1664/SEQ ID NO. 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

The present disclosure further provides a method for treating an inflammatory disease, comprising administering an effective amount of an anti-CXCR5 polypeptide, wherein the anti-CXCR5 polypeptide is selected from the group consisting of a fully human antibody of an IgG class that binds to a CXCR5 epitope with a binding affinity of at least 10^{-6} M, a fully human antibody Fab fragment, having a variable domain region from a heavy chain and a variable domain region from a light chain, a single chain human antibody, having a variable domain region from a heavy chain and a variable domain region from a light chain and a peptide linker connection the heavy chain and light chain variable domain regions, and combinations thereof;

wherein the fully human antibody has a heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ

ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO.
 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ
 ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO.
 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ
 5 ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO.
 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ
 ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO.
 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102,
 SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112,
 10 SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122,
 SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132,
 SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143,
 SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154,
 SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164,
 15 SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185,
 SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195,
 and combinations thereof, and that has a light chain variable domain sequence that is at least
 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO.
 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID
 20 NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24,
 SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID
 NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46,
 SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID
 NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69,
 25 SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID
 NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90,
 SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID
 NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID
 NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID
 30 NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID
 NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID
 NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID
 NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID
 NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID

NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof;

5 wherein the fully human antibody Fab fragment has the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, 10 SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID 15 NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, 20 SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has the light chain variable domain 25 sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID 30 NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97,

SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107,
 SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117,
 SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127,
 SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137,
 5 SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146,
 SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155,
 SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165,
 SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175,
 SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184,
 10 SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194,
 SEQ ID NO. 196, and combinations thereof; and

wherein the single chain human antibody has the heavy chain variable domain sequence
 that is at least 95% identical to the amino acid sequences selected from the group consisting of
 SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO.
 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ
 15 ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO.
 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ
 ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO.
 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ
 20 ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO.
 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ
 ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO.
 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO.
 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO.
 25 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO.
 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO.
 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO.
 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO.
 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO.
 30 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO.
 195, and combinations thereof, and that has the light chain variable domain sequence that is at
 least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID
 NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ
 ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO.

24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof.

Preferably, the fully human antibody has both a heavy chain and a light chain wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2 (called 52A9 herein), SEQ ID NO. 3/SEQ ID NO. 4 (called 52A10 herein), SEQ ID NO. 5/SEQ ID NO. 6 (called 52B10 herein), SEQ ID NO. 7/SEQ ID NO. 8 (called 52C6 herein), SEQ ID NO. 9/SEQ ID NO. 10 (called 52D6 herein), SEQ ID NO. 11/SEQ ID NO. 12 (called 52D7 herein), SEQ ID NO. 13/SEQ ID NO. 14 (called 52D11 herein), SEQ ID NO. 15/SEQ ID NO. 16 (called 52E1 herein), SEQ ID NO. 17/SEQ ID NO. 18 (called 52E10 herein), SEQ ID NO. 19/SEQ ID NO. 20 (called 52H9 herein), SEQ ID NO. 21/SEQ ID NO. 22 (called PC12 herein), SEQ ID NO. 23/SEQ ID NO. 24 (called PD10 herein), SEQ ID NO. 25/SEQ ID NO. 26 (called D3-4 herein), SEQ ID NO. 27/SEQ ID NO. 28 (called E2-1 herein), SEQ ID NO. 29/SEQ ID NO. 30 (called A4 or 7A7 herein), SEQ ID NO. 31/SEQ ID NO. 32 (called A8 herein), SEQ ID NO. 33/SEQ ID NO. 34 (called A12 herein), SEQ ID NO. 35/SEQ ID NO. 36 (called B3 herein), SEQ ID NO. 37/SEQ ID NO. 38 (called C8 herein), SEQ ID NO. 39/SEQ ID NO. 40 (called F8 or 10G9 herein), SEQ ID NO. 41/SEQ ID NO. 42 (called G11 herein), SEQ ID NO. 43/SEQ ID NO. 44 (called H3 herein), SEQ ID NO. 45/SEQ ID NO. 46 (called II5 herein), SEQ ID NO. 47/SEQ ID NO. 48 (called II6

herein), SEQ ID NO. 25/SEQ ID NO. 49 (called 2D3 herein), SEQ ID NO. 50/SEQ ID NO. 51 (called 3A11 herein), SEQ ID NO. 52/SEQ ID NO. 53 (called 3B9 herein), SEQ ID NO. 54/SEQ ID NO. 55 (called 3D11 herein), SEQ ID NO. 56/SEQ ID NO. 57 (called 3D12 or 4E12 herein), SEQ ID NO. 58/SEQ ID NO. 59 (called 3F7 herein), SEQ ID NO. 60/SEQ ID NO. 61 (called 3E12 herein), SEQ ID NO. 62/SEQ ID NO. 63 (called 3F7 herein), SEQ ID NO. 64/SEQ ID NO. 65 (called 3G2 herein), SEQ ID NO. 66/SEQ ID NO. 67 (called 3G7 herein), SEQ ID NO. 68/SEQ ID NO. 69 (called 4A5 herein), SEQ ID NO. 70/SEQ ID NO. 71 (called 4E9 herein), SEQ ID NO. 72/SEQ ID NO. 73 (called 4F1 herein), SEQ ID NO. 74/SEQ ID NO. 75 (called 4F4 herein), SEQ ID NO. 76/SEQ ID NO. 77 (called 4H2 herein), SEQ ID NO. 78/SEQ ID NO. 79 (called 5A8 herein), SEQ ID NO. 80/SEQ ID NO. 81 (called 5F1 herein), SEQ ID NO. 82/SEQ ID NO. 83 (called 6A4 herein), SEQ ID NO. 84/SEQ ID NO. 85 (called 6F9 herein), SEQ ID NO. 15/SEQ ID NO. 86 (called 6G5 herein), SEQ ID NO. 87/SEQ ID NO. 88 (called 7B11 or 8B2 herein), SEQ ID NO. 89/SEQ ID NO. 90 (called 7H10 herein), SEQ ID NO. 15/SEQ ID NO. 91 (called 8D12 herein), SEQ ID NO. 92/SEQ ID NO. 93 (called 8H5 herein), SEQ ID NO. 94/SEQ ID NO. 95 (called 9A10 herein), SEQ ID NO. 96/SEQ ID NO. 97 (called 10A12 herein), SEQ ID NO. 98/SEQ ID NO. 99 (called 10B2 herein), SEQ ID NO. 100/SEQ ID NO. 101 (called 10C3 herein), SEQ ID NO. 102/SEQ ID NO. 103 (called 10C7 herein), SEQ ID NO. 104/SEQ ID NO. 105 (called 11E3 herein), SEQ ID NO. 106/SEQ ID NO. 107 (called 11A12 herein), SEQ ID NO. 108/SEQ ID NO. 109 (called 11A7 herein), SEQ ID NO. 110/SEQ ID NO. 111 (called 11C3 herein), SEQ ID NO. 112/SEQ ID NO. 113 (called 11D3 herein), SEQ ID NO. 114/SEQ ID NO. 115 (called 11D4 herein), SEQ ID NO. 116/SEQ ID NO. 117 (called 11D7 herein), SEQ ID NO. 118/SEQ ID NO. 119 (called 11F3 herein), SEQ ID NO. 120/SEQ ID NO. 121 (called 11G3 herein), SEQ ID NO. 122/SEQ ID NO. 123 (called 12A4 herein), SEQ ID NO. 124/SEQ ID NO. 125 (called 12B11 or 14E10 herein), SEQ ID NO. 126/SEQ ID NO. 127 (called 12B4 herein), SEQ ID NO. 128/SEQ ID NO. 129 (called 12C1 herein), SEQ ID NO. 130/SEQ ID NO. 131 (called 12C6 herein), SEQ ID NO. 132/SEQ ID NO. 133 (called 12D11 herein), SEQ ID NO. 134/SEQ ID NO. 135 (called 12D3 herein), SEQ ID NO. 136/SEQ ID NO. 137 (called 12G10 herein), SEQ ID NO. 138/SEQ ID NO. 139 (called 13E10 herein), SEQ ID NO. 114/SEQ ID NO. 140 (called 13E4 herein), SEQ ID NO. 141/SEQ ID NO. 142 (called 13A3 herein), SEQ ID NO. 143/SEQ ID NO. 144 (called 13F8 herein), SEQ ID NO. 145/SEQ ID NO. 146 (called 13F9 herein), SEQ ID NO. 147/SEQ ID NO. 148 (called 13G9 herein), SEQ ID NO. 149/SEQ ID NO. 150 (called 14E5 herein), SEQ ID NO. 151/SEQ ID NO. 152 (called 14B11 herein), SEQ ID NO. 25/SEQ ID NO. 153 (called 14B4 herein), SEQ ID NO. 154/SEQ ID NO. 155

(called 14C10 herein), SEQ ID NO. 156/SEQ ID NO. 157 (called 14C11 herein), SEQ ID NO. 158/SEQ ID NO. 159 (called 14C3 herein), SEQ ID NO. 160/SEQ ID NO. 161 (called 14D7 herein), SEQ ID NO. 162/SEQ ID NO. 163 (called 14F11 herein), SEQ ID NO. 164/SEQ ID NO. 165 (called 14F8 herein), SEQ ID NO. 166/SEQ ID NO. 167 (called 15C9 herein), SEQ ID NO. 168/SEQ ID NO. 169 (called 15D7 herein), SEQ ID NO. 170/SEQ ID NO. 171 (called 14D9 herein), SEQ ID NO. 172/SEQ ID NO. 173 (called 15F9 herein), SEQ ID NO. 174/SEQ ID NO. 175 (called 15G11 herein), SEQ ID NO. 176/SEQ ID NO. 177 (called 15G7 herein), SEQ ID NO. 179/SEQ ID NO. 178 (called 15G9 herein), SEQ ID NO. 179/SEQ ID NO. 180 (called 15H10 herein), SEQ ID NO. 181/SEQ ID NO. 182 (called 15H12 herein), SEQ ID NO. 183/SEQ ID NO. 184 (called 16E3 herein), SEQ ID NO. 185/SEQ ID NO. 186 (called 16A6 herein), SEQ ID NO. 187/SEQ ID NO. 188 (called 16A8 herein), SEQ ID NO. 189/SEQ ID NO. 190 (called 16B1 herein), SEQ ID NO. 191/SEQ ID NO. 192 (called 16B7 herein), SEQ ID NO. 193/SEQ ID NO. 194 (called 16F8 herein), SEQ ID NO. 195/SEQ ID NO. 196 (called 16F9 herein), and combinations thereof. Preferably, the fully human antibody Fab fragment has both a heavy chain variable domain region and a light chain variable domain region wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2 (called 52A9 herein), SEQ ID NO. 3/SEQ ID NO. 4 (called 52A10 herein), SEQ ID NO. 5/SEQ ID NO. 6 (called 52B10 herein), SEQ ID NO. 7/SEQ ID NO. 8 (called 52C6 herein), SEQ ID NO. 9/SEQ ID NO. 10 (called 52D6 herein), SEQ ID NO. 11/SEQ ID NO. 12 (called 52D7 herein), SEQ ID NO. 13/SEQ ID NO. 14 (called 52D11 herein), SEQ ID NO. 15/SEQ ID NO. 16 (called 52E1 herein), SEQ ID NO. 17/SEQ ID NO. 18 (called 52E10 herein), SEQ ID NO. 19/SEQ ID NO. 20 (called 52H9 herein), SEQ ID NO. 21/SEQ ID NO. 22 (called PC12 herein), SEQ ID NO. 23/SEQ ID NO. 24 (called PD10 herein), SEQ ID NO. 25/SEQ ID NO. 26 (called D3-4 herein), SEQ ID NO. 27/SEQ ID NO. 28 (called E2-1 herein), SEQ ID NO. 29/SEQ ID NO. 30 (called A4 or 7A7 herein), SEQ ID NO. 31/SEQ ID NO. 32 (called A8 herein), SEQ ID NO. 33/SEQ ID NO. 34 (called A12 herein), SEQ ID NO. 35/SEQ ID NO. 36 (called B3 herein), SEQ ID NO. 37/SEQ ID NO. 38 (called C8 herein), SEQ ID NO. 39/SEQ ID NO. 40 (called F8 or 10G9 herein), SEQ ID NO. 41/SEQ ID NO. 42 (called G11 herein), SEQ ID NO. 43/SEQ ID NO. 44 (called H3 herein), SEQ ID NO. 45/SEQ ID NO. 46 (called H5 herein), SEQ ID NO. 47/SEQ ID NO. 48 (called H6 herein), SEQ ID NO. 25/SEQ ID NO. 49 (called 2D3 herein), SEQ ID NO. 50/SEQ ID NO. 51 (called 3A11 herein), SEQ ID NO. 52/SEQ ID NO. 53 (called 3B9 herein), SEQ ID NO. 54/SEQ ID NO. 55 (called 3D11 herein), SEQ ID NO. 56/SEQ ID NO. 57 (called 3D12 or 4E12 herein), SEQ ID NO. 58/SEQ ID NO. 59 (called 3E7 herein), SEQ ID NO.

60/SEQ ID NO. 61 (called 3E12 herein), SEQ ID NO. 62/SEQ ID NO. 63 (called 3F7 herein),
 SEQ ID NO. 64/SEQ ID NO. 65 (called 3G2 herein), SEQ ID NO. 66/SEQ ID NO. 67 (called
 3G7 herein), SEQ ID NO. 68/SEQ ID NO. 69 (called 4A5 herein), SEQ ID NO. 70/SEQ ID
 NO. 71 (called 4F9 herein), SEQ ID NO. 72/SEQ ID NO. 73 (called 4F1 herein), SEQ ID NO.
 5 74/SEQ ID NO. 75 (called 4F4 herein), SEQ ID NO. 76/SEQ ID NO. 77 (called 4H2 herein),
 SEQ ID NO. 78/SEQ ID NO. 79 (called 5A8 herein), SEQ ID NO. 80/SEQ ID NO. 81 (called
 5F1 herein), SEQ ID NO. 82/SEQ ID NO. 83 (called 6A4 herein), SEQ ID NO. 84/SEQ ID
 NO. 85 (called 6F9 herein), SEQ ID NO. 15/SEQ ID NO. 86 (called 6G5 herein), SEQ ID NO.
 87/SEQ ID NO. 88 (called 7B11 or 8B2 herein), SEQ ID NO. 89/SEQ ID NO. 90 (called 7H10
 10 herein), SEQ ID NO. 15/SEQ ID NO. 91 (called 8D12 herein), SEQ ID NO. 92/SEQ ID NO.
 93 (called 8H5 herein), SEQ ID NO. 94/SEQ ID NO. 95 (called 9A10 herein), SEQ ID NO.
 96/SEQ ID NO. 97 (called 10A12 herein), SEQ ID NO. 98/SEQ ID NO. 99 (called 10B2
 herein), SEQ ID NO. 100/SEQ ID NO. 101 (called 10C3 herein), SEQ ID NO. 102/SEQ ID
 NO. 103 (called 10C7 herein), SEQ ID NO. 104/SEQ ID NO. 105 (called 11E3 herein), SEQ
 15 ID NO. 106/SEQ ID NO. 107 (called 11A12 herein), SEQ ID NO. 108/SEQ ID NO. 109
 (called 11A7 herein), SEQ ID NO. 110/SEQ ID NO. 111 (called 11C3 herein), SEQ ID NO.
 112/SEQ ID NO. 113 (called 11D3 herein), SEQ ID NO. 114/SEQ ID NO. 115 (called 11D4
 herein), SEQ ID NO. 116/SEQ ID NO. 117 (called 11D7 herein), SEQ ID NO. 118/SEQ ID
 NO. 119 (called 11F3 herein), SEQ ID NO. 120/SEQ ID NO. 121 (called 11G3 herein), SEQ
 20 ID NO. 122/SEQ ID NO. 123 (called 12A4 herein), SEQ ID NO. 124/SEQ ID NO. 125 (called
 12B11 or 14E10 herein), SEQ ID NO. 126/SEQ ID NO. 127 (called 12B4 herein), SEQ ID
 NO. 128/SEQ ID NO. 129 (called 12C1 herein), SEQ ID NO. 130/SEQ ID NO. 131 (called
 12C6 herein), SEQ ID NO. 132/SEQ ID NO. 133 (called 12D11 herein), SEQ ID NO.
 134/SEQ ID NO. 135 (called 12D3 herein), SEQ ID NO. 136/SEQ ID NO. 137 (called 12G10
 25 herein), SEQ ID NO. 138/SEQ ID NO. 139 (called 13E10 herein), SEQ ID NO. 114/SEQ ID
 NO. 140 (called 13E4 herein), SEQ ID NO. 141/SEQ ID NO. 142 (called 13A3 herein), SEQ
 ID NO. 143/SEQ ID NO. 144 (called 13F8 herein), SEQ ID NO. 145/SEQ ID NO. 146 (called
 13F9 herein), SEQ ID NO. 147/SEQ ID NO. 148 (called 13G9 herein), SEQ ID NO. 149/SEQ
 ID NO. 150 (called 14E5 herein), SEQ ID NO. 151/SEQ ID NO. 152 (called 14B11 herein),
 30 SEQ ID NO. 25/SEQ ID NO. 153 (called 14B4 herein), SEQ ID NO. 154/SEQ ID NO. 155
 (called 14C10 herein), SEQ ID NO. 156/SEQ ID NO. 157 (called 14C11 herein), SEQ ID NO.
 158/SEQ ID NO. 159 (called 14C3 herein), SEQ ID NO. 160/SEQ ID NO. 161 (called 14D7
 herein), SEQ ID NO. 162/SEQ ID NO. 163 (called 14F11 herein), SEQ ID NO. 164/SEQ ID
 NO. 165 (called 14F8 herein), SEQ ID NO. 166/SEQ ID NO. 167 (called 15C9 herein), SEQ

ID NO. 168/SEQ ID NO. 169 (called 15D7 herein), SEQ ID NO. 170/SEQ ID NO. 171 (called 14D9 herein), SEQ ID NO. 172/SEQ ID NO. 173 (called 15F9 herein), SEQ ID NO. 174/SEQ ID NO. 175 (called 15G11 herein), SEQ ID NO. 176/SEQ ID NO. 177 (called 15G7 herein), SEQ ID NO. 179/SEQ ID NO. 180 (called 15H10 herein), SEQ ID NO. 181/SEQ ID NO. 182 (called 15H12 herein), SEQ ID NO. 183/SEQ ID NO. 184 (called 16E3 herein), SEQ ID NO. 185/SEQ ID NO. 186 (called 16A6 herein), SEQ ID NO. 187/SEQ ID NO. 188 (called 16A8 herein), SEQ ID NO. 189/SEQ ID NO. 190 (called 16B1 herein), SEQ ID NO. 191/SEQ ID NO. 192 (called 16B7 herein), SEQ ID NO. 193/SEQ ID NO. 194 (called 16F8 herein), SEQ ID NO. 195/SEQ ID NO. 196 (called 16F9 herein), and combinations thereof. Preferably, the fully human single chain antibody has both a heavy chain variable domain region and a light chain variable domain region, wherein the single chain fully human antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 49/SEQ ID NO. 50, SEQ ID NO. 51/SEQ ID NO. 52, SEQ ID NO. 53/SEQ ID NO. 54, SEQ ID NO. 55/SEQ ID NO. 56, SEQ ID NO. 57/SEQ ID NO. 58/SEQ ID NO. 59, SEQ ID NO. 60/SEQ ID NO. 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO. 65, SEQ ID NO. 66/SEQ ID NO. 67, SEQ ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ ID NO. 71, SEQ ID NO. 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO. 76/SEQ ID NO. 77, SEQ ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ ID NO. 82/SEQ ID NO. 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 86/SEQ ID NO. 87, SEQ ID NO. 88/SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 91/SEQ ID NO. 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO. 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID

NO. 116/SEQ ID NO. 117, SEQ ID NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ ID NO. 139, SEQ ID NO. 140/SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 153/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 166/SEQ ID NO. 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 178/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

Preferably, the disease to be treated is selected from the group consisting of rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, septic arthritis, Lyme arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, inflammatory bowel disease, insulin dependent diabetes mellitus, thyroiditis, asthma, allergic diseases, psoriasis, dermatitis scleroderma, graft versus host disease, organ transplant rejection, acute or chronic immune disease associated with organ transplantation, sarcoidosis, atherosclerosis, disseminated intravascular coagulation, Kawasaki's disease, Grave's disease, nephrotic syndrome, chronic fatigue syndrome, Wegener's granulomatosis, Henoch-Schoenlein purpura, microscopic vasculitis of the kidneys, chronic active hepatitis, uveitis, septic shock, toxic shock syndrome, sepsis syndrome, cachexia, infectious diseases, parasitic diseases, acquired immunodeficiency syndrome, acute transverse myelitis, Huntington's chorea, Parkinson's disease, Alzheimer's disease, stroke, primary biliary cirrhosis, hemolytic anemia, malignancies, heart failure, myocardial infarction, Addison's disease, sporadic, polyglandular deficiency type I and polyglandular deficiency type II, Schmidt's syndrome, adult (acute) respiratory distress syndrome, alopecia, alopecia areata, seronegative arthropathy, arthropathy, Reiter's disease, psoriatic arthropathy, ulcerative colitic arthropathy, enteropathic synovitis, chlamydia, yersinia and salmonella associated arthropathy,

- spondyloarthopathy, atheromatous disease/arteriosclerosis, atopic allergy, autoimmune bullous disease, pemphigus vulgaris, pemphigus foliaceus, pemphigoid, linear IgA disease, autoimmune haemolytic anaemia, Coombs positive haemolytic anaemia, acquired pernicious anaemia, juvenile pernicious anaemia, myalgic encephalitis/Royal Free Disease, chronic
- 5 mucocutaneous candidiasis, giant cell arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, Acquired Immunodeficiency Disease Syndrome, Acquired Immunodeficiency Related Diseases, Hepatitis B, Hepatitis C, common varied immunodeficiency (common variable hypogammaglobulinaemia), dilated cardiomyopathy, female infertility, ovarian failure, premature ovarian failure, fibrotic lung disease, cryptogenic
- 10 fibrosing alveolitis, post-inflammatory interstitial lung disease, interstitial pneumonitis, connective tissue disease associated interstitial lung disease, mixed connective tissue disease associated lung disease, systemic sclerosis associated interstitial lung disease, rheumatoid arthritis associated interstitial lung disease, systemic lupus erythematosus associated lung disease, dermatomyositis/polymyositis associated lung disease, Sjogren's disease associated
- 15 lung disease, ankylosing spondylitis associated lung disease, vasculitic diffuse lung disease, haemosiderosis associated lung disease, drug-induced interstitial lung disease, fibrosis, radiation fibrosis, bronchiolitis obliterans, chronic eosinophilic pneumonia, lymphocytic infiltrative lung disease, postinfectious interstitial lung disease, gouty arthritis, autoimmune hepatitis, type-1 autoimmune hepatitis (classical autoimmune or lupoid hepatitis), type-2
- 20 autoimmune hepatitis (anti-LKM antibody hepatitis), autoimmune mediated hypoglycaemia, type B insulin resistance with acanthosis nigricans, hypoparathyroidism, acute immune disease associated with organ transplantation, chronic immune disease associated with organ transplantation, osteoarthritis, primary sclerosing cholangitis, psoriasis type 1, psoriasis type 2, idiopathic leucopaenia, autoimmune neutropaenia, renal disease NOS, glomerulonephritides,
- 25 microscopic vasulitis of the kidneys, lyme disease, discoid lupus erythematosus, male infertility idiopathic or NOS, sperm autoimmunity, multiple sclerosis (all subtypes), sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture's syndrome, pulmonary manifestation of polyarteritis nodosa, acute rheumatic fever, rheumatoid spondylitis, Still's disease, systemic sclerosis, Sjorgren's syndrome,
- 30 Takayasu's disease/arteritis, autoimmune thrombocytopaenia, idiopathic thrombocytopaenia, autoimmune thyroid disease, hyperthyroidism, goitrous autoimmune hypothyroidism (Hashimoto's disease), atrophic autoimmune hypothyroidism, primary myxoedema, phacogenic uveitis, primary vasculitis, vitiligo acute liver disease, chronic liver diseases, alcoholic cirrhosis, alcohol-induced liver injury, choleosatatis, idiosyncratic liver disease,

Drug-Induced hepatitis, Non-alcoholic Steatohepatitis, allergy and asthma, group B streptococci (GBS) infection, mental disorders (e.g., depression and schizophrenia), Th2 Type and Th1 Type mediated diseases, acute and chronic pain (different forms of pain), and cancers such as lung, breast, stomach, bladder, colon, pancreas, ovarian, prostate and rectal cancer and

5 hematopoietic malignancies (leukemia and lymphoma) Abetalipoproteinemia, Acrocyanosis, acute and chronic parasitic or infectious processes, acute leukemia, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), acute or chronic bacterial infection, acute pancreatitis, acute renal failure, adenocarcinomas, aural ectopic beats, AIDS dementia complex, alcohol-induced hepatitis, allergic conjunctivitis, allergic contact dermatitis, allergic

10 rhinitis, allograft rejection, alpha-1-antitrypsin deficiency, amyotrophic lateral sclerosis, anemia, angina pectoris, anterior horn cell degeneration, anti cd3 therapy, antiphospholipid syndrome, anti-receptor hypersensitivity reactions, aortic and peripheral aneurysms, aortic dissection, arterial hypertension, arteriosclerosis, arteriovenous fistula, ataxia, atrial fibrillation (sustained or paroxysmal), atrial flutter, atrioventricular block, B cell lymphoma, bone graft

15 rejection, bone marrow transplant (BMT) rejection, bundle branch block, Burkitt's lymphoma, Burns, cardiac arrhythmias, cardiac stun syndrome, cardiac tumors, cardiomyopathy, cardiopulmonary bypass inflammation response, cartilage transplant rejection, cerebellar cortical degenerations, cerebellar disorders, chaotic or multifocal atrial tachycardia, chemotherapy associated disorders, chronic myelocytic leukemia (CML), chronic alcoholism,

20 chronic inflammatory pathologies, chronic lymphocytic leukemia (CLL), chronic obstructive pulmonary disease (COPD), chronic salicylate intoxication, colorectal carcinoma, congestive heart failure, conjunctivitis, contact dermatitis, cor pulmonale, coronary artery disease, Creutzfeldt-Jakob disease, culture negative sepsis, cystic fibrosis, cytokine therapy associated disorders, Dementia pugilistica, demyelinating diseases, dengue hemorrhagic fever, dermatitis,

25 dermatologic conditions, diabetes, diabetes mellitus, diabetic atherosclerotic disease, Diffuse Lewy body disease, dilated congestive cardiomyopathy, disorders of the basal ganglia, Down's Syndrome in middle age, drug-induced movement disorders induced by drugs which block CNS dopamine receptors, drug sensitivity, eczema, encephalomyelitis, endocarditis, endocrinopathy, epiglottitis, epstein-barr virus infection, erythromelalgia, extrapyramidal and

30 cerebellar disorders, familial hemophagocytic lymphohistiocytosis, fetal thymus implant rejection, Friedreich's ataxia, functional peripheral arterial disorders, fungal sepsis, gas gangrene, gastric ulcer, glomerular nephritis, graft rejection of any organ or tissue, gram negative sepsis, gram positive sepsis, granulomas due to intracellular organisms, hairy cell leukemia, Hallerorden-Spatz disease, hashimoto's thyroiditis, hay fever, heart transplant

rejection, hemachromatosis, hemodialysis, hemolytic uremic syndrome/thrombolytic thrombocytopenic purpura, hemorrhage, hepatitis (A), His bundle arrhythmias, HIV infection/HIV neuropathy, Hodgkin's disease, hyperkinetic movement disorders, hypersensitivity reactions, hypersensitivity pneumonitis, hypertension, hypokinetic movement disorders,

5 hypothalamic-pituitary-adrenal axis evaluation, idiopathic Addison's disease, idiopathic pulmonary fibrosis, antibody mediated cytotoxicity, Asthenia, infantile spinal muscular atrophy, inflammation of the aorta, influenza a, ionizing radiation exposure, iridocyclitis/uveitis/optic neuritis, ischemia-reperfusion injury, ischemic stroke, juvenile rheumatoid arthritis, juvenile spinal muscular atrophy, Kaposi's sarcoma, kidney transplant

10 rejection, legionella, leishmaniasis, leprosy, lesions of the corticospinal system, lipedema, liver transplant rejection, lymphedema, malaria, malignant Lymphoma, malignant histiocytosis, malignant melanoma, meningitis, meningococcemia, metabolic/idiopathic, migraine headache, mitochondrial multi.system disorder, mixed connective tissue disease, monoclonal gammopathy, multiple myeloma, multiple systems degenerations (Mencel Dejerine-Thomas

15 Shi-Drager and Machado-Joseph), myasthenia gravis, mycobacterium avium intracellulare, mycobacterium tuberculosis, myelodysplastic syndrome, myocardial infarction, myocardial ischemic disorders, nasopharyngeal carcinoma, neonatal chronic lung disease, nephritis, nephrosis, neurodegenerative diseases, neurogenic I muscular atrophies, neutropenic fever, non-hodgkins lymphoma, occlusion of the abdominal aorta and its branches, occlusive arterial

20 disorders, ok13 therapy, orchitis/epididymitis, orchitis/vasectomy reversal procedures, organomegaly, osteoporosis, pancreas transplant rejection, pancreatic carcinoma, paraneoplastic syndrome/hypercalcemia of malignancy, parathyroid transplant rejection, pelvic inflammatory disease, perennial rhinitis, pericardial disease, peripheral atherosclerotic disease, peripheral vascular disorders, peritonitis, pernicious anemia, pneumocystis carinii pneumonia,

25 pneumonia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome), post perfusion syndrome, post pump syndrome, post-MI cardiomyopathy syndrome, preeclampsia, Progressive supranuclear Palsy, primary pulmonary hypertension, radiation therapy, Raynaud's phenomenon and disease, Raynaud's disease, Refsum's disease, regular narrow QRS tachycardia, renovascular hypertension,

30 reperfusion injury, restrictive cardiomyopathy, sarcomas, scleroderma, senile chorea, Senile Dementia of Lewy body type, seronegative arthropathies, shock, sickle cell anemia, skin allograft rejection, skin changes syndrome, small bowel transplant rejection, solid tumors, specific arrhythmias, spinal ataxia, spinocerebellar degenerations, streptococcal myositis, structural lesions of the cerebellum, Subacute sclerosing panencephalitis, Syncope, syphilis of

the cardiovascular system, systemic anaphalaxis, systemic inflammatory response syndrome, systemic onset juvenile rheumatoid arthritis, T-cell or FAB ALL, Telangiectasia, thromboangitis obliterans, thrombocytopenia, toxicity, transplants, trauma/hemorrhage, type III hypersensitivity reactions, type IV hypersensitivity, unstable angina, uremia, urosepsis, 5 urticaria, valvular heart diseases, varicose veins, vasculitis, venous diseases, venous thrombosis, ventricular fibrillation, viral and fungal infections, viral encephalitis/aseptic meningitis, viral-associated hemaphagocytic syndrome, Wernicke-Korsakoff syndrome, Wilson's disease, and xenograft rejection of any organ or tissue.

Brief Description of the Figure

10 Figure 1 shows the binding of various IgG1 clones over time.

Detailed Description

The present disclosure provides a fully human antibody of an IgG class that binds to a CXCR5 epitope with a binding affinity of 10^{-6} M or less, that has a heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the 15 group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, 20 SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the 30 group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID

NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully human antibody has both a heavy chain and a light chain wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2 (called 52A9 herein), SEQ ID NO. 3/SEQ ID NO. 4 (called 52A10 herein), SEQ ID NO. 5/SEQ ID NO. 6 (called 52B10 herein), SEQ ID NO. 7/SEQ ID NO. 8 (called 52C6 herein), SEQ ID NO. 9/SEQ ID NO. 10 (called 52D6 herein), SEQ ID NO. 11/SEQ ID NO. 12 (called 52D7 herein), SEQ ID NO. 13/SEQ ID NO. 14 (called 52D11 herein), SEQ ID NO. 15/SEQ ID NO. 16 (called 52E1 herein), SEQ ID NO. 17/SEQ ID NO. 18 (called 52E10 herein), SEQ ID NO. 19/SEQ ID NO. 20 (called 52H9 herein), SEQ ID NO. 21/SEQ ID NO. 22 (called PC12 herein), SEQ ID NO. 23/SEQ ID NO. 24 (called PD10 herein), SEQ ID NO. 25/SEQ ID NO. 26 (called D3-4 herein), SEQ ID NO. 27/SEQ ID NO. 28 (called E2-1 herein), SEQ ID NO. 29/SEQ ID NO. 30 (called A4 or 7A7 herein), SEQ ID NO. 31/SEQ ID NO. 32 (called A8 herein), SEQ ID NO. 33/SEQ ID NO. 34 (called A12 herein), SEQ ID NO. 35/SEQ ID NO. 36 (called B3 herein), SEQ ID NO. 37/SEQ ID NO. 38 (called C8 herein), SEQ ID NO. 39/SEQ ID NO. 40 (called F8 or 10G9 herein), SEQ ID NO. 41/SEQ ID NO. 42 (called G11 herein), SEQ ID NO. 43/SEQ ID NO. 44 (called II3 herein), SEQ ID NO. 45/SEQ ID NO. 46 (called

H5 herein), SEQ ID NO. 47/SEQ ID NO. 48 (called H6 herein), SEQ ID NO. 25/SEQ ID NO. 49 (called 2D3 herein), SEQ ID NO. 50/SEQ ID NO. 51 (called 3A11 herein), SEQ ID NO. 52/SEQ ID NO. 53 (called 3B9 herein), SEQ ID NO. 54/SEQ ID NO. 55 (called 3D11 herein), SEQ ID NO. 56/SEQ ID NO. 57 (called 3D12 or 4E12 herein), SEQ ID NO. 58/SEQ ID NO. 59 (called 3E7 herein), SEQ ID NO. 60/SEQ ID NO. 61 (called 3E12 herein), SEQ ID NO. 62/SEQ ID NO. 63 (called 3F7 herein), SEQ ID NO. 64/SEQ ID NO. 65 (called 3G2 herein), SEQ ID NO. 66/SEQ ID NO. 67 (called 3G7 herein), SEQ ID NO. 68/SEQ ID NO. 69 (called 4A5 herein), SEQ ID NO. 70/SEQ ID NO. 71 (called 4E9 herein), SEQ ID NO. 72/SEQ ID NO. 73 (called 4F1 herein), SEQ ID NO. 74/SEQ ID NO. 75 (called 4F4 herein), SEQ ID NO. 76/SEQ ID NO. 77 (called 4H2 herein), SEQ ID NO. 78/SEQ ID NO. 79 (called 5A8 herein), SEQ ID NO. 80/SEQ ID NO. 81 (called 5F1 herein), SEQ ID NO. 82/SEQ ID NO. 83 (called 6A4 herein), SEQ ID NO. 84/SEQ ID NO. 85 (called 6F9 herein), SEQ ID NO. 15/SEQ ID NO. 86 (called 6G5 herein), SEQ ID NO. 87/SEQ ID NO. 88 (called 7B11 or 8B2 herein), SEQ ID NO. 89/SEQ ID NO. 90 (called 7H10 herein), SEQ ID NO. 15/SEQ ID NO. 91 (called 8D12 herein), SEQ ID NO. 92/SEQ ID NO. 93 (called 8H5 herein), SEQ ID NO. 94/SEQ ID NO. 95 (called 9A10 herein), SEQ ID NO. 96/SEQ ID NO. 97 (called 10A12 herein), SEQ ID NO. 98/SEQ ID NO. 99 (called 10B2 herein), SEQ ID NO. 100/SEQ ID NO. 101 (called 10C3 herein), SEQ ID NO. 102/SEQ ID NO. 103 (called 10C7 herein), SEQ ID NO. 104/SEQ ID NO. 105 (called 11E3 herein), SEQ ID NO. 106/SEQ ID NO. 107 (called 11A12 herein), SEQ ID NO. 108/SEQ ID NO. 109 (called 11A7 herein), SEQ ID NO. 110/SEQ ID NO. 111 (called 11C3 herein), SEQ ID NO. 112/SEQ ID NO. 113 (called 11D3 herein), SEQ ID NO. 114/SEQ ID NO. 115 (called 11D4 herein), SEQ ID NO. 116/SEQ ID NO. 117 (called 11D7 herein), SEQ ID NO. 118/SEQ ID NO. 119 (called 11F3 herein), SEQ ID NO. 120/SEQ ID NO. 121 (called 11G3 herein), SEQ ID NO. 122/SEQ ID NO. 123 (called 12A4 herein), SEQ ID NO. 124/SEQ ID NO. 125 (called 12B11 or 14E10 herein), SEQ ID NO. 126/SEQ ID NO. 127 (called 12B4 herein), SEQ ID NO. 128/SEQ ID NO. 129 (called 12C1 herein), SEQ ID NO. 130/SEQ ID NO. 131 (called 12C6 herein), SEQ ID NO. 132/SEQ ID NO. 133 (called 12D11 herein), SEQ ID NO. 134/SEQ ID NO. 135 (called 12D3 herein), SEQ ID NO. 136/SEQ ID NO. 137 (called 12G10 herein), SEQ ID NO. 138/SEQ ID NO. 139 (called 13E10 herein), SEQ ID NO. 114/SEQ ID NO. 140 (called 13E4 herein), SEQ ID NO. 141/SEQ ID NO. 142 (called 13A3 herein), SEQ ID NO. 143/SEQ ID NO. 144 (called 13F8 herein), SEQ ID NO. 145/SEQ ID NO. 146 (called 13F9 herein), SEQ ID NO. 147/SEQ ID NO. 148 (called 13G9 herein), SEQ ID NO. 149/SEQ ID NO. 150 (called 14E5 herein), SEQ ID NO. 151/SEQ ID NO. 152 (called 14B11 herein), SEQ ID NO. 25/SEQ ID NO. 153 (called 14B4 herein), SEQ

ID NO. 154/SEQ ID NO. 155 (called 14C10 herein), SEQ ID NO. 156/SEQ ID NO. 157 (called 14C11 herein), SEQ ID NO. 158/SEQ ID NO. 159 (called 14C3 herein), SEQ ID NO. 160/SEQ ID NO. 161 (called 14D7 herein), SEQ ID NO. 162/SEQ ID NO. 163 (called 14F11 herein), SEQ ID NO. 164/SEQ ID NO. 165 (called 14F8 herein), SEQ ID NO. 1664/SEQ ID NO. 167 (called 15C9 herein), SEQ ID NO. 168/SEQ ID NO. 169 (called 15D7 herein), SEQ ID NO. 170/SEQ ID NO. 171 (called 14D9 herein), SEQ ID NO. 172/SEQ ID NO. 173 (called 15F9 herein), SEQ ID NO. 174/SEQ ID NO. 175 (called 15G11 herein), SEQ ID NO. 176/SEQ ID NO. 177 (called 15G7 herein), SEQ ID NO. 19/SEQ ID NO. 178 (called 15G9 herein), SEQ ID NO. 179/SEQ ID NO. 180 (called 15H10 herein), SEQ ID NO. 181/SEQ ID NO. 182 (called 15H12 herein), SEQ ID NO. 183/SEQ ID NO. 184 (called 16E3 herein), SEQ ID NO. 185/SEQ ID NO. 186 (called 16A6 herein), SEQ ID NO. 187/SEQ ID NO. 188 (called 16A8 herein), SEQ ID NO. 189/SEQ ID NO. 190 (called 16B1 herein), SEQ ID NO. 191/SEQ ID NO. 192 (called 16B7 herein), SEQ ID NO. 193/SEQ ID NO. 194 (called 16F8 herein), SEQ ID NO. 195/SEQ ID NO. 196 (called 16F9 herein), and combinations thereof.

The present disclosure provides a fully human antibody Fab fragment, having a variable domain region from a heavy chain and a variable domain region from a light chain, wherein the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO.

189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully human antibody Fab fragment has both a heavy chain variable domain region and a light chain variable domain region wherein the antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 25/SEQ ID NO. 49, SEQ ID NO. 50/SEQ ID NO. 51, SEQ ID NO.

52/SEQ ID NO. 53, SEQ ID NO. 54/SEQ ID NO. 55, SEQ ID NO. 56/SEQ ID NO. 57, SEQ ID NO. 58/SEQ ID NO. 59, SEQ ID NO. 60/SEQ ID NO. 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO. 65, SEQ ID NO. 66/SEQ ID NO. 67, SEQ ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ ID NO. 71, SEQ ID NO. 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO. 76/SEQ ID NO. 77, SEQ ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ ID NO. 82/SEQ ID NO. 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 15/SEQ ID NO. 86, SEQ ID NO. 87/SEQ ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 15/SEQ ID NO. 91, SEQ ID NO. 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO. 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117, SEQ ID NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ ID NO. 139, SEQ ID NO. 114/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 1664/SEQ ID NO. 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

The present disclosure provides a single chain human antibody, having a variable domain region from a heavy chain and a variable domain region from a light chain and a peptide linker connection the heavy chain and light chain variable domain regions, wherein the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO.

5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID

NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof. Preferably, the fully

5 human single chain antibody has both a heavy chain variable domain region and a light chain variable domain region, wherein the single chain fully human antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ

10 ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO.

15 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 49/SEQ ID NO. 50/SEQ ID NO. 51, SEQ ID NO. 52/SEQ ID NO. 53, SEQ ID NO. 54/SEQ ID NO. 55, SEQ ID NO. 56/SEQ ID NO. 57, SEQ ID NO. 58/SEQ ID NO. 59, SEQ ID NO. 60/SEQ ID NO. 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO. 65, SEQ ID NO. 66/SEQ ID NO. 67, SEQ

20 ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ ID NO. 71, SEQ ID NO. 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO. 76/SEQ ID NO. 77, SEQ ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ ID NO. 82/SEQ ID NO. 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 86/SEQ ID NO. 87/SEQ ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 91/SEQ ID NO. 92/SEQ ID NO.

25 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO. 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117, SEQ ID NO. 118/SEQ ID NO. 119,

30 SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ ID NO. 139, SEQ ID NO. 140/SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144,

SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 166/SEQ ID NO. 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

The present disclosure further provides a method for treating a broad spectrum of mammalian cancers or inflammatory diseases or autoimmune diseases, comprising administering an effective amount of an anti-CXCR5 polypeptide, wherein the anti-CXCR5 polypeptide is selected from the group consisting of a fully human antibody of an IgG class that binds to a CXCR5 epitope with a binding affinity of at least 10^{-6} M, a fully human antibody Fab fragment, having a variable domain region from a heavy chain and a variable domain region from a light chain, a single chain human antibody, having a variable domain region from a heavy chain and a variable domain region from a light chain and a peptide linker connection the heavy chain and light chain variable domain regions, and combinations thereof;

wherein the fully human antibody has a heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132,

SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, 5 SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, 10 SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, 15 SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof;

wherein the fully human antibody Fab fragment has the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, 30 SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54,

SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has the light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and combinations thereof; and

wherein the single chain human antibody has the heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7, SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29, SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO. 50, SEQ ID NO. 52, SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74, SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98, SEQ ID NO. 100, SEQ ID NO. 102, SEQ ID NO. 104, SEQ ID NO. 106, SEQ ID NO. 108, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 124, SEQ ID NO. 126, SEQ ID NO. 128, SEQ ID NO. 130, SEQ ID NO. 132, SEQ ID NO. 134, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 141, SEQ ID NO. 143, SEQ ID NO. 145, SEQ ID NO. 147, SEQ ID NO. 149, SEQ ID NO. 151, SEQ ID NO. 154, SEQ ID NO. 156, SEQ ID NO. 158, SEQ ID NO. 160, SEQ ID NO. 162, SEQ ID NO. 164, SEQ ID NO. 176, SEQ ID NO. 179, SEQ ID NO. 181, SEQ ID NO. 183, SEQ ID NO. 185, SEQ ID NO. 187, SEQ ID NO. 189, SEQ ID NO. 191, SEQ ID NO. 193, SEQ ID NO. 195, and combinations thereof, and that has the light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10, SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 34, SEQ ID NO. 36, SEQ ID NO. 38, SEQ ID NO. 40, SEQ ID NO. 42, SEQ ID NO. 44, SEQ ID NO. 46, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 51, SEQ ID NO. 53, SEQ ID NO. 55, SEQ ID NO. 57, SEQ ID NO. 59, SEQ ID NO. 61, SEQ ID NO. 63, SEQ ID NO. 67, SEQ ID NO. 69, SEQ ID NO. 71, SEQ ID NO. 73, SEQ ID NO. 75, SEQ ID NO. 77, SEQ ID NO. 79, SEQ ID NO. 81, SEQ ID NO. 83, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 88, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 93, SEQ ID NO. 95, SEQ ID NO. 97, SEQ ID NO. 99, SEQ ID NO. 101, SEQ ID NO. 103, SEQ ID NO. 105, SEQ ID NO. 107, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 123, SEQ ID NO. 125, SEQ ID NO. 127, SEQ ID NO. 129, SEQ ID NO. 131, SEQ ID NO. 133, SEQ ID NO. 135, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID

NO. 140, SEQ ID NO. 142, SEQ ID NO. 144, SEQ ID NO. 146, SEQ ID NO. 148, SEQ ID
 NO. 150, SEQ ID NO. 152, SEQ ID NO. 153, SEQ ID NO. 155, SEQ ID NO. 157, SEQ ID
 NO. 159, SEQ ID NO. 161, SEQ ID NO. 163, SEQ ID NO. 165, SEQ ID NO. 167, SEQ ID
 NO. 169, SEQ ID NO. 171, SEQ ID NO. 173, SEQ ID NO. 175, SEQ ID NO. 177, SEQ ID
 5 NO. 178, SEQ ID NO. 180, SEQ ID NO. 182, SEQ ID NO. 184, SEQ ID NO. 186, SEQ ID
 NO. 188, SEQ ID NO. 190, SEQ ID NO. 192, SEQ ID NO. 194, SEQ ID NO. 196, and
 combinations thereof.

Preferably, the fully human antibody has both a heavy chain and a light chain wherein
 the antibody has a heavy chain/light chain variable domain sequence selected from the group
 10 consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO.
 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO.
 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ
 ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO.
 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ
 15 ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO.
 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ
 ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO.
 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 25/SEQ
 ID NO. 49, SEQ ID NO. 50/SEQ ID NO. 51, SEQ ID NO. 52/SEQ ID NO. 53, SEQ ID NO.
 20 54/SEQ ID NO. 55, SEQ ID NO. 56/SEQ ID NO. 57, SEQ ID NO. 58/SEQ ID NO. 59, SEQ
 ID NO. 60/SEQ ID NO. 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO.
 65, SEQ ID NO. 66/SEQ ID NO. 67, SEQ ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ
 ID NO. 71, SEQ ID NO. 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO.
 76/SEQ ID NO. 77, SEQ ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ
 25 ID NO. 82/SEQ ID NO. 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 15/SEQ ID NO.
 86, SEQ ID NO. 87/SEQ ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 15/SEQ
 ID NO. 91, SEQ ID NO. 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO.
 96/SEQ ID NO. 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ
 ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID
 30 NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO.
 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117,
 SEQ ID NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ
 ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID
 NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO.

133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO.
 138/SEQ ID NO. 139, SEQ ID NO. 114/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142,
 SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ
 ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID
 5 NO. 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO.
 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO.
 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 1664/SEQ ID NO.
 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO.
 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177,
 10 SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ
 ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID
 NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO.
 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations
 thereof. Preferably, the fully human antibody Fab fragment has both a heavy chain variable
 15 domain region and a light chain variable domain region wherein the antibody has a heavy
 chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO.
 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO.
 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID
 NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18,
 20 SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID
 NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO.
 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ
 ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO.
 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ
 25 ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 25/SEQ ID NO. 49, SEQ ID NO.
 50/SEQ ID NO. 51, SEQ ID NO. 52/SEQ ID NO. 53, SEQ ID NO. 54/SEQ ID NO. 55, SEQ
 ID NO. 56/SEQ ID NO. 57, SEQ ID NO. 58/SEQ ID NO. 59, SEQ ID NO. 60/SEQ ID NO.
 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO. 65, SEQ ID NO. 66/SEQ
 ID NO. 67, SEQ ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ ID NO. 71, SEQ ID NO.
 30 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO. 76/SEQ ID NO. 77, SEQ
 ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ ID NO. 82/SEQ ID NO.
 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 15/SEQ ID NO. 86, SEQ ID NO. 87/SEQ
 ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 15/SEQ ID NO. 91, SEQ ID NO.
 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO. 97, SEQ

ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO. 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107, SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117, SEQ ID NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO. 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO. 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133, SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ ID NO. 139, SEQ ID NO. 114/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO. 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO. 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157, SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 166/SEQ ID NO. 167, SEQ ID NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO. 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO. 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182, SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

Preferably, the fully human single chain antibody has both a heavy chain variable domain region and a light chain variable domain region, wherein the single chain fully human antibody has a heavy chain/light chain variable domain sequence selected from the group consisting of SEQ ID NO. 1/SEQ ID NO. 2, SEQ ID NO. 3/SEQ ID NO. 4, SEQ ID NO. 5/SEQ ID NO. 6, SEQ ID NO. 7/SEQ ID NO. 8, SEQ ID NO. 9/SEQ ID NO. 10, SEQ ID NO. 11/SEQ ID NO. 12, SEQ ID NO. 13/SEQ ID NO. 14, SEQ ID NO. 15/SEQ ID NO. 16, SEQ ID NO. 17/SEQ ID NO. 18, SEQ ID NO. 19/SEQ ID NO. 20, SEQ ID NO. 21/SEQ ID NO. 22, SEQ ID NO. 23/SEQ ID NO. 24, SEQ ID NO. 25/SEQ ID NO. 26, SEQ ID NO. 27/SEQ ID NO. 28, SEQ ID NO. 29/SEQ ID NO. 30, SEQ ID NO. 31/SEQ ID NO. 32, SEQ ID NO. 33/SEQ ID NO. 34, SEQ ID NO. 35/SEQ ID NO. 36, SEQ ID NO. 37/SEQ ID NO. 38, SEQ ID NO. 39/SEQ ID NO. 40, SEQ ID NO. 41/SEQ ID NO. 42, SEQ ID NO. 43/SEQ ID NO. 44, SEQ ID NO. 45/SEQ ID NO. 46, SEQ ID NO. 47/SEQ ID NO. 48, SEQ ID NO. 25/SEQ ID NO. 49, SEQ ID NO. 50/SEQ ID NO. 51, SEQ ID NO. 52/SEQ ID NO. 53, SEQ ID NO. 54/SEQ ID NO. 55, SEQ ID NO. 56/SEQ ID NO. 57, SEQ ID NO. 58/SEQ ID NO. 59, SEQ ID NO. 60/SEQ

ID NO. 61, SEQ ID NO. 62/SEQ ID NO. 63, SEQ ID NO. 64/SEQ ID NO. 65, SEQ ID NO.
 66/SEQ ID NO. 67, SEQ ID NO. 68/SEQ ID NO. 69, SEQ ID NO. 70/SEQ ID NO. 71, SEQ
 ID NO. 72/SEQ ID NO. 73, SEQ ID NO. 74/SEQ ID NO. 75, SEQ ID NO. 76/SEQ ID NO.
 77, SEQ ID NO. 78/SEQ ID NO. 79, SEQ ID NO. 80/SEQ ID NO. 81, SEQ ID NO. 82/SEQ
 5 ID NO. 83, SEQ ID NO. 84/SEQ ID NO. 85, SEQ ID NO. 15/SEQ ID NO. 86, SEQ ID NO.
 87/SEQ ID NO. 88, SEQ ID NO. 89/SEQ ID NO. 90, SEQ ID NO. 15/SEQ ID NO. 91, SEQ
 ID NO. 92/SEQ ID NO. 93, SEQ ID NO. 94/SEQ ID NO. 95, SEQ ID NO. 96/SEQ ID NO.
 97, SEQ ID NO. 98/SEQ ID NO. 99, SEQ ID NO. 100/SEQ ID NO. 101, SEQ ID NO.
 102/SEQ ID NO. 103, SEQ ID NO. 104/SEQ ID NO. 105, SEQ ID NO. 106/SEQ ID NO. 107,
 10 SEQ ID NO. 108/SEQ ID NO. 109, SEQ ID NO. 110/SEQ ID NO. 111, SEQ ID NO. 112/SEQ
 ID NO. 113, SEQ ID NO. 114/SEQ ID NO. 115, SEQ ID NO. 116/SEQ ID NO. 117, SEQ ID
 NO. 118/SEQ ID NO. 119, SEQ ID NO. 120/SEQ ID NO. 121, SEQ ID NO. 122/SEQ ID NO.
 123, SEQ ID NO. 124/SEQ ID NO. 125, SEQ ID NO. 126/SEQ ID NO. 127, SEQ ID NO.
 128/SEQ ID NO. 129, SEQ ID NO. 130/SEQ ID NO. 131, SEQ ID NO. 132/SEQ ID NO. 133,
 15 SEQ ID NO. 134/SEQ ID NO. 135, SEQ ID NO. 136/SEQ ID NO. 137, SEQ ID NO. 138/SEQ
 ID NO. 139, SEQ ID NO. 114/SEQ ID NO. 140, SEQ ID NO. 141/SEQ ID NO. 142, SEQ ID
 NO. 143/SEQ ID NO. 144, SEQ ID NO. 145/SEQ ID NO. 146, SEQ ID NO. 147/SEQ ID NO.
 148, SEQ ID NO. 149/SEQ ID NO. 150, SEQ ID NO. 151/SEQ ID NO. 152, SEQ ID NO.
 25/SEQ ID NO. 153, SEQ ID NO. 154/SEQ ID NO. 155, SEQ ID NO. 156/SEQ ID NO. 157,
 20 SEQ ID NO. 158/SEQ ID NO. 159, SEQ ID NO. 160/SEQ ID NO. 161, SEQ ID NO. 162/SEQ
 ID NO. 163, SEQ ID NO. 164/SEQ ID NO. 165, SEQ ID NO. 1664/SEQ ID NO. 167, SEQ ID
 NO. 168/SEQ ID NO. 169, SEQ ID NO. 170/SEQ ID NO. 171, SEQ ID NO. 172/SEQ ID NO.
 173, SEQ ID NO. 174/SEQ ID NO. 175, SEQ ID NO. 176/SEQ ID NO. 177, SEQ ID NO.
 19/SEQ ID NO. 178, SEQ ID NO. 179/SEQ ID NO. 180, SEQ ID NO. 181/SEQ ID NO. 182,
 25 SEQ ID NO. 183/SEQ ID NO. 184, SEQ ID NO. 185/SEQ ID NO. 186, SEQ ID NO. 187/SEQ
 ID NO. 188, SEQ ID NO. 189/SEQ ID NO. 190, SEQ ID NO. 191/SEQ ID NO. 192, SEQ ID
 NO. 193/SEQ ID NO. 194, SEQ ID NO. 195/SEQ ID NO. 196, and combinations thereof.

Preferably, the broad spectrum of mammalian cancers to be treated the cancer is an
 CXCR5-positive cancer. Preferably, the broad spectrum of mammalian cancers to be treated is
 30 selected from the group consisting of carcinomas, prostate cancer, non-small cell lung cancer,
 breast cancer, endometrial cancer, ovarian cancer, gastric cancers, head and neck cancers, and
 colon cancer.

An "antigen binding protein" is a protein comprising a portion that binds to an antigen
 and, optionally, a scaffold or framework portion that allows the antigen binding portion to

adopt a conformation that promotes binding of the antigen binding protein to the antigen. Examples of antigen binding proteins include antibodies, antibody fragments (*e.g.*, an antigen binding portion of an antibody), antibody derivatives, and antibody analogs. The antigen binding protein can comprise, for example, an alternative protein scaffold or artificial scaffold with grafted CDRs or CDR derivatives. Such scaffolds include, but are not limited to, antibody-derived scaffolds comprising mutations introduced to, for example, stabilize the three-dimensional structure of the antigen binding protein as well as wholly synthetic scaffolds comprising, for example, a biocompatible polymer. See, for example, Korndorfer et al., 2003, *Proteins: Structure, Function, and Bioinformatics*, Volume 53, Issue 1:121-129; Roque et al., 2004, *Biotechnol. Prog.* 20:639-654. In addition, peptide antibody mimetics ("PAMs") can be used, as well as scaffolds based on antibody mimetics utilizing fibronectin components as a scaffold.

An antigen binding protein can have, for example, the structure of a naturally occurring immunoglobulin. An "immunoglobulin" is a tetrameric molecule. In a naturally occurring immunoglobulin, each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. Human light chains are classified as kappa or lambda light chains. Heavy chains are classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 10 more amino acids. See generally, *Fundamental Immunology* Ch. 7 (Paul, W., ed., 2nd ed. Raven Press, N.Y. (1989)) (incorporated by reference in its entirety for all purposes). The variable regions of each light/heavy chain pair form the antibody binding site such that an intact immunoglobulin has two binding sites.

The variable regions of naturally occurring immunoglobulin chains exhibit the same general structure of relatively conserved framework regions (FR) joined by three hypervariable regions, also called complementarity determining regions or CDRs. From N-terminus to C-terminus, both light and heavy chains comprise the domains FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain is in accordance with the definitions of Kabat et al. in *Sequences of Proteins of Immunological Interest*, 5th Ed., US Dept. of Health and Human Services, PHS, NIH, NIH Publication no. 91-3242, 1991. Other

numbering systems for the amino acids in immunoglobulin chains include IMGT.RTM. (international ImMunoGeneTics information system; Lefranc et al, *Dev. Comp. Immunol.* 29:185-203; 2005) and AHo (Honegger and Pluckthun, *J. Mol. Biol.* 309(3):657-670; 2001).

An "antibody" refers to an intact immunoglobulin or to an antigen binding portion thereof that competes with the intact antibody for specific binding, unless otherwise specified. Antigen binding portions may be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies. Antigen binding portions include, *inter alia*, Fab, Fab', F(ab')₂, Fv, domain antibodies (dAbs), and complementarity determining region (CDR) fragments, single-chain antibodies (scFv), chimeric antibodies, diabodies, triabodies, tetra-

10 tetra- bodies, and polypeptides that contain at least a portion of an immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide.

A Fab fragment is a monovalent fragment having the V_L, V_H, C_L and C_{H1} domains; a F(ab')₂ fragment is a bivalent fragment having two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment has the V_H and C_{H1} domains; an Fv fragment has the V_L and V_H domains of a single arm of an antibody; and a dAb fragment has a V_H domain, a V_L domain, or an antigen-binding fragment of a V_H or V_L domain (U.S. Patents 6,846,634; 6,696,245, US Patent Applications 2002/02512; 2004/0202995; 2004/0038291; 2004/0009507; 2003/0039958, and Ward et al., *Nature* 341:544-546, 1989).

15 A single-chain antibody (scFv) is an antibody in which a V_L and a V_H region are joined

via a linker (*e.g.*, a synthetic sequence of amino acid residues) to form a continuous protein chain wherein the linker is long enough to allow the protein chain to fold back on itself and form a monovalent antigen binding site (Bird et al., 1988, *Science* 242:423-26 and Huston et al., 1988, *Proc. Natl. Acad. Sci. USA* 85:5879-83). Diabodies are bivalent antibodies comprising two polypeptide chains, wherein each polypeptide chain comprises V_H and V_L domains joined by a linker that is too short to allow for pairing between two domains on the same chain, thus allowing each domain to pair with a complementary domain on another polypeptide chain (Holliger et al., 1993, *Proc. Natl. Acad. Sci. USA* 90:6444-48, and Poljak et al., 1994, *Structure* 2:1121-23). If the two polypeptide chains of a diabody are identical, then a diabody resulting from their pairing will have two identical antigen binding sites. Polypeptide chains having different sequences can be used to make a diabody with two different antigen binding sites. Similarly, tribodies and tetra-

20 bodies are antibodies comprising three and four polypeptide chains, respectively, and forming three and four antigen binding sites, respectively, which can be the same or different.

25

30

Complementarity determining regions (CDRs) and framework regions (FR) of a given antibody may be identified using the system described by Kabat et al. *supra*; Lefranc et al., *supra* and/or Honegger and Pluckthun, *supra*. One or more CDRs may be incorporated into a molecule either covalently or noncovalently to make it an antigen binding protein. An antigen
5 binding protein may incorporate the CDR(s) as part of a larger polypeptide chain, may covalently link the CDR(s) to another polypeptide chain, or may incorporate the CDR(s) noncovalently. The CDRs permit the antigen binding protein to specifically bind to a particular antigen of interest.

An antigen binding protein may have one or more binding sites. If there is more than
10 one binding site, the binding sites may be identical to one another or may be different. For example, a naturally occurring human immunoglobulin typically has two identical binding sites, while a "bispecific" or "bifunctional" antibody has two different binding sites.

The term "human antibody" includes all antibodies that have one or more variable and constant regions derived from human immunoglobulin sequences. In one embodiment, all of
15 the variable and constant domains are derived from human immunoglobulin sequences (a fully human antibody). These antibodies may be prepared in a variety of ways, examples of which are described below, including through the immunization with an antigen of interest of a mouse that is genetically modified to express antibodies derived from human heavy and/or light chain-encoding genes.

Further, the framework regions may be derived from one of the same anti-CXCR5
20 antibodies, from one or more different antibodies, such as a human antibody, or from a humanized antibody. In one example of a chimeric antibody, a portion of the heavy and/or light chain is identical with, homologous to, or derived from an antibody from a particular species or belonging to a particular antibody class or subclass, while the remainder of the
25 chain(s) is/are identical with, homologous to, or derived from an antibody (-ies) from another species or belonging to another antibody class or subclass. Also included are fragments of such antibodies that exhibit the desired biological activity (*i.e.*, the ability to specifically bind CXCR5).

A "neutralizing antibody" or an "inhibitory antibody" is an antibody that inhibits the
30 activation of CXCR5 when an excess of the anti-CXCR5 antibody reduces the amount of activation by at least about 20% using an assay such as those described herein in the Examples. In various embodiments, the antigen binding protein reduces the amount of amount of activation of CXCR5 by at least 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99%, and 99.9%.

Fragments or analogs of antibodies can be readily prepared by those of ordinary skill in the art following the teachings of this specification and using techniques known in the art. Preferred amino- and carboxy-termini of fragments or analogs occur near boundaries of functional domains. Structural and functional domains can be identified by comparison of the nucleotide and/or amino acid sequence data to public or proprietary sequence databases. Computerized comparison methods can be used to identify sequence motifs or predicted protein conformation domains that occur in other proteins of known structure and/or function. Methods to identify protein sequences that fold into a known three-dimensional structure are known. See, Bowie et al., 1991, *Science* 253:164.

10 A "CDR grafted antibody" is an antibody comprising one or more CDRs derived from an antibody of a particular species or isotype and the framework of another antibody of the same or different species or isotype.

A "multi-specific antibody" is an antibody that recognizes more than one epitope on one or more antigens. A subclass of this type of antibody is a "bi-specific antibody" which
15 recognizes two distinct epitopes on the same or different antigens.

An antigen binding protein "specifically binds" to an antigen (*e.g.*, human CXCR5) if it binds to the antigen with a dissociation constant of 1 nanomolar or less.

An "antigen binding domain," "antigen binding region," or "antigen binding site" is a portion of an antigen binding protein that contains amino acid residues (or other moieties) that
20 interact with an antigen and contribute to the antigen binding protein's specificity and affinity for the antigen. For an antibody that specifically binds to its antigen, this will include at least part of at least one of its CDR domains.

An "epitope" is the portion of a molecule that is bound by an antigen binding protein (*e.g.*, by an antibody). An epitope can comprise non-contiguous portions of the molecule (*e.g.*,
25 in a polypeptide, amino acid residues that are not contiguous in the polypeptide's primary sequence but that, in the context of the polypeptide's tertiary and quaternary structure, are near enough to each other to be bound by an antigen binding protein).

The "percent identity" of two polynucleotide or two polypeptide sequences is determined by comparing the sequences using the GAP computer program (a part of the GCG
30 Wisconsin Package, version 10.3 (Accelrys, San Diego, Calif.)) using its default parameters.

The terms "polynucleotide," "oligonucleotide" and "nucleic acid" are used interchangeably throughout and include DNA molecules (*e.g.*, cDNA or genomic DNA), RNA molecules (*e.g.*, mRNA), analogs of the DNA or RNA generated using nucleotide analogs (*e.g.*, peptide nucleic acids and non-naturally occurring nucleotide analogs), and hybrids

thereof. The nucleic acid molecule can be single-stranded or double-stranded. In one embodiment, the nucleic acid molecules of the invention comprise a contiguous open reading frame encoding an antibody, or a fragment, derivative, mutein, or variant thereof.

Two single-stranded polynucleotides are "the complement" of each other if their
5 sequences can be aligned in an anti-parallel orientation such that every nucleotide in one polynucleotide is opposite its complementary nucleotide in the other polynucleotide, without the introduction of gaps, and without unpaired nucleotides at the 5' or the 3' end of either sequence. A polynucleotide is "complementary" to another polynucleotide if the two polynucleotides can hybridize to one another under moderately stringent conditions. Thus, a
10 polynucleotide can be complementary to another polynucleotide without being its complement.

A "vector" is a nucleic acid that can be used to introduce another nucleic acid linked to it into a cell. One type of vector is a "plasmid," which refers to a linear or circular double stranded DNA molecule into which additional nucleic acid segments can be ligated. Another type of vector is a viral vector (*e.g.*, replication defective retroviruses, adenoviruses and adeno-
15 associated viruses), wherein additional DNA segments can be introduced into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors comprising a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along
20 with the host genome. An "expression vector" is a type of vector that can direct the expression of a chosen polynucleotide.

A nucleotide sequence is "operably linked" to a regulatory sequence if the regulatory sequence affects the expression (*e.g.*, the level, timing, or location of expression) of the nucleotide sequence. A "regulatory sequence" is a nucleic acid that affects the expression (*e.g.*,
25 the level, timing, or location of expression) of a nucleic acid to which it is operably linked. The regulatory sequence can, for example, exert its effects directly on the regulated nucleic acid, or through the action of one or more other molecules (*e.g.*, polypeptides that bind to the regulatory sequence and/or the nucleic acid). Examples of regulatory sequences include promoters, enhancers and other expression control elements (*e.g.*, polyadenylation signals).
30 Further examples of regulatory sequences are described in, for example, Goeddel, 1990, Gene Expression Technology: *Methods in Enzymology* 185, Academic Press, San Diego, Calif. and Baron et al., 1995, *Nucleic Acids Res.* 23:3605-06.

A "host cell" is a cell that can be used to express a nucleic acid, *e.g.*, a nucleic acid of the invention. A host cell can be a prokaryote, for example, *E. coli*, or it can be a eukaryote, for

example, a single-celled eukaryote (*e.g.*, a yeast or other fungus), a plant cell (*e.g.*, a tobacco or tomato plant cell), an animal cell (*e.g.*, a human cell, a monkey cell, a hamster cell, a rat cell, a mouse cell, or an insect cell) or a hybridoma. Examples of host cells include the COS-7 line of monkey kidney cells (ATCC CRL 1651) (see Gluzman et al., 1981, *Cell* 23:175), L cells, C127 cells, 3T3 cells (ATCC CCL 163), Chinese hamster ovary (CHO) cells or their derivatives such as Veggie CHO and related cell lines which grow in serum-free media (see Rasmussen et al., 1998, *Cytotechnology* 28:31) or CHO strain DX-B11, which is deficient in DHFR (see Urlaub et al., 1980, *Proc. Natl. Acad. Sci. USA* 77:4216-20), HeLa cells, BHK (ATCC CRL 10) cell lines, the CV1/EBNA cell line derived from the African green monkey kidney cell line CV1 (ATCC CCL 70) (see McMahan et al., 1991, *EMBO J.* 10:2821), human embryonic kidney cells such as 293,293 EBNA or MSR 293, human epidermal A431 cells, human Colo205 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HL-60, U937, HaK or Jurkat cells. Typically, a host cell is a cultured cell that can be transformed or transfected with a polypeptide-encoding nucleic acid, which can then be expressed in the host cell. The phrase "recombinant host cell" can be used to denote a host cell that has been transformed or transfected with a nucleic acid to be expressed. A host cell also can be a cell that comprises the nucleic acid but does not express it at a desired level unless a regulatory sequence is introduced into the host cell such that it becomes operably linked with the nucleic acid. It is understood that the term host cell refers not only to the particular subject cell but also to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to, *e.g.*, mutation or environmental influence, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

95% Homology

The present disclosure provides a number of antibodies structurally characterized by the amino acid sequences of their variable domain regions. However, the amino acid sequences can undergo some changes while retaining their high degree of binding to their specific targets. More specifically, many amino acids in the variable domain region can be changed with conservative substitutions and it is predictable that the binding characteristics of the resulting antibody will not differ from the binding characteristics of the wild type antibody sequence. There are many amino acids in an antibody variable domain that do not directly interact with the antigen or impact antigen binding and are not critical for determining antibody structure. For example, a predicted nonessential amino acid residue in any of the disclosed antibodies is preferably replaced with another amino acid residue from the same class. Methods of

identifying amino acid conservative substitutions which do not eliminate antigen binding are well-known in the art (see, e.g., Brummell et al., *Biochem.* 32: 1180-1187 (1993); Kobayashi et al. *Protein Eng.* 12(10):879-884 (1999); and Burks et al. *Proc. Natl. Acad. Sci. USA* 94:412-417 (1997)). Near et al. *Mol. Immunol.* 30:369-377, 1993 explains how to impact or not impact binding through site-directed mutagenesis. Near et al. only mutated residues that they thought had a high probability of changing antigen binding. Most had a modest or negative effect on binding affinity (Near et al. Table 3) and binding to different forms of digoxin (Near et al. Table 2).

The recombinant DNA can also include any type of protein tag sequence that may be useful for purifying the protein. Examples of protein tags include but are not limited to a histidine tag, a FLAG tag, a myc tag, an HA tag, or a GST tag. Appropriate cloning and expression vectors for use with bacterial, fungal, yeast, and mammalian cellular hosts can be found in *Cloning Vectors: A Laboratory Manual*, (Elsevier, N.Y., 1985).

The expression construct is introduced into the host cell using a method appropriate to the host cell. A variety of methods for introducing nucleic acids into host cells are known in the art, including, but not limited to, electroporation; transfection employing calcium chloride, rubidium chloride, calcium phosphate, DEAE-dextran, or other substances; microprojectile bombardment; lipofection; and infection (where the vector is an infectious agent). Suitable host cells include prokaryotes, yeast, mammalian cells, or bacterial cells.

Suitable bacteria include gram negative or gram positive organisms, for example, *E. coli* or *Bacillus spp.* Yeast, preferably from the *Saccharomyces* species, such as *S. cerevisiae*, may also be used for production of polypeptides. Various mammalian or insect cell culture systems can also be employed to express recombinant proteins. *Baculovirus* systems for production of heterologous proteins in insect cells are reviewed by Luckow and Summers, (*Bio/Technology*, 6:47, 1988). Examples of suitable mammalian host cell lines include endothelial cells, COS-7 monkey kidney cells, CV-1, L cells, C127, 3T3, Chinese hamster ovary (CHO), human embryonic kidney cells, HeLa, 293, 293T, and BHK cell lines. Purified polypeptides are prepared by culturing suitable host/vector systems to express the recombinant proteins. For many applications, the small size of many of the polypeptides disclosed herein would make expression in *E. coli* as the preferred method for expression. The protein is then purified from culture media or cell extracts.

CXCR5-binding polypeptides can also be produced by chemical synthesis (e.g., by the methods described in Solid Phase Peptide Synthesis, 2nd ed., 1984, The Pierce Chemical Co., Rockford, Ill.). Modifications to the protein can also be produced by chemical synthesis.

The polypeptides of the present disclosure can be purified by isolation/purification methods for proteins generally known in the field of protein chemistry. Non-limiting examples include extraction, recrystallization, salting out (*e.g.*, with ammonium sulfate or sodium sulfate), centrifugation, dialysis, ultrafiltration, adsorption chromatography, ion exchange chromatography, hydrophobic chromatography, normal phase chromatography, reversed-phase chromatography, gel filtration, gel permeation chromatography, affinity chromatography, electrophoresis, countercurrent distribution or any combinations of these. After purification, polypeptides may be exchanged into different buffers and/or concentrated by any of a variety of methods known to the art, including, but not limited to, filtration and dialysis.

10 Post-Translational Modifications of Polypeptides

In certain embodiments, the binding polypeptides of the invention may further comprise post-translational modifications. Exemplary post-translational protein modifications include phosphorylation, acetylation, methylation, ADP-ribosylation, ubiquitination, glycosylation, carbonylation, sumoylation, biotinylation or addition of a polypeptide side chain or of a hydrophobic group. As a result, the modified soluble polypeptides may contain non-amino acid elements, such as lipids, poly- or mono-saccharide, and phosphates. A preferred form of glycosylation is sialylation, which conjugates one or more sialic acid moieties to the polypeptide. Sialic acid moieties improve solubility and serum half-life while also reducing the possible immunogenicity of the protein. See Raju et al. *Biochemistry*. 2001 31; 40(30):8868-20 76.

In one specific embodiment, modified forms of the subject soluble polypeptides comprise linking the subject soluble polypeptides to nonproteinaceous polymers. In one specific embodiment, the polymer is polyethylene glycol ("PEG"), polypropylene glycol, or polyoxyalkylenes, in the manner as set forth in U.S. Patents 4,640,835; 4,496,689; 4,301,144; 25 4,670,417; 4,791,192 or 4,179,337.

PEG is a water soluble polymer that is commercially available or can be prepared by ring-opening polymerization of ethylene glycol according to methods well known in the art (Sandler and Karo, *Polymer Synthesis*, Academic Press, New York, Vol. 3, pages 138-161). The term "PEG" is used broadly to encompass any polyethylene glycol molecule, without regard to size or to modification at an end of the PEG, and can be represented by the formula: 30 $X-O(CH_2CH_2O)_n-1CH_2CH_2OH$ (1), where n is 20 to 2300 and X is H or a terminal modification, *e.g.*, a C_{1-4} alkyl. In one embodiment, the PEG of the invention terminates on one end with hydroxy or methoxy, *i.e.*, X is H or CH_3 ("methoxy PEG"). A PEG can contain further chemical groups which are necessary for binding reactions; which results from the

chemical synthesis of the molecule; or which is a spacer for optimal distance of parts of the molecule. In addition, such a PEG can consist of one or more PEG side-chains which are linked together. PEGs with more than one PEG chain are called multiarmed or branched PEGs. Branched PEGs can be prepared, for example, by the addition of polyethylene oxide to various polyols, including glycerol, pentaerythriol, and sorbitol. For example, a four-armed branched PEG can be prepared from pentaerythriol and ethylene oxide. Branched PEG are described in, for example, EP-A 0 473 084 and U.S. Patent. 5,932,462. One form of PEGs includes two PEG side-chains (PEG2) linked via the primary amino groups of a lysine (Monfardini et al., *Bioconjugate Chem.* 6 (1995) 62-69).

Although PEG is well-known, this is the first demonstration that a pegylated ^{10}F n3 polypeptide can be pegylated and retain ligand binding activity. In a preferred embodiment, the pegylated ^{10}F n3 polypeptide is produced by site-directed pegylation, particularly by conjugation of PEG to a cysteine moiety at the N- or C-terminus. Accordingly, the present disclosure provides a target-binding ^{10}F n3 polypeptide with improved pharmacokinetic properties, the polypeptide comprising: a ^{10}F n3 domain having from about 80 to about 150 amino acids, wherein at least one of the loops of said ^{10}F n3 domain participate in target binding; and a covalently bound PEG moiety, wherein said ^{10}F n3 polypeptide binds to the target with a K_D of less than 100 nM and has a clearance rate of less than 30 mL/hr/kg in a mammal. The PEG moiety may be attached to the ^{10}F n3 polypeptide by site directed pegylation, such as by attachment to a Cys residue, where the Cys residue may be positioned at the N-terminus of the ^{10}F n3 polypeptide or between the N-terminus and the most N-terminal beta or beta-like strand or at the C-terminus of the ^{10}F n3 polypeptide or between the C-terminus and the most C-terminal beta or beta-like strand. A Cys residue may be situated at other positions as well, particularly any of the loops that do not participate in target binding. A PEG moiety may also be attached by other chemistry, including by conjugation to amines.

PEG conjugation to peptides or proteins generally involves the activation of PEG and coupling of the activated PEG-intermediates directly to target proteins/peptides or to a linker, which is subsequently activated and coupled to target proteins/peptides (see Abuchowski et al., *J. Biol. Chem.*, 252, 3571 (1977) and *J. Biol. Chem.*, 252, 3582 (1977), Zalipsky, et al., and Harris et. al., in: *Poly(ethylene glycol) Chemistry: Biotechnical and Biomedical Applications*; (J. M. Harris ed.) Plenum Press: New York, 1992; Chap.21 and 22). It is noted that a binding polypeptide containing a PEG molecule is also known as a conjugated protein, whereas the protein lacking an attached PEG molecule can be referred to as unconjugated.

A variety of molecular mass forms of PEG can be selected, *e.g.*, from about 1,000 Daltons (Da) to 100,000 Da (*n* is 20 to 2300), for conjugating to CXCR5-binding polypeptides. The number of repeating units "*n*" in the PEG is approximated for the molecular mass described in Daltons. It is preferred that the combined molecular mass of PEG on an activated
 5 linker is suitable for pharmaceutical use. Thus, in one embodiment, the molecular mass of the PEG molecules does not exceed 100,000 Da. For example, if three PEG molecules are attached to a linker, where each PEG molecule has the same molecular mass of 12,000 Da (each *n* is about 270), then the total molecular mass of PEG on the linker is about 36,000 Da (total *n* is about 820). The molecular masses of the PEG attached to the linker can also be different, *e.g.*,
 10 of three molecules on a linker two PEG molecules can be 5,000 Da each (each *n* is about 110) and one PEG molecule can be 12,000 Da (*n* is about 270).

In a specific embodiment of the disclosure an CXCR5 binding polypeptide is covalently linked to one poly(ethylene glycol) group of the formula: $--CO--(CH_2)_x--(OCH_2CH_2)_m--OR$, with the $--CO$ (*i.e.* carbonyl) of the poly(ethylene glycol) group forming
 15 an amide bond with one of the amino groups of the binding polypeptide; *R* being lower alkyl; *x* being 2 or 3; *m* being from about 450 to about 950; and *n* and *m* being chosen so that the molecular weight of the conjugate minus the binding polypeptide is from about 10 to 40 kDa. In one embodiment, a binding polypeptide's 6-amino group of a lysine is the available (free) amino group.

The above conjugates may be more specifically presented by formula (II): $P--NHCO--(CH_2)_x--(OCH_2CH_2)_m--OR$ (II), wherein *P* is the group of a binding polypeptide as described herein, (*i.e.* without the amino group or amino groups which form an amide linkage with the carbonyl shown in formula (II); and wherein *R* is lower alkyl; *x* is 2 or 3; *m* is from about 450 to about 950 and is chosen so that the molecular weight of the conjugate minus the binding
 25 polypeptide is from about 10 to about 40 kDa. As used herein, the given ranges of "*m*" have an orientational meaning. The ranges of "*m*" are determined in any case, and exactly, by the molecular weight of the PEG group.

In another embodiment, the pegylated binding polypeptides of the invention will preferably retain at least 25%, 50%, 60%, 70%, 80%, 85%, 90%, 95% or 100% of the
 30 biological activity associated with the unmodified protein. In one embodiment, biological activity refers to its ability to bind to CXCR5, as assessed by *KD*, *k_{on}* or *k_{off}*. In one specific embodiment, the pegylated binding polypeptide protein shows an increase in binding to CXCR5 relative to unpegylated binding polypeptide.

The serum clearance rate of PEG-modified polypeptide may be decreased by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or even 90%, relative to the clearance rate of the unmodified binding polypeptide. The PEG-modified polypeptide may have a half-life ($t_{1/2}$) which is enhanced relative to the half-life of the unmodified protein. The half-life of PEG-binding polypeptide may be enhanced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 250%, 300%, 400% or 500%, or even by 1000% relative to the half-life of the unmodified binding polypeptide. In some embodiments, the protein half-life is determined *in vitro*, such as in a buffered saline solution or in serum. In other embodiments, the protein half-life is an *in vivo* half life, such as the half-life of the protein in the serum or other bodily fluid of an animal.

Therapeutic Formulations and Modes of Administration

The present disclosure features methods for treating conditions or preventing pre-conditions which respond to an inhibition of CXCR5 biological activity. Preferred examples are conditions that are characterized by inflammation or cellular hyperproliferation. Techniques and dosages for administration vary depending on the type of specific polypeptide and the specific condition being treated but can be readily determined by the skilled artisan. In general, regulatory agencies require that a protein reagent to be used as a therapeutic is formulated so as to have acceptably low levels of pyrogens. Accordingly, therapeutic formulations will generally be distinguished from other formulations in that they are substantially pyrogen free, or at least contain no more than acceptable levels of pyrogen as determined by the appropriate regulatory agency (*e.g.*, FDA).

Therapeutic compositions of the present disclosure may be administered with a pharmaceutically acceptable diluent, carrier, or excipient, in unit dosage form. Administration may be parenteral (*e.g.*, intravenous, subcutaneous), oral, or topical, as non-limiting examples. In addition, any gene therapy technique, using nucleic acids encoding the polypeptides of the invention, may be employed, such as naked DNA delivery, recombinant genes and vectors, cell-based delivery, including *ex vivo* manipulation of patients' cells, and the like.

The composition can be in the form of a pill, tablet, capsule, liquid, or sustained release tablet for oral administration; or a liquid for intravenous, subcutaneous or parenteral administration; gel, lotion, ointment, cream, or a polymer or other sustained release vehicle for local administration.

Methods well known in the art for making formulations are found, for example, in "Remington: The Science and Practice of Pharmacy" (20th ed., ed. A. R. Gennaro A R., 2000, Lippincott Williams & Wilkins, Philadelphia, Pa.). Formulations for parenteral administration

may, for example, contain excipients, sterile water, saline, polyalkylene glycols such as polyethylene glycol, oils of vegetable origin, or hydrogenated naphthalenes. Biocompatible, biodegradable lactide polymer, lactide/glycolide copolymer, or polyoxyethylene-polyoxypropylene copolymers may be used to control the release of the compounds.

- 5 Nanoparticulate formulations (*e.g.*, biodegradable nanoparticles, solid lipid nanoparticles, liposomes) may be used to control the biodistribution of the compounds. Other potentially useful parenteral delivery systems include ethylene-vinyl acetate copolymer particles, osmotic pumps, implantable infusion systems, and liposomes. The concentration of the compound in the formulation varies depending upon a number of factors, including the dosage of the drug to
10 be administered, and the route of administration.

The polypeptide may be optionally administered as a pharmaceutically acceptable salt, such as non-toxic acid addition salts or metal complexes that are commonly used in the pharmaceutical industry. Examples of acid addition salts include organic acids such as acetic, lactic, pantoic, maleic, citric, malic, ascorbic, succinic, benzoic, palmitic, suberic, salicylic,
15 tartaric, methanesulfonic, toluenesulfonic, or trifluoroacetic acids or the like; polymeric acids such as tannic acid, carboxymethyl cellulose, or the like; and inorganic acid such as hydrochloric acid, hydrobromic acid, sulfuric acid phosphoric acid, or the like. Metal complexes include zinc, iron, and the like. In one example, the polypeptide is formulated in the presence of sodium acetate to increase thermal stability.

20 Formulations for oral use include tablets containing the active ingredient(s) in a mixture with non-toxic pharmaceutically acceptable excipients. These excipients may be, for example, inert diluents or fillers (*e.g.*, sucrose and sorbitol), lubricating agents, glidants, and anti-adhesives (*e.g.*, magnesium stearate, zinc stearate, stearic acid, silicas, hydrogenated vegetable oils, or talc).

25 Formulations for oral use may also be provided as chewable tablets, or as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium.

A therapeutically effective dose refers to a dose that produces the therapeutic effects for which it is administered. The exact dose will depend on the disorder to be treated, and may be
30 ascertained by one skilled in the art using known techniques. In general, the polypeptide is administered at about 0.01 $\mu\text{g/kg}$ to about 50 mg/kg per day, preferably 0.01 mg/kg to about 30 mg/kg per day, most preferably 0.1 mg/kg to about 20 mg/kg per day. The polypeptide may be given daily (*e.g.*, once, twice, three times, or four times daily) or preferably less frequently (*e.g.*, weekly, every two weeks, every three weeks, monthly, or quarterly). In addition, as is

known in the art, adjustments for age as well as the body weight, general health, sex, diet, time of administration, drug interaction, and the severity of the disease may be necessary, and will be ascertainable with routine experimentation by those skilled in the art.

Exemplary Uses

5 The CXCR5 binding proteins described herein and their related variants are useful in a number of therapeutic and diagnostic applications. These include the inhibition of the biological activity of CXCR5 by competing for or blocking the binding to a CXCR5 as well as the delivery of cytotoxic or imaging moieties to cells, preferably cells expressing CXCR5. The small size and stable structure of these molecules can be particularly valuable with respect to
10 manufacturing of the drug, rapid clearance from the body for certain applications where rapid clearance is desired or formulation into novel delivery systems that are suitable or improved using a molecule with such characteristics.

 On the basis of their efficacy as inhibitors of CXCR5 biological activity, the polypeptides of this disclosure are effective against a number of cancer conditions as well as
15 complications arising from cancer, such as pleural effusion and ascites, colorectal cancers, head and neck cancers, small cell lung cancer, non-small cell lung cancer (NSCLC) and pancreatic cancer. Non-limiting examples of cancers include bladder, blood, bone, brain, breast, cartilage, colon kidney, liver, lung, lymph node, nervous tissue, ovary, pancreatic, prostate, skeletal muscle, skin, spinal cord, spleen, stomach, testes, thymus, thyroid, trachea,
20 urogenital tract, ureter, urethra, uterus, or vaginal cancer.

 In certain embodiments, the subject anti-CXCR5 antibodies agents of the invention can be used alone. Alternatively, the subject agents may be used in combination with other conventional anti-cancer therapeutic approaches directed to treatment or prevention of proliferative disorders (*e.g.*, tumor). For example, such methods can be used in prophylactic
25 cancer prevention, prevention of cancer recurrence and metastases after surgery, and as an adjuvant of other conventional cancer therapy. The present disclosure recognizes that the effectiveness of conventional cancer therapies (*e.g.*, chemotherapy, radiation therapy, phototherapy, immunotherapy, and surgery) can be enhanced through the use of a subject polypeptide therapeutic agent.

30 A wide array of conventional compounds have been shown to have anti-neoplastic activities. These compounds have been used as pharmaceutical agents in chemotherapy to shrink solid tumors, prevent metastases and further growth, or decrease the number of malignant cells in leukemic or bone marrow malignancies. Although chemotherapy has been effective in treating various types of malignancies, many anti-neoplastic compounds induce

undesirable side effects. It has been shown that when two or more different treatments are combined, the treatments may work synergistically and allow reduction of dosage of each of the treatments, thereby reducing the detrimental side effects exerted by each compound at higher dosages. In other instances, malignancies that are refractory to a treatment may respond to a combination therapy of two or more different treatments.

When a polypeptide therapeutic agent of the present invention is administered in combination with another conventional anti-neoplastic agent, either concomitantly or sequentially, such therapeutic agent may be found to enhance the therapeutic effect of the anti-neoplastic agent or overcome cellular resistance to such anti-neoplastic agent. This allows decrease of dosage of an anti-neoplastic agent, thereby reducing the undesirable side effects, or restores the effectiveness of an anti-neoplastic agent in resistant cells.

Pharmaceutical compounds that may be used for combinatory anti-tumor therapy include, merely to illustrate: aminoglutethimide, amsacrine, anastrozole, asparaginase, bcl-2, bicalutamide, bleomycin, buserelin, busulfan, camptothecin, capecitabine, carboplatin, carmustine, chlorambucil, cisplatin, cladribine, clodronate, colchicine, cyclophosphamide, cyproterone, cytarabine, dacarbazine, dactinomycin, daunorubicin, dienestrol, diethylstilbestrol, docetaxel, doxorubicin, epirubicin, estradiol, estramustine, etoposide, exemestane, filgrastim, fludarabine, fludrocortisone, fluorouracil, fluoxymesterone, flutamide, gemcitabine, genistein, goserelin, hydroxyurea, idarubicin, ifosfamide, imatinib, interferon, irinotecan, irinotecan, letrozole, leucovorin, leuprolide, levamisole, lomustine, mechlorethamine, medroxyprogesterone, megestrol, melphalan, mercaptopurine, mesna, methotrexate, mitomycin, mitotane, mitoxantrone, nilutamide, nocodazole, octreotide, oxaliplatin, paclitaxel, pamidronate, pentostatin, plicamycin, porfimer, procarbazine, raltitrexed, rituximab, streptozocin, suramin, tamoxifen, temozolomide, teniposide, testosterone, thioguanine, thiotepa, titanocene dichloride, topotecan, trastuzumab, tretinoin, vinblastine, vincristine, vindesine, and vinorelbine.

Certain chemotherapeutic anti-tumor compounds may be categorized by their mechanism of action into, for example, following groups: anti-metabolites/anti-cancer agents, such as pyrimidine analogs (5-fluorouracil, floxuridine, capecitabine, gemcitabine and cytarabine) and purine analogs, folate antagonists and related inhibitors (mercaptopurine, thioguanine, pentostatin and 2-chlorodeoxyadenosine (cladribine)); antiproliferative/antimitotic agents including natural products such as vinca alkaloids (vinblastine, vincristine, and vinorelbine), microtubule disruptors such as taxane (paclitaxel, docetaxel), vincristin, vinblastin, nocodazole, epothilones and navelbine, epidipodophyllotoxins (etoposide,

- teniposide), DNA damaging agents (actinomycin, amsacrine, anthracyclines, bleomycin, busulfan, camptothecin, carboplatin, chlorambucil, cisplatin, cyclophosphamide, cytoxan, dactinomycin, daunorubicin, doxorubicin, epirubicin, hexamethylmelamineoxaliplatin, iphosphamide, melphalan, merchloroethamine, mitomycin, mitoxantrone, nitrosourea,
- 5 plicamycin, procarbazine, taxol, taxotere, teniposide, triethylenethiophosphoramidate and etoposide (VP16)); antibiotics such as dactinomycin (actinomycin D), daunorubicin, doxorubicin (adriamycin), idarubicin, anthracyclines, mitoxantrone, bleomycins, plicamycin (mithramycin) and mitomycin; enzymes (L-asparaginase which systemically metabolizes L-asparagine and deprives cells which do not have the capacity to synthesize their own
- 10 asparagine); antiplatelet agents; antiproliferative/antimitotic alkylating agents such as nitrogen mustards (mechlorethamine, cyclophosphamide and analogs, melphalan, chlorambucil), ethylenimines and methylmelamines (hexamethylmelamine and thiotepa), alkyl sulfonates--busulfan, nitrosoureas (carmustine (BCNU) and analogs, streptozocin), trazenes--dacarbazine (DTIC); antiproliferative/antimitotic antimetabolites such as folic acid analogs (methotrexate);
- 15 platinum coordination complexes (cisplatin, carboplatin), procarbazine, hydroxyurea, mitotane, aminoglutethimide; hormones, hormone analogs (estrogen, tamoxifen, goserelin, bicalutamide, nilutamide) and aromatase inhibitors (letrozole, anastrozole); anticoagulants (heparin, synthetic heparin salts and other inhibitors of thrombin); fibrinolytic agents (such as tissue plasminogen activator, streptokinase and urokinase), aspirin, dipyridamole, ticlopidine, clopidogrel,
- 20 abciximab; antimigratory agents; antisecretory agents (breveldin); immunosuppressives (cyclosporine, tacrolimus (FK-506), sirolimus (rapamycin), azathioprine, mycophenolate mofetil); anti-angiogenic compounds (TNP-470, genistein) and growth factor inhibitors (*e.g.*, VEGF inhibitors, fibroblast growth factor (FGF) inhibitors); angiotensin receptor blocker; nitric oxide donors; anti-sense oligonucleotides; antibodies (trastuzumab); cell cycle inhibitors
- 25 and differentiation inducers (tretinoin); mTOR inhibitors, topoisomerase inhibitors (doxorubicin (adriamycin), amsacrine, camptothecin, daunorubicin, dactinomycin, eniposide, epirubicin, etoposide, idarubicin and mitoxantrone, topotecan, irinotecan), corticosteroids (cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, and prednisolone); growth factor signal transduction kinase inhibitors; mitochondrial dysfunction inducers and
- 30 caspase activators; and chromatin disruptors.

Depending on the nature of the combinatory therapy, administration of the polypeptide therapeutic agents may be continued while the other therapy is being administered and/or thereafter. Administration of the polypeptide therapeutic agents may be made in a single dose, or in multiple doses. In some instances, administration of the polypeptide therapeutic agents is

commenced at least several days prior to the conventional therapy, while in other instances, administration is begun either immediately before or at the time of the administration of the conventional therapy.

In one example of a diagnostic application, a biological sample, such as serum or a tissue biopsy, from a patient suspected of having a condition characterized by inappropriate angiogenesis is contacted with a detectably labeled polypeptide of the disclosure to detect levels of CXCR5. The levels of CXCR5 detected are then compared to levels of CXCR5 detected in a normal sample also contacted with the labeled polypeptide. An increase of at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% in the levels of the CXCR5 may be considered a diagnostic indicator.

In certain embodiments, the CXCR5 binding polypeptides are further attached to a label that is able to be detected (*e.g.*, the label can be a radioisotope, fluorescent compound, enzyme or enzyme co-factor). The active moiety may be a radioactive agent, such as: radioactive heavy metals such as iron chelates, radioactive chelates of gadolinium or manganese, positron emitters of oxygen, nitrogen, iron, carbon, or gallium, ^{43}K , ^{52}Fe , ^{57}Co , ^{67}Cu , ^{67}Ga , ^{68}Ga , ^{123}I , ^{125}I , ^{131}I , ^{132}I , or ^{99}Tc . A binding agent affixed to such a moiety may be used as an imaging agent and is administered in an amount effective for diagnostic use in a mammal such as a human and the localization and accumulation of the imaging agent is then detected. The localization and accumulation of the imaging agent may be detected by radioscintigraphy, nuclear magnetic resonance imaging, computed tomography or positron emission tomography. Immunoscintigraphy using CXCR5 binding polypeptides directed at CXCR5 may be used to detect and/or diagnose cancers and vasculature. For example, any of the binding polypeptide against a CXCR5 marker labeled with ^{99}Tc Technetium, ^{111}In Indium, or ^{125}I Iodine may be effectively used for such imaging. As will be evident to the skilled artisan, the amount of radioisotope to be administered is dependent upon the radioisotope. Those having ordinary skill in the art can readily formulate the amount of the imaging agent to be administered based upon the specific activity and energy of a given radionuclide used as the active moiety. Typically 0.1-100 millicuries per dose of imaging agent, preferably 1-10 millicuries, most often 2-5 millicuries are administered. Thus, compositions according to the present invention useful as imaging agents comprising a targeting moiety conjugated to a radioactive moiety comprise 0.1-100 millicuries, in some embodiments preferably 1-10 millicuries, in some embodiments preferably 2-5 millicuries, in some embodiments more preferably 1-5 millicuries.

The CXCR5 binding polypeptides can also be used to deliver additional therapeutic agents (including but not limited to drug compounds, chemotherapeutic compounds, and radiotherapeutic compounds) to a cell or tissue expressing CXCR5. In one example, the CXCR5 binding polypeptide is fused to a chemotherapeutic agent for targeted delivery of the chemotherapeutic agent to a tumor cell or tissue expressing CXCR5.

The CXCR5 binding polypeptides are useful in a variety of applications, including research, diagnostic and therapeutic applications. For instance, they can be used to isolate and/or purify receptor or portions thereof, and to study receptor structure (*e.g.*, conformation) and function.

In certain embodiments, the binding polypeptides or fragments thereof can be labeled or unlabeled for diagnostic purposes. Typically, diagnostic assays entail detecting the formation of a complex resulting from the binding of a binding polypeptide to CXCR5. The binding polypeptides or fragments can be directly labeled, similar to antibodies. A variety of labels can be employed, including, but not limited to, radionuclides, fluorescers, enzymes, enzyme substrates, enzyme cofactors, enzyme inhibitors and ligands (*e.g.*, biotin, haptens). Numerous appropriate immunoassays are known to the skilled artisan (see, for example, U.S. Patents. 3,817,827; 3,850,752; 3,901,654; and 4,098,876). When unlabeled, the binding polypeptides can be used in assays, such as agglutination assays. Unlabeled binding polypeptides can also be used in combination with another (one or more) suitable reagent which can be used to detect the binding polypeptide, such as a labeled antibody reactive with the binding polypeptide or other suitable reagent (*e.g.*, labeled protein A).

In one embodiment, the binding polypeptides of the present invention can be utilized in enzyme immunoassays, wherein the subject polypeptides are conjugated to an enzyme. When a biological sample comprising a CXCR5 protein is combined with the subject binding polypeptides, binding occurs between the binding polypeptides and the CXCR5 protein. In one embodiment, a sample containing cells expressing a CXCR5 protein (*e.g.*, endothelial cells) is combined with the subject antibodies, and binding occurs between the binding polypeptides and cells bearing a CXCR5 protein recognized by the binding polypeptide. These bound cells can be separated from unbound reagents and the presence of the binding polypeptide-enzyme conjugate specifically bound to the cells can be determined, for example, by contacting the sample with a substrate of the enzyme which produces a color or other detectable change when acted on by the enzyme. In another embodiment, the subject binding polypeptides can be unlabeled, and a second, labeled polypeptide (*e.g.*, an antibody) can be added which recognizes the subject binding polypeptide.

In certain aspects, kits for use in detecting the presence of a CXCR5 protein in a biological sample can also be prepared. Such kits will include a CXCR5 binding polypeptide which binds to a CXCR5 protein or portion of said receptor, as well as one or more ancillary reagents suitable for detecting the presence of a complex between the binding polypeptide and the receptor protein or portions thereof. The polypeptide compositions of the present invention can be provided in lyophilized form, either alone or in combination with additional antibodies specific for other epitopes. The binding polypeptides and/or antibodies, which can be labeled or unlabeled, can be included in the kits with adjunct ingredients (*e.g.*, buffers, such as Tris, phosphate and carbonate, stabilizers, excipients, biocides and/or inert proteins, *e.g.*, bovine serum albumin). For example, the binding polypeptides and/or antibodies can be provided as a lyophilized mixture with the adjunct ingredients, or the adjunct ingredients can be separately provided for combination by the user. Generally these adjunct materials will be present in less than about 5% weight based on the amount of active binding polypeptide or antibody, and usually will be present in a total amount of at least about 0.001% weight based on polypeptide or antibody concentration. Where a second antibody capable of binding to the binding polypeptide is employed, such antibody can be provided in the kit, for instance in a separate vial or container. The second antibody, if present, is typically labeled, and can be formulated in an analogous manner with the antibody formulations described above.

Similarly, the present disclosure also provides a method of detecting and/or quantitating expression of CXCR5, wherein a composition comprising a cell or fraction thereof (*e.g.*, membrane fraction) is contacted with a binding polypeptide which binds to a CXCR5 or portion of the receptor under conditions appropriate for binding thereto, and the binding is monitored. Detection of the binding polypeptide, indicative of the formation of a complex between binding polypeptide and CXCR5 or a portion thereof, indicates the presence of the receptor. Binding of a polypeptide to the cell can be determined by standard methods, such as those described in the working examples. The method can be used to detect expression of CXCR5 on cells from an individual. Optionally, a quantitative expression of CXCR5 on the surface of endothelial cells can be evaluated, for instance, by flow cytometry, and the staining intensity can be correlated with disease susceptibility, progression or risk.

The present disclosure also provides a method of detecting the susceptibility of a mammal to certain diseases. To illustrate, the method can be used to detect the susceptibility of a mammal to diseases which progress based on the amount of CXCR5 present on cells and/or the number of CXCR5-positive cells in a mammal.

Polypeptide sequences are indicated using standard one- or three-letter abbreviations. Unless otherwise indicated, each polypeptide sequence has amino termini at the left and a carboxy termini at the right; each single-stranded nucleic acid sequence, and the top strand of each double-stranded nucleic acid sequence, has a 5' termini at the left and a 3' termini at the right. A particular polypeptide sequence also can be described by explaining how it differs from a reference sequence.

Antigen Binding Proteins

Antigen binding proteins (*e.g.*, antibodies, antibody fragments, antibody derivatives, antibody muteins, and antibody variants) are polypeptides that bind to EGFR, (preferably, human CXCR5). Antigen binding proteins include antigen binding proteins that inhibit a biological activity of CXCR5.

Oligomers that contain one or more antigen binding proteins may be employed as CXCR5 antagonists. Oligomers may be in the form of covalently-linked or non-covalently-linked dimers, trimers, or higher oligomers. Oligomers comprising two or more antigen binding protein are contemplated for use, with one example being a homodimer. Other oligomers include heterodimers, homotrimers, heterotrimers, homotetramers, heterotetramers, etc.

One embodiment is directed to oligomers comprising multiple antigen binding proteins joined via covalent or non-covalent interactions between peptide moieties fused to the antigen binding proteins. Such peptides may be peptide linkers (spacers), or peptides that have the property of promoting oligomerization. Leucine zippers and certain polypeptides derived from antibodies are among the peptides that can promote oligomerization of antigen binding proteins attached thereto, as described in more detail below.

In particular embodiments, the oligomers comprise from two to four antigen binding proteins. The antigen binding proteins of the oligomer may be in any form, such as any of the forms described above, *e.g.*, variants or fragments. Preferably, the oligomers comprise antigen binding proteins that have CXCR5 binding activity.

In one embodiment, an oligomer is prepared using polypeptides derived from immunoglobulins. Preparation of Fusion Proteins Comprising Certain Heterologous Polypeptides Fused to Various Portions of antibody-derived polypeptides (including the Fc domain) has been described, *e.g.*, by Ashkenazi et al., 1991, *Proc. Natl. Acad. Sci. USA* 88:10535; Byrn et al., 1990, *Nature* 344:677; and Hollenbaugh et al., 1992 "Construction of Immunoglobulin Fusion Proteins", in *Current Protocols in Immunology*, Suppl. 4, pages 10.19.1-10.19.11.

One embodiment is directed to a dimer comprising two fusion proteins created by fusing a CXCR5 binding fragment of an anti-CXCR5 antibody to the Fc region of an antibody. The dimer can be made by, for example, inserting a gene fusion encoding the fusion protein into an appropriate expression vector, expressing the gene fusion in host cells transformed with
5 the recombinant expression vector, and allowing the expressed fusion protein to assemble much like antibody molecules, whereupon interchain disulfide bonds form between the Fc moieties to yield the dimer.

The term "Fc polypeptide" includes native and mutein forms of polypeptides derived from the Fc region of an antibody. Truncated forms of such polypeptides containing the hinge
10 region that promotes dimerization also are included. Fusion proteins comprising Fc moieties (and oligomers formed therefrom) offer the advantage of facile purification by affinity chromatography over Protein A or Protein G columns.

Another method for preparing oligomeric antigen binding proteins involves use of a leucine zipper. Leucine zipper domains are peptides that promote oligomerization of the
15 proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., 1988, *Science* 240:1759), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble oligomeric proteins are described in WO 94/10308, and the leucine
20 zipper derived from lung surfactant protein D (SPD) described in Hoppe et al., 1994, *FEBS Letters* 344:191. The use of a modified leucine zipper that allows for stable trimerization of a heterologous protein fused thereto is described in Fanslow et al., 1994, *Semin. Immunol.* 6:267-78. In one approach, recombinant fusion proteins comprising an anti-CXCR5 antibody fragment or derivative fused to a leucine zipper peptide are expressed in suitable host cells, and
25 the soluble oligomeric anti-CXCR5 antibody fragments or derivatives that form are recovered from the culture supernatant.

Antigen-binding fragments of antigen binding proteins of the invention may be produced by conventional techniques. Examples of such fragments include, but are not limited to, Fab and F(ab')₂ fragments.

30 The present disclosure provides monoclonal antibodies that bind to CXCR5. Monoclonal antibodies may be produced using any technique known in the art, e.g., by immortalizing spleen cells harvested from the transgenic animal after completion of the immunization schedule. The spleen cells can be immortalized using any technique known in the art, e.g., by fusing them with myeloma cells to produce hybridomas. Myeloma cells for use

in hybridoma-producing fusion procedures preferably are non-antibody-producing, have high fusion efficiency, and enzyme deficiencies that render them incapable of growing in certain selective media which support the growth of only the desired fused cells (hybridomas).

Examples of suitable cell lines for use in mouse fusions include Sp-20, P3-X63/Ag8, P3-X63-Ag8.653, NS1/1.Ag 4 1, Sp210-Ag14, FO, NSO/U, MPC-11, MPC11-X45-GTG 1.7 and S194/5XX0 Bul; examples of cell lines used in rat fusions include R210.RCY3, Y3-Ag 1.2.3, IR983F and 48210. Other cell lines useful for cell fusions are U-266, GM1500-GRG2, LICR-LON-HMy2 and UC729-6.

Antigen binding proteins directed against CXCR5 can be used, for example, in assays to detect the presence of CXCR5 polypeptides, either *in vitro* or *in vivo*. The antigen binding proteins also may be employed in purifying CXCR5 proteins by immunoaffinity chromatography. Blocking antigen binding proteins can be used in the methods disclosed herein. Such antigen binding proteins that function as CXCR5 antagonists may be employed in treating any CXCR5-induced condition, including but not limited to various cancers.

Antigen binding proteins may be employed in an *in vitro* procedure, or administered *in vivo* to inhibit CXCR5-induced biological activity. Disorders caused or exacerbated (directly or indirectly) by the proteolytic activation of CXCR5, examples of which are provided herein, thus may be treated. In one embodiment, the present invention provides a therapeutic method comprising *in vivo* administration of a CXCR5 blocking antigen binding protein to a mammal in need thereof in an amount effective for reducing a CXCR5-induced biological activity.

Antigen binding proteins include fully human monoclonal antibodies that inhibit a biological activity of CXCR5.

Antigen binding proteins may be prepared by any of a number of conventional techniques. For example, they may be purified from cells that naturally express them (*e.g.*, an antibody can be purified from a hybridoma that produces it), or produced in recombinant expression systems, using any technique known in the art. See, for example, Monoclonal Antibodies, Hybridomas: A New Dimension in Biological Analyses, Kennet et al. (eds.), Plenum Press, New York (1980); and Antibodies: A Laboratory Manual, Harlow and Land (eds.), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., (1988).

Any expression system known in the art can be used to make the recombinant polypeptides of the invention. In general, host cells are transformed with a recombinant expression vector that comprises DNA encoding a desired polypeptide. Among the host cells that may be employed are prokaryotes, yeast or higher eukaryotic cells. Prokaryotes include gram negative or gram positive organisms, for example *E. coli* or *bacilli*. Higher eukaryotic

cells include insect cells and established cell lines of mammalian origin. Examples of suitable mammalian host cell lines include the COS-7 line of monkey kidney cells (ATCC CRL 1651) (Gluzman et al., 1981, *Cell* 23:175), L cells, 293 cells, C127 cells, 3T3 cells (ATCC CCL 163), Chinese hamster ovary (CHO) cells, HeLa cells, BHK (ATCC CRL 10) cell lines, and the CV1/EBNA cell line derived from the African green monkey kidney cell line CV1 (ATCC CCL 70) as described by McMahan et al., 1991, *EMBO J.* 10: 2821. Appropriate cloning and expression vectors for use with bacterial, fungal, yeast, and mammalian cellular hosts are described by Pouwels et al. (Cloning Vectors: A Laboratory Manual, Elsevier, N.Y., 1985).

The transformed cells can be cultured under conditions that promote expression of the polypeptide, and the polypeptide recovered by conventional protein purification procedures. One such purification procedure includes the use of affinity chromatography, *e.g.*, over a matrix having all or a portion (*e.g.*, the extracellular domain) of CXCR5 bound thereto. Polypeptides contemplated for use herein include substantially homogeneous recombinant mammalian anti-CXCR5 antibody polypeptides substantially free of contaminating endogenous materials.

Antigen binding proteins may be prepared, and screened for desired properties, by any of a number of known techniques. Certain of the techniques involve isolating a nucleic acid encoding a polypeptide chain (or portion thereof) of an antigen binding protein of interest (*e.g.*, an anti-CXCR5 antibody), and manipulating the nucleic acid through recombinant DNA technology. The nucleic acid may be fused to another nucleic acid of interest, or altered (*e.g.*, by mutagenesis or other conventional techniques) to add, delete, or substitute one or more amino acid residues, for example.

Single chain antibodies may be formed by linking heavy and light chain variable domain (Fv region) fragments via an amino acid bridge (short peptide linker), resulting in a single polypeptide chain. Such single-chain Fvs (scFvs) have been prepared by fusing DNA encoding a peptide linker between DNAs encoding the two variable domain polypeptides (V_L and V_H). The resulting polypeptides can fold back on themselves to form antigen-binding monomers, or they can form multimers (*e.g.*, dimers, trimers, or tetramers), depending on the length of a flexible linker between the two variable domains (Kortt et al., 1997, *Prot. Eng.* 10:423; Kortt et al., 2001, *Biomol. Eng.* 18:95-108). By combining different V_L and V_H -comprising polypeptides, one can form multimeric scFvs that bind to different epitopes (Kriangkum et al., 2001, *Biomol. Eng.* 18:31-40). Techniques developed for the production of single chain antibodies include those described in U.S. Patent 4,946,778; Bird, 1988, *Science*

242:423; Huston et al., 1988, *Proc. Natl. Acad. Sci. USA* 85:5879; Ward et al., 1989, *Nature* 334:544, de Graaf et al., 2002, *Methods Mol. Biol.* 178:379-87.

Techniques are known for deriving an antibody of a different subclass or isotype from an antibody of interest, *i.e.*, subclass switching. Thus, IgG antibodies may be derived from an
5 IgM antibody, for example, and vice versa. Such techniques allow the preparation of new antibodies that possess the antigen-binding properties of a given antibody (the parent antibody), but also exhibit biological properties associated with an antibody isotype or subclass different from that of the parent antibody. Recombinant DNA techniques may be employed. Cloned DNA encoding particular antibody polypeptides may be employed in such procedures,
10 *e.g.*, DNA encoding the constant domain of an antibody of the desired isotype (Lantto et al., 2002, *Methods Mol. Biol.* 178:303-16). Moreover, if an IgG4 is desired, it may also be desired to introduce a point mutation (CPSCP->CPPCP) in the hinge region (Bloom et al., 1997, *Protein Science* 6:407) to alleviate a tendency to form intra-H chain disulfide bonds that can lead to heterogeneity in the IgG4 antibodies.

15 In particular embodiments, antigen binding proteins of the present invention have a binding affinity (K_a) for CXCR5 of at least 10^6 . In other embodiments, the antigen binding proteins exhibit a K_a of at least 10^7 , at least 10^8 , at least 10^9 , or at least 10^{10} . In another embodiment, the antigen binding protein exhibits a K_a substantially the same as that of an antibody described herein in the Examples.

20 In another embodiment, the present disclosure provides an antigen binding protein that has a low dissociation rate from CXCR5. In one embodiment, the antigen binding protein has a K_{off} of 1×10^{-4} to $^{-1}$ or lower. In another embodiment, the K_{off} is 5×10^{-5} to $^{-1}$ or lower. In another embodiment, the K_{off} is substantially the same as an antibody described herein. In another embodiment, the antigen binding protein binds to CXCR5 with substantially the same
25 K_{off} as an antibody described herein.

In another aspect, the present disclosure provides an antigen binding protein that inhibits an activity of CXCR5. In one embodiment, the antigen binding protein has an IC_{50} of 1000 nM or lower. In another embodiment, the IC_{50} is 100 nM or lower; in another embodiment, the IC_{50} is 10 nM or lower. In another embodiment, the IC_{50} is substantially the
30 same as that of an antibody described herein in the Examples. In another embodiment, the antigen binding protein inhibits an activity of CXCR5 with substantially the same IC_{50} as an antibody described herein.

In another aspect, the present disclosure provides an antigen binding protein that binds to human CXCR5 expressed on the surface of a cell and, when so bound, inhibits CXCR5

signaling activity in the cell without causing a significant reduction in the amount of CXCR5 on the surface of the cell. Any method for determining or estimating the amount of CXCR5 on the surface and/or in the interior of the cell can be used. In other embodiments, binding of the antigen binding protein to the CXCR5-expressing cell causes less than about 75%, 50%, 40%,
5 30%, 20%, 15%, 10%, 5%, 1%, or 0.1% of the cell-surface CXCR5 to be internalized.

In another aspect, the present disclosure provides an antigen binding protein having a half-life of at least one day *in vitro* or *in vivo* (e.g., when administered to a human subject). In one embodiment, the antigen binding protein has a half-life of at least three days. In another embodiment, the antigen binding protein has a half-life of four days or longer. In another
10 embodiment, the antigen binding protein has a half-life of eight days or longer. In another embodiment, the antigen binding protein is derivatized or modified such that it has a longer half-life as compared to the underivatized or unmodified antigen binding protein. In another embodiment, the antigen binding protein contains one or more point mutations to increase serum half life, such as described in WO00/09560, incorporated by reference herein.

The present disclosure further provides multi-specific antigen binding proteins, for example, bispecific antigen binding protein, e.g., antigen binding protein that bind to two different epitopes of CXCR5, or to an epitope of CXCR5 and an epitope of another molecule, via two different antigen binding sites or regions. Moreover, bispecific antigen binding protein as disclosed herein can comprise an CXCR5 binding site from one of the herein-described
15 antibodies and a second CXCR5 binding region from another of the herein-described antibodies, including those described herein by reference to other publications. Alternatively, a bispecific antigen binding protein may comprise an antigen binding site from one of the herein described antibodies and a second antigen binding site from another CXCR5 antibody that is known in the art, or from an antibody that is prepared by known methods or the methods
20 described herein.

Numerous methods of preparing bispecific antibodies are known in the art. Such methods include the use of hybrid-hybridomas as described by Milstein et al., 1983, *Nature* 305:537, and chemical coupling of antibody fragments (Brennan et al., 1985, *Science* 229:81; Glennie et al., 1987, *J. Immunol.* 139:2367; U.S. Patent 6,010,902). Moreover, bispecific
25 antibodies can be produced via recombinant means, for example by using leucine zipper moieties (i.e., from the *Fos* and *Jun* proteins, which preferentially form heterodimers; Kostelny et al., 1992, *J. Immunol.* 148:1547) or other lock and key interactive domain structures as described in U.S. Patent 5,582,996. Additional useful techniques include those described in U.S. Patents 5,959,083; and 5,807,706.

In another aspect, the antigen binding protein comprises a derivative of an antibody. The derivatized antibody can comprise any molecule or substance that imparts a desired property to the antibody, such as increased half-life in a particular use. The derivatized antibody can comprise, for example, a detectable (or labeling) moiety (*e.g.*, a radioactive, colorimetric, antigenic or enzymatic molecule, a detectable bead (such as a magnetic or electrodeposited (*e.g.*, gold bead), or a molecule that binds to another molecule (*e.g.*, biotin or streptavidin), a therapeutic or diagnostic moiety (*e.g.*, a radioactive, cytotoxic, or pharmaceutically active moiety), or a molecule that increases the suitability of the antibody for a particular use (*e.g.*, administration to a subject, such as a human subject, or other *in vivo* or *in vitro* uses). Examples of molecules that can be used to derivatize an antibody include albumin (*e.g.*, human serum albumin) and polyethylene glycol (PEG). Albumin-linked and PEGylated derivatives of antibodies can be prepared using techniques well known in the art. In one embodiment, the antibody is conjugated or otherwise linked to transthyretin (TTR) or a TTR variant. The TTR or TTR variant can be chemically modified with, for example, a chemical selected from the group consisting of dextran, poly(n-vinyl pyrrolidone), polyethylene glycols, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols and polyvinyl alcohols.

Therapeutic Methods and Administration of Antigen Binding Proteins

Certain methods provided herein comprise administering a CXCR5 binding antigen binding protein to a subject, thereby reducing a CXCR5-induced biological response that plays a role in a particular condition. In particular embodiments, methods of the invention involve contacting endogenous CXCR5 with an CXCR5 binding antigen binding protein, *e.g.*, via administration to a subject or in an *ex vivo* procedure.

The term "treatment" encompasses alleviation or prevention of at least one symptom or other aspect of a disorder, or reduction of disease severity, and the like. An antigen binding protein need not effect a complete cure, or eradicate every symptom or manifestation of a disease, to constitute a viable therapeutic agent. As is recognized in the pertinent field, drugs employed as therapeutic agents may reduce the severity of a given disease state, but need not abolish every manifestation of the disease to be regarded as useful therapeutic agents. Similarly, a prophylactically administered treatment need not be completely effective in preventing the onset of a condition in order to constitute a viable prophylactic agent. Simply reducing the impact of a disease (for example, by reducing the number or severity of its symptoms, or by increasing the effectiveness of another treatment, or by producing another beneficial effect), or reducing the likelihood that the disease will occur or worsen in a subject,

is sufficient. One embodiment of the invention is directed to a method comprising administering to a patient a CXCR5 antagonist in an amount and for a time sufficient to induce a sustained improvement over baseline of an indicator that reflects the severity of the particular disorder.

5 Use of antigen binding proteins in *ex vivo* procedures also is contemplated. For example, a patient's blood or other bodily fluid may be contacted with an antigen binding protein that binds CXCR5 *ex vivo*. The antigen binding protein may be bound to a suitable insoluble matrix or solid support material.

Advantageously, antigen binding proteins are administered in the form of a
10 composition comprising one or more additional components such as a physiologically acceptable carrier, excipient or diluent. Optionally, the composition additionally comprises one or more physiologically active agents, for example, a second inflammation- or immune-inhibiting substance, an anti-angiogenic substance, an analgesic substance, etc., non-exclusive examples of which are provided herein. In various particular embodiments, the composition
15 comprises one, two, three, four, five, or six physiologically active agents in addition to an EGFR binding antigen binding protein

Combination Therapy

In another aspect, the present disclosure provides a method of treating a subject with an CXCR5 inhibiting antigen binding protein and one or more other treatments. In one
20 embodiment, such a combination therapy achieves synergy or an additive effect by, for example, attacking multiple sites or molecular targets in a tumor. Types of combination therapies that can be used in connection with the present invention include inhibiting or activating (as appropriate) multiple nodes in a single disease-related pathway, multiple pathways in a target cell, and multiple cell types within a target tissue.

25 In another embodiment, a combination therapy method comprises administering to the subject two, three, four, five, six, or more of the CXCR5 agonists or antagonists described herein. In another embodiment, the method comprises administering to the subject two or more treatments that together inhibit or activate (directly or indirectly) CXCR5-mediated signal transduction. Examples of such methods include using combinations of two or more CXCR5
30 inhibiting antigen binding proteins, of an CXCR5 inhibiting antigen binding protein and one or more other therapeutic moiety having anti-cancer properties (for example, cytotoxic agents, and/or immunomodulators), or of an CXCR5 inhibiting antigen binding protein and one or more other treatments (*e.g.*, surgery, or radiation). Furthermore, one or more anti-CXCR5 antibodies or antibody derivatives can be used in combination with one or more molecules or

other treatments, wherein the other molecule(s) and/or treatment(s) do not directly bind to or affect CXCR5, but which combination is effective for treating or preventing the condition being treated. In one embodiment, one or more of the molecule(s) and/or treatment(s) treats or prevents a condition that is caused by one or more of the other molecule(s) or treatment(s) in the course of therapy, *e.g.*, nausea, fatigue, alopecia, cachexia, insomnia, etc. In every case where a combination of molecules and/or other treatments is used, the individual molecule(s) and/or treatment(s) can be administered in any order, over any length of time, which is effective, *e.g.*, simultaneously, consecutively, or alternately. In one embodiment, the method of treatment comprises completing a first course of treatment with one molecule or other treatment before beginning a second course of treatment. The length of time between the end of the first course of treatment and beginning of the second course of treatment can be any length of time that allows the total course of therapy to be effective, *e.g.*, seconds, minutes, hours, days, weeks, months, or even years.

In another embodiment, the method comprises administering one or more of the CXCR5 antagonists described herein and one or more other treatments (*e.g.*, a therapeutic or palliative treatment). Where a method comprises administering more than one treatment to a subject, it is to be understood that the order, timing, number, concentration, and volume of the administrations is limited only by the medical requirements and limitations of the treatment, *i.e.*, two treatments can be administered to the subject, *e.g.*, simultaneously, consecutively, alternately, or according to any other regimen.

Example 1

This example describes a cellular binding assay to determine the EC_{50} for anti-CXCR5 antibodies binding to human CXCR5. This example shows the binding characteristics for these antibodies in terms of the maximal cell binding and the concentration at which 50% binding saturation (EC_{50}) is reached. In this example, CHO-CXCR5 cells were lifted from culture flasks using non-enzymatic Cell Dissociation Buffer – PBS based (Life Technologies #13151-014). Cells were resuspended in FACS Buffer (2% Fetal Bovine Serum in PBS) at 1×10^6 cells/ml and 50 μ l (0.5×10^5 cells) were aliquoted into the wells of a 96-well plate. Plated cells were spun down and the supernatant discarded. Cells were resuspended in 30 μ l FACS Buffer serially diluted concentrations of CXCR5 IgG in triplicate. Plates were incubated for 1 hr at 4 °C and then washed 2x with FACS Buffer. Cells were resuspended in 50 μ l goat anti-human IgG (γ -chain specific)-PE conjugated secondary antibody (Southern Biotech # 2040-09) diluted 1:500 in FACS Buffer. Cells were further incubated for 30 min at 4 °C and then washed 1x with FACS Buffer. The cells were resuspended in a final volume of 30 μ l FACS Buffer and

analyzed using the Intellicyt Flow Cytometer. Median fluorescence in the FL-2H channel was determined using FlowJo software and EC₅₀ value was determined by plotting the data in GraphPad Prism and analyzing using a variable slope non-linear regression. The results are shown in Table 1.

- 5 Table 1 EC₅₀ of anti-CXCR5 antibodies to human CXCR5. N/A = little detectable binding.

Name	EC50 (nM), hu-CHO
4C10	0.7
11A7	0.9
11D3	2.7
11E3-0	10
11E3	1.8
11G3	2.6
12C1	12
12D3	1.3
12D11	2.1
12G10	0.5
13A3	7.4
13E4	0.9
13E10	0.7
13F9	1.6
13G9	3
14B11	10
14C10	0.7
14C11	21
14D7	4
14D9	22
14E5	0.3
14F8	2.5
14F11	3.8
15G11	0.4
15H2	6.1
16A8	2.3
16F8	3.6
16F9	0.7
52A10	0.5
52B10	0.5
52C6	3
16E3	250

15H10	132
11F3	13
16A6	37
12B11	53
16B7	88
14E10	57
14C3	21
PC12	4.2
52D6	24
52A9*	31
52B10	0.46
52C6	2.8
52H9	4
52A10	0.54

Example 2

This example shows a cellular binding assay to determine the EC₅₀ for anti-CXCR5 antibodies binding to murine CXCR5. This example shows the binding characteristics for these antibodies in terms of the maximal cell binding and the concentration at which 50% binding saturation (EC₅₀) is reached. In this example, mouse spleen cells were harvested from either C57Bl/6 or athymic nu/nu mice. Cells were cultured at 2x10⁶ per ml with LPS at 10 micrograms per ml in RPMI+10%FCS for up to 4 days at 37 °C in 5% CO₂. Cells were harvested, washed and resuspended in FACS Buffer (2% Fetal Bovine Serum in PBS) at 1 x 10⁶ cells/ml and 50 µl (0.5 x 10⁵ cells) were aliquoted into the wells of a 96-well plate. Plated cells were spun down and the supernatant discarded. Cells were resuspended in 30 µl FACS Buffer containing serially diluted concentrations of CXCR5 IgG in triplicate. Plates were incubated for 1 hr at 4 °C and then washed 2x with FACS Buffer. Cells were resuspended in 50 µl goat anti-human IgG (γ-chain specific)-PE conjugated secondary antibody (Southern Biotech # 2040-09) diluted 1:500 in FACS Buffer. Cells were further incubated for 30 min at 4 °C and then washed 1x with FACS Buffer. The cells were resuspended in a final volume of 30 µl FACS Buffer and analyzed using the Intellicyt Flow Cytometer. Median fluorescence in the FL-2H channel was determined using FlowJo software and EC₅₀ value was determined by plotting the data in GraphPad Prism and analyzing using a variable slope non-linear regression. The results are shown in Table 2.

Table 2. EC₅₀ of anti-CXCR5 antibodies to murine CXCR5. N/A = little detectable binding.

Name	EC50 (nM), mur
------	----------------

11A7	>100
11D3	N/A
11E3	11
11G3	37
12C1	N/A
12D3	27
12D11	N/A
12G10	2.5
13E4	5.5
13E10	25
13F9	23
13G9	>50
14B11	N/A
14C10	375
14E5	2.8
14F11	N/A
15G11	4.8
16A8	>100
16F8	15
16F9	3.1
12B11	N/A
16B7	N/A

Example 3

In this example, CHO-CXCR5 cells were lifted from culture flasks using non-enzymatic Cell Dissociation Buffer – PBS based (Life Technologies #13151-014). Cells were resuspended in FACS Buffer (2% Fetal Bovine Serum in PBS) with sodium azide at 1×10^6 cells/ml and 800 μ l were aliquoted into a tube for each antibody. Antibody was added to a final concentration of 5 μ g/ml and incubated at room temperature for 1h. The samples were then placed on ice and a 105 μ l aliquot at various time points was removed and added to 190 μ l FACS buffer in a 96-well plate and centrifuged for 3 min. Supernatant was discarded, the cells were resuspended in 105 μ l of FACS buffer, aliquoted (50 μ l) in duplicates into another 96-well plate containing 150 μ l FACS buffer and incubated at room temperature. After all of the time points were collected, the plate was centrifuged for 3 min, supernatant discarded and the cells were resuspended in 50 μ l goat anti-human IgG (γ -chain specific)-PE conjugated secondary antibody (Southern Biotech # 2040-09) diluted 1:500 in FACS Buffer. Cells were further incubated for 30 min at 4 °C and then washed 1x with FACS Buffer. The cells were

resuspended in a final volume of 30 μ l FACS Buffer and analyzed using the Intellicyt Flow Cytometer. The binding of various IgG1 clones over time is shown in Figure 1.

Example 4

This example shows a Calcium assay with CHO-CXCR5 cells. CHO-CXCR5 cells (CHO cells transfected with human CXCR5 gene) were used in the calcium assay. Cells (0.1×10^5) were seeded in 20 μ l of growth medium per well of a 384 well plate (#781091, Greiner) and incubated for 20 hours. The growth medium is F-12K (#21127, Life Technologies) plus 10% FBS. Serial diluted doses of mAbs (5 μ l) were added into 20 μ l cells and incubated 20 min at room temperature. Then, 25 μ l of Calcium 4 Assay kit reagent (R8142, Molecular Devices), including 0.5 mM probenecid (Sigma #P8761-25G), were added to the 25 μ l cells pre-incubated with the mAbs. After 1 h incubation at 37°C, 5% CO₂, followed by 15 minutes at room temperature, 12.5 μ l of 5X dose of ligand was added to each well of the plate as a challenge agonist with detection of the calcium response on the FlexStation3 (Molecular Devices). The final concentration of ligand used in the assay was 9 nM of CXCL13 (#801-CX-025/CF, R&D). The IC₅₀ value of each mAb indicated Table 3 was calculated by Prism5. Each IC₅₀ value represents Mean $\pm$ S.D. (n=2) and one of two independent experiments which had similar results. R&D mAb (Cat# MAB190, R&D) was used as a control anti-CXCR5 antibody. Antibody 11A7 is a fully human IgG1.

Table 3: IC₅₀ [nM] of mAbs in calcium flux assay using CHO-CXCR5 cells

	R&D mAb	11A7
CXCL13	10	5

Example 6

This example shows a chemotaxis assay with Sultan cells. Human B lymphocyte SH-Sultan cell line (CRL-1484, ATCC) was used for the chemotaxis assays. The chemotaxis assays were set up using 96-well chemotaxis chamber (ChemoTX; NeuroProbe, Gaithersburg, MD) with the 2 compartments separated by a 5- μ m polycarbonate membrane. Assay buffer used for chemotaxis was RPMI plus 0.5% FBS, 0.5 mM sodium pyruvate and 0.5% BSA. Serial diluted concentrations of mAbs were pre-incubated with the activated T cells (0.1×10^6 cells in 25 μ l of the assay buffer) at room temperature for 20 min. Ligand (CXCL13) at 25 nM was loaded in the wells of plate in the lower chambers, whereas the pre-incubated cells with mAbs were loaded on top of membrane. After 4 h incubation at 37 °C, 5% CO₂, migrated cells in the lower chamber were transferred to an opaque white 96 well plate and incubated with CellTiter GLO (Cat#G7571, Promega) for 10 min at room temperature. Luminescent signals

generated from the cells in each well were detected by a fluorescent plate reader (FlexStation3, Molecular Devices). The IC₅₀ value of each mAb indicated in Table 4 was calculated by Prism5. Each IC₅₀ value represents Mean±S.D. (n=3) and one of two independent experiments which had similar results. The SAR113244 antibody used as a control in the assay is a Sanofi antibody expressed as an IgG1.

Table 4: IC₅₀ [nM] of mAbs in chemotaxis assay using HS-Sultan cells

	SAR113244	11A7	R&D mAb
CXCL13	4.7	4.8	4.1

Sequence Listing

	Heavy chain variable domain region	Light chain variable domain region
52A9	EVQLVESGGGVVQGRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKVPFYSSSS DYWGQGTLLTVSS SEQ ID NO. 1	QSVVTQPASVSGSPGQSITISCTGTSSDVGG SKYVSWFQQHPGKAPKLMYDVSNRPSGV SYRFSGSKSGNTASLTISGLQAEDEADYYCTS YTSSRTWVFGGGTKLTVL SEQ ID NO. 2
52A10	QVQLVQSGAEVKKPGASVKVCKASGYTFTSYGISW VRQAPGQGLEWVGWISAYNGNTNYAQKLQGRVT MTTDTSTSTAYMELRSLRSDDTAVYYCARGSDYWG QGTLTVSS SEQ ID NO. 3	SYELTQPPSASGTPGQRVTISCSGSSSNIGSN YVYWYQQLPGTAPKLLIYRNNQRPSGVPDR FSGSKSGTSASLAISGLRSEDEADYYCAAWD DSLSPVFGGGTQLTVL SEQ ID NO. 4
52B10	EVQLLESGGGLVQPGGSLRLSCAGSESTFGDSWLN WVRQAPGKGLEWVANINKDGSKEYVESVKGRFTI SRDNAKKSIVYLQMNSLRVEDTAVYYCLLKGVWGQ GTLTVSS SEQ ID NO. 5	AIQLTQSPSFLSASVGDRVTITCRASQGISSY LAWYQQKPGKAPKLLIYAASLTQSGVPSRFS GSGSGTEFTLTISLQPEDFATYYCQQLNSYP ITFGPGTKVDIK SEQ ID NO. 6
52C6	QVQLVESGGGLVQPGGSLRLSCAASGFTFDDYAMH WVRQAPGKGLQWVAVISHDGS AKYYADSVKGRFTI SRDNAKNSLYLQMNSLRAEDTAVYYCARSRWGDN WGQGTLLTVSS SEQ ID NO. 7	SYELMQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVSKRPSGV SNRFSGSKSGNTASLTISGLQAEDEADYYCS SYTSSSTPYVFGTGTGLTVL SEQ ID NO. 8
52D6	EVQLLESGGGLVQPGRSLRLSCAASGFNFDAYAMH WVRQAPGKGLEWVSGISWNSGYIAYADSVEGRFAI SRDNSKNTVFLQMNSLRAEDTAIYYCARDRWLSYW GQGTLLTVSS SEQ ID NO. 9	QSVLTQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVSKRPSGV SNRFSGSKSGNTASLTISGLQAEDEAEYYCS SYAGSNFVFGGGTKLTVL SEQ ID NO. 10
52D7	QVQLVQSGAEVKKPGASVKISCKASGYTITTHYIHW VRQAPGQGLEWMGIINPNSGRTPKQKFGQGRVTM TRDTSTNTVYMEVNSLRSED TAVYYCATGSGSYGN WFDPWGQGTLLTVSS SEQ ID NO. 11	QTVVTQPPSVSGAPGQRVTISCTGSSSNIG SVVTQPPSVSAAPGQKVTISCSGSSSNIGNN YVSWYQQLPGTAPKLLIYDNNKRPSGIPDRF SGSKSGTSATLGITGLQTGDEADYYCGTWD SSLTLVFGTGTGLTVL SEQ ID NO. 12
52D11	QVQLVQSGGEVKKPGALVKVCKASGYTFSTHGIS WVRQAPGQGLAWMGWISAYNGKATYAQTQGR VTMTTDTSTNTAYMELRNLRSDDTAVYYCARVGAV TGMDSWGQGTLLTVSS SEQ ID NO. 13	QSVVTQPPSVSAAPGQVTISCSGSSSNIGS KFVSWYQHVPGTAPKLLIYDNDKRPSGIPD RFSGSKSGTSATLGITGLQTGDEADYYCGT WDSSLSAYVFGTGTGLTVL SEQ ID NO. 14

52E1	EVQLLESGAEVKKPGASVKVSCASGYTFSRYAMH WVRQAPGQRLEWMGWIHAGNGNTKYSQKFQGR VTISRDTASTAYMELSSLRSEDTAVYYCARGSIAAA GGFDYWGGQGLTVTVSS SEQ ID NO. 15	QAVLTQPPSASGTPGQRVTLSGSGSSNIGR NYVYWYQQLPGTAPKLVLYVNDKRPSGIPD RFGSGSGTSATLGITGLQTGDEADYYCGT WDSSLRAYVFGTGKVTVL SEQ ID NO. 16 QAGLTQPPSASGSPGQSVTISCTGTSSDVG GYNVSWYQQHPGKAPKLMIEVSKRPSG VPDRFSGSGSGNTASLTVSGLQAEDEADYY CSSYAGSNKGVVFGGGTKLTVL SEQ ID NO. 18 QSVLTQPASVSGSPGQSVTISCTGTSRDVG GYNFVSWYQQHPGKAPKLMIDVSNRPSG VSNRFTGSGSGNTASLTISGLQAEDEADYHC SSYRRGDTLVFGGGTKLTVL SEQ ID NO. 20
52E10	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKKYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKGANFDY WGQGLTVTVSS SEQ ID NO. 17	
52H9	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKKYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKLSGPTAKF DYWGQGLTVTVSS SEQ ID NO. 19	
PC12	EVQLLESGAEVKKPGASVKVSCASGYTFTSYVHVH VRQAPGQGLEWMGIINPSGGTTSYAQKFQGRVTM TRDTSTSTVYMELSSLRSEDTAVYYCVRDRRVAAAT TPSAFDVWGQGTMTVTVSS SEQ ID NO. 21	QSVVTQPPSVSAAPGQKVTISCSGSSSNIGN NYVSWYQQLPGTAPKLLIYDNNKRPSGIPD RFGSGSGTSATLGIVGLQTGDEADYYCAT WDGSLSTFLFGPGTKLTVL SEQ ID NO. 22
PD10	QMQLVQSGSEVKKPGASVKVSCRASGYLFTNYGIS WVRQAPGQGLEWMGWVSAHGEFTKYAPSLQDR VTMTSDISTTTAYMELRSLRSDDTGVYYCARDRGAD HFDTWGQGLTVTVSS SEQ ID NO. 23	DIVMTQTPLSSPVTLGQPASISCRSSQSLVH SDGNTYLSWLQQRPGQPPRLIIYKISNRFSG VPDRFSGSGAGTDFTLKISRVEADVGYYC TQATQFPFTFGQGTKEIK SEQ ID NO. 24
D3-4	QVQLQQSGPGLLNPSQTLSTLCVISGDSVSSNSATW NWIRQPSRGLLEWLGRITYRSQWFNDYAVSVKSRI TINPDTSKNQFSLQLSSVTPEDTAVYYCARWLHVW GQGTTVTVSS SEQ ID NO. 25	LPVLTQPPSASGTPGQRVTISCSGGTSNIGN NNVYWYQQVPGMAPKLLIFRNSQRPSGVP DRFSGSGSGNTASLTISGLQAEDEGDYYCGS YAGPRTYVFGSGTKVTVL SEQ ID NO. 26
E2-1	EVQLLESGGGLVQPGSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKKYADSVKGRFTI SRDNSKNTLYLQLNSLRAEDTAVYYCARGQNLDYW GQGLTVTVSS SEQ ID NO. 27	QPVLTQPASVSGSPGQSITISCTGTSSDVGG YNYISWYQQHPGKAPKLMIEVSNRPSGVS NRFGSGSGNTASLTISGLQAEDEADYYCSS YRSSSTQVFGGGTKLTVL SEQ ID NO. 28
A4 and 7A7	QMQLVQSGAVVKPPGSSVKVSCASGGTISRYVIS WVRQAPGQRLEWMGWINAANGRTKYLDKFQGR VTFTMDMSTSTASMESSLTSEDTAVYFCARSLREQ VGGNYYYLMDVWGRGTTVTVSS SEQ ID NO. 29	DIQLTQSPSSLSASVGDRVTITCRASQGIGTY LAWFQQKPGKVPKPLIYAASLTQSGVPSRFS GSGSGADFTLTISLQPEDVATYYCQKYNSV PQTFGQGTKEIK SEQ ID NO. 30 NFMLTQPPSVSKGLRQTATLTCTGNSNNV QSALTQPRSVSGSPGQSVTISCTGTSSDVGT YNYVSWYQQHPGKAPKLIIDVSIKPSGVSN RFGSGSGNTASLTITGLQAEDEADYYCQSY DSSLSGVFGGGTQLTVL SEQ ID NO. 32 LPVLTQPPSASGTPGQRVTISCSGNVSNIAN NYVYWYRHLPGTAPKLLMYRNNKRPSGVP DRFTASKSGTSASLAISGLRSEDEADYYCAA WDDSLHGYVFGTGKVTVL SEQ ID NO. 34
A8	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVGRIKSKTDGGTTDYAAPVKGR FTISRDDSKNTLYLQMNSLKTEDTAVYYCTTGRHSG SYLRGTLTVTVSS SEQ ID NO. 31	
A12	QVQLVQSGAEVKKPGASVKVSCASGNTLSNYAIH WVRQAPGQGLEWMGWINAVNGNTKYSQKFQGR VTATRDTSATIFYLESSLRSEDTAVYYCVLITGAYWG EGTTVTVTVSS SEQ ID NO. 33	

B3	QVQLVESGGGLVKPGGSLRLSCAASGFTFSYYMV WVRRSPGKGLEWISYISSGGTIIYADSVKGRFTISRH NSENTLYLQMNSLRAEDTAVYYCATRSKGHALDVW GQGTTVTVSS SEQ ID NO. 35	LPVLTQSPASGTPGQRTVISCSSSSNIGSN YVYWYQQLPGTAPKLLIYRNNQRPSGVPDR FSGSKSGTSASLAISGLQPEDEAYYCASWD DRLTGYVFGSGTKVTVL SEQ ID NO. 36 QAVLTQPPSVSKGLRQTATLTCTGNSNNVG NQGAVWLQHQHQPPLSSRKNNRPSGI SERFSASRSGNTASLTITGLQPDDEADYYCS AWDSSLSSWVFGGGTKLTVL SEQ ID NO. 38
C8	QVQLVESGGGVVQPRSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARRAVAGH YYGMDVWGQGTTLTVSS SEQ ID NO. 37	QPVLTQPPASGTPGQRTVISCSSSSNIGS NYVYWYQQLPGTAPKLLIYRNNQRPSGVPD RFGSKSGTSASLAISGLRSEDEADYYCAAW DDSLSGRVFGGGTKLTVL SEQ ID NO. 40
F8 and 10G9	EVQLVESGGGLVQPGGSLRLSCSGSGFSSNYAMH WVRQAPGKGLEHVSIAISSNGGSIYADSVKGRFTIS RDNSKNMLYFQMSSLRTEDTAVYYCVKRPVGSNF DYWGQGTTLTVSS SEQ ID NO. 39	QSVLTQPPASGTPGQRTVISCSSSSNIGSF YVYWYQHVPGTAPKLLIYRNNRRPSGVPDR FSGSKSGNTASLTISGLQAEDEADYYCSSYPR NTVLFGGGTKLTVL SEQ ID NO. 42
G11	QVQLVESGGGLVQSGGSLRLSCAASGFTFSSYGMQ WVRQAPGKGLEWVSSISSGGSTFYADSVKGRFTIS RDNSKNTLYLQMNSLRAEDAAVYFCVKGGLMPAA YFWGQGTTLTVSS SEQ ID NO. 41	QVLTQPPASGTPGQRTVISCSSSSNIGSF YVYWYQHVPGTAPKLLIYRNNRRPSGVPDR FSGSKSGNTASLTISGLQAEDEADYYCSSYPR NTVLFGGGTKLTVL SEQ ID NO. 42
H3	QVQLVESGAEVKKPGASVKVSCASGWTRNYMH WVRQAPGQGLEWMGWINPKNGGTNYAQKFQDR VTMTDSSISTAYMELSSLRSEDVAVYYCATGIRSTV RGLDNWGQGTTLTVSS SEQ ID NO. 43	QSALTQPASVSGSPGQSITISCSGSNRDVG YFVSWYQKHGPKAPRLMIYDVINRPSGVP DRFSGSKSGNTASLTISGLQPEDEGEYCYSSF TSSRTLAFGGGTKLTVL SEQ ID NO. 44 LPVLTQPPSVSGAPGQRTVISCSSSSNIGA AYDVHWYQQLPGTAPKLLIYNNRPSGVP DRFSGSKSGTSASLAISGLQSEDEADYYCAA WDDSLNGYVFGTGKTLTVL SEQ ID NO. 46
H5	QVQLVESGAEVKKPGASVKVSCASGYLTSSYMH WVRQAPGQGLEWMGIINPSGGNTSYAQKFQGRV TMTRDTSTSTVYMELSSLRPDDTAVYYCATDGELEI AAYWGQGTTLTVSS SEQ ID NO. 45	QAGLTQPASVSGSPGQSITISCTGTSTDIGVY DHVSWYQKHGPKAPRLISGVYKRPSAVSD RFFGSKSGSTASLTISGLQPDDEAEYRCMSY TTSKTYVFGTGKTLTVL SEQ ID NO. 48 QAGLTQPSSLSASPGASALTCTLRSGINVG TYRIYWYQKPGSPPQYLLMYKSDSDKQQ GSGVPSRFSGSKDASANAGILLISGLQSEDE ADYYCMIWHSSAYVFGTGKTVTVL SEQ ID NO. 49
H6	EVQLLESGGGVVQPRSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKHRRGDHG DYWGQGTTLTVSS SEQ ID NO. 47	QAGLTQPASVSGSPGQSITISCTGTSTDIGVY DHVSWYQKHGPKAPRLISGVYKRPSAVSD RFFGSKSGSTASLTISGLQPDDEAEYRCMSY TTSKTYVFGTGKTLTVL SEQ ID NO. 48 QAGLTQPSSLSASPGASALTCTLRSGINVG TYRIYWYQKPGSPPQYLLMYKSDSDKQQ GSGVPSRFSGSKDASANAGILLISGLQSEDE ADYYCMIWHSSAYVFGTGKTVTVL SEQ ID NO. 49
2D3	QVQLQQSGPGLNPSQTLSTCVISGDSVSSNSATW NWIRQSPSRGLEWLGRTYYRSQWFNDYAVSVKSRI TINPDTSKNQFSLQLSSVTPEDTAVYYCARWLHVW GQGTTVTVSS SEQ ID NO. 25	QAGLTQPASVSGSPGQSITISCTGTSTDIGVY DHVSWYQKHGPKAPRLISGVYKRPSAVSD RFFGSKSGSTASLTISGLQPDDEAEYRCMSY TTSKTYVFGTGKTLTVL SEQ ID NO. 48 QAGLTQPSSLSASPGASALTCTLRSGINVG TYRIYWYQKPGSPPQYLLMYKSDSDKQQ GSGVPSRFSGSKDASANAGILLISGLQSEDE ADYYCMIWHSSAYVFGTGKTVTVL SEQ ID NO. 49
3A11	QVQLVQSGGGVVQPRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAHGGDYYW GQGTPVTVSS SEQ ID NO. 50	QSALTQPPSVSAAPGQKVTISCSGSSSNIGN NYVSWYQQLPGTAPKLLIYDNNKRPSGIPD RFGSKSGTSATLGITGLQTDGADYYCGT WDSSLASGVFGGGTKLTVL SEQ ID NO. 51
3B9	EVQLVESGGGLVKPGESLRLSCAASGFTFKSYPM WVRQAPGKGLEWVSSISSGDHRYADSVKGRFTIS RDNARNLSLQMNLLRAEDTAVYYCPAGRDFDHW GRGTLTVSS SEQ ID NO. 52	QAGLTQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQKHGPKAPKLLIYEVFNRPSSS NRFGSKSGNTASLTISGLQAEDEADYYCSS PTTSKTLVFGGGTKVTVL SEQ ID NO. 53

3D11	EVQLVQSGGGLVQPGGSLRLSCSASGFTFSSYAMH WVRQAPGKGLEYSVAISSNGGSTYYADSVKGRFTIS RDNSKNTLYLQMSSLRAEDTAVYYCVKGRTRDGY NDWGQGTLLTVSS SEQ ID NO. 54	DIVMTQSPPSLSASVGDVAITCRASQDIRN DLGWFQKPGTAPKRLIFAASGLQSGVPSR FRSGSGTEFTLTINNLPEDSATYYCLQHY RFRPVFGQGTKEIK SEQ ID NO. 55 QSVVTQPPSVSGAPGQRVTVSCTGSSSNIG SRYAVNWWYQQLPGRAPKLLIYGNTNRPSGV PDRFSASKSGTSASLAISGLQAEDEADYYCQ SFDSSLRGYVFGTGKVTVL SEQ ID NO. 57
3D12 and 4E12	EVQLVESGGGLVQPGGSPRLSCAASGFTFSSYAMS WVRQAPGKGLEWVSVISGSGGTYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTALYYCAKAVRGVSPF DYWGQGTLLTVSS SEQ ID NO. 56	
3E7	QVQLQQSGPGLVRPSQTVSLTCVISGDSVSSNRVG WNWLRQSPSRGLEWLGGTAYRSTWRLYYPPSLKSR VTITPDTSRNQFSLNLSVTPDDTAVYYCARGFVEAF DVWGQGTMTVTSS SEQ ID NO. 58	QAGLTQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVKRPSGV SHRFSGSKSGNTASLTISGLQAEDEADYYCS SYRSRSTLVFGGGTQLTVL SEQ ID NO. 59
3E12	QVQLQQSGPGLVKPSQTLTCAISGDSVSSNSAA WNWIRQSPSRGLEWLGRTYYRSKWFDYAVSVKS RITINPDTSKNQFSLQLSSVTPEDTAVYYCARWLHV WGQGTTLTVSS SEQ ID NO. 60	QSVLTQPPSASGTPGQRVTIPCSGSSSNIGS KTVSWYQQLPGTAPKLLIYSSDQRPSPGVPD RFSASKSGTSASLAISGLQSEDEADYYCAAW DGSLDGYVFGTGKVTVL SEQ ID NO. 61 QAVLTQPPSVSQALRQTATLTCTGNSNNVG SQGAAWLQQHQGHPPKLLSYRNNNRPSGI SERFSASRSGDTASLTISGLQPEDEADYFCSA WDNSLRAWVFGGGTKLTVL SEQ ID NO. 63
3F7	QVQLVESGGGVVQPGRSLRLSCAASGFTFSDYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARIQARSGSS LGQGTLLTVSS SEQ ID NO. 62	DIQLTQSPLSLPVTLGQPASISCMSSQSLVHS DGNTYLNWFQQRPGQSPRRLIYKVSNRDS GVPDRFSGSGSGTDFTLKISRVEAEDVGVVY CMQGSHPWRTFGQGTREIK SEQ ID NO. 65
3G2	QMQLVQSGAEVKKPGASVKVCKASGYTFTSYAM HWVRQAPGQRLEWMGWINAGNGNTKYSQKFQG RVTITADKSTSTAYMELSSLRSEDVAVYYCARGRVVR NQNYYYGMDVWGQGTTLTVSS SEQ ID NO. 64	DVVMQTQSPLSLPVTLGQPASISCRSSQSLVH SDGNTYLNWFQQRPGQSPRRLIYKVSNRDS GVPDRFSGSGSGTDFTLKISRVEAEDVGVVY CMQGTHWPPWTFGGGKLEIK SEQ ID NO. 67
3G7	EVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARGALAGYW GQGTLLTVSS SEQ ID NO. 66	
4A5	EVQLVESGGGLIQPGGSLTSCAASGVIVSSYYMSW VRQAPGKGLEWVSVPSPSGRTYYKDSVKGRFTISR TSKNTVSLQMNNLRGEDAAIYYCTRTSGLYGTDVW GQGTTLTVSS SEQ ID NO. 68	AIRMTQSPSSVSASVGDRTITCRASQSISS WLAWYQKPGKAPKLLIYKASSLQSGVPSR FSGSGSGTEFSLTISSLPDDFATYYCQYNS YTYTFGQGTKEIK SEQ ID NO. 69 DIVMTQSPLSPVTLGQPASISCRSSQSLVHS NGNTYLSWLQQRPGQPPRLLYRISNRFSG VPDRFSGSGAGTNFTLKISRVEAEDVGVVY MQATQFPRTFGQGTQVDIK SEQ ID NO. 71
4E9	QVQLVESGGGVVQPGRSLRLSCAASGLDFSNYAMH WVRQAPGKGLEWVAVISYDGTKKYYADSVKGRFTI SRDNSKNTLYLQMNSLETEDTAVYYCTRGRIFGYW GQGTLLTVSS SEQ ID NO. 70	
4F1	EVQLVQSGAEVKKPGASVKVCKASGYTFSYYMH WVRQAPGEGLEWMGWINPNSGDTNYPQKFQGR VTIMTRDTSISTAYMELSSLRSDDTAVYYCAREMAKL GIRNLDYWGQGTLLTVSS SEQ ID NO. 72	QSALTQPPSASGTPGQRVTISCSGSSSNIGS YRVNWWYQQLSGAAPKLLIYRNNQRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSAVVFGGGTKLTVL SEQ ID NO. 73

4F4	QVQLQQSGPGLVKPSQTLSTLCVISGDSVSNRAA WNWIRQSPSGGLEWLGRTYYRSKWYSDYGASVK RITVNPDTSKNQFSLQVNSVTPDDTAVYYCARGKVS AFDIWGGQTMVTVSS SEQ ID NO. 74	QSVLTQPPSASGTPGQRTVITSCSGSSNIGR HAVNWWYQQLPGTAPKLLIYRSNQRP SGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSTPYVFGTGKLTVL SEQ ID NO. 75 DIVMTQSPSLPVTLGQPASISCRSSQSLVHS NGITYLNWFQQRPGQSPRRLIYKVSNRDSG VPDRFSGSGSGTDFTLKISRLEAEDVGYYC MQGTHWPPTFGQGTKVEIK SEQ ID NO. 77
4H2	EVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMS WIRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISR DNAKNSLYLQMNSLTVEDTAVYYCARGGYPRGWG QGTLTVSS SEQ ID NO. 76	
5A8	QVQLVQSGAEVKKPGASVKVCKASGYFTNYGIS WVRQAPGQGLEWMGWISAYNGNTNYAQKFQGR VTMTTDTSTSTAYMELSSLKSEDTAVYYCATLGGAT WGQGTITVTVSS SEQ ID NO. 78	LPVLTQPASVSGSPGQSITISCTGTSSDVGGY NYVSWYQQHPGKAPKLMYDVSKRPSGV NRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSTVVFGGGTKLTVL SEQ ID NO. 79
5F1	QVQLQQSGPGLVKPSQTLSTLCVISGDSVSSNSAA WNWIRQSPSGALEWLGRTYYRSKWYNDYAPSVKS RITINPDTSKNQFSLQLNSVTPEDTAVYYCAKWSLV WGQGTITVTVSS SEQ ID NO. 80	QAGLTQPPSASGTPGQRTVITPCSGSSNIGS KTVSWYQQLPGTAPKLLIYSSDQRP SGV RFSASKSGTSASLAISGLQSEDEADYYCAAW DGS LDGYVFGTGKLTVL SEQ ID NO. 81
6A4	QVQLVQSGSVLKKPGASVKVSCETSGYSFTSYGLHW LRQAPGQGLQWMGWIHNTGNPSYAPGFTGRYV FSRDTSVSTTYLQINSLEDGDTAIYFCARARYGLDVW GQGTITVTVSS SEQ ID NO. 82	QTVVTQPPSVSAAPGQKVTISCSGSSNIGS HFVSWYQQLPGTAPKLLIYDNKKRPSGIPDR FSGSKSGTSATLGITGLQTGDEADYYCGTW DSSLAGVFGGTGKVTVL SEQ ID NO. 83 QPVLTPPPSVSKGLRQTATLTCTGNSSNVG NLGAAWLQQHQGRPPKLLSYRNNNRPSGI SERLSASRSGNTASLTITGLQPEDEADYYCA AWDTSLRVVWFGGTGKLTVL SEQ ID NO. 85
6F9	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMS WIRQAPGKGLEWVSYISSSGSTMYADSVKGRFTIS RDNAKNSLFLQMNSLRDDDTAVYYCARGGYPRYW GQGTITVTVSS SEQ ID NO. 84	
6G5	EVQLLESGAEVKKPGASVKVCKASGYTFSRYAMH WVRQAPGQRLWGMWGHAGNGNTKYSQKFQGR VTISRDTASTAYMELSSLRSEDTAVYYCARGSIAAA GGFDYWGGTGLTVTVSS SEQ ID NO. 15	SYVLTQPPSASGTPGQRTVITSCSGSSNIGR NYVYVYQQLPGTAPKLVLYVNDKRPSGIPD RFSGSKSGTSATLGITGLQTGDEADYYCGT WDSSLRAYVFGTGQTTLTVL SEQ ID NO. 86
7B11 and 8B2	QVTLRESGGGLVQPGGSLRLSCAASGFTFSPYWMS WVRQAPGKGLEWVASIKKDASGEYYVDSVKGRFSI SRDNAKNSVYLQMNSLRAEDTAVYYCARGGWVLD VWGQGTITVTVSS SEQ ID NO. 87	ETTLTQSPGTLSPGERATLSCRASQSVRS YLAWYQQKPGQAPRLIYGASSRATGIPDRF SGSGSGTDFTLTISRLEPEDFAVYYCQQYGSS PLTFGQGTKVEIK SEQ ID NO. 88
7H10	EVQLVESGGGLIQPGGSLRLSCASGFTLNYYMN WVRQAPGKGLEWVSYISSGGNTFYADSVKGRFIISR DSSKNILYLQMNSLRAEDTAVYYCARKYCSGGYCKY DYWGQGTITVTVSS SEQ ID NO. 89	QPVLTPPPSASGTPGQRTVITSCSGSSNIGS NFVYVYQQFPGMAPKLLIYRNNQRPSGVP DRFSGSKSGTSASLVISGLRSEDEATYYCAS WETSLSGPRVFGGTGKL SEQ ID NO. 90
8D12	EVQLLESGAEVKKPGASVKVCKASGYTFSRYAMH WVRQAPGQRLWGMWGHAGNGNTKYSQKFQGR VTISRDTASTAYMELSSLRSEDTAVYYCARGSIAAA GGFDYWGGTGLTVTVSS SEQ ID NO. 15	LLVLTQSPSASGTPGQRTVITSCSGSSNIGR NYVYVYQQLPGTAPKLVLYVNDKRPSGIPD RFSGSKSGTSATLGITGLQTGDEADYYCGT WDSSLRAYVFGTGKVTVL SEQ ID NO. 91
8H5	QVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMS WIRQAPGKGLEWVSYISSSGSTMYADSVKGRFTIS RDNAKNSLFLQMNSLRDDDTAVYYCARGGYPRYW GQGTITVTVSS SEQ ID NO. 92	QSVLTQPPSVSKGLRQTATLTCTGNSSNVG NLGAAWLQQHQGRPPKLLSYRNNNRPSGI SERLSASRSGNTASLTITGLQPEDEADYYCA AWDTSLRVVWFGGTGQTTLTVL SEQ ID NO.

93

9A10	EVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMS WVRQAPGKGLEWVSYISSSGSTIYYADSVKGRFTISR DNAKNSLYLQMNSLRAEDTAVYYCASGLSGVGATN VHYWGQGTLLTVSS SEQ ID NO. 94	LPVLTQPPSVSKGLRQTATLTCTGNTNNVG NQGAAWLQQHQGHPPKLLSYRNNNRPSG ISERLSASRSGNTASLTITGLQPEDEADYYCS AWDSSLNVWVFGGGTKLTVL SEQ ID NO. 95
10A12	EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAMH WVRRAPGQRLEWMGWINAGNGNTKYSQKFQGR VTITRDTASTAYMELSSLRSEDVAVYYCARDGIVATI WGQGTLLTVSS SEQ ID NO. 96	QPVLTPASVSGSPGQSITISCTGTRSDVGT YNLVSQYQRHPGRAPKLMIEVSKRPSGIS NLFSGSKSGNTASLTISGLQSEDEADYYCCSY TGRLLTVFGGGTKLTVL SEQ ID NO. 97
10B2	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVT MTTDTSTSTAYMELRSLRSDDTAVYYCARARAVAG RGSYWGQGTLLTVSS SEQ ID NO. 98	QPVLTPRVSVSGSPGQSVTISCTGTSSDVGS YNLVSQYQRHPGKAPKLVIEVVKRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSSTYVFGTGKTLTVL SEQ ID NO. 99
10C3	QVQLVESGGGVVQPGRLRLSCAASGFTFSSNYAMH WVRLAPGKGLEWVAVISYDGSNKYYGDSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARRNNDY WGQGTLLTVSS SEQ ID NO. 100	QPVLTPPSASGSPGQSVTISCTGTSSDIGR YNYVSWYQQYPGKAPKLVIEVVKRPSGVP DRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSRTLTVFGGGTKLTVL SEQ ID NO. 101
10C7	QVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYSMN WVRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISR DNSKNTLYLQMNSLRAEDTAIYYCARKGLAAPGKGY WGQGTLLTVSS SEQ ID NO. 102	LPVLTQPRSVSGSPGQSVTISCTGTSSDVGR YGYVSWYQQHPGKAPQLMIYEVNKRPSGV PDRFSGSKSDNTASLTISGLQAEDEADYYCS SYTSSSTRVFGTGKTVL SEQ ID NO. 103
11E3	EVQLVESGGGVVQPGRLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARLPIPKQST VAGTSYWGQGTLLTVSS SEQ ID NO. 104	LPVLTQPASVSGSPGQSITISCTGTSSDVGGY NYVSWYQQHPGNAPKLMIDVSNRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSS YTSSSTLYVFGTGKTLTVL SEQ ID NO. 105
11A12	EVQLVESGGGVVQPGGSLRLSCETSGFVFSYAMH WVRQAPGKGLDWVAVMSSDGSNKYYGNSVKGRF TISRDNKNTLYLQMNSLRGEDTAVYFCARTNTRLF FGGKLRGDFWGQGTLLTVSS SEQ ID NO. 106	QSVLTQPPSVSKGLRQTATLTCTGNSNNVG NQGAAWLQQHQGHPPKLLFYRNNNRPSG ISERFSASRSGNTASLTITGLQPEDEADYYCS AWDSSLARVFGGGTKLTVL SEQ ID NO. 107
11A7	EVQLVESGGGLVQPGGSLRLSCAASGFTVSSNYMS WVRQAPGKGLEWVSVYSGGSTYYADSVKGRFTISR HNSKNTLYLQMNSLRAEDTAVYYCARGYVWVGQ TLTVSS SEQ ID NO. 108	QPVLTPPSVSKDLRQTATLTCTGNSNNVG NQGATWLQQHQGHPPKLLSYKNNNRPSGI SERFSASRSGNTASLTITGLQPEDEADYYCSA WDSSLASVFGGGTQLTVL SEQ ID NO. 109
11C3	QVQLVESGGGLVKPGGSLRLSCEASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNKNTLYLQLSSLRAEDTALYYCATGRMTALWG QGTTVTVSS SEQ ID NO. 110	QAVLTQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKFMIDVSKRPSGV SDRFSGSKSGNTASLTISGLQAEDEADYYCS SYTSSSTLVFGGGTKLTVL SEQ ID NO. 111

11D3	QVQLVQSGGGVVQPGRSLRLSCAASGFTFSNFGM HWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRF TISRDNSKNTLYLQMNSLRAEDTAVYYCARNTVTYH DVWGQGTTVTVSS SEQ ID NO. 112	QPVLTPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMINDVSNRPSGV SSRFGSGKSGNTASLTISGLQAEDEADYYCSS YTSSTLVFGGGKTLTVL SEQ ID NO. 113
11D4	QITLKESGGGVVQPGRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCANNGWATY PDYWGQGTLTVSS SEQ ID NO. 114	QSVLTQPASVSGSQGQSITISCTGTSSDVGA YNYVSWYQQYPGEAPRLILYDVSRPSGIS NRFGSGKSGNMASTISGLQAEDEADYYCSS YRSSSTVVFGGGKTVTVL SEQ ID NO. 115
11D7	EVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKLSGPTAKF DYWGQGTLTVSS SEQ ID NO. 116	QAGLTQPASVSGSPGQSITISCTGTSSDVGG YKYVSWYQQHPGKAPKLMYDVSKRPSGV NRFGSGKSGNTASLTISGLQAEDEADYYCSS YTSRSTLVFVGTGKTVTVL SEQ ID NO. 117
11F3	QVQLVESGGGVVQPGRSLRLYCAASGFIFSSYAIHW VRQAPGKGLEWVAVISYDGSKKYYADSVGRFTISR DNSKNSLYLQMNSLRVDDTAVYYCAHRQLGYWG QGTLTVSS SEQ ID NO. 118	QSVLTQPPSASGSPGQSVTISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVSKRPSGV SNRFGSGKSGNTASLTISGLQAEDEADYYCS SYTSSSTLVFGGGKTLTVL SEQ ID NO. 119 DIVMTQTPLSLPVTLGQPASISCRSSQSLVHS DGNTYLNWFQQRPGQSPRRLIYKVSNRDS GVPDRFGSGSGTDFTLKISRVEADVGYY CMQGTWPPFTFGGQGTKVEIK SEQ ID NO. 121
11G3	EVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARLTRGSDYY GSGRSMNDYWGQGTLTVSS SEQ ID NO. 120	
12A4	QVQLVESGGGLVQPGRSLRLSCTASGFTFGDYAVT WVRQAPGKGLEWVGFIISMITYGGPTQYAASVKGR FTISRDDSKGIAYLQMNRLKTEDTAVYFCTVAGQH WGQGTLTVSS SEQ ID NO. 122	SYELTQPLSVSVALGQTARITCGGNNIGSKN VHWYQQKPGQAPVLVIYRDSNRPSGIPERF SGNSGNTATLTISRAQAGDEADYYCQVW DSSTHNYVFGTGKTVTVL SEQ ID NO. 123
12B11 and 14E10	EVQLVESGGGLVKPGRSLRLSCTASGFPGDYAMS WFRQAPGKGLEWVALISYDGRNNYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVFYCARDRMGRP GGRFYHHAMDVWGQGTTVTVSS SEQ ID NO. 124	SYELMQPPSVSRGLRQTATLTCASTRNDVG NEGASWLQHQHPPKLLSYRDTNRPSGIS DRFSASRSGNTASLTISGLQPEDEADYYCSA WDSSLRAWVFGGGKTLTVL SEQ ID NO. 125
12B4	QVTLRESGGGLVKPGSLRLSCAASGFTFSDYYMT WIRQAPGKGLEWVSYISTGGTIYYADSVKGRFTISR NAKNSLYLQMDSLRAEDTAVYYCAGGARDCGGGT CKRRGFHWGQGTLTVSS SEQ ID NO. 126	QPVLTPRSVSGSPGQSVTISCTGTSSDVGS YDYVSWYQQHPGKAPKVMYDVSKRPSGV SNRFGSGKSGNTASLTISGLQDEDEADYYCR SYTSSATYVFGTGKTVTVL SEQ ID NO. 127
12C1	EVQLLESGGGLVKPGSLRLSCAASGFTFNYYAMH WVRQAPGKGLEWLTVISFYGGKQYYADSVKGRFTI SRDNSRNTLYLQMNSLRADDTAVYYCARDNGRHF DYWGQGTLTVSS SEQ ID NO. 128	QPVLTPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVSKRPSGV SNRFGSGKSGNTASLTISGLQAEDEADYYCT SYRSGRTYVFGSGTKTVTVL SEQ ID NO. 129
12C6	EVQLVQSGAEVKKPGASVKISCKASGYTITTHYIHW VRQAPGQGLEWMGIINPNSGRTKYPQKFQGRVTM TRDTSTNTVYMEVNSLRSEDYAVYYCATGSGSYGN WFDPPWGQGTLTVSS SEQ ID NO. 130	QSVVTQPPSVSAAPGQKVTISCSGSSNIGN NYVSWYQQLPGTAPKLLIYDNNKRPSGIPD RFGSGSGTSATLGITGLQTGDEADYYCGT WDSSLTLVFGTGKTLTVL SEQ ID NO. 131

12D11	EVQLVQSGAEVKKPGASVKVSCASGYTFTGYLN WVRQAPGQGLEWMGWINPNNGGTNYAQRFGG RVTMTTRDTSISTAYMDLSRLRSDDTAVYYCVRGTRK YYHDSNGRRRDYYYGMDVWGQGTITVTVSS SEQ ID NO. 132	AIRMTQSPSSLSASVGDRTITCRASQSISSY LNWYQQKPGKAPKLLIYAASSLQSGVPSKFS GSGSGTEFTLTISLQPEDFATYYCQQYKFYP PNFGGGTKVEI SEQ ID NO. 133 QPVLTPASVSGSPGQSIASCTGTSSDVGS NNRVSWYQQHPGKAPKLMIEVDKRPSPGV SNRFGSKSGNTASLTISGLQAEDEADYYCG TWDSSLSAYVFGTGKLTVL SEQ ID NO. 135 SYELMQPPSVSGTPGQRTVITSCSGSTSNVGS NTVNWYRQFPGTAPKLLIYANNQRPSPGV DRFGSKSGTSASLAISGLQSENEADYYCAA WDDSLNGYVFGTGKLTVL SEQ ID NO. 137 QPVLTPQLSASGTPGQRTVITSCSGSSNIGS NYYVWYQQLPGTAPKLLIYRNYQRPSPGVPD RFGSGTSGTSASLAISGLRSEDEADYHCAAW DGSMRGWVFGGGTKLTVL SEQ ID NO. 139
12D3	EVQLVESGGGLVQPGKSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARLRWLDY WGQGTITVTVSS SEQ ID NO. 134	
12G10	EVQLVESGGGVVQPGKSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARIAGVAGTHF DYWGQGTITVTVSS SEQ ID NO. 136	
13E10	EVQLVQSGAEVKKPGASLKISCRASGYTFTRNYIHW VRQAPGQGLEWLGIIINPNNGGSTRYSQKFQGRVTM TRDTSTRVYMESSLRSEDVAVYYCAREAPKYCSGS SCYSGGVVDYWGQGTITVTVSS SEQ ID NO. 138	
13E4	QITLKESGGGVVQPGKSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCANNGWATY PDYWGQGTITVTVSS SEQ ID NO. 114	QPVLTPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLMIYDVSNRPSGV SNRFGSKSGNTASLTISGLQAEDEADYYCS SYTSSSTLVFGGGTKLTVL SEQ ID NO. 140
13A3	EVQLVQSGGGVVQPGKSLRLSCVASGFTFRTYGMH WVRQAPGKGLEWVAVISHDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARATFGQGTI VTVSS SEQ ID NO. 141	QAGLTQPASVSGSPGQSITISCTGTSSDVGS YNLVSWYQQHPGKAPKLMIEGSKRPSGV NRFGSKSGNTASLTISGLQAEDEADYYCCS HAGSSTYVFGTGKVTVL SEQ ID NO. 142 DIVMTQSPSLPVTLGQPAISCRSSQSLVHS DGNTYLNWFQQRPGQSPRRLIYKVSNRDS GVPDRFGSGSGTDFTLKISRVEAEDVGVYY CMQGTHTWPTFGGQGTLEIK SEQ ID NO. 144
13F8	EVQLLESGGGVVQPGKSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARLTRGSDYY GSGRSMNDYWGQGTITVTVSS SEQ ID NO. 143	
13F9	EVQLLESGGGLIQPGSLRLSCAASGFIFSRYGMMHW VRQAPGKGLEWVAVTSDGRSKYYTDSVQGRFTIS RDNSKNTLDLQMNSLRAEDTAVYYCARLHTVGPW HFDLWGRGTITVTVSS SEQ ID NO. 145	SYELTQPRSVSGSPGQSVTISCTGTSSDVGG YNYVSWYQQHPGKVPKLMIEVSNRPSGV SNRFGSKSGNAASLTISGLQAEDEADYYCS SYTSSSTLVFGGGTKLTVL SEQ ID NO. 146
13G9	EVQLVESGGGVVQPGKSLRLSCAASGFTFSRYGMH WVRQSPGKGLEWVAGISYDGSCKYYADSVKGRFTI SRANSKNTLFLQMNSLRAEDTAVYYCARARGLDYV GQGTITVTVSS SEQ ID NO. 147	QAVLTQPASVSGSPGQSITISCTGTSSDIGSY NLVSWYQQHPGKAPKLLIYEVNKRPSGVSN RFGSKSGNTASLTISGLQAEDEADYYCSSYR SINTVVFGGGTQLTVL SEQ ID NO. 148
14E5	EVQLVESGGGVVQPGKSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKVSRGSDY WGQGTITVTVSS SEQ ID NO. 149	QSVLTQPASVSGSPGQSITISCTGTSSDVGG YNYVSWYQQHPGKAPKLLIYDVSRPSGISS RFGSKSGNTASLTISGLQTEDDGDYCLSYT TSRAVVFGGGTQLTVL SEQ ID NO. 150

14B11	QVQLVESGGGVVQPGMSLRSLSCAASGFTFSSHAM HWVRQAPGKGLEWVAQIWSGDSNRYSDSVKGR FTISRQSKNTVSLQMNSLRAEDTAVYFCARDGQS MAPYAMDVWGQGTMTVTSS SEQ ID NO. 151	DIVMTQTPLSLPVTGPGEPAISCRSSQSLHKK NGNNYLDWYLQRPQSPQLLIYLASNRASG VPDRFSGSGSGTDFTLEISRVPEDVGYYC MQGLQTPTFGPGRKVEIK SEQ ID NO. 152 QSVVTQPPSVSAAPGQKVTISCSGSSSNIGS KAVNWWYQQLPGTAPKLLIYGNNQRPSGVP DRFSGSKSGTSASLAISGLQSEDEADYYCAA WDASLNGYVFGTGKVTVL SEQ ID NO. 153
14B4	QVQLQQSGPGLNPSQTLSTCVISGDSVSSNSATW NWIRQSPSRGLEWLGRYYRSQWFNDYAVSVKSRI TINPDTSKNQFSLQLSSVTPEDTAVYYCARWLHVW GQGTITVTSS SEQ ID NO. 25	QSVLTQPASVSGSPGQSITISCTGTSSDVGG YKYSWYQQHPGKAPKLMYDVTKRPSGV SNRFAGSKSGNTASLTISGLQAEDEADYYCS SYTSSSTFMVFGGGTKLTVL SEQ ID NO. 155
14C10	EVQLLESGGGLIQPGGSLRLSCAASGFTFNSYGMH WVRQAPGKGLEWVAVISYDGSNTYYADSVKGRFT MSRDNSKNTLYLQMNSLRAEDTAVYYCARLQKQV RQLLRNDAFDIWGQGTMTVTSS SEQ ID NO. 154	QAGLTQPPSASGTPGQRTVITISCSGSSSNIGS NYVYWYQQLPGTAPKLLIYRNNQRPSGVPD RFSGSKSGTSASLAISGLRSEDEADYYCAAW DDSLSGWVFGGGTKLTVL SEQ ID NO. 157
14C11	QVQLQQSGPGLVKPSQTLSTCAISGDTVSTNRAA WYWRQSPSRGLEWLGRTHYRSRWLNDYAPSVKS RITINPDTSKNQFSLQLNSVTPEDTAVYYCARGAAG RAFDIWGQGTITVTSS SEQ ID NO. 156	DIVMTQSPSSLSASVGDRTITCRASQTISTY LNWYQKPKGAPKLLIYDASSLQSGVPSRFT GSASGTDFTLTISLQPEDFATYYCQSYSIP LTFGGGTKEIK SEQ ID NO. 159
14C3	QVQLVQSGGGVVQPGRLRLSCAASGFAFNNGM HWVRQAPGKGLEWMAVISNDGNRQYYVDSVKGR FLISRDNPTRTVYLEMNSLTDDTGTYCAKPSSGW FRAFDVWGPMTMTVTSS SEQ ID NO. 158	ETTLTQSPGTLSPGERATLSCRASQSVSS NLAWYQKPKGQAPRLIYGASTRATGIPAR FSGSGSGTDFTLTISLEPEDFAVYYCQQRN NWPLTFGGGTKEIK SEQ ID NO. 161 LPVLTQPRSVSGSPRQSVTISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVSKRPSGV PDRFSGSKSGNTASLTISGLQAEDEAHYYCK SYTTSRTWVFGGGTKLTVL SEQ ID NO. 163
14D7	QVQLVQSGGGVVQPGRLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKWGRGA PDYWGQGTITVTSS SEQ ID NO. 160	QSVLTQPPSASGTPGQRTVITISCTGSSSNIGS RYDVHWYQQLPGGAPKLLIYSNTNRPSGVP DRFASKSGTSASLAISGLQAGDEADYFCQS FDSSLRGYVFGTGKVTVL SEQ ID NO. 165
14F11	EVQLVQSGAEVKKPGASVKVCKASGSTFTNYYIHW VRQAPGQGLEWMGIINPSGSGSIGSPQKFQGRVTM TRDTSTNTVYMESSLRSEDYAVYYCASRSFGNDGV FDIWGQGTMTVTSS SEQ ID NO. 162	QSVLTQPPSVSGAPGQRTVITISCTGSSSNIGA GYDVHWYQQLPGTAPKLLIYRNSNRPSGVP DRFSGSKSDTSASLTISGLQAEDEADYYCSSY RSGSTPYVFGTGKLTVL SEQ ID NO. 167 SYELMQPPSASETPGQRTVITISCSGSSSNIGS NFVYWYQQLPGMAPKLLIYKNDQRPSGVP DRFSGSKSGTSASLAISGLRSEDEADYYCAAR DDSLSGSVVFGGGTKVTVL SEQ ID NO. 169
14F8	QVQLVESGGGVVQPGRLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKNRYFDY WGQGTITVTSS SEQ ID NO. 164	
15C9	EVQLVQSGAEVKKPGASVKVCKASGYFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVT MTTDTSTSTAYMELRSLRSDDTAVYYCARVRLVGR LGAFDIWGQGTMTVTSS SEQ ID NO. 166	
15D7	QVQLVQSGAEVKKPGASVKVCKASGYFTSYGISW VRQAPGQGLEWMGWISAYNGNTNYAQKLQGRVT MTTDTSTSTAYMELRSLRSDDTAVYYCARGSDYWG QGTLVTSS SEQ ID NO. 168	

14D9	EVQLVESGGGVVQPGKSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARSAWLDS WGQGTLVTVSS SEQ ID NO. 170	QAGLTQPHSVSGSPGQSVTISCTGTSSDVG SYNHVSWYQQHPGKAPKLMYDVS KRPSG VSNRFGSGSKGNTASLTISGLQAEDEADYYC SSYTSSTYVFGTGKVTVL SEQ ID NO. 171
15F9	QVQLVQSGAEVKKPGASVKVSCKASGYTFSSYYMH WVRQAPGQGPPEWMGIINPIGGSTTYAQKFQGRVT MTSDTATSTAYMELSLRSEDTAIYYCARSRKNQW HYGMDVWGEGTTVTVSS SEQ ID NO. 172	AIQLTQSPSSLSASVGDRTITCRASQSISSYL NWKYQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISLQPEDFATYYCQSSHVS PPTFGQGTKVEIK SEQ ID NO. 173 DVVMTQSPLSSPVTLGQPASISCRSSQSLVH SDGTTYLSWLQQRPGQPPRLIYKISNRFSG VPDRFSGSGAGTDFTLKISRVEAEDVGVYYC MQTTQFPFMFGQGTKVEIK SEQ ID NO. 175
15G11	QVQLVQSGGGVVQPGGSLRLSCAASGFAFNRYGM HWVRQAPGQGLEWVAVISYDGSNKYYADSVKGRF TISRDNNSNTLYLQMNSLSADDTAVYYCAKGGGAAL DSWGQGTLLTVSS SEQ ID NO. 174	QSVLTQPASVSGSPGQSSISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVS NRPSGIS DRFGSGSKGNTASLTISGLQAEDEADYYCSS YRRSSTPWVFGGGTKLTVL SEQ ID NO. 177
15G7	QVQLVQSGGGVVQPGKSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKLSGPTAKF DYWGQGTLLTVSS SEQ ID NO. 176	QSVLTQPPASGSPGQSVTISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVS KWPSGIS SRFGSGSKGNTASLTISGLQAEDEADYYCSSY TKNKTLLFGGGTKLTVL SEQ ID NO. 178 QPVLTQPASVSGSPGQSVTISCTGTSSDVGG GYNYVSWYQQHPGKAPKLMYDVT KRPSG VSNRFGSGSKGNTASLTISGLQAEDEADYYC SSYTSSTPYVFGTGKVTVL SEQ ID NO. 180
15G9	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAKLSGPTAKF DYWGQGTLLTVSS SEQ ID NO. 179	DIVMTQTPLSLPVTLGQPASISCRSSQSLVYR DGNTYLNWFQQRPGQSPRRLLIYKVS NRDS GVPDRFSGSGSGTDFTLKISRVEAEDVGVYY CMQGTHTWPLTFGQGTKVEI SEQ ID NO. 182
15H10	EVQLVESGGGVVQPGKSLRLSCAASGFTFSDYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARATFGQGT LTVSS SEQ ID NO. 179	QSVLTQPASVSGSPGQSVTISCTGTSSDVGG YNYVSWYQQHPGKAPKLMYDVTYRPSGV SNRFGSGSKGNTASLTISGLQAEDEADYYCS SYTSSSTLVFGTGKVTVL SEQ ID NO. 184 QSALTQPPASGTPGQRVTISCSGSRSNIGS NTVNWYQQLPGTAPKLLIHSNTQRPSGVP DRFGSGSGTSASLAISGLQSEDEADYYCAT WDDSLNGYVFGSGTKVTVL SEQ ID NO. 186
15H2	EVQLVESGGGVVQPGKSLRLSCAASGFTFSSYAMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARVGIAAAV GMDVWGQGTTVTVSS SEQ ID NO. 181	LPVLTQPASVSGSPGQSVTISCTGTSSDVGGY NYVSWYQQHPGKAPKLMYDVS NRPSGVS DRFGSGSKGNTASLNISGLQPDDEAEYYCSS YRTKNTLVFGGGTKLTVL SEQ ID NO. 188
16E3	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGMH WVRQAPGKGLEWVAISYNGRNQYYADSLKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCATPAATLDY WGQGTLVTVSS SEQ ID NO. 183	
16A6	QMQLVQSGGGVVQPGKSLRLSCAASGFTFSSYGM HWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRF TISRDNKNTLYLQMNSLRAEDTAVYYCARATFGQG TLTVSS SEQ ID NO. 185	
16A8	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNYGMH WVRQAPGKGLEWVATISYDGSNNYYAASVKGRFT VSRDNSTLYLQMNSLRAEDTAVYYCAGAIAAAGVW GQGTLLTVSS SEQ ID NO. 187	

16B1	EVQLVESGGGVVQPGRSLRLSCAASGFTFSTYGMH WVRQAPGKGLEWVAALAYDGTNKKYAESVKGRFA ISRDN SKNTVFLQMNSLRAEDTAIYYCARDRWLSY WGQGLTVTVSS SEQ ID NO. 189	QAGLTQPPSLSGSPGQTVTISCTGTSSDVGG YNHVS WYQQHPDKAPQVIYDVNKR PSEV PDRFSGSKSGNTASLTISGLQPEDEAHYYCT SYAGSHKLLFGGGTKLTVL SEQ ID NO. 190
16B7	QVQLVESGAEVKKPGASVKVCKASGYFTSYVH WVRQAPGQGLEWMGIINPSGGTTSYAQKFQGRVT MTRDTSTSTVYMESSLRSED TAVYYCVRDRRVVAA TTPSAFDVWGQGTMTVTVSS SEQ ID NO. 191	QSVVTQPPSVSAAPGQRTISCSGSTSNIGS NYVSWYHQLPGTAPKLLVYHNDKRPSGIPD RFSGSKSGTSATLGITGLQTGDEADYYCGT WDSSLVWVFGGGTKVTVL SEQ ID NO. 192
16F8	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTI SRDN SKNTLYLQLNSLRAEDTAVYYCARGQNLDYW GQGLTVTVSS SEQ ID NO. 193	QPVLTPASVSGSPGQSITISCTGTSSDVGG YNYISWYQQHPGKAPKLMIEVSNRPSGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSS YRSSTQVFGGGTKLTVL SEQ ID NO. 194 SYELTQPRSVSGSPGQSVTISCTGTSSDVGG
16F9	EVQLVESGGEVKKPGASVKLSCKSSGYFTSYMH WVRQAPGQGLEWMGIINPSGGSTSSAQKFQGRVT MTRDTSTRTVYMESSLRSED TAVYYCARGAPNWN YARTLFDYWGQGLTVTVSS SEQ ID NO. 195	YNSVSWYQQHPGKAPKLMYDVSKRPSGV PDRFSGSKSGNTASLTISGLQAEDEADYYCS SYSSSTTHVFGGGTKLTVL SEQ ID NO. 196

We claim:

1. A recombinant fully human anti-CXC chemokine receptor 5 (CXCR5) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising
5 complementarity determining regions (CDRs) as set forth in a heavy chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174; and comprising a light chain variable domain comprising CDRs as set forth in a light chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO.: 137, SEQ ID NO. 139, SEQ ID NO. 150,
10 and SEQ ID NO. 175.
2. The recombinant fully human anti-CXCR5 antibody, or antigen binding fragment thereof, of claim 1, wherein the heavy chain variable domain is selected from the group consisting of
 - a) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 108
15 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 108;
 - b) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 136 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 136;
 - c) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 138 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 138;
 - 20 d) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 149 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 149; and
 - e) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 174 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 174; andwherein the light chain variable domain is selected from the group consisting of
 - 25 a) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 109 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 109;
 - b) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 137 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 137;
 - c) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 139
30 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 139
 - d) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 150 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 150; and
 - e) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 175 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 175.

3. The recombinant fully human anti-CXCR5 antibody fragment of claim 2, which is a Fab fragment.
- 5 4. The recombinant fully human anti-CXCR5 antibody, or antigen binding-fragment, of claim 1, wherein the heavy chain variable domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174, and the light chain variable domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 150, and SEQ ID NO. 175.
- 10 5. The recombinant fully human anti-CXCR5 antibody of claim 1, wherein the antibody is an IgG.
- 15 6. The recombinant fully human anti-CXCR5 antibody of claim 5, wherein the antibody is an IgG1 or an IgG4.
7. The recombinant fully human anti-CXCR5 antigen-binding fragment of claim 1, wherein the fragment is a Fab fragment.
- 20 8. The recombinant fully human anti-CXCR5 antigen-binding fragment of claim 1, which is a single chain antibody.
9. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 108/SEQ ID NO. 109.
- 25 10. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 136/SEQ ID NO. 137.
- 30 11. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 138/SEQ ID NO. 139.

12. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 149/SEQ ID NO. 150.
- 5
13. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 174/SEQ ID NO. 175.
- 10
14. A pharmaceutical composition comprising the recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, and a pharmaceutically acceptable excipient.
- 15
15. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 108 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 109.
- 20
16. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 136 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 137.
- 25
17. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 138 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 139.
- 30
18. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 149 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 150.

19. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 174 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 175.

5