

## **ANTI-ADGRE2 ANTIBODIES AND USES THEREOF**

### **CROSS REFERENCED APPLICATIONS**

**[0001]** This application claims priority to, and the benefit of, U.S. provisional application No. 63/179,756, filed on April 26, 2021, the contents of which is hereby incorporated by reference in its entirety.

### **SEQUENCE LISTING**

**[0002]** The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on April 19, 2022, is named MIL-018WO\_SL.txt and is 38,304bytes in size.

### **BACKGROUND**

**[0003]** Anti-ADGRE2 antibodies bind Adhesion G Protein-coupled Receptor E2, ADGRE2 antigen, also known as EMR2, CD312, VBU or CD97. ADGRE2 is expressed by monocytes, macrophages, dendritic cells and granulocytes. ADGRE2 is expressed on cancer cells in cancers, including acute myeloid leukemia. ADGRE2 binds to the chondroitin sulfate moiety of glycosaminoglycan chains and promotes cell attachment. ADGRE2 is highly expressed in cancerous cells, including acute myeloid leukemia cells.

### **SUMMARY**

**[0004]** The present disclosure provides humanized anti-ADGRE2 antibodies and antigen-binding fragments thereof, for the treatment of autoimmune diseases and cancers, including leukemia, lymphoma, or myeloma, including, for example, relapsed and refractory acute myeloid leukemia. The antibodies and fragments thereof of the present disclosure can be used alone, in fusion proteins or conjugated to at least one diagnostic and/or therapeutic agent or in combination with other treatment modalities.

**[0005]** In one aspect, the present disclosure provides a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSSASSSVSYMHWYQQKSGQSPKRWIYDTSKLSAG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSSASSSVSYMHWYQQKSGLSPKRWIYDTSKLSAGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSSASSSVSYMHWYQQKSGLSPKRWIYDTSKLSAGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12); or

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLGSGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAVYYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLGSGVP  
DRFSGSGSGTDYFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16);

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLGSGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYYPGD

GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGKLEIK (SEQ ID  
NO: 31).

**[0005a]** In another aspect, the present disclosure provides a use of the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof as described herein in the manufacture of a medicament for treating cancer. In another aspect, the present disclosure provides a pharmaceutical composition comprising a humanized anti-ADGRE2 antibody or fragment thereof and a pharmaceutically acceptable carrier, wherein the humanized ADGRE2 antibody or antibody fragment thereof comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGKLEIK (SEQ ID  
NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDNAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGV

PDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLAGSV  
PDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLAGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLAGVP  
DRFSGSGSGTDYTFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPG LAPRRWIYDTSK LASGV  
PDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSK LASG  
V PARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0005b]** In some examples, provided herein is a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGAPRLLIYDTSKLGASGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLGASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLGASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12); or

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMGAVYP

GDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLLTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCASSSVSYMHWYQQKSGQSPKRWIYDTSKLSG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLLTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLSGVP  
DRFSGSGSGTDYFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16);

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTMSCASSSVSYMHWYQQKPGLAPRRWIYDTSKLSGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18);

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that  
is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSSASSSVSYMHWYQQKSGQSPKRWIYDTSKLSAG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0006]** In some examples, provided herein is a humanized anti-ADGRE2 antibody or  
antigen-binding fragment thereof comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
of

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPLAPRLLIYDTSKLSAGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
of

EIVLTQSPATMSASPGERVMTMSSASSSVSYMHWYQQKSGLSPKRWIYDTSKLSAGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG

DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLGSGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12); or

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of  
QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDRHTQKFKGRVTMTRDTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
of  
EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLGSG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of  
QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLGSGVP  
DRFSGSGSGTDYFTIRRLEPEDFATYYCQQWSSNPLTFGGQGTKVEIK (SEQ ID NO:  
16);

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPG LAPRRWIYDTSK LASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18);

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGV PARFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0007]** In some examples, provided herein is a humanized anti-ADGRE2 antibody or  
antigen-binding fragment thereof comprising:

a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid  
sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid sequence  
of VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid sequence of  
ARGFTAYGMDY (SEQ ID NO: 3); and

a light chain complementarity determining region (LCDR) 1 comprising an amino acid  
sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid sequence of DTS  
(SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of QQWSSNPLT (SEQ  
ID NO: 6).

**[0008]** In some examples, provided herein is a humanized anti-ADGRE2 antibody or  
antigen-binding fragment thereof, wherein the anti-ADGRE2 antibody or fragment thereof is  
selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM  
antibody, bi- or multi- specific antibody, Fab fragment, Fab' fragment, F(ab')<sub>2</sub>

fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody, cameloid antibody; masked antibody, Small Modular ImmunoPharmaceutical ("SMIPs™"), single chain, Tandem diabody, VHHs, Anticalin, Nanobody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Trans-body; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.

**[0009]** In some examples, the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).

**[0010]** In some examples, the humanized anti-ADGRE2 antibody or fragment thereof is an antibody comprising an IgG constant region.

**[0011]** In some examples, the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is a single-chain variable fragment (scFv).

**[0012]** In some examples, the scFv comprises a signal sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.

**[0013]** In some examples, the scFv comprises a sequence having at least about 80% identity to:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGA  
VYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGQSPKRWIYDTSKLSGVPARFSGSGSGTDYFTFTISSMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLSGVPDRFSGSGSGTDYFTTISRMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS

VSYMHWYQQKSGLSPKRWIYDTSKLAGVPDRFSGSGSGTDYFTISRMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMG  
AVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDNAVYYCARGFTAYG  
MDYWGGQGLTVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSA  
SSSVSYMHWYQQKPLAPRLLIYDTSKLAGIPDRFSGSGSGTDFTLTISRLEPEDFAV  
YYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

**[0014]** In some examples, the single-chain variable fragment (scFv) comprises a sequence of:

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGG  
GTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGQSPKRWIYDTSKLAGVPARFSGSGSGTDYFTISSMEPEDFATYYCQQ  
WSSNPLTFGGGKLEIK (SEQ ID NO: 19);

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGG  
GTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGLSPKRWIYDTSKLAGVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQ  
WSSNPLTFGGGKLEIK (SEQ ID NO: 20);

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMELSSLRSEDNAVYYCARGFTAYGMDYWG  
QGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGLSPKRWIYDTSKLAGVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQ  
WSSNPLTFGGGKLEIK (SEQ ID NO: 21); or

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMGAVYYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDNAVYYCARGFTAYGMDYW  
GQGLTVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSASSSVS  
YMHWYQQKPLAPRLLIYDTSKLAGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQ  
QWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

**[0015]** In some examples, the humanized anti-ADGRE2 antibody has a disassociation constant ( $K_D$ ) is than less than about  $10^{-8}$  M  $K_D$ , less than about  $10^{-9}$  M  $K_D$ ,

less than about  $10^{-10}$  M  $K_D$ , less than about  $10^{-11}$  M  $K_D$ , less than about  $10^{-12}$  M  $K_D$ , or less than about  $10^{-13}$  M  $K_D$ .

[0016] In some examples, the humanized anti-ADGRE2 antibody has EC50 between about 1 – 100 nM.

[0017] In some examples, the EC50 is between about 10 – 95 nM.

[0018] In some examples, the EC50 is between about 25 – 75 nM.

[0019] In some examples, provided herein is a method of treating a cancer comprising administering the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof.

[0020] In some examples, the cancer is selected from leukemia, lymphoma, and myeloma.

[0021] In some examples, a pharmaceutical composition comprising a humanized anti-ADGRE2 antibody or fragment thereof and a pharmaceutically acceptable carrier, wherein the humanized anti-ADGRE2 antibody or antibody fragment thereof comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGDGD  
TRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGQGTTV  
TVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGAPRLLIYDTSKSLASGIPDRFS  
GSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGDGD  
TRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQGTTVT  
VSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKSLASGV

PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFQGRVTMTRDTSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 14);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFQGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLASGVP  
DRFSGSGSGTDYFTIRRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVTMSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
that is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0022]** In some examples, the pharmaceutical composition comprises a humanized  
anti-ADGRE2 antibody or antigen-binding fragment, wherein the humanized anti-ADGRE2  
antibody or antigen-binding fragment comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence  
of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD

GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKSLASGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence  
of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKSLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence  
of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKSLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence  
of

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDNAVYYCARGFTAYGMDYW  
GQGTTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKSLASG  
VPAFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFQKGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLGAVP  
DRFSGSGSGTDYFTIRRLPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPG LAPRRWIYDTSKLGAVP  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFQKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0023]** In some examples, the pharmaceutical composition comprises a humanized anti-ADGRE2 antibody or antibody fragment thereof comprises:

a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid sequence of VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid sequence of ARGFTAYGMDY (SEQ ID NO: 3); and

a light chain complementarity determining region (LCDR) 1 comprising an amino acid sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid sequence of DTS (SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of QQWSSNPLT (SEQ ID NO: 6).

**[0024]** In some examples, the pharmaceutical composition comprises a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof, wherein the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi- specific antibody, Fab fragment, Fab' fragment, F(ab')<sub>2</sub> fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody, cameloid antibody; masked antibody, Small Modular ImmunoPharmaceutical ("SMIPs™"), single chain, Tandem diabody, VHHs, Anticalin, Nanobody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Trans-body; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.

**[0025]** In some examples, the pharmaceutical composition comprises a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof, wherein the anti-ADGRE2 antibody or fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).

**[0026]** In some examples, the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is an antibody comprising an IgG constant region.

**[0027]** In some examples, the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is a single-chain variable fragment (scFv).

**[0028]** In some examples, the scFv comprises a signal sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.

**[0029]** In some examples, the scFv comprises a sequence having at least about 80% identity to:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGA  
VYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGQSPKRWIYDTSKLGVPARFSGSGSGTDYFTFTISSMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLGVPDRFSGSGSGTDYFTFTISRMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLGVPDRFSGSGSGTDYFTFTISRMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMG  
AVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMESSLRSEDVAVYYCARGFTAYG  
MDYWGQGTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSA  
SSSVSYMHWYQQKPLAPRLLIYDTSKLGIPDRFSGSGSGTDFTLTISRLEPEDFAV  
YYCQQWSSNPLTFGQGKVEIK (SEQ ID NO: 22).

**[0030]** In some examples, the single-chain variable fragment (scFV) comprises a sequence of:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGA  
VYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGQSPKRWIYDTSKLGVPARFSGSGSGTDYFTFTISSMEPEDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS

VSYMHWYQQKSGLSPKRWIYDTSKLASGVDPDRFSGSGSGTDYTFTISRMPEPDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTMSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLASGVDPDRFSGSGSGTDYTFTISRMPEPDFATY  
YCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWMG  
AVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARGFTAYG  
MDYWGGQGLTVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSA  
SSSVSYMHWYQQKPLAPRLLIYDTSKLASGIPDRFSGSGSGTDFTLTISRLEPEDFAV  
YYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

**[0031]** In another aspect, provided herein is a nucleic acid sequence encoding an amino acid sequence that is at least about 90% identical to any one of SEQ ID Nos: 7-18.

**[0032]** In another aspect, provided herein is a vector comprising the nucleic acid sequence as described herein.

**[0033]** In another aspect, the present disclosure provides an isolated cell comprising the vector as described herein. In some examples, provided herein is a cell comprising the vector.

**[0034]** In another aspect, the present disclosure provides a use of a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating cancer in a subject in need thereof, the humanized anti-ADGRE2 antibody comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASG  
VPAFSGSGSGTDYFTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that  
is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that  
is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFQGRVTMTRDTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that  
is at least about 80% identical to

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPLAPRLLIYDTSKLASGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLLTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKL  
ASGVDPDRFSGSGSGTDYFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK  
(SEQ ID NO: 16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPG LAPRRWIYDTSKLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLAGS  
VPA RFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGGTKLEIK (SEQ ID  
NO: 31).

**[0034a]** In some examples, provided herein is a method of treating cancer comprising administering a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof to a subject in need thereof, the humanized anti-ADGRE2 antibody comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to  
QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSED TAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to  
EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLAGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQG GTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGG  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLGSGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDTAVYYCARGFTAYGMDYWGG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLGSGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFQGRVTMTRDTSTSTVYMEVSSLRSEDTAVYYCARGFTAYGMDYWGG  
QGTLTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLGSG  
VPAFSGSGSGTDYFTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMESSLRSEDVAVYYCARGFTAYGMDYW  
GQGLTVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLASGVP  
DRFSGSGSGTDYFTIRRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

**[0035]** In some examples, provided herein is a method of treating cancer comprising administering a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof to a subject in need thereof, wherein the humanized anti-ADGRE2 antibody comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFQKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGAPRLLIYDTSKSLASGIPD  
RFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKSLASGV  
PDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGMDYWG  
QGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKSLASGV

PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTMSCASSSVSYMHWYQQKSGQSPKRWIYDTSKLSAG  
VPAFSGSGSGTDYFTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 14);

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYYPG  
DGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSEDVAVYYCARGFTAYGMDYW  
GQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLSAGVP  
DRFSGSGSGTDYFTFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO:  
16); or

(h) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYYPGD  
GDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLASGV  
PDRFSGSGSGTDYFTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO:  
18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGMDYWGQ  
GTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence  
that of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPA  
RFSGSGSGTDYFTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 31).

**[0036]** In some examples, provided herein is a method of treating cancer comprising  
administering a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof to a  
subject in need thereof, wherein the humanized anti-ADGRE2 antibody comprises:

a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid  
sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid sequence of  
VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid sequence of  
ARGFTAYGMDY (SEQ ID NO: 3); and

a light chain complementarity determining region (LCDR) 1 comprising an amino acid  
sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid sequence of DTS  
(SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of QQWSSNPLT (SEQ ID  
NO: 6).

**[0037]** In some examples, provided herein is a method of treating cancer comprising  
administering a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof to a  
subject in need thereof, wherein the humanized anti-ADGRE2 antibody or antigen-binding  
fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).

**[0038]** In some examples, provided herein is a method of treating cancer comprising  
administering a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof to a

subject in need thereof, wherein the humanized anti-ADGRE2 antibody or fragment thereof is an antibody comprising an IgG constant region.

**[0039]** In some examples, the anti-humanized ADGRE2 antibody or fragment thereof is a single-chain variable fragment (scFv).

**[0040]** In some examples, the scFv comprises a leader sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.

**[0041]** In some examples, the scFv comprises a sequence having at least about 80% identity to:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGA  
VYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSS  
VSYMHWYQQKSGQSPKRWIYDTSKLGSGVDFSGSGSGTDYTFITISMEPEDFATY  
YCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLGSGVDFSGSGSGTDYTFITISMEPEDFATY  
YCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGA  
VYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSS  
VSYMHWYQQKSGLSPKRWIYDTSKLGSGVDFSGSGSGTDYTFITISMEPEDFATY  
YCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVCKASGYTFTNYWMQWVRQAPGQGLEWMG  
AVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMEVSSLRSEDNAVYYCARGFTAYG  
MDYWGQGTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSA  
SSSVSYMHWYQQKPLAPRLIYDTSKLGSGIPDFSGSGSGTDFTLTISRLEPEDFAV  
YYCQQWSSNPLTFGGGTKVEIK (SEQ ID NO: 22).

**[0042]** In some examples, the single-chain variable fragment (scFv) comprises a sequence of:

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGD  
GDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGQ  
GTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQ  
WSSNPLTFGGGGTKLEIK (SEQ ID NO: 19);

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGD  
GDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQ  
GTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGLSPKRWIYDTSKLASGVPRFSGSGSGTDYTFTISRMEPEDFATYYCQQ  
WSSNPLTFGGGGTKLEIK (SEQ ID NO: 20);

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPG  
DGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYWG  
QGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSASSSVSYMH  
WYQQKSGLSPKRWIYDTSKLASGVPRFSGSGSGTDYTFTISRMEPEDFATYYCQQ  
WSSNPLTFGGGGTKLEIK (SEQ ID NO: 21); or

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYP  
GDGDTRHTQKFKGRVTMTRDTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYWG  
GQGTTLTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCSASSSVS  
YMHWYQQKPGAPRLLIYDTSKLASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQ  
QWSSNPLTFGGQGTKVEIK (SEQ ID NO: 22).

**[0043]** In some examples, the cancer is selected from leukemia, lymphoma, or myeloma.

**[0044]** In some examples, the treatment comprises administration of one or more additional agents.

**[0045]** In some examples, the one or more additional agents is selected from an antibody, a chemotherapeutic, or radiation therapy.

## DEFINITIONS

**[0046]** *A or An:* The articles “a” and “an” are used herein to refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, “an element” means one element or more than one element.

## CLAIMS

1. A humanized anti-ADGRE2 antibody or antigen-binding fragment thereof comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGA  
VYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFT  
AYGMDYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12); or

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSED TAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to  
EIVLTQSPATLSLSPGERATLSCSASSSVSYMHYQQKPGLAPRLLIYDTSKLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID  
NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSED TAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to  
QIVLTQSPATLSLSPGERATLTCSASSSVSYMHYQQKPGLSPKRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTIRRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ  
ID NO: 16);

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 18); or

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSK  
LASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK  
(SEQ ID NO: 31).

2. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of claim 1 comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIG  
AVYPPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARG  
FTAYGMDYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of (SEQ ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12); or

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFQGRVTMTRDTSTSTVYMEVSSLRSEDVAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHYQQKPGLAPRLIYDTSKLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID  
NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSEDNAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPLSPKRWIYDTSKLAS  
GVPDRFSGSGSGTDYFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ  
ID NO: 16);

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSK  
LASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK  
(SEQ ID NO: 31).

3. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of claim 1 or 2 comprising:

a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid sequence of VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid sequence of ARGFTAYGMDY (SEQ ID NO: 3); and

a light chain complementarity determining region (LCDR) 1 comprising an amino acid sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid sequence of DTS (SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of QQWSSNPLT (SEQ ID NO: 6).

4. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the anti-ADGRE2 antibody or fragment thereof is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi- specific antibody, Fab fragment, Fab' fragment, F(ab')<sub>2</sub> fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody, cameloid antibody; masked antibody, Small Modular ImmunoPharmaceutical ("SMIPs<sup>TM</sup>"), single chain, Tandem diabody, VHHs, Anticalin, Nanobody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Trans-body; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.

5. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the anti-ADGRE2 antibody or fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).

6. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the humanized anti-ADGRE2 antibody or fragment thereof is an antibody comprising an IgG constant region.
7. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the ADGRE2 antibody or fragment thereof is a single-chain variable fragment (scFv).
8. The humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of claim 7, wherein the scFv comprises a signal sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.
9. The humanized anti-ADGRE2 antibody or antigen-binding fragment of claim 8, wherein the scFV comprises a sequence having at least about 80% identity to:
  - (a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWI  
GAVYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYTFTISS  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);
  - (b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWI  
GAVYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSLSPKRWIYDTSKLASGVPDRFSGSGSGTDYTFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);
  - (c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEW  
IGAVYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT

SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEW  
MGAVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARGF  
TAYGMDYWGQGTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGER  
ATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLASGIPDRFSGSGSGTDFTLTI  
SRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

10. The humanized anti-ADGRE2 antibody or antigen-binding fragment of claim 8, wherein the scFV comprises a sequence of:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWI  
GAVYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYFTISS  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWI  
GAVYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEW  
IGAVYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEW  
MGAVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMELSSLRSEDVAVYYCARGF  
TAYGMDYWGQGTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGER

ATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLASGIPDRFSGSGSGTDFTLTI  
SRLEPEDFAVYYCQQWSSNPLTFGQGKVEIK (SEQ ID NO: 22).

11. The humanized anti-ADGRE2 antibody of any one of the preceding claims, wherein the disassociation constant ( $K_D$ ) is than less than about  $10^{-8}$  M  $K_D$ , less than about  $10^{-9}$  M  $K_D$ , less than about  $10^{-10}$  M  $K_D$ , less than about  $10^{-11}$  M  $K_D$ , less than about  $10^{-12}$  M  $K_D$ , or less than about  $10^{-13}$  M  $K_D$ .
12. The humanized anti-ADGRE2 antibody of any one of the preceding claims, wherein the EC50 is between 1 – 100 nM.
13. The humanized anti-ADGRE2 antibody of claim 12, wherein the EC50 is between 10 – 95 nM.
14. The humanized anti-ADGRE2 antibody of claim 12, wherein the EC50 is between 25 – 75 nM.
15. Use of the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof of any one of the proceeding claims in the manufacture of a medicament for treating cancer.
16. The use according to claim 17, wherein the cancer is selected from leukemia, lymphoma, or myeloma.
17. A pharmaceutical composition comprising a humanized anti-ADGRE2 antibody or fragment thereof and a pharmaceutically acceptable carrier, wherein the humanized ADGRE2 antibody or antibody fragment thereof comprises:
  - (a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to  
EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQKPGAPRLLIYDTSKSLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSCKASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFQGRVTMTADKSTSTVYMELSSLRSEDTAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQKPGLSPKRWIYDTSKSLAS  
GVPDRFSGSGSGTDYFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that  
is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASG  
VPAFRFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID  
NO: 31).

18. The pharmaceutical composition of claim 17, wherein the humanized anti-ADGRE2  
antibody or antibody fragment thereof comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPAFRFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY

PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFGRVTMTRDTSTSTVYMESSLRSEDVAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID  
NO: 8);

(h) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino  
acid sequence of

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSEDNAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ  
ID NO: 16); or

(i) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an  
amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTISRMPEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence of

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSK  
LASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK  
(SEQ ID NO: 31).

19. The pharmaceutical composition of claim 17 or 18, wherein the humanized anti-ADGRE2 antibody or antibody fragment thereof comprises:
- a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid sequence of VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid sequence of ARGFTAYGMDY (SEQ ID NO: 3); and
- a light chain complementarity determining region (LCDR) 1 comprising an amino acid sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid sequence of DTS (SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of QQWSSNPLT (SEQ ID NO: 6).
20. The pharmaceutical composition of any one of claims 17-19, wherein the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi-specific antibody, Fab fragment, Fab' fragment, F(ab')<sub>2</sub> fragment, Fd' fragment, Fd fragment, isolated CDRs or sets thereof; single-chain variable fragment (scFv), polypeptide-Fc fusion, single domain antibody, cameloid antibody; masked antibody, Small Modular ImmunoPharmaceutical ("SMIPs<sup>TM</sup>"), single chain, Tandem diabody, VHs, Anticalin, Nanobody, minibodies, BiTE, ankyrin repeat protein, DARPIN, Avimer, DART, TCR-like antibody, Adnectin, Affilin, Trans-body; Affibody, TrimerX, MicroProtein, Fynomer, Centyrin; and KALBITOR.
21. The pharmaceutical composition of any one of claims 17-20, wherein the anti-ADGRE2 antibody or fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).
22. The pharmaceutical composition of claim 21, wherein the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is an antibody comprising an IgG constant region.

23. The pharmaceutical composition of any one of claims 17-22, wherein the humanized anti-ADGRE2 antibody or antigen-binding fragment thereof is a single-chain variable fragment (scFv).
24. The pharmaceutical composition of claim 23, wherein the scFv comprises a signal sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.
25. The pharmaceutical composition of claim 24, wherein the scFV comprises a sequence having at least about 80% identity to:
- (a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFTAYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERV  
TMSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);
- (b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERV  
TMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVDPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);
- (c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERV  
TMSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVDPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or
- (d) QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVYPGDGDTRHTQKFKGRVTMTRDTSTSTVYMESSLRSEDNAVYYCARGFTAYGMDYWGQGTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSP

GERATLSCSASSSVSYMHWHYQQKPGLAPRLLIYDTSKLASGIPDRFSGSGSGT  
DFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGKVEIK (SEQ ID NO: 22).

26. The pharmaceutical composition of claim 25, wherein the scFV comprises a sequence of:

- (a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDFAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWHYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYFTTIS  
MEPEDFATYYCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 19);
- (b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSAS  
SSSVSYMHWHYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYFTTISRMEPE  
DFATYYCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 20);
- (c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDFAVYYCARGFTAYGM  
DYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMTSCSAS  
SSSVSYMHWHYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYFTTISRMEPE  
DFATYYCQQWSSNPLTFGGGKLEIK (SEQ ID NO: 21); or
- (d) QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAVY  
YPGDGDTRHTQKFKGRVTMTRDTSTSTVYMEVSSLRSEDFAVYYCARGFTAYG  
MDYWGQGTSLTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLS  
CSASSSVSYMHWHYQQKPGLAPRLLIYDTSKLASGIPDRFSGSGSGTDFTLTISRLE  
PEDFAVYYCQQWSSNPLTFGQGKVEIK (SEQ ID NO: 22).

27. A nucleic acid sequence encoding an amino acid sequence at least about 90% identical to any one of SEQ ID Nos: 7-18.

28. A vector comprising the nucleic acid sequence of claim 27.

29. An isolated cell comprising the vector of claim 28.

30. Use of a humanized anti-ADGRE2 antibody or antigen-binding fragment thereof in the manufacture of a medicament for treating cancer in a subject in need thereof, the humanized anti-ADGRE2 antibody comprising:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFQKATLTADKSTSTAYMEVSSLRSEDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical

toEIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKL  
ASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK  
(SEQ ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFQGRVTMTRDTSTSTVYMESSLRSEDNAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to  
EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLIYDTSKLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID  
NO: 8);

(e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino  
acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKVSCASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFQGRVTMTADKSTSTVYMESSLRSEDNAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence that is at least about 80% identical to

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLAS  
GVPDRFSGSGSGTDYFTIRRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ  
ID NO: 16); or

(f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGGTKLEIK (SEQ  
ID NO: 18); or

(g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence that is at least about 80% identical to

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSK  
LASGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGGTKLEIK  
(SEQ ID NO: 31).

31. The use according to claim 30, wherein the humanized anti-ADGRE2 antibody comprises:

(a) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 7), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLA  
SGVPARFSGSGSGTDYTFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 14);

(b) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 9), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 10);

(c) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 11), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATMSASPGERVMTSCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLA  
SGVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 12);

(d) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVCKASGYTFTNYWMQWVRQAPGQGLEWMGAV  
YPGDGDTRHTQKFQGRVTMTRDTSTSTVYMEVSSLRSEDVAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 13), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGLAPRLLIYDTSKLASG  
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID  
NO: 8);

- (e) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEWIGAV  
YPGDGDTRHTQKFKGRVTMTADKSTSTVYMELSSLRSEDVAVYYCARGFTAYG  
MDYWGQGTLVTVSS (SEQ ID NO: 15), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

QIVLTQSPATLSLSPGERATLTCSASSSVSYMHWYQQKPGLSPKRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTIRLEPEDFATYYCQQWSSNPLTFGQGTKVEIK (SEQ  
ID NO: 16); or

- (f) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWIGAVY  
PGDGDTRYTQKFQGRATLTADTSTSTAYMEVSSLRSEDVAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 17), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid sequence of

EIVLTQSPATLSASPGERVMTSCSASSSVSYMHWYQQKPGLAPRRWIYDTSKLAS  
GVPDRFSGSGSGTDYTFTISRMEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ  
ID NO: 18); or

- (g) an immunoglobulin heavy chain variable ( $V_H$ ) region comprising an amino acid sequence of

QVQLVQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWIGAVY  
PGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDTAVYYCARGFTAYGM  
DYWGQGTTVTVSS (SEQ ID NO: 30), and

an immunoglobulin light chain variable ( $V_L$ ) region comprising an amino acid  
sequence of

EIVLTQSPATMSASPGERVMTMSCSASSSVSYMHYQQKSGQSPKRWIYDTSK  
LASGVPARFSGSGSGTDYFTISSMEPEDFATYYCQQWSSNPLTFGGGTKLEIK  
(SEQ ID NO: 31).

32. The use according to claim 30 or 31, wherein the humanized anti-ADGRE2 antibody or  
antibody fragment thereof comprises:

a heavy chain complementarity determining region (HCDR) 1 comprising an amino  
acid sequence of GYTFTNYW (SEQ ID NO: 1), an HCDR2 comprising an amino acid  
sequence of VYPGDGDT (SEQ ID NO: 2), an HCDR3 comprising an amino acid  
sequence of ARGFTAYGMDY (SEQ ID NO: 3); and

a light chain complementarity determining region (LCDR) 1 comprising an amino  
acid sequence of SSVSY (SEQ ID NO: 4), an LCDR2 comprising an amino acid  
sequence of DTS (SEQ ID NO: 5), and an LCDR3 comprising an amino acid sequence of  
QQWSSNPLT (SEQ ID NO: 6).

33. The use according to any one of claims 30-32, wherein the humanized anti-ADGRE2  
antibody or antigen-binding fragment thereof is a monoclonal antibody or a single-chain  
variable fragment (scFv).

34. The use according to any one of claims 30-33, wherein the humanized anti-ADGRE2  
antibody or fragment thereof is an antibody comprising an IgG constant region.

35. The use according to any one of claims 30-34, wherein the humanized anti-ADGRE2 antibody or fragment thereof is a single-chain variable fragment (scFv).
36. The use according to claim 35, wherein the scFv comprises a leader sequence, a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.
37. The use according to claim 36, wherein the scFV comprises a sequence having at least about 80% identity to:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWI  
GAVYPGDGDTRHTQKFKGKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYTFTISS  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWI  
GAVYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDNAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYTFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEW  
IGAVYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDRFSGSGSGTDYTFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEW  
MGAVYPGDGDTRHTQKFKGRTMTRDTSTSTVYMEVSSLRSEDNAVYYCARGF  
TAYGMDYWGQGTTLVTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGER  
ATLSCSASSSVSYMHWYQQKPGLAPRLIYDTSKLASGIPDRFSGSGSGTDFTLT  
SRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

38. The use according to claim 37, wherein the scFV comprises a sequence of:

(a) QVQLQQSGAEVAKPGASVKLSCKASGYTFTNYWMQWIKQAPGQGLEWI  
GAVYPGDGDTRHTQKFQKATLTADKSTSTAYMEVSSLRSEDNAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGQSPKRWIYDTSKLASGVPARFSGSGSGTDYTFTISS  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 19);

(b) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWIRQAPGQGLEWI  
GAVYPGDGDTRYTQKFQGRATLTADTSISTAYMEVSRLRSDDTAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDFSGSGSGTDYTFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 20);

(c) QVQLQQSGAEVKKPGASVKLSCKASGYTFTNYWMQWVRQAPGQGLEW  
IGAVYPGDGDTRYTQKFQGRATLTADTSTSTVYMEVSSLRSEDNAVYYCARGFT  
AYGMDYWGQGTTVTVSSGGGGSGGGGSGGGGSEIVLTQSPATMSASPGERVMT  
SCSASSSVSYMHWYQQKSGLSPKRWIYDTSKLASGVPDFSGSGSGTDYTFTISR  
MEPEDFATYYCQQWSSNPLTFGGGTKLEIK (SEQ ID NO: 21); or

(d) QVQLQQSGAEVKKPGASVKVSKASGYTFTNYWMQWVRQAPGQGLEW  
MGAVYPGDGDTRHTQKFQGRVTMTRDTSTSTVYMEVSSLRSEDNAVYYCARGF  
TAYGMDYWGQGTTLTVSSASTGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGER  
ATLSCSASSSVSYMHWYQQKPLAPRLIYDTSKLASGIPDRFSGSGSGTDFTLTI  
SRLEPEDFAVYYCQQWSSNPLTFGQGTKVEIK (SEQ ID NO: 22).

39. The use according to any one of claims 30-38, wherein the cancer is selected from leukemia, lymphoma, or myeloma.

40. The use according to any one of claims 30-39, comprising that one or more additional agents is to be administered.

41. The use according to claim 40, wherein the one or more additional agents is selected from an antibody, a chemotherapeutic, or radiation therapy.