What is claimed is:

1. An isolated fully human monoclonal antibody that binds Jagged 1 and Jagged 2.

2. The antibody of claim 1, wherein the antibody comprises a VH CDR1 sequence comprising the amino acid sequence SYAMS (SEQ ID NO: 200); a VH CD2 sequence comprising the amino acid sequence SIDPEGRQTYYADSVKG (SEQ ID NO: 208); a VH CDR3 sequence comprising the amino acid sequence DIGGRSAFDY (SEQ ID NO: 209); a VL CDR1 sequence comprising the amino acid sequence RASQSISSY (SEQ ID NO: 210); a VL CDR2 sequence comprising the amino acid sequence AASSLQS (SEQ ID NO: 211); and a VL CDR3 sequence comprising the amino acid sequence QQTVVAPPL (SEQ ID NO: 212).

3. The antibody of claim 1, wherein the antibody comprises a combination of a VH CDR1 sequence, a VH CDR2 sequence, a VH CDR3 sequence, a VL CDR1 sequence, a VL CDR2 sequence, and a VL CDR3 sequence selected from the combinations shown in Table 2.

4. The antibody of claim 3, wherein the antibody comprises a combination of a variable heavy chain region and a variable light chain region from the combinations listed in Table 4.

5. The antibody of claim 1, wherein the antibody binds Jagged 1 and Jagged 2 and prevents one or more of Jagged 1 or Jagged 2 from binding a Notch receptor.

6. The antibody of claim 1, wherein said antibody is an IgG isotype.

7. The antibody of claim 6, wherein said antibody is an IgG1 isotype.

8. The antibody of claim 1 comprising an agent conjugated to the antibody.

9. The antibody of claim 8, wherein the agent is a therapeutic agent, an antineoplastic agent, a toxin or fragment thereof, a detectable moiety or a diagnostic agent.

10. The antibody of claim 8, wherein the agent is conjugated to the antibody via a linker.

11. The antibody of claim 10, wherein the linker is a cleavable linker.

12. A pharmaceutical composition comprising an antibody of any one of the preceding claims and a carrier.

13. An activatable antibody that in an activated state binds Jagged 1 and Jagged 2 comprising:

an antibody or an antigen binding fragment thereof (AB) that specifically binds to Jagged 1 and Jagged 2;

a masking moiety (MM) that inhibits the binding of the AB to Jagged 1 and Jagged 2 when the activatable antibody is in an uncleaved state; and

a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.

14. The activatable antibody of claim 13, wherein the MM has an equilibrium dissociation constant for binding to the AB which is greater than the equilibrium dissociation constant of the AB to Jagged 1 and Jagged 2.

15. The activatable antibody of claim 13, wherein the MM does not interfere or compete with the AB for binding to Jagged 1 and Jagged 2 when the activatable antibody is in a cleaved state.

16. The activatable antibody of claim 13, wherein the protease is co-localized with Jagged 1 and/or Jagged 2 in a tissue, and wherein the protease cleaves the CM in the activatable antibody when the activatable antibody is exposed to the protease.

17. The activatable antibody of claim 13, wherein the activatable antibody in the uncleaved state has the structural arrangement from N-terminus to C-terminus as follows: MM-CM-AB or AB-CM-MM.

18. The activatable antibody of claim 13, wherein the activatable antibody comprises a linking peptide between the MM and the CM.

19. The activatable antibody of claim 13, wherein the activatable antibody comprises a linking peptide between the CM and the AB.

20. The activatable antibody of claim 13, wherein the activatable antibody comprises a first linking peptide (LP1) and a second linking peptide (LP2), and wherein the activatable antibody follows in the uncleaved state has the structural arrangement from N-terminus to C-terminus as: MM-LP1-CM-LP2-AB or AB-LP2-CM-LP1-MM.

21. The activatable antibody of claim 20, wherein the two linking peptides need not be identical to each other.

22. The activatable antibody of claim 20, wherein each of LP1 and LP2 is a peptide of about 1 to 20 amino acids in length.

23. The activatable antibody of claim 13, wherein the MM is a polypeptide of about 2 to 40 amino acids in length.

24. The activatable antibody of claim 13, wherein the MM polypeptide sequence is different from that of Jagged 1 and Jagged 2 and wherein the MM polypeptide sequence is no more than 50% identical to any natural binding partner of the AB.

25. The activatable antibody of claim 13, wherein the CM is a polypeptide of up to 15 amino acids in length.

26. The activatable antibody of claim 13, wherein the antigen binding fragment thereof is selected from the group consisting of a Fab fragment, a $F(ab')_2$ fragment, a scFv, a scab, a dAb, a single domain heavy chain antibody, and a single domain light chain antibody.

27. The activatable antibody of claim 13, wherein the CM is a substrate for an enzyme selected from the group consisting of uPA, legumain, MT-SP1, ADAM17, BMP-1, TMPRSS3, TMPRSS4, MMP-9, MMP-12, MMP-13, and MMP-14.

28. The activatable antibody of claim 13 comprising an agent conjugated to the AB.

29. The activatable antibody of claim 28, wherein the agent is a therapeutic agent, an antineoplastic agent, a toxin or fragment thereof, a detectable moiety or a diagnostic agent.

30. The activatable antibody of claim 28, wherein the agent is conjugated to the AB via a linker.

31. The activatable antibody of claim 30, wherein the linker is a cleavable linker.

32. The activatable antibody of claim 13, wherein the MM comprises a sequence selected from the group consisting of the sequences shown in Table 9, Table 11, Table 12, Table 13, Table 14, Table 19, Table 20, Table 21, Table 22, or Table 23.

33. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a VH CDR1 sequence comprising the amino acid sequence SYAMS (SEQ ID NO: 200); a VH CD2 sequence comprising the amino acid sequence SIDPEGRQTYYADSVKG (SEQ ID NO: 208); a VH CDR3 sequence comprising the amino acid sequence DIGGRSAFDY (SEQ ID NO: 209); a VL CDR1 sequence comprising the amino acid sequence RASQSISSY (SEQ ID NO: 210); a VL CDR2 sequence comprising the amino acid sequence AASSLQS (SEQ ID NO: 211); and a VL CDR3 sequence comprising the amino acid sequence QQTVVAPPL (SEQ ID NO: 212).

34. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a combination of a VH CDR1 sequence, a VH CDR2 sequence, a VH CDR3 sequence, a VL CDR1 sequence, a VL CDR2 sequence, and a VL CDR3 sequence selected from the combinations shown in Table 2.

35. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a combination of a variable heavy chain region and a variable light chain region from the combinations listed in Table 4.

36. The activatable antibody of claim 13 comprising a light chain amino acid sequence selected from the group consisting of SEQ ID NOs: 74, 132, 134, 136, 138, 140, 142, 144, 146,

180, 182, 184, 186, 188, 190, 192, 194, and 196, and a heavy chain amino acid sequence selected from the group consisting of SEQ ID NOs: 76 and 148.

37. An isolated nucleic acid molecule encoding the antibody of claim 1 or the activatable antibody of claim 13.

38. A vector comprising the isolated nucleic acid molecule of claim 37.

39. A method of producing an antibody or an activatable antibody by culturing a cell under conditions that lead to expression of the antibody or the activatable antibody, wherein the cell comprises the nucleic acid molecule of claim 37.

40. A method of manufacturing an activatable antibody that binds Jagged 1 and Jagged 2 in an activated state, the method comprising:

(a) culturing a cell comprising a nucleic acid construct that encodes the activatable antibody under conditions that lead to expression of the activatable antibody, wherein the activatable antibody comprises a masking moiety (MM), a cleavable moiety (CM), and an antibody or an antigen binding fragment thereof (AB) that specifically binds Jagged 1 and Jagged 2,

and

(b) recovering the activatable antibody.

41. The method of claim 40, wherein the CM is a polypeptide that functions as a substrate for a protease.

42. The method of claim 40, wherein the CM is positioned in the activatable antibody such that, in an uncleaved state, the MM interferes with specific binding of the AB to Jagged 1 and Jagged 2 and in a cleaved state the MM does not interfere or compete with specific binding of the AB to Jagged 1 and Jagged 2

43. A method of alleviating a symptom of a clinical indication associated with cancer in a subject, the method comprising administering the antibody of claim 1 or the activatable

antibody of claim 13 to a subject in need thereof in an amount sufficient to alleviate the symptom of the clinical indication associated with cancer.

44. A method of reducing angiogenesis comprising administering the antibody of claim 1 or the activatable antibody of claim 13 to a subject in need thereof in an amount sufficient to reduce angiogenesis.

45. A method of reducing Jagged 1 and/or Jagged 2 signaling comprising administering the antibody of claim 1 or the activatable antibody of claim 13 to a subject in need thereof in an amount sufficient to reduce Jagged 1 and/or Jagged 2 signaling.

46. The method of any one of claims 43 to 45, wherein said subject is a human.

47. A method of alleviating a symptom of a fibrotic disorder, wherein the method comprises administering the antibody of claim 1 or the activatable antibody of claim 13 to a subject in need thereof in an amount sufficient to alleviate the symptom of the fibrotic disorder in the subject.

48. The method of claim 47, wherein said subject is a human.

What is claimed is:

1. An isolated fully human monoclonal antibody that binds Jagged 1 and Jagged 2.

2. The antibody of claim 1, wherein the antibody comprises a VH CDR1 sequence comprising the amino acid sequence SYAMS (SEQ ID NO: 200); a VH CD2 sequence comprising the amino acid sequence SIDPEGRQTYYADSVKG (SEQ ID NO: 208); a VH CDR3 sequence comprising the amino acid sequence DIGGRSAFDY (SEQ ID NO: 209); a VL CDR1 sequence comprising the amino acid sequence RASQSISSY (SEQ ID NO: 210); a VL CDR2 sequence comprising the amino acid sequence AASSLQS (SEQ ID NO: 211); and a VL CDR3 sequence comprising the amino acid sequence QQTVVAPPL (SEQ ID NO: 212).

3. The antibody of claim 1, wherein the antibody comprises a combination of a VH CDR1 sequence, a VH CDR2 sequence, a VH CDR3 sequence, a VL CDR1 sequence, a VL CDR2 sequence, and a VL CDR3 sequence selected from the combinations shown in Table 2.

4. The antibody of claim 3, wherein the antibody comprises a combination of a variable heavy chain region and a variable light chain region from the combinations listed in Table 4.

5. The antibody of claim 1, wherein the antibody binds Jagged 1 and Jagged 2 and prevents one or more of Jagged 1 or Jagged 2 from binding a Notch receptor.

6. The antibody of claim 1, wherein said antibody is an IgG isotype.

7. The antibody of claim 6, wherein said antibody is an IgG1 isotype.

8. The antibody of claim 1 comprising an agent conjugated to the antibody.

9. The antibody of claim 8, wherein the agent is a therapeutic agent, an antineoplastic agent, a toxin or fragment thereof, a detectable moiety or a diagnostic agent.

10. The antibody of claim 8, wherein the agent is conjugated to the antibody via a linker.

11. The antibody of claim 10, wherein the linker is a cleavable linker.

12. A pharmaceutical composition comprising an antibody of any one of the preceding claims and a carrier.

13. An activatable antibody that in an activated state binds Jagged 1 and Jagged 2 comprising:

an antibody or an antigen binding fragment thereof (AB) that specifically binds to Jagged 1 and Jagged 2;

a masking moiety (MM) that inhibits the binding of the AB to Jagged 1 and Jagged 2 when the activatable antibody is in an uncleaved state; and

a cleavable moiety (CM) coupled to the AB, wherein the CM is a polypeptide that functions as a substrate for a protease.

14. The activatable antibody of claim 13, wherein the MM has an equilibrium dissociation constant for binding to the AB which is greater than the equilibrium dissociation constant of the AB to Jagged 1 and Jagged 2.

15. The activatable antibody of claim 13, wherein the MM does not interfere or compete with the AB for binding to Jagged 1 and Jagged 2 when the activatable antibody is in a cleaved state.

16. The activatable antibody of claim 13, wherein the protease is co-localized with Jagged 1 and/or Jagged 2 in a tissue, and wherein the protease cleaves the CM in the activatable antibody when the activatable antibody is exposed to the protease.

17. The activatable antibody of claim 13, wherein the activatable antibody in the uncleaved state has the structural arrangement from N-terminus to C-terminus as follows: MM-CM-AB or AB-CM-MM.

18. The activatable antibody of claim 13, wherein the activatable antibody comprises a linking peptide between the MM and the CM.

19. The activatable antibody of claim 13, wherein the activatable antibody comprises a linking peptide between the CM and the AB.

20. The activatable antibody of claim 13, wherein the activatable antibody comprises a first linking peptide (LP1) and a second linking peptide (LP2), and wherein the activatable antibody follows in the uncleaved state has the structural arrangement from N-terminus to C-terminus as: MM-LP1-CM-LP2-AB or AB-LP2-CM-LP1-MM.

21. The activatable antibody of claim 20, wherein the two linking peptides need not be identical to each other.

22. The activatable antibody of claim 20, wherein each of LP1 and LP2 is a peptide of about 1 to 20 amino acids in length.

23. The activatable antibody of claim 13, wherein the MM is a polypeptide of about 2 to 40 amino acids in length.

24. The activatable antibody of claim 13, wherein the MM polypeptide sequence is different from that of Jagged 1 and Jagged 2 and wherein the MM polypeptide sequence is no more than 50% identical to any natural binding partner of the AB.

25. The activatable antibody of claim 13, wherein the CM is a polypeptide of up to 15 amino acids in length.

26. The activatable antibody of claim 13, wherein the antigen binding fragment thereof is selected from the group consisting of a Fab fragment, a $F(ab')_2$ fragment, a scFv, a scab, a dAb, a single domain heavy chain antibody, and a single domain light chain antibody.

27. The activatable antibody of claim 13, wherein the CM is a substrate for an enzyme selected from the group consisting of uPA, legumain, MT-SP1, ADAM17, BMP-1, TMPRSS3, TMPRSS4, MMP-9, MMP-12, MMP-13, and MMP-14.

28. The activatable antibody of claim 13 comprising an agent conjugated to the AB.

29. The activatable antibody of claim 28, wherein the agent is a therapeutic agent, an antineoplastic agent, a toxin or fragment thereof, a detectable moiety or a diagnostic agent.

30. The activatable antibody of claim 28, wherein the agent is conjugated to the AB via a linker.

31. The activatable antibody of claim 30, wherein the linker is a cleavable linker.

32. The activatable antibody of claim 13, wherein the MM comprises a sequence selected from the group consisting of the sequences shown in Table 9, Table 11, Table 12, Table 13, Table 14, Table 19, Table 20, Table 21, Table 22, or Table 23.

33. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a VH CDR1 sequence comprising the amino acid sequence SYAMS (SEQ ID NO: 200); a VH CD2 sequence comprising the amino acid sequence SIDPEGRQTYYADSVKG (SEQ ID NO: 208); a VH CDR3 sequence comprising the amino acid sequence DIGGRSAFDY (SEQ ID NO: 209); a VL CDR1 sequence comprising the amino acid sequence RASQSISSY (SEQ ID NO: 210); a VL CDR2 sequence comprising the amino acid sequence AASSLQS (SEQ ID NO: 211); and a VL CDR3 sequence comprising the amino acid sequence QQTVVAPPL (SEQ ID NO: 212).

34. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a combination of a VH CDR1 sequence, a VH CDR2 sequence, a VH CDR3 sequence, a VL CDR1 sequence, a VL CDR2 sequence, and a VL CDR3 sequence selected from the combinations shown in Table 2.

35. The activatable antibody of claim 13, wherein the antibody or antigen-binding fragment thereof that binds Jagged 1 and Jagged 2 comprises a combination of a variable heavy chain region and a variable light chain region from the combinations listed in Table 4.

36. The activatable antibody of claim 13 comprising a light chain amino acid sequence selected from the group consisting of SEQ ID NOs: 74, 132, 134, 136, 138, 140, 142, 144, 146, 180, 182, 184, 186, 188, 190, 192, 194, and 196, and a heavy chain amino acid sequence selected from the group consisting of SEQ ID NOs: 76 and 148.

37. An isolated nucleic acid molecule encoding the antibody of claim 1 or the activatable antibody of claim 13.

38. A vector comprising the isolated nucleic acid molecule of claim 37.

39. A method of producing an antibody or an activatable antibody by culturing a cell under conditions that lead to expression of the antibody or the activatable antibody, wherein the cell comprises the nucleic acid molecule of claim 37.

40. A method of manufacturing an activatable antibody that binds Jagged 1 and Jagged 2 in an activated state, the method comprising:

(a) culturing a cell comprising a nucleic acid construct that encodes the activatable antibody under conditions that lead to expression of the activatable antibody, wherein the activatable antibody comprises a masking moiety (MM), a cleavable moiety (CM), and an antibody or an antigen binding fragment thereof (AB) that specifically binds Jagged 1 and Jagged 2,

and

(b) recovering the activatable antibody.

41. The method of claim 40, wherein the CM is a polypeptide that functions as a substrate for a protease.

42. The method of claim 40, wherein the CM is positioned in the activatable antibody such that, in an uncleaved state, the MM interferes with specific binding of the AB to Jagged 1 and Jagged 2 and in a cleaved state the MM does not interfere or compete with specific binding of the AB to Jagged 1 and Jagged 2

43. Use of the antibody of claim 1 or the activatable antibody of claim 13 in the manufacture of a medicament for treatment of cancer.

44. Use of the antibody of claim 1 or the activatable antibody of claim 13 in the manufacture of a medicament for treatment of a fibrotic disorder.