

CLAIMS

1. An isolated antibody or antigen binding fragment that (i) binds to natriuretic peptide receptor 1 (NPR1); and (ii) is capable of activating NPR1 in the absence of atrial natriuretic peptide (ANP).

5

2. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of claim 1 which is ANP non-competitive.

3. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of claim 1 which is ANP competitive.

10

4. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of claim 1 or 2, wherein the antibody or antigen binding fragment thereof binds to an epitope within amino acids 99-133 of SEQ ID NO: 1.

15

5. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of any one of claims 1, 2, or 4, wherein the antibody or antigen binding fragment thereof binds to a conformational epitope of human NPR1, and wherein the conformational epitope comprises at least one amino acid residue within each of (i) amino acids 99-103 of SEQ ID NO: 1, (ii) 105-111 of SEQ ID NO: 1, (iii) 131-134 of SEQ ID NO: 1, and additionally binds to amino acid 375 and/or 378 of SEQ ID NO: 1.

20

6. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of claim 1 or 3, wherein the antibody or antigen binding fragment thereof binds to an epitope within amino acids 188-219 of SEQ ID NO: 1.

25

7. An isolated anti-NPR1 antibody or antigen binding fragment; or the isolated antibody or antigen binding fragment of any one of claims 1, 3, or 6, wherein the antibody or antigen binding fragment thereof binds to a conformational epitope within NPR1, and wherein the conformational epitope comprises at least one amino acid residue within each of (i) amino acids 188-198 of SEQ ID NO: 1, (ii) 201-208 of SEQ ID NO: 1, (iii) 215-238 of SEQ ID NO: 1, and (iv) 294-297 of SEQ ID NO: 1, optionally wherein the antibody or antigen binding fragment thereof binds to at least amino acids 188, 192, 194, 197, 201, 208, and 219 of SEQ ID NO: 1.

30

8. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 2, 4, or 5, wherein the antibody or antigen binding fragment comprises

35

three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), and wherein:

- (a) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 28; HCDR2 comprises or consists of an amino acid sequence as set forth in
 5 X₁IX₂SX₃GX₄YX₅X₆YADSVKG (SEQ ID NO: 429), wherein X₁ is A or V, X₂ is S or E, X₃ is D or K, X₄ is S or N, X₅ is I or T, and X₆ is Y or F; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30; LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41; LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42; and LCDR3 comprises or consists of an amino acid
 10 sequence as set forth in Y₁QY₂Y₃Y₄Y₅PRT (SEQ ID NO: 430); wherein Y₁ is M or Q, Y₂ is S, E, T, or I, Y₃ is Y or W, Y₄ is E, V, R, A, T, or M, and Y₅ is K, V, R, or A;
- (II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 31; HCDR2 comprises or consists of an amino acid sequence as set forth in
 15 X₁IX₂SX₃GX₄YX₅X₆YADSVKG (SEQ ID NO: 429), wherein X₁ is A or V, X₂ is S or E, X₃ is D or K, X₄ is S or N, X₅ is I or T, and X₆ is Y or F; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42, and LCDR3 comprises or consists of an amino acid sequence as set forth in Y₁QY₂Y₃Y₄Y₅PRT (SEQ ID NO: 430); wherein Y₁ is M or Q, Y₂ is S, E,
 20 T, or I, Y₃ is Y or W, Y₄ is E, V, R, A, T, or M, and Y₅ is K, V, R, or A;
- (III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 32, HCDR2 comprises or consists of an amino acid sequence as set forth in X₁SX₂GX₃Y (SEQ ID NO: 431), wherein X₁ is S or E, X₂ is D or K, or X₃ is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an
 25 amino acid sequence as set forth in SEQ ID NO: 44, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in Y₁Y₂Y₃Y₄PR (SEQ ID NO: 432); wherein Y₁ is S, E, T, or I, Y₂ is Y or W, Y₃ is E, V, R, A, T, or M, and Y₄ is K, V, R, or A; or
- (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID
 30 NO: 34, HCDR2 comprises or consists of an amino acid sequence as set forth in IX₁SX₂GX₃YX₄ (SEQ ID NO: 433), wherein X₁ is S or E, X₂ is D or K, X₃ is S or N, and X₄ is I or T, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 36, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 47, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3
 35 comprises or consists of an amino acid sequence as set forth in Y₁QY₂Y₃Y₄Y₅PRT (SEQ ID NO: 430); wherein Y₁ is M or Q, Y₂ is S, E, T, or I, Y₃ is Y or W, Y₄ is E, V, R, A, T, or M, and Y₅ is K, V, R, or A;

(b) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 28; HCDR2 comprises or consists of an amino acid sequence as set forth in $X_1IX_2SX_3GX_4YX_5X_6YADSVKG$ (SEQ ID NO: 429), wherein X_1 is A or V, X_2 is S or E, X_3 is D or K, X_4 is S or N, X_5 is I or T, and X_6 is Y or F; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30; LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41; LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42; and LCDR3 comprises or consists of an amino acid sequence as set forth in $QQY_1WY_2Y_3PRT$ (SEQ ID NO: 434); wherein Y_1 is S, E, T, or I, Y_2 is V, R, A, T, or M, and Y_3 is K, V, R, or A;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 31; HCDR2 comprises or consists of an amino acid sequence as set forth in $X_1IX_2SX_3GX_4YX_5X_6YADSVKG$ (SEQ ID NO: 429), wherein X_1 is A or V, X_2 is S or E, X_3 is D or K, X_4 is S or N, X_5 is I or T, and X_6 is Y or F; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42, and LCDR3 comprises or consists of an amino acid sequence as set forth in $QQY_1WY_2Y_3PRT$ (SEQ ID NO: 434); wherein Y_1 is S, E, T, or I, Y_2 is V, R, A, T, or M, and Y_3 is K, V, R, or A;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 32, HCDR2 comprises or consists of an amino acid sequence as set forth in $X_1SX_2GX_3Y$ (SEQ ID NO: 431), wherein X_1 is S or E, X_2 is D or K, or X_3 is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 44, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in $Y_1WY_2Y_3PR$ (SEQ ID NO: 435); wherein Y_1 is S, E, T, or I, Y_2 is V, R, A, T, or M, and Y_3 is K, V, R, or A; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 34, HCDR2 comprises or consists of an amino acid sequence as set forth in $IX_1SX_2GX_3YX_4$ (SEQ ID NO: 433), wherein X_1 is S or E, X_2 is D or K, X_3 is S or N, and X_4 is I or T, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 36, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 47, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in $QQY_1WY_2Y_3PRT$ (SEQ ID NO: 434); wherein Y_1 is S, E, T, or I, Y_2 is V, R, A, T, or M, and Y_3 is K, V, R, or A;

(c) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 28; HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 119; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30; LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41; LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42; and LCDR3 comprises or consists of an amino acid sequence as set forth in QQY₁WY₂Y₃PRT (SEQ ID NO: 434); wherein Y₁ is S, E, T, or I, Y₂ is V, R, A, T, or M, and Y₃ is K, V, R, or A;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 31; HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 119; HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42, and LCDR3 comprises or consists of an amino acid sequence as set forth in QQY₁WY₂Y₃PRT (SEQ ID NO: 434); wherein Y₁ is S, E, T, or I, Y₂ is V, R, A, T, or M, and Y₃ is K, V, R, or A;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 32, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 120, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 44, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in Y₁WY₂Y₃PR (SEQ ID NO: 435); wherein Y₁ is S, E, T, or I, Y₂ is V, R, A, T, or M, and Y₃ is K, V, R, or A; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 34, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 121, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 36, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 47, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in QQY₁WY₂Y₃PRT (SEQ ID NO: 434); wherein Y₁ is S, E, T, or I, Y₂ is V, R, A, T, or M, and Y₃ is K, V, R, or A;

(d) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁THYIH (SEQ ID NO: 436), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in SIY₁Y₂Y₃GY₄Y₅TY₆YADSVKG (SEQ ID NO: 437), wherein Y₁ is S or G, Y₂ is S or G, Y₃ is S or Q, Y₄ is S, Q, or G, Y₅ is S, N, or M, and Y₆ is Y or L, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 7, HCDR2 comprises or consists of an amino acid sequence as set forth in SIY₁Y₂Y₃GY₄Y₅TY₆YADSVKG (SEQ ID NO: 437), wherein Y₁ is S or G, Y₂ is S or G, Y₃ is S or Q, Y₄ is S, Q, or G, Y₅ is S, N, or M, and Y₆ is Y or L, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁TH (SEQ ID NO: 438), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁Y₂Y₃GY₄Y₅ (SEQ ID NO: 439), wherein Y₁ is S or G, Y₂ is S or G, Y₃ is S or Q, Y₄ is S, Q, or G, and Y₅ is S, N, or M, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 20, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 22; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁THY (SEQ ID NO: 440), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in IY₁Y₂Y₃GY₄Y₅T (SEQ ID NO: 441), wherein Y₁ is S or G, Y₂ is S or G, Y₃ is S or Q, Y₄ is S, Q, or G, and Y₅ is S, N, or M, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 12, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 23, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(e) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁THYIH (SEQ ID NO: 436), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in SISY₁SGY₂Y₃TYYADSVKG (SEQ ID NO: 442), wherein Y₁ is S or G, Y₂ is S or Q, and Y₃ is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 7, HCDR2 comprises or consists of an amino acid sequence as set forth in SISY₁SGY₂Y₃TYYADSVKG (SEQ ID NO: 442), wherein Y₁ is S or G, Y₂ is S or Q, and Y₃ is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6,

LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁TH (SEQ ID NO: 438), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in SY₁SGY₂Y₃ (SEQ ID NO: 443), wherein Y₁ is S or G, Y₂ is S or Q, and Y₃ is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 20, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 22; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁THY (SEQ ID NO: 440), wherein X₁ is N, S, or Q, HCDR2 comprises or consists of an amino acid sequence as set forth in ISY₁SGY₂Y₃T (SEQ ID NO: 444), wherein Y₁ is S or G, Y₂ is S or Q, and Y₃ is S or N, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 12, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 23, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19;

(f) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂YX₃X₄X₅ (SEQ ID NO: 445), wherein X₁ is S or T, X₂ is S, K, or R, X₃ is W or Y, X₄ is I or L, and X₅ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁IY₂QY₃Y₄Y₅EY₆Y₇YVESVKG (SEQ ID NO: 446), wherein Y₁ is S or N, Y₂ is K or H, Y₃ is S, Q, or H, Y₄ is G or A, Y₅ is S, H, or L, Y₆ is T or K, and Y₇ is Y, K, or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in X₁YX₂X₃X₄ (SEQ ID NO: 447), wherein X₁ is S, K, or R, X₂ is W or Y, X₃ is I or L, and X₄ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁IY₂QY₃Y₄Y₅EY₆Y₇YVESVKG (SEQ ID NO: 446), wherein Y₁ is S or N, Y₂ is K or H, Y₃ is S, Q, or H, Y₄ is G or A, Y₅ is S, H, or L, Y₆ is T or K, and Y₇ is Y, K, or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂Y (SEQ ID NO: 448), wherein X₁ is S or T, and X₂ is S, K, or R, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁QY₂Y₃Y₄E (SEQ ID NO: 449), wherein Y₁ is K or H, Y₂ is S, Q, or H, Y₃ is G or A, and Y₄ is S, H, or L, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 240, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 242; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂YX₃ (SEQ ID NO: 450), wherein X₁ is S or T, X₂ is S, K, or R, and X₃ is W or Y, HCDR2 comprises or consists of an amino acid sequence as set forth in IY₁QY₂Y₃Y₄EY₅ (SEQ ID NO: 451), wherein Y₁ is K or H, Y₂ is S, Q, or H, Y₃ is G or A, Y₄ is S, H, or L, and Y₅ is T or K, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 232, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 243, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(g) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂YX₃X₄X₅ (SEQ ID NO: 445), wherein X₁ is S or T, X₂ is S, K, or R, X₃ is W or Y, X₄ is I or L, and X₅ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in SIHQY₁Y₂Y₃EY₄Y₅YVESVKG (SEQ ID NO: 453), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, Y₄ is T or K, and Y₅ is K or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in X₁YX₂X₃X₄ (SEQ ID NO: 447), wherein X₁ is S, K, or R, X₂ is W or Y, X₃ is I or L, and X₄ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in SIHQY₁Y₂Y₃EY₄Y₅YVESVKG (SEQ ID NO: 453), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, Y₄ is T or K, and Y₅ is K or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂Y (SEQ ID NO: 448), wherein X₁ is S or T, and X₂ is S, K, or R, HCDR2 comprises or consists of

an amino acid sequence as set forth in HQY₁Y₂Y₃E (SEQ ID NO: 456), wherein Y₁ is Q or H, Y₂ is G or A, and Y₃ is H or L, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 240, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 242; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFX₁FSX₂YX₃ (SEQ ID NO: 450), wherein X₁ is S or T, X₂ is S, K, or R, and X₃ is W or Y, HCDR2 comprises or consists of an amino acid sequence as set forth in IHQY₁Y₂Y₃EY₄ (SEQ ID NO: 458), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, and Y₄ is T or K, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 232, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 243, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(h) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁YX₂IX₃ (SEQ ID NO: 452), wherein X₁ is S or R, X₂ is W or Y, and X₃ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁IY₂QY₃Y₄Y₅EY₆Y₇YVESVKG (SEQ ID NO: 446), wherein Y₁ is S or N, Y₂ is K or H, Y₃ is S, Q, or H, Y₄ is G or A, Y₅ is S, H, or L, Y₆ is T or K, and Y₇ is Y, K, or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in X₁YX₂IX₃ (SEQ ID NO: 454), wherein X₁ is S or R, X₂ is W or Y, and X₃ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁IY₂QY₃Y₄Y₅EY₆Y₇YVESVKG (SEQ ID NO: 446), wherein Y₁ is S or N, Y₂ is K or H, Y₃ is S, Q, or H, Y₄ is G or A, Y₅ is S, H, or L, Y₆ is T or K, and Y₇ is Y, K, or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁Y (SEQ ID NO: 455), wherein X₁ is S or R, HCDR2 comprises or consists of an amino acid sequence as set forth in Y₁QY₂Y₃Y₄E (SEQ ID NO: 449), wherein Y₁ is K or H, Y₂ is S, Q, or H, Y₃ is G or A, and Y₄ is S, H, or L, HCDR3 comprises or consists of an amino acid sequence as set

forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 240, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 242; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁YX₂ (SEQ ID NO: 457), wherein X₁ is S or R, and X₂ is W or Y, HCDR2 comprises or consists of an amino acid sequence as set forth in IY₁QY₂Y₃Y₄EY₅ (SEQ ID NO: 451), wherein Y₁ is K or H, Y₂ is S, Q, or H, Y₃ is G or A, Y₄ is S, H, or L, and Y₅ is T or K, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 232, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 243, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239; or

(i) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁YX₂IX₃ (SEQ ID NO: 452), wherein X₁ is S or R, X₂ is W or Y, and X₃ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in SIHQY₁Y₂Y₃EY₄Y₅YVESVKG (SEQ ID NO: 453), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, Y₄ is T or K, and Y₅ is K or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in X₁YX₂IX₃ (SEQ ID NO: 454), wherein X₁ is S or R, X₂ is W or Y, and X₃ is S or N, HCDR2 comprises or consists of an amino acid sequence as set forth in SIHQY₁Y₂Y₃EY₄Y₅YVESVKG (SEQ ID NO: 453), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, Y₄ is T or K, and Y₅ is K or R, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁Y (SEQ ID NO: 455), wherein X₁ is S or R, HCDR2 comprises or consists of an amino acid sequence as set forth in HQY₁Y₂Y₃E (SEQ ID NO: 456), wherein Y₁ is Q or H, Y₂ is G or A, and Y₃ is H or L, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 240, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 242; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFSX₁YX₂ (SEQ ID NO: 457), wherein X₁ is S or R, and X₂ is W or Y, HCDR2 comprises or consists of an amino acid sequence as set forth in IHQY₁Y₂Y₃EY₄ (SEQ ID NO: 458), wherein Y₁ is Q or H, Y₂ is G or A, Y₃ is H or L, and Y₄ is T or K, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 232, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 243, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239.

9. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 3, 6, or 7, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), and wherein:

(a) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 310, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 311, HCDR3 comprises or consists of an amino acid sequence as set forth in GX₁X₂X₃GX₄LGFDH (SEQ ID NO: 459), wherein X₁ is A or S, X₂ is V or L, X₃ is A or P, and X₄ is Q or L, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 320, LCDR2 comprises or consists of an amino acid sequence as set forth in GNSNRPY₁ (SEQ ID NO: 460), wherein Y₁ is S or N, and LCDR3 comprises or consists of an amino acid sequence as set forth in QSYZ₁Z₂Z₃Z₄Z₅Z₆Z₇V (SEQ ID NO: 461), wherein Z₁ is Y, D, or G, Z₂ is T, S, or A, Z₃ is S, P, or F, Z₄ is S, T, or P, Z₅ is H, S, or R, Z₆ is G, S, or F, and Z₇ is P, S, or V;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 229, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 311, HCDR3 comprises or consists of an amino acid sequence as set forth in GX₁X₂X₃GX₄LGFDH (SEQ ID NO: 459), wherein X₁ is A or S, X₂ is V or L, X₃ is A or P, and X₄ is Q or L, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 320, LCDR2 comprises or consists of an amino acid sequence as set forth in GNSNRPY₁ (SEQ ID NO: 460), wherein Y₁ is S or N, and LCDR3 comprises or consists of an amino acid sequence as set forth in QSYZ₁Z₂Z₃Z₄Z₅Z₆Z₇V (SEQ ID NO: 461), wherein Z₁ is Y, D, or G, Z₂ is T, S, or A, Z₃ is S, P, or F, Z₄ is S, T, or P, Z₅ is H, S, or R, Z₆ is G, S, or F, and Z₇ is P, S, or V;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 80, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 313, HCDR3 comprises or consists of an amino acid sequence as set forth in GX₁X₂X₃GX₄LGFDH (SEQ ID NO: 459), wherein X₁ is A or S, X₂ is V or L, X₃ is A or P, and X₄ is Q or L, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 323, LCDR2

comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 324, and LCDR3 comprises or consists of an amino acid sequence as set forth in $YZ_1Z_2Z_3Z_4Z_5Z_6Z_7$ (SEQ ID NO: 462), wherein Z_1 is Y, D, or G, Z_2 is T, S, or A, Z_3 is S, P, or F, Z_4 is S, T, or P, Z_5 is H, S, or R, Z_6 is G, S, or F, and Z_7 is P, S, or V; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 82, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 314, HCDR3 comprises or consists of an amino acid sequence as set forth in $ARGX_1X_2X_3GX_4LGFDH$ (SEQ ID NO: 463), wherein X_1 is A or S, X_2 is V or L, X_3 is A or P, and X_4 is Q or L, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 326, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 324, and LCDR3 comprises or consists of an amino acid sequence as set forth in $QSYZ_1Z_2Z_3Z_4Z_5Z_6Z_7V$ (SEQ ID NO: 461), wherein Z_1 is Y, D, or G, Z_2 is T, S, or A, Z_3 is S, P, or F, Z_4 is S, T, or P, Z_5 is H, S, or R, Z_6 is G, S, or F, and Z_7 is P, S, or V;

(b) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in $GFTFX_1X_2YAX_3X_4$ (SEQ ID NO: 464), wherein X_1 is S or G, X_2 is S or T, X_3 is I or M, and X_4 is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in $Y_1ISY_2Y_3GY_4Y_5Y_6Y_7YAY_8SVKG$ (SEQ ID NO: 465), wherein Y_1 is A or S, Y_2 is A, S, or G, Y_3 is S or H, Y_4 is G or Y, Y_5 is S or Y, Y_6 is T or A, Y_7 is Y, R, or N, and Y_8 is E or G, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in $X_1YAX_2X_3$ (SEQ ID NO: 466), wherein X_1 is S or T, X_2 is I or M, and X_3 is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in $Y_1ISY_2Y_3GY_4Y_5Y_6Y_7YAY_8SVKG$ (SEQ ID NO: 465), wherein Y_1 is A or S, Y_2 is A, S, or G, Y_3 is S or H, Y_4 is G or Y, Y_5 is S or Y, Y_6 is T or A, Y_7 is Y, R, or N, and Y_8 is E or G, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in $GFTFX_1X_2Y$ (SEQ ID NO: 467), wherein X_1 is S or G, and X_2 is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in $SY_1Y_2GY_3Y_4$ (SEQ ID NO: 468), wherein Y_1 is A, S, or G, Y_2 is S or H, Y_3 is G or Y, and Y_4 is S or Y, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino

acid sequence as set forth in SEQ ID NO: 340, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 342; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁X₂YA (SEQ ID NO: 469), wherein X₁ is S or G, and X₂ is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in ISY₁Y₂GY₃Y₄T (SEQ ID NO: 470), wherein Y₁ is S or G, Y₂ is S or H, Y₃ is G or Y, and Y₄ is S or Y, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 332, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 343, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339; or

(c) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁X₂YAX₃X₄ (SEQ ID NO: 464), wherein X₁ is S or G, X₂ is S or T, X₃ is I or M, and X₄ is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in SISY₁Y₂GYYY₃Y₄YAY₅SVKG (SEQ ID NO: 471), wherein Y₁ is A or S, Y₂ is S or H, Y₃ is T or A, Y₄ is R or N, and Y₅ is E or G, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339;

(II) HCDR1 comprises or consists of an amino acid sequence as set forth in X₁YAX₂X₃ (SEQ ID NO: 466), wherein X₁ is S or T, X₂ is I or M, and X₃ is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in SISY₁Y₂GYYY₃Y₄YAY₅SVKG (SEQ ID NO: 471), wherein Y₁ is A or S, Y₂ is S or H, Y₃ is T or A, Y₄ is R or N, and Y₅ is E or G, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339;

(III) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁X₂Y (SEQ ID NO: 467), wherein X₁ is S or G, and X₂ is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in SY₁Y₂GY (SEQ ID NO: 472), wherein Y₁ is A or S, and Y₂ is S or H, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 340, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 342; or

(IV) HCDR1 comprises or consists of an amino acid sequence as set forth in GFTFX₁X₂YA (SEQ ID NO: 469), wherein X₁ is S or G, and X₂ is S or T, HCDR2 comprises or consists of an amino acid sequence as set forth in ISY₁Y₂G (SEQ ID NO: 473), wherein Y₁ is A, S, or G, and Y₂ is S or H, HCDR3 comprises or consists of an amino acid sequence as set forth in
 5 SEQ ID NO: 332, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 343, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339.

10 10. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 2, 4, 5, or 8, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), and wherein:

(a) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID
 15 NO: 28, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 29, 119, and 190, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 41, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42, and LCDR3
 20 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 43, 126, 134, 145, 172, 178, and 184; (II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 31, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 29, 119, and 190, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid
 25 sequence as set forth in SEQ ID NO: 41, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 42, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 43, 126, 134, 145, 172, 178, and 184; (III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 32, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 33, 120, and 191, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 30, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 44, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3
 30 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 46, 127, 135, 146, 173, 179, and 185; or (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 34, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 35, 121, and 192, HCDR3 comprises or consists of an amino acid
 35 sequence as set forth in SEQ ID NO: 36, LCDR1 comprises or consists of an amino acid

sequence as set forth in SEQ ID NO: 47, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 45, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 43, 126, 134, 145, 172, 178, and 184;

(b) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 4, 112, and 165, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 100, and 151, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19; (II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 7, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 5, 100, and 151, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 17, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 18, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19; (III) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 8, 113, and 166, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 9, 101, and 152, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 6, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 20, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 22; or (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 10, 114, and 167, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 11, 102, and 153, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 12, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 23, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 21, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 19; or

(c) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 226, 367, and 378, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 227, 368, and 379, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239; (II) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 229, 369, and 380, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 227, 368, and 379,

HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 237, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 238, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239; (III) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 32, 370, and 381, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 230, 371, and 382, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 228, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 240, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 242; or (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 34, 372, and 383, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 231, 373, and 384, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 232, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 243, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 241, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 239.

11. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 3, 6, 7, or 9, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3), and wherein:

(a) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 310, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 311, HCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 312 and 348, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 320, LCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 321 and 354, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 322, 355, and 361; (II) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 229, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 311, HCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 312 and 348, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 320, LCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 321 and 354, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 322, 355, and 361; (III) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 80, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 313,

HCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 312 and 348, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 323, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 324, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 325, 356, and 362; or (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 82, HCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 314, HCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 315 and 349, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 326, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 324, and LCDR3 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 322, 355, and 361; or

(b) (I) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 270 and 407, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 271, 389, and 408, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339; (II) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 273 and 409, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 271, 389, and 408, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 337, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 338, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339; (III) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 32 and 410, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 274, 390, and 411, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 331, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 340, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 342; or (IV) HCDR1 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 275 and 412, HCDR2 comprises or consists of an amino acid sequence as set forth in any one of SEQ ID NOs: 276, 391, and 413, HCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 332, LCDR1 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 343, LCDR2 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 341, and LCDR3 comprises or consists of an amino acid sequence as set forth in SEQ ID NO: 339.

12. The antibody or antigen binding fragment of any one of claims 1, 2, 4, 5, 8, or 10, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) selected from:

(a) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 135 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 134 (LCDR3);

(b) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 126 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 126 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 127 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 126 (LCDR3);

(c) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 145 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 145 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 146 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 145 (LCDR3);

(d) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30

(HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 173 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 172 (LCDR3);

5 (e) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 178 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 178 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30
10 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 179 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 178 (LCDR3);

(f) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30
15 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 184 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 184 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 185
20 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 184 (LCDR3);

(g) (I) SEQ ID NO: 4 (HCDR1), SEQ ID NO: 100 (HCDR2), SEQ ID NO: 6 (HCDR3),
SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (II) SEQ
25 ID NO: 7 (HCDR1), SEQ ID NO: 100 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO: 8 (HCDR1), SEQ ID NO: 101 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1),
SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 10 (HCDR1),
SEQ ID NO: 102 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO:
30 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(h) (I) SEQ ID NO: 112 (HCDR1), SEQ ID NO: 100 (HCDR2), SEQ ID NO: 6
(HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3);
(II) SEQ ID NO: 7 (HCDR1), SEQ ID NO: 100 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID
NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO:
35 113 (HCDR1), SEQ ID NO: 101 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1),
SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 114 (HCDR1),

SEQ ID NO: 102 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(i) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 43 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 119 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 43 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 120 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 46 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 121 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 43 (LCDR3);

(j) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 126 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 126 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 127 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 126 (LCDR3);

(k) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 135 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 134 (LCDR3);

(l) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 145 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 145 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 146 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 145 (LCDR3);

(m) (I) SEQ ID NO: 4 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (II) SEQ ID NO: 7 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17

(LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO: 8 (HCDR1), SEQ ID NO: 152 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 10 (HCDR1), SEQ ID NO: 153 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(n) (I) SEQ ID NO: 112 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (II) SEQ ID NO: 7 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO: 113 (HCDR1), SEQ ID NO: 152 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 114 (HCDR1), SEQ ID NO: 153 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(o) (I) SEQ ID NO: 165 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (II) SEQ ID NO: 7 (HCDR1), SEQ ID NO: 151 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO: 166 (HCDR1), SEQ ID NO: 152 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 167 (HCDR1), SEQ ID NO: 153 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(p) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 173 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 172 (LCDR3);

(q) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 178 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 178 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 179 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 178 (LCDR3);

(r) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 184 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 184 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 185 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 184 (LCDR3);

(s) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 190 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 190 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 134 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 191 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 135 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 192 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 134 (LCDR3);

(t) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 190 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 190 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 172 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 191 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 173 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 192 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 172 (LCDR3);

(u) (I) SEQ ID NO: 4 (HCDR1), SEQ ID NO: 5 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (II) SEQ ID NO: 7 (HCDR1), SEQ ID NO: 5 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 17 (LCDR1), SEQ ID NO: 18 (LCDR2), and SEQ ID NO: 19 (LCDR3); (III) SEQ ID NO: 8 (HCDR1), SEQ ID NO: 9 (HCDR2), SEQ ID NO: 6 (HCDR3), SEQ ID NO: 20 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 22 (LCDR3); or (IV) SEQ ID NO: 10 (HCDR1), SEQ ID NO: 11 (HCDR2), SEQ ID NO: 12 (HCDR3), SEQ ID NO: 23 (LCDR1), SEQ ID NO: 21 (LCDR2), and SEQ ID NO: 19 (LCDR3);

(v) (I) SEQ ID NO: 28 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41 (LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 43 (LCDR3); (II) SEQ ID NO: 31 (HCDR1), SEQ ID NO: 29 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 41

(LCDR1), SEQ ID NO: 42 (LCDR2), and SEQ ID NO: 43 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 33 (HCDR2), SEQ ID NO: 30 (HCDR3), SEQ ID NO: 44 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 46 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 35 (HCDR2), SEQ ID NO: 36 (HCDR3), SEQ ID NO: 47 (LCDR1), SEQ ID NO: 45 (LCDR2), and SEQ ID NO: 43 (LCDR3);

(w) (I) SEQ ID NO: 367 (HCDR1), SEQ ID NO: 368 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (II) SEQ ID NO: 369 (HCDR1), SEQ ID NO: 368 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (III) SEQ ID NO: 370 (HCDR1), SEQ ID NO: 371 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 240 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 242 (LCDR3); or (IV) SEQ ID NO: 372 (HCDR1), SEQ ID NO: 373 (HCDR2), SEQ ID NO: 232 (HCDR3), SEQ ID NO: 243 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 239 (LCDR3);

(x) (I) SEQ ID NO: 378 (HCDR1), SEQ ID NO: 379 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (II) SEQ ID NO: 380 (HCDR1), SEQ ID NO: 379 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (III) SEQ ID NO: 381 (HCDR1), SEQ ID NO: 382 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 240 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 242 (LCDR3); or (IV) SEQ ID NO: 383 (HCDR1), SEQ ID NO: 384 (HCDR2), SEQ ID NO: 232 (HCDR3), SEQ ID NO: 243 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 239 (LCDR3);

(y) (I) SEQ ID NO: 226 (HCDR1), SEQ ID NO: 227 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (II) SEQ ID NO: 229 (HCDR1), SEQ ID NO: 227 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 239 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 230 (HCDR2), SEQ ID NO: 228 (HCDR3), SEQ ID NO: 240 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 242 (LCDR3); or (IV) SEQ ID NO: 34 (HCDR1), SEQ ID NO: 231 (HCDR2), SEQ ID NO: 232 (HCDR3), SEQ ID NO: 243 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 239 (LCDR3);

(z) (I) SEQ ID NO: 270 (HCDR1), SEQ ID NO: 271 (HCDR2), SEQ ID NO: 272 (HCDR3), SEQ ID NO: 282 (LCDR1), SEQ ID NO: 261 (LCDR2), and SEQ ID NO: 283 (LCDR3); (II) SEQ ID NO: 273 (HCDR1), SEQ ID NO: 271 (HCDR2), SEQ ID NO: 272 (HCDR3), SEQ ID NO: 282 (LCDR1), SEQ ID NO: 261 (LCDR2), and SEQ ID NO: 283 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 274 (HCDR2), SEQ ID NO: 272

(HCDR3), SEQ ID NO: 284 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 285 (LCDR3); or (IV) SEQ ID NO: 275 (HCDR1), SEQ ID NO: 276 (HCDR2), SEQ ID NO: 277 (HCDR3), SEQ ID NO: 286 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 283 (LCDR3); or

(aa) (I) SEQ ID NO: 291 (HCDR1), SEQ ID NO: 292 (HCDR2), SEQ ID NO: 293 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 304 (LCDR3); (II) SEQ ID NO: 294 (HCDR1), SEQ ID NO: 292 (HCDR2), SEQ ID NO: 293 (HCDR3), SEQ ID NO: 237 (LCDR1), SEQ ID NO: 238 (LCDR2), and SEQ ID NO: 304 (LCDR3); (III) SEQ ID NO: 295 (HCDR1), SEQ ID NO: 296 (HCDR2), SEQ ID NO: 293 (HCDR3), SEQ ID NO: 240 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 305 (LCDR3); or (IV) SEQ ID NO: 297 (HCDR1), SEQ ID NO: 298 (HCDR2), SEQ ID NO: 299 (HCDR3), SEQ ID NO: 243 (LCDR1), SEQ ID NO: 241 (LCDR2), and SEQ ID NO: 304 (LCDR3).

13. The antibody or antigen binding fragment of any one of claims 1, 3, 6, 7, 9, or 11, wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) selected from:

(a) (I) SEQ ID NO: 52 (HCDR1), SEQ ID NO: 53 (HCDR2), SEQ ID NO: 54 (HCDR3), SEQ ID NO: 65 (LCDR1), SEQ ID NO: 66 (LCDR2), and SEQ ID NO: 67 (LCDR3); (II) SEQ ID NO: 55 (HCDR1), SEQ ID NO: 53 (HCDR2), SEQ ID NO: 54 (HCDR3), SEQ ID NO: 65 (LCDR1), SEQ ID NO: 66 (LCDR2), and SEQ ID NO: 67 (LCDR3); (III) SEQ ID NO: 56 (HCDR1), SEQ ID NO: 57 (HCDR2), SEQ ID NO: 54 (HCDR3), SEQ ID NO: 68 (LCDR1), SEQ ID NO: 69 (LCDR2), and SEQ ID NO: 70 (LCDR3); or (IV) SEQ ID NO: 58 (HCDR1), SEQ ID NO: 59 (HCDR2), SEQ ID NO: 60 (HCDR3), SEQ ID NO: 71 (LCDR1), SEQ ID NO: 69 (LCDR2), and SEQ ID NO: 67 (LCDR3);

(b) (I) SEQ ID NO: 76 (HCDR1), SEQ ID NO: 77 (HCDR2), SEQ ID NO: 78 (HCDR3), SEQ ID NO: 89 (LCDR1), SEQ ID NO: 90 (LCDR2), and SEQ ID NO: 91 (LCDR3); (II) SEQ ID NO: 79 (HCDR1), SEQ ID NO: 77 (HCDR2), SEQ ID NO: 78 (HCDR3), SEQ ID NO: 89 (LCDR1), SEQ ID NO: 90 (LCDR2), and SEQ ID NO: 91 (LCDR3); (III) SEQ ID NO: 80 (HCDR1), SEQ ID NO: 81 (HCDR2), SEQ ID NO: 78 (HCDR3), SEQ ID NO: 92 (LCDR1), SEQ ID NO: 93 (LCDR2), and SEQ ID NO: 94 (LCDR3); or (IV) SEQ ID NO: 82 (HCDR1), SEQ ID NO: 83 (HCDR2), SEQ ID NO: 84 (HCDR3), SEQ ID NO: 95 (LCDR1), SEQ ID NO: 93 (LCDR2), and SEQ ID NO: 91 (LCDR3);

(c) (I) SEQ ID NO: 310 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 348 (HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 354 (LCDR2), and SEQ ID NO: 361 (LCDR3); (II) SEQ ID NO: 229 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 348

(HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 354 (LCDR2), and SEQ ID NO: 361 (LCDR3); (III) SEQ ID NO: 80 (HCDR1), SEQ ID NO: 313 (HCDR2), SEQ ID NO: 348 (HCDR3), SEQ ID NO: 323 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 362 (LCDR3); or (IV) SEQ ID NO: 82 (HCDR1), SEQ ID NO: 314 (HCDR2), SEQ ID NO: 349 (HCDR3), SEQ ID NO: 326 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 361 (LCDR3);

(d) (I) SEQ ID NO: 270 (HCDR1), SEQ ID NO: 389 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339 (LCDR3); (II) SEQ ID NO: 273 (HCDR1), SEQ ID NO: 389 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339 (LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 390 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 340 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 342 (LCDR3); or (IV) SEQ ID NO: 275 (HCDR1), SEQ ID NO: 391 (HCDR2), SEQ ID NO: 332 (HCDR3), SEQ ID NO: 343 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 339 (LCDR3);

(e) (I) SEQ ID NO: 407 (HCDR1), SEQ ID NO: 408 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339 (LCDR3); (II) SEQ ID NO: 409 (HCDR1), SEQ ID NO: 408 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339 (LCDR3); (III) SEQ ID NO: 410 (HCDR1), SEQ ID NO: 411 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 340 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 342 (LCDR3); or (IV) SEQ ID NO: 412 (HCDR1), SEQ ID NO: 413 (HCDR2), SEQ ID NO: 332 (HCDR3), SEQ ID NO: 343 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 339 (LCDR3);

(f) (I) SEQ ID NO: 310 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 312 (HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 321 (LCDR2), and SEQ ID NO: 322 (LCDR3); (II) SEQ ID NO: 229 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 312 (HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 321 (LCDR2), and SEQ ID NO: 322 (LCDR3); (III) SEQ ID NO: 80 (HCDR1), SEQ ID NO: 313 (HCDR2), SEQ ID NO: 312 (HCDR3), SEQ ID NO: 323 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 325 (LCDR3); or (IV) SEQ ID NO: 82 (HCDR1), SEQ ID NO: 314 (HCDR2), SEQ ID NO: 315 (HCDR3), SEQ ID NO: 326 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 322 (LCDR3);

(g) (I) SEQ ID NO: 270 (HCDR1), SEQ ID NO: 271 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339 (LCDR3); (II) SEQ ID NO: 273 (HCDR1), SEQ ID NO: 271 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 337 (LCDR1), SEQ ID NO: 338 (LCDR2), and SEQ ID NO: 339

(LCDR3); (III) SEQ ID NO: 32 (HCDR1), SEQ ID NO: 274 (HCDR2), SEQ ID NO: 331 (HCDR3), SEQ ID NO: 340 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 342 (LCDR3); or (IV) SEQ ID NO: 275 (HCDR1), SEQ ID NO: 276 (HCDR2), SEQ ID NO: 332 (HCDR3), SEQ ID NO: 343 (LCDR1), SEQ ID NO: 341 (LCDR2), and SEQ ID NO: 339 (LCDR3); or

(h) (I) SEQ ID NO: 310 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 348 (HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 354 (LCDR2), and SEQ ID NO: 355 (LCDR3); (II) SEQ ID NO: 229 (HCDR1), SEQ ID NO: 311 (HCDR2), SEQ ID NO: 348 (HCDR3), SEQ ID NO: 320 (LCDR1), SEQ ID NO: 354 (LCDR2), and SEQ ID NO: 355 (LCDR3); (III) SEQ ID NO: 80 (HCDR1), SEQ ID NO: 313 (HCDR2), SEQ ID NO: 348 (HCDR3), SEQ ID NO: 323 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 356 (LCDR3); or (IV) SEQ ID NO: 82 (HCDR1), SEQ ID NO: 314 (HCDR2), SEQ ID NO: 349 (HCDR3), SEQ ID NO: 326 (LCDR1), SEQ ID NO: 324 (LCDR2), and SEQ ID NO: 355 (LCDR3).

14. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 2, 4, 5, 8, 10, or 12, wherein the antibody or antigen binding fragment comprises:

(a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 136;

(b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 136;

(c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 128;

(d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 128;

(e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 147;

(f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 147;

(g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 174;

(h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 174;

(i) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 180;

- (j) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 180;
- (k) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 201, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 186;
- 5 (l) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 186;
- (m) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 103, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 24;
- (n) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 115, and a light
10 chain variable region comprising an amino acid sequence of SEQ ID NO: 24;
- (o) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 122, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 48;
- (p) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 128;
- 15 (q) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 136;
- (r) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 147;
- (s) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 154, and a light
20 chain variable region comprising an amino acid sequence of SEQ ID NO: 24;
- (t) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 161, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 24;
- (u) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 168, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 24;
- 25 (v) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 174;
- (w) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 180;
- (x) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light
30 chain variable region comprising an amino acid sequence of SEQ ID NO: 186;
- (y) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 193, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 136;
- (z) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 193, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 174;
- 35 (aa) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 13, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 24;

- (bb) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 37, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 48;
- (cc) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 374, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 244;
- 5 (dd) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 385, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 244;
- (ee) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 233, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 244;
- (ff) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 278, and a light
- 10 chain variable region comprising an amino acid sequence of SEQ ID NO: 287; or
- (gg) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 300, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 306.

15. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding
 15 fragment of any one of claims 1, 3, 6, 7, 9, 11, or 13, wherein the antibody or antigen binding fragment comprises:

- (a) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 61, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 72;
- (b) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 85, and a light
- 20 chain variable region comprising an amino acid sequence of SEQ ID NO: 96;
- (c) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 350, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 363;
- (d) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 392, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 344;
- 25 (e) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 414, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 344;
- (f) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 316, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 327;
- (g) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 333, and a light
- 30 chain variable region comprising an amino acid sequence of SEQ ID NO: 344; or
- (h) a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 350, and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 357.

16. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding
 35 fragment of any one of claims 1, 2, 4, 5, 8, 10, 12, or 14, wherein the antibody or antigen binding fragment comprises:

- (a) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising an amino acid sequence of SEQ ID NO: 138;
- (b) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising an amino acid sequence of SEQ ID NO: 138;
- 5 (c) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising an amino acid sequence of SEQ ID NO: 130;
- (d) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising an amino acid sequence of SEQ ID NO: 130;
- (e) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising
10 an amino acid sequence of SEQ ID NO: 149;
- (f) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising an amino acid sequence of SEQ ID NO: 149;
- (g) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising an amino acid sequence of SEQ ID NO: 176;
- 15 (h) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising an amino acid sequence of SEQ ID NO: 176;
- (i) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising an amino acid sequence of SEQ ID NO: 182;
- (j) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising
20 an amino acid sequence of SEQ ID NO: 182;
- (k) a heavy chain comprising an amino acid sequence of SEQ ID NO: 203, and a light chain comprising an amino acid sequence of SEQ ID NO: 188;
- (l) a heavy chain comprising an amino acid sequence of SEQ ID NO: 208, and a light chain comprising an amino acid sequence of SEQ ID NO: 188;
- 25 (m) a heavy chain comprising an amino acid sequence of SEQ ID NO: 105, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- (n) a heavy chain comprising an amino acid sequence of SEQ ID NO: 108, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- (o) a heavy chain comprising an amino acid sequence of SEQ ID NO: 117, and a light chain comprising
30 an amino acid sequence of SEQ ID NO: 26;
- (p) a heavy chain comprising an amino acid sequence of SEQ ID NO: 124, and a light chain comprising an amino acid sequence of SEQ ID NO: 50;
- (q) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 130;
- 35 (r) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 138;

- (s) a heavy chain comprising an amino acid sequence of SEQ ID NO: 141, and a light chain comprising an amino acid sequence of SEQ ID NO: 138;
- (t) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 149;
- 5 (u) a heavy chain comprising an amino acid sequence of SEQ ID NO: 156, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- (v) a heavy chain comprising an amino acid sequence of SEQ ID NO: 159, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- (w) a heavy chain comprising an amino acid sequence of SEQ ID NO: 163, and a light chain comprising
10 an amino acid sequence of SEQ ID NO: 26;
- (x) a heavy chain comprising an amino acid sequence of SEQ ID NO: 170, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- (y) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 176;
- 15 (z) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 182;
- (aa) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 188;
- (bb) a heavy chain comprising an amino acid sequence of SEQ ID NO: 195, and a light chain comprising
20 an amino acid sequence of SEQ ID NO: 138;
- (cc) a heavy chain comprising an amino acid sequence of SEQ ID NO: 195, and a light chain comprising an amino acid sequence of SEQ ID NO: 176;
- (dd) a heavy chain comprising an amino acid sequence of SEQ ID NO: 15, and a light chain comprising an amino acid sequence of SEQ ID NO: 26;
- 25 (ee) a heavy chain comprising an amino acid sequence of SEQ ID NO: 39, and a light chain comprising an amino acid sequence of SEQ ID NO: 50;
- (ff) a heavy chain comprising an amino acid sequence of SEQ ID NO: 376, and a light chain comprising an amino acid sequence of SEQ ID NO: 246;
- (gg) a heavy chain comprising an amino acid sequence of SEQ ID NO: 387, and a light chain comprising
30 an amino acid sequence of SEQ ID NO: 246;
- (hh) a heavy chain comprising an amino acid sequence of SEQ ID NO: 235, and a light chain comprising an amino acid sequence of SEQ ID NO: 246;
- (ii) a heavy chain comprising an amino acid sequence of SEQ ID NO: 280, and a light chain comprising an amino acid sequence of SEQ ID NO: 289; or
- 35 (jj) a heavy chain comprising an amino acid sequence of SEQ ID NO: 302, and a light chain comprising an amino acid sequence of SEQ ID NO: 308.

17. An isolated anti-NPR1 antibody or antigen binding fragment; or the antibody or antigen binding fragment of any one of claims 1, 3, 6, 7, 9, 11, 13, or 15, wherein the antibody or antigen binding fragment comprises:

(a) a heavy chain comprising an amino acid sequence of SEQ ID NO: 63, and a light chain comprising an amino acid sequence of SEQ ID NO: 74;

(b) a heavy chain comprising an amino acid sequence of SEQ ID NO: 87, and a light chain comprising an amino acid sequence of SEQ ID NO: 98;

(c) a heavy chain comprising an amino acid sequence of SEQ ID NO: 352, and a light chain comprising an amino acid sequence of SEQ ID NO: 365;

(d) a heavy chain comprising an amino acid sequence of SEQ ID NO: 394, and a light chain comprising an amino acid sequence of SEQ ID NO: 346;

(e) a heavy chain comprising an amino acid sequence of SEQ ID NO: 416, and a light chain comprising an amino acid sequence of SEQ ID NO: 346;

(f) a heavy chain comprising an amino acid sequence of SEQ ID NO: 318, and a light chain comprising an amino acid sequence of SEQ ID NO: 329;

(g) a heavy chain comprising an amino acid sequence of SEQ ID NO: 335, and a light chain comprising an amino acid sequence of SEQ ID NO: 346; or

(h) a heavy chain comprising an amino acid sequence of SEQ ID NO: 352, and a light chain comprising an amino acid sequence of SEQ ID NO: 359.

18. The antibody or antigen binding fragment of any one of claims 1-17, which is an antigen binding fragment selected from the group consisting of a Fab, Fab', F(ab')₂, Fv, single domain antibody (dAb), and a single chain variable fragment (scFv).

19. The antibody or antigen binding fragment of any one of claims 1-19, wherein the antibody or antigen binding fragment is therapeutic.

20. An isolated nucleic acid or nucleic acids encoding the amino acid sequence of the antibody or antigen binding fragment of any one of claims 1-19.

21. A vector comprising the isolated nucleic acid(s) of claim 20.

22. A host cell comprising the isolated nucleic acid(s) of claim 20 or the vector of claim 21.

23. A method of producing the antibody or antigen binding fragment of any one of claims 1-19, comprising culturing the host cell of claim 22 under conditions suitable to produce the antibody or

antigen binding fragment, optionally wherein the method additionally comprises purification of the antibody or antigen binding fragment.

24. A pharmaceutical composition comprising an antibody or antigen binding fragment of any one of claims 1-19 or produced by the method of claim 23 and a pharmaceutically acceptable carrier; optionally wherein the composition further comprises an additional therapeutic agent.

25. The pharmaceutical composition of claim 24, or a combination comprising an antibody or antigen binding fragment of any one of claims 1-19, wherein the additional therapeutic agent is selected from an ACE (angiotensin-converting-enzyme) inhibitor, an angiotensin receptor blocker (ARB), a neprilysin inhibitor, a beta blocker, a diuretic, a calcium channel blocker, a cardiac glycoside, a sodium-glucose co-transporter 2 inhibitor (SGLT2i), an angiotensin receptor-neprilysin inhibitor (ARNi), a corticosteroid, a leukotriene modifier, a bronchodilator, a beta-adrenoceptor antagonist, a carbonic anhydrase inhibitor, an alpha 2-adrenoceptor agonist, a parasympathomimetic, a prostaglandin analog, a rho kinase inhibitor, and combinations thereof.

26. The antibody or antigen binding fragment of any one of claims 1-19, or the pharmaceutical composition of claim 24 or 25, for use in the treatment of a disorder or disease associated with natriuretic peptide receptor activity in a subject in need of such treatment.

27. The antibody or antigen binding fragment of any one of claims 1-19, or the pharmaceutical composition or combination of claim 24 or 25, for use in the treatment of a cardiovascular disorder in a subject in need of such treatment, optionally wherein the cardiovascular disorder is selected from: hypertension, peripheral vascular disease, heart failure, coronary artery disease (CAD), ischemic heart disease (IHD), mitral stenosis and regurgitation, angina, hypertrophic cardiomyopathy, diabetic cardiomyopathy, supraventricular and ventricular arrhythmias, cardiac dysrhythmia, atrial fibrillation (AF), new onset of atrial fibrillation, recurrent atrial fibrillation, cardiac fibrosis, atrial flutter, detrimental vascular remodeling, plaque stabilization, and myocardial infarction (MI).

28. The antibody or antigen binding fragment of any one of claims 1-19, or the pharmaceutical composition or combination of claim 24 or 25, for use in the treatment of heart failure, hypertrophic cardiomyopathy (HCM), hypertension, preeclampsia, asthma, glaucoma, a kidney disorder, and/or cytokine release syndrome in a subject in need of such treatment, optionally wherein the heart failure is selected from a heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), heart failure after acute myocardial infarct, or acute decompensated heart failure.

29. Use of the antibody or antigen binding fragment of any one of claims 1-19, or the pharmaceutical composition or combination of claim 24 or 25 in the manufacture of a medicament for the treatment of a cardiovascular disorder in a subject in need of such treatment, optionally wherein the cardiovascular disorder is selected from: hypertension, peripheral vascular disease, heart failure, coronary artery disease (CAD), ischemic heart disease (IHD), mitral stenosis and regurgitation, angina, hypertrophic cardiomyopathy, diabetic cardiomyopathy, supraventricular and ventricular arrhythmias, cardiac dysrhythmia, atrial fibrillation (AF), new onset of atrial fibrillation, recurrent atrial fibrillation, cardiac fibrosis, atrial flutter, detrimental vascular remodeling, plaque stabilization, and myocardial infarction (MI).

10

30. Use of the antibody or antigen binding fragment of any one of claims 1-19, or the pharmaceutical composition or combination of claim 24 or 25 in the manufacture of a medicament for the treatment of heart failure, hypertrophic cardiomyopathy (HCM), hypertension, preeclampsia, asthma, glaucoma, a kidney disorder, and/or cytokine release syndrome in a subject in need of such treatment, optionally wherein the heart failure is selected from a heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), heart failure after acute myocardial infarct, or acute decompensated heart failure.

15