

What is claimed is:

1. A method of treating kidney fibrosis in a subject having kidney disease, the method comprising administering to the subject an effective amount of an anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment thereof, thereby treating kidney fibrosis.
- 5 2. A method of reducing or attenuating kidney fibrosis in a subject having kidney disease, the method comprising administering to a subject in need thereof an effective amount of an anti- $\alpha\beta 8$ integrin antibody or an antigen-binding fragment thereof, thereby reducing or attenuating fibrosis in the kidney.
3. A method of abrogating the activity of $\alpha\beta 8$ integrin associated with kidney fibrosis, the
10 method comprising administering to a subject in need thereof an effective amount of an anti- $\alpha\beta 8$ integrin antibody or an antigen-binding fragment thereof, thereby abrogating the activity of $\alpha\beta 8$ integrin associated with kidney fibrosis.
4. A method of treating kidney fibrosis by blocking the activation of TGF- β from its latent form in kidney cells and tissue, the method comprising administering to a subject in need thereof
15 an effective amount of an anti- $\alpha\beta 8$ integrin antibody or an antigen-binding fragment thereof, thereby treating the kidney fibrosis.
5. A method of treating kidney damage characterized by an increase in plasma creatinine and/or urinary protein excretion levels, the method comprising administering to a subject in need thereof an effective amount of an anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment
20 thereof, wherein said administration of the anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment thereof abrogates the plasma creatinine and/or urinary protein excretion levels in the subject, thereby treating kidney damage.
6. The method of any one of claims 3-5, wherein the subject has kidney disease.
7. The method of any one of claims 1-6, wherein the kidney disease is selected from
25 diabetic 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 method of claim 7, wherein the kidney disease is CKD.
9. The method of any one of claims 1-8, wherein the antibody or an antigen binding
5 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. A method of detecting kidney fibrosis in kidney tissue, the method comprising contacting kidney tissue with an effective amount of a detectably labeled anti- $\alpha\text{v}\beta 8$ integrin antibody or an antigen binding fragment thereof, thereby detecting the binding of the anti- $\alpha\text{v}\beta 8$ integrin
10 antibody to $\alpha\text{v}\beta 8$ integrin in the kidney tissue.
11. The method 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:
15 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)
20 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:
25 YANRLVD; and
- (f) a light chain variable region CDR3 comprising the amino acid sequence:
LQYDEFPTY.

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

EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRYWMSWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTITVTVSS;

5 and

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

DIQLTQSPSSLSASVGDRVTITCKASQDINSYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQYDEFPYTFGGGTKVEIK.

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

(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

15 (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:

20 YANRLVD; and

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

LQYDVFPYT.

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

25 EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRSWISWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTITVTVSS and

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

DIQLTQSPSSLSASVGDRVTITCKASQDINKYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCLQYDVFPYTFGGGTKVEIK.

15. The method of any one of claims 1-14, wherein the antibody, or an antigen binding fragment 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.
- 5 16. The method of any one of claims 1-9, or 11-15, wherein the antibody or an antigen binding fragment thereof, is administered to the subject in combination with an adjunct therapeutic agent or treatment for kidney disease.
17. The method of claim 16, wherein the antibody or an antigen binding fragment thereof, is administered to the subject prior to, at the same time as, or after the administration of the adjunct
10 therapeutic agent or treatment.
18. An anti- $\alpha\text{v}\beta 8$ 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:
15 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;
 - 20 (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- $\alpha\text{v}\beta 8$ integrin antibody or an antigen binding fragment thereof of claim 18,
25 comprising a heavy chain variable region (V_H) amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRYWMSWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTITVTVSS;
and
a light chain variable region (V_L) amino acid sequence:

DIQLTQSPSSLSASVGDRVTITCKASQDINSYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDFPPTFGGGTKVEIK.

20. An anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment thereof, comprising:
- (a) a heavy chain variable region CDR1 comprising the amino acid sequence
5 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
 - 10 (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.
21. The anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment thereof of claim 20, comprising a heavy chain variable region (V_H) amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGFVFSRSWISWVRQAPGKGLEWIGEINPDSSTIN
YTSSLKDRFTISRDNKNSLYLQMNSLRAEDTAVYYCAILITTEDYWGQGTTVTVSS and
20 a light chain variable region (V_L) amino acid sequence:
DIQLTQSPSSLSASVGDRVTITCKASQDINKYLSWFQQKPGKAPKSLIYYANRLVDGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQYDVFPPTFGGGTKVEIK.
22. An anti- $\alpha\beta 8$ integrin antibody or an antigen binding fragment thereof that competes for binding to $\alpha\beta 8$ integrin with the antibody or an antigen binding fragment thereof of any one of
25 claims 18-21.
23. The antibody or an antigen binding fragment thereof of any one of claims 18-22, for use in a method of treating kidney fibrosis, wherein said antibody or an antigen binding fragment thereof specifically binds to $\alpha\beta 8$ 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 the activity of $\alpha\text{v}\beta 8$ integrin associated with kidney fibrosis to treat kidney disease.

5 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.

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

gaggtgcagctggtggaaagcggcggaggactggtgcagcctggcggcagcctgagactgagct
gcgccgtgtccggcttcgtgttcagccggagctggatcagctgggtccgccaggccccaggaa
gggcttggaaatggatcggcgagatcaaccccgacagcagcaccatcaactacaccagcagcctg
aaggaccggttcaccatcagccgggacaacgccaagaacagcctgtacctgcagatgaacagcc
15 tgcggggccgaggacaccgccgtgtactactgcgccatcctcatcaccaccgaggactactgggg
ccagggcaccaccgtgaccgtgtcctct;

and the V_L region coding sequence comprises nucleic acid sequence:

gacatccagctgaccagagccccagcagcctgagcgccagcgtgggcgacagagtgaccatca
catgcaaggccagccaggacatcaacaagtacctgagctgggtccagcagaagcccggaaggc
20 cccaagagcctgatctactacgccaaccggctggtggacggcgtgccagcagattttctggc
agcggcagcggcaccgacttcaccctgaccatcagcagcctgcagcccaggacttcgccacct
actactgcctgcagtacgacgtgttcccctacaccttcggcggaggcaccaaggtggaaatcaa
g.

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

25 29. The expression vector of claim 28, which is a prokaryotic, eukaryotic, or mammalian 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 diluent.
33. A pharmaceutical composition comprising the polynucleotide of any one of claims 25-27,
5 and a pharmaceutically acceptable carrier, excipient, or diluent.
34. A kit comprising the antibody or an antigen binding fragment thereof that specifically binds to $\alpha v \beta 8$ integrin of any one of claims 18-24, or a pharmaceutical composition comprising the antibody or the antigen binding fragment thereof.