

CLAIMS

1. A method of treating a disorder in a mammal that is responsive to TIM-3 inhibition, which method comprises administering an effective amount of the composition comprising (a) the TIM-3-binding agent comprising the immunoglobulin heavy chain polypeptide which comprises the amino acid sequence Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Xaa1 Ala Xaa2 Ser Gly Phe Xaa3 Xaa4 Xaa5 Thr Phe Ser Xaa6 Tyr Xaa7 Met Xaa8 Trp Val Arg Gln Ala Xaa9 Gly Lys Gly Leu Xaa10 Trp Val Ser Xaa11 Ile Ser Xaa12 Gly Gly Xaa13 Tyr Thr Tyr Tyr Gln Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Xaa14 Glu Asp Thr Ala Val Tyr Tyr Cys Xaa15 Ser Xaa16 Xaa17 Xaa18 Xaa19 Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala (SEQ ID NO: 1), wherein

- (a) Xaa1 is deleted or is alanine (Ala),
 - (b) Xaa2 is alanine (Ala), proline (Pro), aspartic acid (Asp), glycine (Gly), threonine (Thr), or valine (Val),
 - (c) the subsequence Xaa3 Xaa4 Xaa5 is deleted or is Thr-Phe-Ile,
 - (d) Xaa6 is serine (Ser), asparagine (Asn), arginine (Arg), or threonine (Thr),
 - (e) Xaa7 is aspartic acid (Asp) or alanine (Ala),
 - (f) Xaa8 is serine (Ser) or threonine (Thr),
 - (g) Xaa9 is proline (Pro) or leucine (Leu),
 - (h) Xaa10 is aspartic acid (Asp) or glutamic acid (Glu),
 - (i) Xaa11 is threonine (Thr) or alanine (Ala),
 - (j) Xaa12 is glycine (Gly) or serine (Ser),
 - (k) Xaa13 is serine (Ser), threonine (Thr), aspartic acid (Asp), glycine (Gly), asparagine (Asn), or lysine (Lys),
 - (l) Xaa14 is alanine (Ala) or valine (Val),
 - (m) Xaa15 is alanine (Ala) or threonine (Thr), and
 - (n) the subsequence Xaa16 Xaa17 Xaa18 Xaa19 is deleted or is Pro-Tyr-Tyr-Ala,
- and/or the immunoglobulin light chain polypeptide which comprises the amino acid sequence Asp Ile Gln Met Thr Xaa1 Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Xaa2 Ser Gln Ser Ile Xaa3 Xaa4 Tyr Leu Asn Trp Tyr Xaa5 Gln Lys Xaa6 Xaa7 Lys Ala Pro Lys Leu Leu Xaa8 Tyr Xaa9 Ala Ser Xaa10 Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe

Ala Xaa11 Tyr Tyr Cys Gln Gln Xaa12 Xaa13 Xaa14 Xaa15 Pro Xaa16 Thr Phe Gly Xaa17
Gly Thr Lys Xaa18 Glu Ile Lys Arg (SEQ ID NO: 45), wherein

- (a) Xaa1 is glutamine (Gln) or histidine (His),
- (b) Xaa2 is alanine (Ala) or threonine (Thr),
- (c) Xaa3 is serine (Ser), arginine (Arg), asparagine (Asn), or threonine (Thr),
- (d) Xaa4 is serine (Ser), arginine (Arg), aspartic acid (Asp), threonine (Thr), or glycine (Gly),
- (e) Xaa5 is glutamine (Gln) or histidine (His),
- (f) Xaa6 is proline (Pro) or alanine (Ala),
- (g) Xaa7 is glycine (Gly), lysine (Lys), or arginine (Arg),
- (h) Xaa8 is isoleucine (Ile) or methionine (Met),
- (i) Xaa9 is alanine (Ala), glycine (Gly), aspartic acid (Asp), threonine (Thr), serine (Ser), valine (Val), or isoleucine (Ile),
- (j) Xaa10 is serine (Ser) or threonine (Thr),
- (k) Xaa11 is valine (Val), methionine (Met), or alanine (Ala)
- (l) Xaa12 is serine (ser) or arginine (Arg),
- (m) Xaa13 is tyrosine (Tyr), histidine (His), phenylalanine (Phe), aspartic acid (Asp), serine (Ser), or asparagine (Asn),
- (n) Xaa14 is serine (Ser) or asparagine (Asn),
- (o) Xaa15 is threonine (Thr), serine (Ser), alanine (Ala), or proline (Pro),
- (p) Xaa16 is leucine (Leu) or histidine (His),
- (q) Xaa17 is glycine (Gly), arginine (Arg), or glutamic acid (Glu), and

Xaa18 is valine (Val) or leucine (Leu), or the vector comprising the isolated nucleic acid sequence encoding the TIM-3-binding agent comprising the immunoglobulin heavy chain polypeptide which comprises the amino acid sequence Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Xaa1 Ala Xaa2 Ser Gly Phe Xaa3 Xaa4 Xaa5 Thr Phe Ser Xaa6 Tyr Xaa7 Met Xaa8 Trp Val Arg Gln Ala Xaa9 Gly Lys Gly Leu Xaa10 Trp Val Ser Xaa11 Ile Ser Xaa12 Gly Gly Xaa13 Tyr Thr Tyr Tyr Gln Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Xaa14 Glu Asp Thr Ala Val Tyr Tyr Cys Xaa15 Ser Xaa16 Xaa17 Xaa18 Xaa19 Met Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala (SEQ ID NO: 1), wherein

- (a) Xaa1 is deleted or is alanine (Ala),

(b) Xaa2 is alanine (Ala), proline (Pro), aspartic acid (Asp), glycine (Gly), threonine (Thr), or valine (Val),

(c) the subsequence Xaa3 Xaa4 Xaa5 is deleted or is Thr-Phe-Ile,

(d) Xaa6 is serine (Ser), asparagine (Asn), arginine (Arg), or threonine (Thr),

(e) Xaa7 is aspartic acid (Asp) or alanine (Ala),

(f) Xaa8 is serine (Ser) or threonine (Thr),

(g) Xaa9 is proline (Pro) or leucine (Leu),

(h) Xaa10 is aspartic acid (Asp) or glutamic acid (Glu),

(i) Xaa11 is threonine (Thr) or alanine (Ala),

(j) Xaa12 is glycine (Gly) or serine (Ser),

(k) Xaa13 is serine (Ser), threonine (Thr), aspartic acid (Asp), glycine (Gly), asparagine (Asn), or lysine (Lys),

(l) Xaa14 is alanine (Ala) or valine (Val),

(m) Xaa15 is alanine (Ala) or threonine (Thr), and

(n) the subsequence Xaa16 Xaa17 Xaa18 Xaa19 is deleted or is Pro-Tyr-Tyr-Ala, and/or the immunoglobulin light chain polypeptide which comprises the amino acid sequence Asp Ile Gln Met Thr Xaa1 Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Xaa2 Ser Gln Ser Ile Xaa3 Xaa4 Tyr Leu Asn Trp Tyr Xaa5 Gln Lys Xaa6 Xaa7 Lys Ala Pro Lys Leu Leu Xaa8 Tyr Xaa9 Ala Ser Xaa10 Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Xaa11 Tyr Tyr Cys Gln Gln Xaa12 Xaa13 Xaa14 Xaa15 Pro Xaa16 Thr Phe Gly Xaa17 Gly Thr Lys Xaa18 Glu Ile Lys Arg (SEQ ID NO: 45), wherein

(a) Xaa1 is glutamine (Gln) or histidine (His),

(b) Xaa2 is alanine (Ala) or threonine (Thr),

(c) Xaa3 is serine (Ser), arginine (Arg), asparagine (Asn), or threonine (Thr),

(d) Xaa4 is serine (Ser), arginine (Arg), aspartic acid (Asp), threonine (Thr), or glycine (Gly),

(e) Xaa5 is glutamine (Gln) or histidine (His),

(f) Xaa6 is proline (Pro) or alanine (Ala),

(g) Xaa7 is glycine (Gly), lysine (Lys), or arginine (Arg),

(h) Xaa8 is isoleucine (Ile) or methionine (Met),

(i) Xaa9 is alanine (Ala), glycine (Gly), aspartic acid (Asp), threonine (Thr), serine (Ser), valine (Val), or isoleucine (Ile),

- (j) Xaa10 is serine (Ser) or threonine (Thr),
- (k) Xaa11 is valine (Val), methionine (Met), or alanine (Ala)
- (l) Xaa12 is serine (Ser) or arginine (Arg),
- (m) Xaa13 is tyrosine (Tyr), histidine (His), phenylalanine (Phe), aspartic acid (Asp), serine (Ser), or asparagine (Asn),
- (n) Xaa14 is serine (Ser) or asparagine (Asn),
- (o) Xaa15 is threonine (Thr), serine (Ser), alanine (Ala), or proline (Pro),
- (p) Xaa16 is leucine (Leu) or histidine (His),
- (q) Xaa17 is glycine (Gly), arginine (Arg), or glutamic acid (Glu), and
Xaa18 is valine (Val) or leucine (Leu), and
- (b) a pharmaceutically acceptable carrier,

to a mammal having a disorder that is responsive to TIM-3 inhibition, whereupon the disorder is treated in the mammal.