WO2006/055809 discloses the activity of VEGFR1 antibodies in multiple cancer xenograft models. Activity against certain non-neoplastic, angiogenic diseases, such as insulin-dependent diabetes mellitus and autoimmune nephritis, were also disclosed. However, to date, no antibody targeting VEGFR1 has been taught or suggested for therapeutic use for diabetic nephropathy or other forms of progressive CKD.

There remains a need to provide alternative methods to treat CKD. In particular, there remains a need to provide methods to treat diabetic nephropathy.

In one aspect, the present disclosure provides use of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for the treatment of chronic kidney disease.

In another aspect, the present disclosure provides use of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing proteinurea.

In another aspect, the present disclosure provides use of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of

RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing albuminuria.

In another aspect, the present disclosure provides use of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing the loss of glomerular filtration rate reflected by an increase in serum creatinine.

In another aspect, the present disclosure provides use of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for protecting against renal histopathological lesions.

In another aspect, the present disclosure provides a VEGFR1 antibody for use in the treatment of chronic kidney disease, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is

the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

In another aspect, the present disclosure provides a VEGFR1 antibody for use in decreasing proteinuria, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

In another aspect, the present disclosure provides a VEGFR1 antibody for use in decreasing albuminuria, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

In another aspect, the present disclosure provides a VEGFR1 antibody for use in decreasing the loss of glomerular filtration rate reflected by an increase in serum creatinine, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of

VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

In another aspect, the present disclosure provides a VEGFR1 antibody for use in protecting against renal histopathological lesions, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

Accordingly, the present invention provides a method of treating chronic kidney disease in a patient, comprising administering to the patient an effective amount of a VEGFR1 antibody. In another embodiment, the present invention provides a method of treating chronic kidney disease in a patient, comprising administering to the patient an effective amount of a VEGFR1 antibody, wherein the chronic kidney disease is caused by diabetes mellitus. More particularly, the methods of the present invention provide for a patient at stage 3 or stage 4 of chronic kidney disease.

In an embodiment, the present invention provides a method of treating chronic kidney disease in a patient, comprising administering to a patient in need thereof, an effective amount of a VEGFR1 antibody, wherein the chronic kidney disease is diabetic nephropathy. In another embodiment, the present invention provides a method of treating chronic kidney disease in a patient, comprising administering to a patient in need thereof, an effective amount of a VEGFR1 antibody, wherein the chronic kidney disease is focal segmental glomerulosclerosis. In an embodiment, the present invention provides a method of treating chronic kidney disease in a patient, comprising administering to a patient in need thereof, an effective amount of a VEGFR1 antibody, wherein the chronic kidney disease is nephrotic syndrome.

In an embodiment, the present invention provides a method of decreasing proteinuria in a patient, comprising administering to a patient in need thereof, an effective amount of a VEGFR1 antibody. In a further embodiment, the present invention provides a method of decreasing proteinuria in a patient, comprising administering to a patient in need thereof, an effective amount of a VEGFR1 antibody, wherein the proteinuria is caused by chronic kidney disease. In a further embodiment, the present invention

WE CLAIM:

1. Use~~A method of treating chronic kidney disease in a patient, comprising administering to a patient in need thereof, an effective amount~~ of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for the treatment of chronic kidney disease.

2. The ~~method~~ use according to Claim 1, wherein the chronic kidney disease is caused by diabetes mellitus.

3. The ~~method~~ use according to Claim 1 or 2, wherein the patient is at stage 3 or stage 4 of chronic kidney disease.

4. The ~~method~~ use according to any one of Claims 1-3, wherein the chronic kidney disease is diabetic nephropathy or focal segmental glomerulosclerosis.

5. Use ~~A method of decreasing proteinuria in a patient, comprising administering to a patient in need thereof, an effective amount~~ of a VEGFR1 antibody,

wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing proteinurea.

6. The ~~method~~ use according to Claim 5, wherein the proteinuria is caused by diabetic nephropathy.

7. Use ~~A method of decreasing albuminuria in a patient, comprising administering to a patient in need thereof, an effective amount~~ of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing albuminuria.

8. The ~~method~~ use according to Claim 7, wherein the albuminuria is caused by diabetic nephropathy.

9. Use ~~A method of decreasing the loss of glomerular filtration rate reflected by an increase in serum creatinine in a patient, comprising administering to a patient in need thereof, an effective amount~~ of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for decreasing the loss of glomerular filtration rate reflected by an increase in serum creatinine.

10. Use ~~A method of protecting against renal histopathological lesions in a patient, comprising administering to a patient in need thereof, an effective amount~~ of a VEGFR1 antibody, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO:

3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4) in the manufacture of a medicament for protecting against renal histopathological lesions.

11. The ~~method~~ use according to any one of Claims 1-10, wherein the VEGFR1 antibody has a K_D for VEGFR1 of less than 80 pM as determined by surface plasmon resonance.

12. The ~~method~~ use according to any one of Claims 1-11, wherein the VEGFR1 antibody neutralizes VEGF-A binding *in vitro* to VEGFR1 with an IC_{50} less than 2.0 nM.

13. The ~~method~~ use according to any one of Claims 1-12, wherein the VEGFR1 antibody neutralizes PlGF binding *in vitro* to VEGFR1 with an IC_{50} less than 2.0 nM.

14. The ~~method~~ use according to any one of Claims 1-13, wherein the VEGFR1 antibody comprises a LCVR that is the polypeptide of SEQ ID NO: 11, and a HCVR that is the polypeptide of SEQ ID NO: 5.

15. The ~~method~~ use according to any one of Claims 1-14, wherein the VEGFR1 antibody comprises a light chain (LC) and a heavy chain (HC), wherein the LC is the polypeptide of SEQ ID NO: 12, and the HC is the polypeptide of SEQ ID NO: 6.

16. The ~~method~~ use according to any one of Claims 1-14, wherein the VEGFR1 antibody comprises a light chain (LC) and a heavy chain (HC), wherein the LC is the polypeptide of SEQ ID NO: 12, and the HC is the polypeptide of SEQ ID NO: 7.

17. The ~~method~~ use according to any one of Claims 1-15, wherein the VEGFR1 antibody comprises two light chains and two heavy chains, wherein each light chain is the polypeptide of SEQ ID NO: 12, and each heavy chain is the polypeptide of SEQ ID NO: 6.

18. The ~~method~~ use according to any one of Claims 1-14 or 16, wherein the VEGFR1 antibody comprises two light chains and two heavy chains, wherein each light chain is the polypeptide of SEQ ID NO: 12, and each heavy chain is the polypeptide of SEQ ID NO: 7.

19. A VEGFR1 antibody for use in the treatment of chronic kidney disease, wherein the VEGFR1 antibody is an antibody comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises the complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3, and the HCVR comprises the CDRs HCDR1, HCDR2, and HCDR3, wherein the LCDR1 is the polypeptide of RASQSVSSSYLA (SEQ ID NO: 8), the LCDR2 is the polypeptide of GASSRAT (SEQ ID NO: 9), the LCDR3 is the polypeptide of QQYGSSPLT (SEQ ID NO: 10), the HCDR1 is the polypeptide of GFAFSSYGMH (SEQ ID NO: 2), the HCDR2 is the polypeptide of VIWYDGSNKYYADSVRG (SEQ ID NO: 3), and the HCDR3 is the polypeptide of DHYGSGVHHYFYYGLDV (SEQ ID NO: 4).

20. A VEGFR1 antibody for use according to Claim 19, wherein the chronic kidney disease is caused by diabetes mellitus.

21. A VEGFR1 antibody for use according to Claim 19 or 20, wherein the chronic kidney disease is at stage 3 or stage 4.