complex deposition in the glomerular mesangium. *See, e.g.,* Lai, et al., Nature Reviews Disease Primers, 2, pp.16001, 2016. Definitive diagnosis requires kidney biopsy and demonstration of mesangial IgA deposition by immunofluorescence microscopy. Recent advances in the understanding of the initiating events triggering IgA nephropathy have revealed that an aberrant mucosal immune response stimulates the production of galactose deficient IgA1 which is recognized as an autoantigen by circulating antiglycan autoantibodies. Immune recognition results in the formation of nephritogenic immune complexes that deposit in the kidney and activate mesangial cells. Activated mesangial cells proliferate and produce excess amounts of extracellular matrix components, cytokines and chemokines. *See, e.g.,* Suzuki, et al., J. Am. Soc. Nephrol., Vol. 22, pp. 1795-1803 (2011). Up to 40% of patients with biopsy-proven IgA nephropathy progress to end stage kidney disease at some point during long term follow up. The role of ET-1 or the ETA receptor in mesangial cell activation has not been previously reported and atrasentan has not been previously tested in IgA nephropathy. As further described herein, atrasentan can be administered at an efficacious dose with acceptable toxicity, and has the appropriate selectivity to minimize undesired side effects while still treating the underlying IgAN and improving subjects' quality of life. Some examples provide a method of inhibiting mesangial cell activation in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to the subject; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV/AIDS, or acute kidney failure.

[005] Some examples provide a method of inhibiting PDGF signaling (e.g., decreasing the activity and/or expression of one or more of PIK3R1, PDGFRA, NFKBIA, PIK3CG, PLA2G4A, TIAM1, PDGFB, NFKB1, and MAP3K1) in a mesangial cell in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to the subject; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV/AIDS, or acute kidney failure.

[006] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV/AIDS, or acute kidney failure.

[007] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically

acceptable salt thereof, to a subject in need thereof; wherein the subject does not have one or more of diabetic nephropathy, HIV/AIDS, or acute kidney failure.

[008] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject does not suffer from one or more of diabetic nephropathy, HIV/AIDS, or acute kidney failure.

[009] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV/AIDS, prostate cancer, or acute kidney failure.

[0010] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV-related nephropathy, prostate cancer, or acute kidney failure.

[0011] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has not been previously diagnosed with one or more of diabetic nephropathy, HIV-related nephropathy, or acute kidney failure.

[0012] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject is not being treated for one or more of diabetic nephropathy, HIV-related nephropathy, or acute kidney failure.

[0013] Some examples provide a method of treating IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has been determined to have controlled serum glucose levels; and wherein the subject has not been diagnosed with one or more of HIV-related nephropathy or acute kidney failure.

[0014] Some examples provide a method of decreasing renal inflammation and/or fibrosis in a subject having IgA nephropathy, comprising administering a therapeutically

effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0015] Some examples provide a method of decreasing the occurrence of hematuria in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0016] Some examples provide a method of stabilizing eGFR in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0017] Some examples provide a method of decreasing the number of IgA-nephropathy associated disease flares in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0018] Some examples provide a method of delaying the onset of ESRD in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0019] Some examples provide a method of decreasing proteinuria in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

[0020] Some examples provide a method of decreasing fatigue in a subject having IgA nephropathy, comprising administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to a subject in need thereof; wherein the subject has been determined not to suffer from one or more of diabetic nephropathy, HIV-related nephropathy, prostate cancer, or acute kidney failure.

[0021] Some examples provide a method of inhibiting mesangial cell activation, comprising contacting a mesangial cell with an effective amount of atrasentan, or a pharmaceutically acceptable salt thereof.

[0022] Some examples provide a method of reducing activation of a mesangial cell in contact with an IgA immune complex, comprising contacting a mesangial cell with an effective amount of atrasentan, or a pharmaceutically acceptable salt thereof.

[0023] Some examples provide a method of treating IgA nephropathy in a subject in need thereof, comprising: a) determining that the subject has elevated serum Gd-IgA1 levels; and b) administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to the subject

[0024] Some examples provide a method of treating IgA nephropathy in a subject in need thereof, comprising: a) determining that the subject has elevated levels of mesangial activation; and b) administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to the subject.

[0025] Some examples provide a method of treating IgA nephropathy in a subject in need thereof, comprising: a) determining that the subject has elevated levels of IgA-immune complexes in the kidney; and b) administering a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, to the subject.

[0025a] In one aspect, the present disclosure provides use of a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving kidney function in a subject in need thereof; wherein the subject has been previously diagnosed with IgA nephropathy; and wherein the diagnosis of IgA nephropathy comprises a kidney biopsy, detecting anti-glycan antibodies, detecting deposition of IgA-immune complexes in the kidney, or a combination of any of the foregoing.

BRIEF DESCRIPTION OF THE FIGURES

[0026] Figure 1A illustrates that treatment with atrasentan reduces the proliferation of primary human mesangial cells exposed to immune complexes derived from subjects with IgAN.

[0027] Figure 1B illustrates the content of galactose-deficient (Gd)-IgA and total IgA following purification of immune complexes from IgAN or healthy control serum.

[0028] Figure 2A illustrates the decrease in proliferation (after 48 hours) of primary human mesangial cells stimulated with endothelin 1 (ET-1) upon treatment with increasing concentrations of atrasentan shown in log scale, demonstrating an IC_{50} of about 5.1 nM.

[0029] Figure 2B illustrates the decrease in proliferation (after 72 hours) of primary human mesangial cells stimulated with endothelin 1 (ET-1) upon treatment with increasing concentrations of atrasentan shown in log scale, demonstrating an IC_{50} of about 50.8 nM.

[0030] Figure 3A illustrates the increase in IL-6 production by primary human mesangial cells exposed to ET-1 over 48 hours (about a 6-fold increase)and the decrease in IL-6 levels upon treatment with increasing concentrations of atrasentan shown in log scale, demonstrating an IC_{50} of about 1 nM.

[0031] Figure 3B illustrates the increase in IL-6 production by primary human mesangial cells exposed to ET-1 over 72 hours (about a 2.2-fold increase) and the decrease in IL-6 levels upon treatment with increasing concentrations of atrasentan shown in log scale, demonstrating an IC_{50} of about 1 nM.

[0032] Figure 4 illustrates UACR levels in g-ddY mice, at baseline, prior to atrasentan administration, and following approximately 5 days of treatment with atrasentan at 0 (control), 10, 20 or 30 mg/kg/day in the drinking water. (*$P < 0.05$ compared to baseline levels, paired t-test).

WHAT IS CLAIMED:

1. Use of a therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for improving kidney function in a subject in need thereof;

wherein the subject has been previously diagnosed with IgA nephropathy; and

wherein the diagnosis of IgA nephropathy comprises a kidney biopsy, detecting anti-glycan antibodies, detecting deposition of IgA-immune complexes in the kidney, or a combination of any of the foregoing.

2. The use of Claim 1, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.20 mg to about 1.5 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

3. The use of Claim 2, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

4. The use of Claim 3, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.40 mg to about 0.85 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

5. The use of Claim 4, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is about 0.75 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

6. The use of Claim 1, wherein the atrasentan is to be administered as a pharmaceutically acceptable salt.

7. The use of Claim 6, wherein the atrasentan is to be administered as atrasentan hydrochloride or atrasentan mandelate.

8. The use of Claim 7, wherein the atrasentan is to be administered as atrasentan hydrochloride.

9. The use of Claim 7, wherein the atrasentan is to be administered as atrasentan mandelate.

10. The use of Claim 1, wherein the atrasentan is to be administered as the free base.

11. The use of Claim 1, wherein the subject is excreting an average of about 0.5 grams or more of protein in the urine per day for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

12. The use of Claim 11, wherein the subject is excreting an average of about 0.3 grams to 2.0 grams of protein in the urine per day for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

13. The use of Claim 11, wherein the subject is excreting an average of about 0.5 grams to 1.5 grams of protein in the urine per day for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

14. The use of Claim 11, wherein the subject is excreting an average of about 0.75 grams to 1.5 grams of protein in the urine per day for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

15. The use of Claim 1, wherein the subject has an average eGFR of about 20 to about 90 mL/min/1.73m^2 for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

16. The use of Claim 15, wherein the subject has an average eGFR of about 30 to about 90 mL/min/1.73m^2 for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

17. The use of Claim 15, wherein the subject has an average eGFR of about 20 to about 60 mL/min/1.73m^2 for at least about 3 months prior to the first administration of atrasentan, or a pharmaceutically acceptable salt thereof.

18. The use of Claim 11, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.20 mg to about 1.5 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

19. The use of Claim 18, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

20. The use of Claim 19, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.40 mg to about 0.85 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

21. The use of Claim 20, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is about 0.75 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

22. The use of Claim 18, wherein the atrasentan is to be administered as a pharmaceutically acceptable salt.

23. The use of Claim 22, wherein the atrasentan is to be administered as atrasentan hydrochloride or atrasentan mandelate.

24. The use of Claim 18, wherein the atrasentan is to be administered as the free base.

25. The use of Claim 15, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.20 mg to about 1.5 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

26. The use of Claim 25, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.25 mg to about 1.25 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

27. The use of Claim 26, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is from about 0.40 mg to about 0.85 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

28. The use of Claim 27, wherein the therapeutically effective amount of atrasentan, or a pharmaceutically acceptable salt thereof, is about 0.75 mg of atrasentan, or an equivalent amount of a pharmaceutically acceptable salt thereof.

29. The use of Claim 25, wherein the atrasentan is to be administered as a pharmaceutically acceptable salt.

30. The use of Claim 29, wherein the atrasentan is to be administered as atrasentan hydrochloride or atrasentan mandelate.