

What is claimed is:

1. Use of an anti- α v β 8 integrin antibody or an antigen binding fragment thereof in the manufacture of a medicament for treating kidney fibrosis in a subject having kidney disease.
2. Use of an anti- α v β 8 integrin antibody or an antigen binding fragment thereof in the
5 manufacture of a medicament for reducing or attenuating kidney fibrosis in a subject having kidney disease.
3. Use of an anti- α v β 8 integrin antibody or an antigen binding fragment thereof in the manufacture of a medicament for abrogating the activity of α v β 8 integrin associated with kidney fibrosis.
- 10 4. Use of an anti- α v β 8 integrin antibody or an antigen binding fragment thereof in the manufacture of a medicament for treating kidney fibrosis by blocking the activation of TGF- β from its latent form in kidney cells and tissue.
5. Use of an anti- α v β 8 integrin antibody or an antigen binding fragment thereof in the manufacture of a medicament for treating kidney damage characterized by an increase in plasma
15 creatinine and/or urinary protein excretion levels, wherein the anti- α v β 8 integrin antibody or an antigen binding fragment thereof abrogates the plasma creatinine and/or urinary protein excretion levels in the subject.
6. The use of any one of claims 3-5, wherein the subject has kidney disease.
7. The use of any one of claims 1-6, wherein the kidney disease is selected from diabetic
20 nephropathy (DN), chronic kidney disease (CKD), acute kidney disease, hypertension-associated kidney disease, hyperglycemia-associated kidney disease, renal fibrosis, inflammation-associated kidney disease, end stage renal disease (ESRD), autoimmune-associated kidney fibrosis (for example, lupus nephritis) and fibrosis post-kidney transplant.
8. The use of claim 7, wherein the kidney disease is CKD.

9. The use of any one of claims 1-8, wherein the antibody or an antigen binding fragment thereof binds to $\alpha\text{v}\beta 8$ integrin expressed on kidney cells and/or tissue and blocks the activation of TGF- β from its latent form in the kidney cell and/or tissue.

10. Use of a detectably labeled anti- $\alpha\text{v}\beta 8$ integrin antibody or an antigen binding fragment thereof in the manufacture of an article for detecting kidney fibrosis in kidney tissue.

11. The use of any one of claims 1-10, wherein the anti- $\alpha\text{v}\beta 8$ integrin antibody, or an antigen-binding fragment thereof, comprises:

(a) a heavy chain variable region complementarity determining region 1 (CDR1) comprising the amino acid sequence:

RYWMS;

(b) a heavy chain variable region complementarity determining region 2 (CDR2) CDR2 comprising the amino acid sequence:

EINPDSSTINYTSSL; and

(c) a heavy chain variable region complementarity determining region 3 (CDR3) CDR3 comprising the amino acid sequence:

LITTEDY; and

(d) a light chain variable region CDR1 comprising the amino acid sequence: KASQDINSYLS;

(e) a light chain variable region CDR2 comprising the amino acid sequence:

YANRLVD; and

(f) a light chain variable region CDR3 comprising the amino acid sequence: LQYDEFPYT.

12. The use of claim 11, wherein the anti- $\alpha\text{v}\beta 8$ integrin antibody, or an antigen-binding fragment thereof, comprises a heavy chain variable region (V_H) amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCA VSGFVFSRYWMSWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDN AKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTTVTVSS;

and

a light chain variable region (V_L) amino acid sequence:

DIQLTQSPSSLSASVGDRVTITCKASQDINSYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDEFPTYTFGGGTKVEIK.

13. The use of any one of claims 1-10, wherein the anti- $\alpha\text{v}\beta 8$ integrin antibody, or an antigen-binding fragment thereof, comprises:

- 5 (a) a heavy chain variable region CDR1 comprising the amino acid sequence:
RSWIS;
- (b) a heavy chain variable region CDR2 comprising the amino acid sequence:
EINPDSSTINYTSSL; and
- 10 (c) a heavy chain variable region CDR3 comprising the amino acid sequence:
LITTEDY; and
- (d) a light chain variable region CDR1 comprising the amino acid sequence:
KASQDINKYLS;
- (e) a light chain variable region CDR2 comprising the amino acid sequence:
YANRLVD; and
- 15 (f) a light chain variable region CDR3 comprising the amino acid sequence:
LQYDVFPYT.

14. The use of claim 13, wherein the anti- $\alpha\text{v}\beta 8$ integrin antibody, or an antigen-binding fragment thereof, comprises a heavy chain variable region (V_H) amino acid sequence:

20 EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRSWISWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWQGQTTVTVSS and
a light chain variable region (V_L) amino acid sequence:

DIQLTQSPSSLSASVGDRVTITCKASQDINKYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDVFPPTYTFGGGTKVEIK.

15. The use of any one of claims 1-14, wherein the antibody, or an antigen binding fragment
25 thereof, attenuates or abrogates fibrosis associated with increased expression of $\alpha\text{v}\beta 8$ integrin in podocytes and interstitial tubule cells in kidney tissue of the subject with kidney disease.

16. The use of any one of claims 1-9, or 11-15, wherein the antibody or an antigen binding fragment thereof, is to be administered to the subject in combination with an adjunct therapeutic agent or treatment for kidney disease.

17. The use of claim 16, wherein the antibody or an antigen binding fragment thereof, is to be administered to the subject prior to, at the same time as, or after the adjunct therapeutic agent or treatment is to be administered.

18. An anti- α v β 8 integrin antibody, or an antigen binding fragment thereof, comprising:

- (a) a heavy chain variable region CDR1 comprising the amino acid sequence:
RYWMS;
- (b) a heavy chain variable region CDR2 comprising the amino acid sequence:
EINPDSSTINYTSSL; and
- (c) a heavy chain variable region CDR3 comprising the amino acid sequence:
LITTEDY; and
- (d) a light chain variable region CDR1 comprising the amino acid sequence:
KASQDINSYLS;
- (e) a light chain variable region CDR2 comprising the amino acid sequence:
YANRLVD; and
- (f) a light chain variable region CDR3 comprising the amino acid sequence:
LQYDEFPYT.

19. The anti- α v β 8 integrin antibody or an antigen binding fragment thereof of claim 18, comprising a heavy chain variable region (V_H) amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRYWMSWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTTVTVSS;
and

a light chain variable region (V_L) amino acid sequence:

DIQLTQSPSSLSASVGDRVTITCKASQDINSYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDEFPYTFGGGTKVEIK.

20. An anti- α v β 8 integrin antibody or an antigen binding fragment thereof, comprising:

- (a) a heavy chain variable region CDR1 comprising the amino acid sequence
RSWIS;
- (b) a heavy chain variable region CDR2 comprising the amino acid sequence
EINPDSSTINYTSSL;

- (c) a heavy chain variable region CDR3 comprising the amino acid sequence
LITTEDY; and
- (d) a light chain variable region CDR1 comprising the amino acid sequence
KASQDINKYLS;
- 5 (e) a light chain variable region CDR2 comprising the amino acid sequence
YANRLVD; and
- (f) a light chain variable region CDR3 comprising the amino acid sequence
LQYDVFPYT.

21. The anti- $\alpha\text{v}\beta 8$ integrin antibody or an antigen binding fragment thereof of claim 20,
10 comprising a heavy chain variable region (V_H) amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRSWISWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTTVTVSS and
a light chain variable region (V_L) amino acid sequence:
DIQLTQSPSSLSASVGDRVTITCKASQDINKYLSWFQQKPGKAPKSLIYYANRLVDGVP
15 SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDVFPYTFGGGTKVEIK.

22. An anti- $\alpha\text{v}\beta 8$ integrin antibody or an antigen binding fragment thereof that competes for
binding to $\alpha\text{v}\beta 8$ integrin with the antibody or an antigen binding fragment thereof of any one of
claims 18-21.

23. The antibody or an antigen binding fragment thereof of any one of claims 18-22, for use
20 in a method of treating kidney fibrosis, wherein said antibody or an antigen binding fragment
thereof specifically binds to $\alpha\text{v}\beta 8$ integrin, thereby treating kidney fibrosis.

24. The antibody or an antigen-binding fragment thereof of claim 23, wherein said antibody
or an antigen-binding fragment thereof specifically binds to $\alpha\text{v}\beta 8$ integrin expressed on fibrotic
kidney cells and tissue and blocks binding of $\alpha\text{v}\beta 8$ integrin to latent TGF- β , thereby abrogating
25 the activity of $\alpha\text{v}\beta 8$ integrin associated with kidney fibrosis to treat kidney disease.

25. A polynucleotide encoding the antibody or an antigen binding fragment thereof of claim
18 or claim 19.

26. A polynucleotide encoding the antibody or an antigen binding fragment thereof of claim 20 or claim 21.

27. The polynucleotide of claim 26, wherein the V_H region coding sequence comprises nucleic acid sequence:

5 gaggtgcagctggtggaaagcggcggaggactggtgcagcctggcggcagcctgagactgagct
gcgccgtgtccggcttcgtgttcagccggagctggatcagctgggtccgcccaggccccagggaa
gggcctggaatggatcggcgagatcaaccccgacagcagcaccatcaactacaccagcagcctg
aaggaccggttcaccatcagccgggacaacgccaagaacagcctgtacctgcagatgaacagcc
10 tgcggggccgaggacaccgccgtgtactactgcgccatcctcatcaccaccgaggactactgggg
ccagggcaccaccgtgaccgtgtcctct;

and the V_L region coding sequence comprises nucleic acid sequence:

gacatccagctgacccagagccccagcagcctgagcgccagcgtgggcgacagagtgaccatca
catgcaaggccagccaggacatcaacaagtacctgagctgggtccagcagaagccccggcaaggc
15 ccccaagagcctgatctactacgccaaccggctggtggacggcgtgccagcagattttctggc
agcggcagcggcaccgacttcaccctgaccatcagcagcctgcagcccaggacttcgccacct
actactgcctgcagtacgacgtgttcccctacaccttcggcggaggcaccaaggtggaaatcaa
g.

28. An expression vector which comprises the polynucleotide of any one of claims 25-27.

29. The expression vector of claim 28, which is a prokaryotic, eukaryotic, or mammalian
20 expression vector.

30. A cell comprising the expression vector of claim 28 or claim 29.

31. The cell of claim 30, which is a prokaryotic, a eukaryotic, or a mammalian host cell.

32. A pharmaceutical composition comprising the antibody or an antigen-binding fragment
thereof of any one of claims 18-24, and a pharmaceutically acceptable carrier, excipient, or
25 diluent.

33. A pharmaceutical composition comprising the polynucleotide of any one of claims 25-27,
and a pharmaceutically acceptable carrier, excipient, or diluent.

34. A kit comprising the antibody or an antigen binding fragment thereof that specifically
binds to $\alpha\text{v}\beta 8$ integrin of any one of claims 18-24, or a pharmaceutical composition comprising
30 the antibody or the antigen binding fragment thereof.