

What is claimed is:

1. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises: a heavy chain variable region (VH) comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:25, and a light chain variable region (VL) comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:26.

2. The antibody of claim 1, wherein:

(a) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:4, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(b) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:7, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:8, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:9, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:10, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(c) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:12, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:2, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3, the VL-CDR1 comprises the

amino acid sequence set forth in SEQ ID NO:4, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(d) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:13, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:14, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:15, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:16, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:17;

(e) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:18, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:19, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:20, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:21, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:22, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:23; or

(f) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:1, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:24, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:3, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:4, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:5, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6.

3. The antibody of claim 1 or 2, wherein:

(i) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:25;

(ii) the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;

(iii) the VH comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25;

(iv) the VL comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;

(v) the VH comprises the amino acid sequence set forth in SEQ ID NO:25;

(vi) the VL comprises the amino acid sequence set forth in SEQ ID NO:26;

(vii) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;

(viii) the VH comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:25 and the VL comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:26;

(ix) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:220;

(x) the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:221;

(xi) the VH comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:220;

(xii) the VL comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:221;

(xiii) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:220 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:221; or

(xiv) the VH comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:220 and the VL comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence set forth in SEQ ID NO:221.

4. The antibody of claim 1 or 2, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:25 and the VL comprises the amino acid sequence set forth in SEQ ID NO:26.

5. The antibody of claim 1 or 2, where the VH comprises the amino acid sequence set forth in SEQ ID NO:220.

6. The antibody of claim 1 or 2, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:221.

7. The antibody of any one of claims 1 to 6, which is a chimeric antibody, a bispecific antibody, a multispecific antibody, an IgG antibody, or a recombinant antibody.

8. The antibody of any one of claims 1 to 4, which is a humanized antibody.

9. The antibody of any one of claims 1 to 6, which is an antibody fragment comprising at least one antigen-binding site.

10. The antibody of any one of claims 1 to 6, wherein the antibody is a Fab, a Fab', a F(ab')₂, an Fv, a disulfide-linked Fv, an Fd, a linear antibody, a single chain antibody molecule, a diabody, a tribody, a tetrabody, a minibody, a dual variable domain antibody, a single variable domain antibody, or a multispecific antibody formed from antibody fragments.

11. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), wherein the antibody comprises: a VH comprising the amino acid sequence set forth in SEQ ID NO:220 and a VL comprising the amino acid sequence set forth in SEQ ID NO:221.

12. The antibody of claim 11, which is an antibody fragment comprising at least one antigen-binding site.

13. The antibody of claim 11, wherein the antibody is a Fab, a Fab', a F(ab')₂, an Fv, a disulfide-linked Fv, an Fd, a linear antibody, a single chain antibody molecule, a diabody, a tribody, a tetrabody, a minibody, a dual variable domain antibody, a single variable domain antibody, or a multispecific antibody formed from antibody fragments.

14. The antibody of any one of claims 1 to 8 and 11, which comprises an IgG1, IgG2, or IgG4 heavy chain constant region.

15. The antibody of claim 14, wherein the IgG1, IgG2, or IgG4 heavy chain constant region is a human IgG1, human IgG2, or human IgG4 heavy chain constant region.

16. The antibody of any one of claims 1 to 8 and 11, which comprises a kappa or lambda light chain constant region.

17. The antibody of claim 16, wherein the kappa or lambda light chain constant region is a human kappa or human lambda light chain constant region.

18. The antibody of any one of claims 1 to 8 and 11, which comprises an IgG1 heavy chain constant region and a kappa light chain constant region.

19. The antibody of claim 18, wherein the IgG1 heavy chain constant region is a human IgG1 heavy chain constant region and the kappa light chain constant region is a human kappa light chain constant region.

20. The antibody of any one of claims 1 to 6 and 11, which comprises a heavy chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:234

21. The antibody of any one of claims 1 to 6 and 11, which comprises a light chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:236.

22. The antibody of any one of claims 1 to 6 and 11, which comprises: (i) a heavy chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:234; and (ii) a light chain that is at least 90% identical to the amino acid sequence set forth in SEQ ID NO:236.

23. The antibody of claim 1 or 2, which comprises a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:234.

24. The antibody of claim 1 or 2, which comprises a light chain comprising the amino acid sequence set forth in SEQ ID NO:236.

25. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), wherein the antibody comprises: (i) a heavy chain comprising the amino acid sequence

set forth in SEQ ID NO:234; and (ii) a light chain comprising the amino acid sequence set forth in SEQ ID NO:236.

26. An antibody that specifically binds human glucagon receptor (GCGR; SEQ ID NO:223), which comprises:

(a) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:51, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:52;

(b) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:71, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:72;

(c) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:97, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:98;

(d) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:122, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:123;

(e) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:144, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:145;

(f) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:164, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:165;

(g) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:188, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:189;

(h) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:203, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:204; or

(i) a VH comprising VH-CDR1, VH-CDR2, and VH-CDR3 from the amino acid sequence set forth in SEQ ID NO:218, and a VL comprising VL-CDR1, VL-CDR2, and VL-CDR3 from the amino acid sequence set forth in SEQ ID NO:219.

27. The antibody of claim 26, wherein:

(i) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:27, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:28, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:29, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:30, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;

(2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:33, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:34, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:35, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:36, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:37, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:38, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:28, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:29, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:30, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:39, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:40, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:41, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:42, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:37, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:43;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:44, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:45, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:46, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:47, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:48, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:49; or

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:27, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:50, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:29, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:30, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;

- (ii) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:53, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:54, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:55, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:56, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;
- (2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:57, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:58, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:59, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:60, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:37, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;
- (3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:61, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:54, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:55, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:56, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;

- (4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:62, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:40, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:63, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:64, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:37, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:43;
- (5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:65, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:66, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:67, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:68, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:69, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:49; or
- (6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:53, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:70, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:55, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:56, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:31, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:32;
- (iii) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:73, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:74, the VH-CDR3 comprising the amino acid sequence set forth in SEQ ID NO:75, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:76, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:77, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:78;

(2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:79, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:80, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:81, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:82, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:83, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:78;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:84, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:74, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:75, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:76, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:77, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:78;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:85, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:86, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:87, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:88, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:83, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:89;

- (5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:90, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:91, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:92, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:93, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:94, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:95; or
- (6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:73, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:96, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:75, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:76, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:77, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:78;
- (iv) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:99, the VH-CDR2 comprising the amino acid sequence set forth in SEQ ID NO:100, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:101, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:102, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:103, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:104;
- (2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:105, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:106, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:108, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:109, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:104;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:110, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:100, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:101, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:102, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:103, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:104;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:111, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:86, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:112, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:113, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:109, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:114;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:115, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:116, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:117, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:118, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:119, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:120; or

- (6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:99, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:121, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:101, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:102, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:103, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:104;
- (v) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:124, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:125, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:126, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:127, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprising the amino acid sequence set forth in SEQ ID NO:6;
- (2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:129, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:130, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:131, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:132, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;
- (3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:133, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:125, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:126, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:127, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:134, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:135, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:136, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:137, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:17;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:138, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:139, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:140, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:141, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:142, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:23; or

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:124, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:143, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:126, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:127, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

- (vi) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:146, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:147, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:148, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:149, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;
- (2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:150, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:151, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:152, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:153, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;
- (3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:154, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:147, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:148, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:149, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;
- (4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:155, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:156, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:157, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:158, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:17;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:159, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:160, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:161, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:162, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:142, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:23;

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:146, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:163, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:148, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:149, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6; or

(vii) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:166, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:167, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:168, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:170, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:171;

(2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:172, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:173, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:174, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:175, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:171;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:176, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:167, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:168, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:170, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:171;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:177, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:178, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:179, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:180, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:181;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:182, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:183, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:184, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:185, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:142, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:186; or

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:166, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:187, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:168, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:170, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:171;

(viii) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:190, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:191, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:192, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:193;

(2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:172, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:194, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:195, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:175, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:193;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:154, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:191, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:192, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:193;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:177, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:156, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:196, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:180, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:197;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:198, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:199, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:200, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:185, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:142, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:201; or

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:190, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:202, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:192, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID

NO:169, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:193;

(ix) (1) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:190, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:205, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:206, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:207, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(2) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:172, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:208, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:209, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:210, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(3) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:154, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:205, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:206, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:207, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

(4) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:177, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:211, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:212, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:213, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:11, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:17;

(5) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:198, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:214, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:215, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:216, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:142, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:23; or

(6) the VH-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:190, the VH-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:217, the VH-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:206, the VL-CDR1 comprises the amino acid sequence set forth in SEQ ID NO:207, the VL-CDR2 comprises the amino acid sequence set forth in SEQ ID NO:128, and the VL-CDR3 comprises the amino acid sequence set forth in SEQ ID NO:6;

28. The antibody of claim 26 or 27, wherein:

(a) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:51 and the VL comprises an amino acid

sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:52;

(b) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:71 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:72;

(c) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:97 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:98;

(d) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:122 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:123;

(e) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:144 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:145;

(f) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:164 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:165;

(g) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:188 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:189;

(h) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:203 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:204; or

(i) the VH comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:218 and the VL comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:219.

29. The antibody of claim 26 or 27, wherein:

(a) the VH comprises the amino acid sequence set forth in SEQ ID NO:51 and the VL comprises the amino acid sequence set forth in SEQ ID NO:52;

(b) the VH comprises the amino acid sequence set forth in SEQ ID NO:71 and the VL comprises the amino acid sequence set forth in SEQ ID NO:72;

(c) the VH comprises the amino acid sequence set forth in SEQ ID NO:97 and the VL comprises the amino acid sequence set forth in SEQ ID NO:98;

(d) the VH comprises the amino acid sequence set forth in SEQ ID NO:122 and the VL comprises the amino acid sequence set forth in SEQ ID NO:123;

(e) the VH comprises the amino acid sequence set forth in SEQ ID NO:144 and the VL comprises the amino acid sequence set forth in SEQ ID NO:145;

(f) the VH comprises the amino acid sequence set forth in SEQ ID NO:164 and the VL comprises the amino acid sequence set forth in SEQ ID NO:165;

(g) the VH comprises the amino acid sequence set forth in SEQ ID NO:188 and the VL comprises the amino acid sequence set forth in SEQ ID NO:189;

(h) the VH comprises the amino acid sequence set forth in SEQ ID NO:203 and the VL comprises the amino acid sequence set forth in SEQ ID NO:204; or

(i) the VH comprises the amino acid sequence set forth in SEQ ID NO:218 and the VL comprises the amino acid sequence set forth in SEQ ID NO:219.

30. The antibody of any one of claims 1 to 29, which:

- (a) inhibits GCGR signaling in cells expressing GCGR;
- (b) inhibits GCGR activity in a cell;
- (c) inhibits GCGR activity in a cell wherein the GCGR activity is induced by glucagon; and/or
- (d) inhibits cAMP activity.

31. The antibody of any one of claims 1 to 29, which:

- (i) reduces blood glucose levels;
- (ii) increases the level of C-peptide; and/or

(iii) increases the level of insulin.

32. A pharmaceutical composition comprising the antibody of any one of claims 1 to 31 and a pharmaceutically acceptable carrier.

33. An isolated polynucleotide or polynucleotides encoding the antibody of any one of claims 1 to 31.

34. A vector or vectors comprising the polynucleotide or polynucleotides of claim 33.

35. A cell comprising the polynucleotide or polynucleotides of claim 33 or the vector or vectors of claim 34.

36. A method of making the antibody of any one of claims 1 to 31, comprising: (a) culturing the cell of claim 33, and (b) isolating the antibody.

37. Use of the antibody of any one of claims 1 to 31 for the preparation of a medicament for the treatment of a glucose utilization disorder or the sequelae associated therewith.

38. The use of claim 37, wherein the glucose utilization disorder or sequelae associated therewith is diabetes mellitus, latent autoimmune diabetes of adults, gestational diabetes, insulin resistance, pre-diabetes, diseases associated with abnormal glucose metabolism, hyperglycemia, or a physiological disorder associated with, or that results from, a hyperglycemic condition.

39. The use of claim 37, wherein the glucose utilization disorder or sequelae associated therewith is Type 1 diabetes or Type 2 diabetes.

40. Use of the antibody of any one of claims 1 to 31 for the preparation of a medicament for the treatment of metabolic syndrome or a disease or disorder associated with metabolic syndrome.

41. The use of claim 40, wherein the disease or disorder associated with metabolic syndrome is obesity and elevated body mass, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), hypertension, cardiovascular disease, stroke, or heart failure.

42. Use of the antibody of any one of claims 1 to 31 for the preparation of a medicament for the treatment of dyslipidemia or the sequelae associated therewith.

43. The use of claim 42, wherein the sequelae associated therewith is atherosclerosis, coronary artery disease, or a cerebrovascular disorder.

44. The use of any one of claims 37 to 43, wherein the medicament is for administration to the subject in combination with at least one additional therapeutic agent to the subject.

45. The use of claim 44, wherein the at least one additional therapeutic agent is a diabetes or hyperglycemia drug.

46. The use of claim 45, wherein the diabetes or hyperglycemia drug is a biguanide, a sulfonylurea, a meglitinide derivative, an alpha-glucosidase inhibitor, a thiazolidinedione (TZD), a glucagon-like peptide-I (GLP-1) agonist, a dipeptidyl peptidase 4 (DPP-4) inhibitor, a selective sodium-glucose transporter-2 (SGLT-2) inhibitor, an insulin or insulin mimetic, an amylinomimetic, a bile acid sequestrant, and/or a dopamine agonist.

47. The use of any one of claims 37 to 46, wherein the subject is a human.