CLAIMS

1. An antibody binding to human CD38 and encoded by a nucleotide sequence selected from the group consisting of:

(i) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:1 and SEQ ID No:6, respectively;

(ii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:11 and SEQ ID No:16, respectively;

(iii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:21 and SEQ ID No:26, respectively; and

(iv) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions, which are conservative sequence modifications of the sequences as set forth in (i), (ii) or (iii).

2. An antibody binding to human CD38 comprising a V_H CDR3 having the sequence as set forth in SEQ ID No:10.

3. An antibody according to claim 2, comprising a V_L CDR3 having the sequence as set forth in SEQ ID No:5 and a V_H CDR3 having the sequence as set forth in SEQ ID No:10.

4. An antibody according to claim 2, comprising human light chain and human heavy variable regions, wherein the light chain variable region comprises a V_L CDR1 having the sequence as set forth in SEQ ID No:3, a V_L CDR2 having the sequence as set forth in SEQ ID No:4 and a V_L CDR3 having the sequence as set forth in SEQ ID No:5, and the heavy chain variable region comprises a V_H CDR1 having the sequence as set forth in SEQ ID No:8, a V_H CDR2 having the sequence as set forth in SEQ ID No:9 and a V_H CDR3 having the sequence as set forth in SEQ ID No:10.

5. An antibody binding to human CD38, comprising a V_L region having the amino acid sequence as set forth in SEQ ID No:2.

6. An antibody binding to human CD38, comprising a V_L region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence as set forth in SEQ ID No:2.

7. An antibody binding to human CD38, comprising a V_H region having the amino acid sequence as set forth in SEQ ID No:7.

8. An antibody binding to human CD38, comprising a V_H region comprising the amino acid sequence spanning the V_H CDR1 - V_H CDR3 region of SEQ ID No:7.

9. An antibody binding to human CD38, comprising a V_H region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence as set forth in SEQ ID No:7 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:7.

10. An antibody binding to human CD38, comprising a V_H region having 1 to 5, preferably 1 to 3 amino acid substitutions, deletions or additions compared to the sequence as set forth in SEQ ID No:7 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:7.

11. An antibody binding to human CD38, comprising a V_L region as defined in claim 5 and a V_H region as defined in claim 7.

12. An antibody binding to human CD38, comprising a V_H CDR3 having the sequence as set forth in SEQ ID No:20.

13. An antibody according to claim 12, comprising a V_L CDR3 having the sequence as set forth in SEQ ID No:15 and a V_H CDR3 having the sequence as set forth in SEQ ID No:20.

14. An antibody according to claim 12, comprising human light chain and human heavy variable regions, wherein the light chain variable region comprises a V_L CDR1 having the sequence as set forth in SEQ ID No:13, a V_L CDR2 having the sequence as

set forth in SEQ ID No:14 and a V_L CDR3 having the sequence as set forth in SEQ ID No:15, and the heavy chain variable region comprises a V_H CDR1 having the sequence as set forth in SEQ ID No:18, a V_H CDR2 having the sequence as set forth in SEQ ID No:19 and a V_H CDR3 having the sequence as set forth in SEQ ID No:20.

15. An antibody binding to human CD38, comprising a V_L region having the amino acid sequence as set forth in SEQ ID No:12.

16. An antibody binding to human CD38, comprising a V_L region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence according to SEQ ID No:12.

17. An antibody binding to human CD38, comprising a V_H region having the amino acid sequence as set forth in SEQ ID No:17.

18. An antibody binding to human CD38, comprising a V_H region comprising the amino acid sequence spanning the V_H CDR1 - V_H CDR3 region of SEQ ID No:17.

19. An antibody binding to human CD38, comprising a V_H region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence as set forth in SEQ ID No:17 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:17.

20. An antibody binding to human CD38, comprising a V_H region having 1 to 5, preferably 1 to 3 amino acid substitutions, deetions or additions compared to the sequence as set forth in SEQ ID No:17 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:17.

21. An antibody binding to human CD38, comprising a V_L region as defined in claim 15 and a V_H region as defined in claim 17.

22. An antibody binding to human CD38, comprising a V_H CDR3 having the sequence as set forth in SEQ ID No:30.

23. An antibody according to claim 22, comprising a V_L CDR3 having the sequence as set forth in SEQ ID No:25 and a V_H CDR3 having the sequence as set forth in SEQ ID No:30.

24. An antibody according to claim 22, comprising human light chain and human heavy variable regions, wherein the light chain variable region comprises a V_L CDR1 having the sequence as set forth in SEQ ID No:23, a V_L CDR2 having the sequence as set forth in SEQ ID No:24 and a V_L CDR3 having the sequence as set forth in SEQ ID No:25, and the heavy chain variable region comprises a V_H CDR1 having the sequence as set forth in SEQ ID No:28, a V_H CDR2 having the sequence as set forth in SEQ ID No:29 and a V_H CDR3 having the sequence as set forth in SEQ ID No:30.

25. An antibody binding to human CD38, comprising a V_L region having the amino acid sequence as set forth in SEQ ID No:22.

26. An antibody binding to human CD38, comprising a V_L region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence according to SEQ ID No:22.

27. An antibody binding to human CD38, comprising a V_H region having the amino acid sequence as set forth in SEQ ID No:27.

28. An antibody binding to human CD38, comprising a V_H region comprising the amino acid sequence spanning the V_H CDR1 - V_H CDR3 region of SEQ ID No:27.

29. An antibody binding to human CD38, comprising a V_H region having at least about 90%, preferably at least about 95% amino acid sequence identity to the sequence according to SEQ ID No:27 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:27.

30. An antibody binding to human CD38, comprising a V_H region having 1 to 5, preferably 1 to 3 amino acid substitutions, deletions or additions compared to the sequence as set forth in SEQ ID No:27 or to the V_H CDR1 - V_H CDR3 spanning region of SEQ ID No:27.

31. An antibody binding to human CD38, comprising a V_L region as defined in claim 25 and a V_H region as defined in claim 27.

32. A peptide which binds to human CD38 (SEQ ID No:31), and which does not bind to a mutant human CD38, wherein

(i) the serine residue in position 274 has been substituted with a phenylalanine residue (SEQ ID No:34), to the same degree that it binds to human CD38 (SEQ ID No:31);

(ii) the glutamine residue in position 272 has been substituted with an arginine residue (SEQ ID No:33), to the same degree that it binds to human CD38 (SEQ ID No:31); or

(iii) the threonine residue in position 237 has been substituted with an alanine residue (SEQ ID No:32), to the same degree that it binds to human CD38 (SEQ ID No:31).

33. A peptide according to claim 32, wherein the EC_{50} of the binding of the peptide of (i) to a mutant human CD38, when the serine residue in position 274 has been substituted with a phenylalanine residue (SEQ ID No:34), is less than 50%, preferably less than 10%, more preferably less than 5% or even more preferably less than 1% of the EC_{50} of the binding of the peptide to human CD38 (SEQ ID No:31).

34. A peptide according to claim 32, wherein the EC_{50} of the binding of the peptide of (ii) to a mutant human CD38, when the glutamine residue in position 272 has been substituted with an arginine residue (SEQ ID No:33), is less than 50%, preferably less than 10%, more preferably less than 5% or even more preferably less than 1% of the EC_{50} of the binding of the peptide to human CD38 (SEQ ID No:31).

35. A peptide according to claim 32, wherein the EC_{50} of the binding of the peptide of (iii) to a mutant human CD38, when the threonine residue in position 237 has been substituted with an alanine residue (SEQ ID No:32) corresponds to 75% - 125% of the EC_{50} of the binding of the peptide to human CD38 (SEQ ID No:31).

36. A peptide which binds to human CD38 (SEQ ID No:31), wherein the peptide possesses the following binding characteristics: (i) binds to a mutant human CD38, wherein the serine residue in position 274 has been substituted with a phenylalanine residue (SEQ ID No:34), to the same degree that it binds to human CD38 (SEQ ID No:31), (ii) binds to a mutant human CD38, wherein the glutamine residue in position 272 has been substituted with an arginine residue (SEQ ID No:33), to the same degree that it binds to human CD38 (SEQ ID No:31), and (iii) binds to a mutant human CD38, wherein the threonine residue in position 237 has been substituted with an alanine residue (SEQ ID No:32), to the same degree that it binds to human CD38 (SEQ ID No:31).

37. A peptide which binds to human CD38 (SEQ ID No:31), wherein the peptide possesses the following binding characteristics: (i) does not bind to a mutant human CD38, wherein the serine residue in position 274 has been substituted with a phenylalanine residue (SEQ ID No:34), to the same degree that it binds to human CD38 (SEQ ID No:31), (ii) does not bind to a mutant human CD38, wherein the glutamine residue in position 272 has been substituted with an arginine residue (SEQ ID No:33), to the same degree that it binds to human CD38 (SEQ ID No:31), (iii) binds to a mutant human CD38, wherein the threonine residue in position 237 has been substituted with an alanine residue (SEQ ID No:32), to the same degree that it binds to human CD38 (SEQ ID No:31).

38. A peptide according to any one of claims 33, 34 or 35, wherein the EC_{50} is determined by use of an ELISA as described in Example 17 of the specification.

39. A peptide which competes with an antibody according to claim 1 for binding to CD38.

40. A peptide according to claim 39, wherein the competition is determined by use of an ELISA as described in Example 8 or 9 of the specification, wherein competition is defined by a signal of at least 90% as assessed by absorption, or by use of cross-blocking measurements as described in Example 7 of the specification, wherein competition is defined by a signal of at least 90% as assessed by fluorescence.

41. A peptide that specifically binds to a CD38 epitope, which epitope is also specifically bound by an antibody according to claim 1.

42. A peptide that specifically binds to the region SKRNIQFSCKNIYR and the region EKVQTLEAWVIHGG of human CD38 (SEQ ID No:31).

43. A peptide having substantially the same specific binding characteristics for binding human CD38 as an antibody according to claim 1.

44. An antibody or peptide according to any one of claims 1 to 43, wherein said antibody or peptide binds to human CD38, and said antibody or peptide possesses one or more of the following characteristics:

(i) acts as an antagonist of CD38;

(ii) does not induce significant proliferation of peripheral blood mononuclear cells as determined by the method described in Example 18 of the specification;

(iii) does not induce release of significant IL-6 by human monocytes or peripheral blood mononuclear cells as determined by the method described in Example 19 of the specification;

(iv) does not induce release of detectable IFN-γ by human T cells or peripheral blood mononuclear cells as determined by the method described in Example 20 of the specification;

(v) is internalized by CD38 expressing cells; such as internalized by CHO-CD38 cells within 5 to 15 minutes at 37°C by the method as described in Example 12 of the specification;

(vi) induces ADCC; such as with an EC_{50} value of below 15 ng/ml, such as below 10 ng/ml in Daudi-luc cells and with an EC_{50} value of below 75 ng/ml, such as below 50 ng/ml, 30 ng/ml or 10 ng/ml in MM cells as determined by the method described in example 5 of the specification;

(vii) induces CDC in the presence of complement; such as with an EC_{50} value of below 5 µg/ml, such as below 1 µg/ml in daudi-luc or CD38-CHO cells by the method described in Example 6 of the specification;

(viii) inhibits the synthesis of cGDPR;

(ix) inhibits the synthesis of cADPR;

(x) binds to human CD38 with an affinity (K_D) of below 10^{-8} M, such as in the range of from 10^{-8} M to – 10^{-11} M, for example in the range of from 7 x 10^{-9} M to – 10^{-10} M, as determined by surface plasmon resonance as described in Example 20 of the specification.

45. An antibody or peptide according to claim 44, which inhibits the synthesis of cGDPR by at least 25%, preferably at least 30% after 90 minutes at a concentration of 3 µg/ml as determined by the spectophotometric method described in Example 24 of the specification.

46. An antibody or peptide according to claim 44, which inhibits the synthesis of cADPR by at least 25%, preferably at least 30% after 90 minutes at a concentration of 3 µg/ml as determined by the HPLC method described in Munshi et al., J. Biol. Chem. 275, 21566-21571 (2000).

47. An antibody or peptide according to any one of claims 32 to 46, wherein the antibody is a human monoclonal antibody or a peptide derived from a human monoclonal antibody.

48. An antibody according to any one of claims 1 to 31 or 47, characterized in that it is a full length IgG1, IgG2, IgG3, IgG4, IgD, IgA, IgE, or IgM antibody, such as an IgG1 antibody, preferably an IgG1,κ antibody or an IgM antibody, preferably an IgM,κ antibody.

49. An isolated human monoclonal antibody comprising:
(i) a heavy chain variable region amino acid sequence derived from a human Hv1263/3M28 (V_HI) germline sequence and a light chain variable region amino acid sequence derived from a human L15 (VκI) germline sequence, wherein the human antibody binds to human CD38; or
(ii) a heavy chain variable region amino acid sequence derived from a human V_H3-DP-47/V3-23 (V_HIII) germline sequence and a light chain variable region amino acid sequence derived from a human L6 (VκI) germline sequence, wherein the human antibody binds to human CD38.

50. An antibody or peptide according to any one of claims 1 to 49, wherein the antibody or peptide is glycosylated in a eukaryotic cell.

51. An antibody according to any one of claims 1 to 31 or 47 to 49, which is an antibody fragment or a single chain antibody.

52. An antibody or peptide according to any one of claims 1 to 51, further comprising a chelator linker for attaching a radioisotope.

53. An isolated nucleic acid encoding an antibody or peptide according to any one of claims 1 to 52.

54. An expression vector comprising a nucleic acid sequence which encodes an antibody or peptide according to any one of claims 1 to 53.

55. An expression vector comprising a nucleotide sequence selected from the group consisting of:

(i) a V_L nucleotide sequence of SEQ ID No:1,

(ii) a V_H nucleotide sequence of SEQ ID No:6,

(iii) a V_L nucleotide sequence of SEQ ID No:1 and a V_H nucleotide sequence of SEQ ID No:6;

(iv) a V_L nucleotide sequence of SEQ ID No:11;

(v) a V_H nucleotide sequence of SEQ ID No:16;

(vi) a V_L nucleotide sequence of SEQ ID No:11 and a V_H nucleotide sequence of SEQ ID No:16;

(vii) a V_L nucleotide sequence of SEQ ID No:21;

(viii) a V_H nucleotide sequence of SEQ ID No:26; and

(ix) a V_L nucleotide sequence of SEQ ID No:21 and a V_H nucleotide sequence of SEQ ID No:26.

56. An expression vector according to claim 54 or 55, further comprising a nucleotide sequence encoding the constant region of a light chain, a heavy chain or both light and heavy chains of a human antibody.

57. An expression vector according to claim 56, wherein the nucleotide sequence encoding the constant region of a light chain, a heavy chain or both light and heavy chains of a human antibody encodes an IgG1 antibody.

58. A hybridoma which produces a human monoclonal anti-CD38 antibody encoded by human light chain and human heavy chain nucleic acids selected from the group consisting of:

(i) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:1 and SEQ ID No:6, respectively;

(ii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:11 and SEQ ID No:16, respectively;

(iii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:21 and SEQ ID No:26, respectively; and

(iv) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions, which are conservative sequence modifications of the sequences set forth in (i), (ii) or (iii).

59. A hybridoma which produces a human monoclonal anti-CD38 antibody having human heavy chain and light chain variable regions selected from the group consisting of:

(i) the human light chain variable amino acid sequence as set forth in SEQ ID No:2, and the human heavy chain variable amino sequence as set forth in SEQ ID No:7;

(ii) the human light chain variable amino acid sequence as set forth in SEQ ID No:12, and the human heavy chain variable amino sequence as set forth in SEQ ID No:17;

(iii) the human light chain variable amino acid sequence as set forth in SEQ ID No:22, and the human heavy chain variable amino sequence as set forth in SEQ ID No:27; and

(iv) conservative sequences modifications of the human light chain and human heavy chain variable amino acid sequences as set forth in (i), (ii) or (iii).

60. A transfectoma which produces a human monoclonal anti-CD38 antibody encoded by human light chain and human heavy chain nucleic acids selected from the group consisting of:

(i) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:1 and SEQ ID No:6, respectively;

(ii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:11 and SEQ ID No:16, respectively;

(iii) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions as set forth in SEQ ID No:21 and SEQ ID No:26, respectively; and

(iv) human light chain and human heavy chain nucleic acids comprising nucleotide sequences in their variable regions, which are conservative sequence modifications of the sequences set forth in (i), (ii) or (iii).

61. A transfectoma which produces a human monoclonal anti-CD38 antibody having human heavy chain and light chain variable regions selected from the group consisting of:

(i) the human light chain variable amino acid sequence as set forth in SEQ ID No:2, and the human heavy chain variable amino sequence as set forth in SEQ ID No:7;

(ii) the human light chain variable amino acid sequence as set forth in SEQ ID No:12, and the human heavy chain variable amino sequence as set forth in SEQ ID No:17;

(iii) the human light chain variable amino acid sequence as set forth in SEQ ID No:22, and the human heavy chain variable amino sequence as set forth in SEQ ID No:27; and

(iv) conservative sequences modifications of the human light chain and human heavy chain variable amino acid sequences as set forth in (i), (ii) or (iii).

62. A eukaryotic or prokaryotic host cell which produces an antibody or peptide according to any one of claims 1 to 52.

63. A eukaryotic or prokaryotic host cell containing an expression vector according to any one of claims 54 to 57.

64. A transgenic nonhuman animal or plant comprising nucleic acids encoding a human heavy chain and a human light chain, wherein the animal or plant produces a detectable amount of an antibody or peptide according to any one of claims 1 to 52.

65. An immunoconjugate comprising an antibody or peptide according to any one of claims 1 to 52 linked to a cytotoxic agent, a radioisotope, or a drug.

66. An immunoconjugate comprising an antibody or peptide according to any one of claims 1 to 52, wherein the antibody or peptide is a monomeric IgM antibody linked to a cytotoxic agent, a radioisotope, or a drug.

67. A bispecific or multispecific molecule comprising an antibody or peptide according to any one of claims 1 to 52 and a binding specificity for a human effector cell.

68. A bispecific or multispecific molecule comprising an antibody or peptide according to any one of claims 1 to 52 and a binding specificity for CD3, CD4, CD138, IL-15R, membrane bound or receptor bound TNF-α, a human Fc receptor, or membrane bound or receptor bound IL-15.

69. A pharmaceutical composition comprising an antibody or peptide according to any one of claims 1 to 52 or an immunoconjugate according to claim 65 or 66 and a pharmaceutically acceptable carrier.

70. A pharmaceutical composition according to claim 69, comprising one or more further therapeutic agents.

71. An antibody or peptide according to any one of claims 1 to 52, an immunoconjugate according to claim 65 or 66, a pharmaceutical composition according to claim 69 or 70, or an expression vector according to any one of claims 54 to 57, for use in a method of inhibiting growth and/or proliferation of a cell expressing CD38, comprising administration to the cell of the antibody, peptide, immunoconjugate,

pharmaceutical composition, or expression vector, such that the growth and/or proliferation of the cell is inhibited.

72. An antibody or peptide according to any one of claims 1 to 52, an immunoconjugate according to claim 65 or 66, a pharmaceutical composition according to claim 70 or 71, or an expression vector according to any one of claims 54 to 57 for use in a method of preventing and/or treating a disease or disorder involving cells expressing CD38 in a subject, which method comprises administration of a therapeutically effective amount of the antibody, peptide, immunoconjugate, pharmaceutical composition, or expression vector to a subject in need thereof.

73. An antibody, peptide, immunoconjugate, pharmaceutical composition or expression vector for use according to claim 72, wherein the disease or disorder is rheumatoid arthritis or multiple myeloma.

74. An antibody, peptide, immunoconjugate, pharmaceutical composition or expression vector for use according to any one of claims 71 to 73, wherein the method comprises administration of one or more further therapeutic agents to the cell or subject, wherein the one or more therapeutic agents are selected from the group consisting of chemotherapeutic agents, anti-inflammatory agents, and immunosuppressive and/or immunomodulatory agents.

75. An antibody, peptide, immunoconjugate, pharmaceutical composition or expression vector for use according to claim 74, wherein the one or more further therapeutic agents are selected from the group consisting of cisplatin, gefitinib, cetuximab, rituximab, bevacizumab, erlotinib, bortezomib, thalidomide, pamidronate, zoledronic acid, clodronate, risendronate, ibandronate, etidronate, alendronate, tiludronate, arsenic trioxide, lenalidomide, filgrastim, pegfilgrastim, sargramostim, suberoylanilide hydroxamic acid, and SCIO-469.

76. An *in vitro* method for detecting the presence of CD38 antigen, or a cell expressing CD38, in a sample comprising:

a) contacting the sample with an antibody or peptide according to any one of claims 1 to 52 under conditions that allow for formation of a complex between the antibody or peptide and CD38; and

b) detecting the formation of a complex.

77. An *in vivo* method for detecting CD38 antigen, or a cell expressing CD38, in a subject comprising:

a) administering an antibody or peptide according to any one of claims 1 to 52 under conditions that allow for formation of a complex between the antibody or peptide and CD38; and

b) detecting the formed complex.

78. An anti-idiotypic antibody binding to an antibody according to any one of claims 1 to 31, 47 to 49 or 51.

79. Use of an anti-idiotypic antibody according to claim 78 for detecting the level of a antibody according to any one of claims 1 to 31, 47 to 49 or 51 in a sample.

80. Use of an anti-idiotypic antibody according to claim 78 for detecting the level of human monoclonal antibody against CD38 in a sample.

81 The use of an antibody or peptide according to any one of claims 1 to 52, an immunoconjugate according to claim 65 or 66, a pharmaceutical composition according to claim 69 or 70, or an expression vector according to any one of claims 54 to 57 in the manufacture of a medicament for inhibiting growth and/or proliferation of a cell expressing CD38.

82. The use of a therapeutically effective amount of an antibody or peptide according to any one of claims 1 to 52, an immunoconjugate according to claim 65 or 66, a pharmaceutical composition according to claim 70 or 71, or an expression vector according to any one of claims 54 to 57 in the manufacture of a medicament for preventing and/or treating a disease or disorder involving cells expressing CD38 in a subject.

83. The use according to claim 82, wherein the disease or disorder is rheumatoid arthritis or multiple myeloma.

84. The use according to any one of claims 81 to 83, wherein the inhibiting growth and/or proliferation of a cell expressing CD38 or preventing and/or treating a disease or disorder involving cells expressing CD38 in a subject wherein the medicament is to be administered together with one or more further therapeutic agents to the cell or subject, wherein the one or more therapeutic agents are selected from the group consisting of chemotherapeutic agents, anti-inflammatory agents, and immunosuppressive and/or immunomodulatory agents.

85. The use according to claim 84, wherein the one or more further therapeutic agents are selected from the group consisting of cisplatin, gefitinib, cetuximab, rituximab, bevacizumab, erlotinib, bortezomib, thalidomide, pamidronate, zoledronic acid, clodronate, risendronate, ibandronate, etidronate, alendronate, tiludronate, arsenic trioxide, lenalidomide, filgrastim, pegfilgrastim, sargramostim, suberoylanilide hydroxamic acid, and SCIO-469.