

using corticosteroids and immunosuppressive drugs. Unfortunately, these anti-inflammatory agents have had little to no clinical effect. Currently there are no effective treatments or therapeutics for fibrosis, but both animal studies and anecdotal human reports suggest that fibrotic tissue damage may be reversed (Tampe and Zeisberg, *Nat Rev Nephrol*, Vol 10:226-237, 2014).

The kidney has a limited capacity to recover from injury. Various renal pathologies result in local inflammation that causes scarring and fibrosis of renal tissue. The perpetuation of inflammatory stimuli drives tubulointerstitial inflammation and fibrosis and progressive renal functional impairment in chronic kidney disease. Its progression to end-stage renal failure is associated with significant morbidity and mortality. Since tubulointerstitial fibrosis is the common end point of multiple renal pathologies, it represents a key target for therapies aimed at preventing renal failure. Risk factors (e.g., proteinuria) independent of the primary renal disease contribute to the development of renal fibrosis and loss of renal excretory function by driving local inflammation, which in turn enhances disease progression.

In view of the role of fibrosis in many diseases and disorders, such as, for example, tubulointerstitial fibrosis leading to chronic kidney disease, there is a pressing need to develop therapeutically effective agents for treating diseases and conditions caused or exacerbated by fibrosis. In further view of the paucity of new and existing treatments targeting inflammatory pro-fibrotic pathways in renal disease, there is a need to develop therapeutically effective agents to treat, inhibit, prevent and/or reverse renal fibrosis and thereby prevent progressive chronic kidney disease.

SUMMARY

This summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This summary is not intended to identify key features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

In one aspect, the present disclosure refers to use of a MASP-2 inhibitory monoclonal antibody or antigen-binding fragment thereof in an amount effective to reduce or prevent proteinuria in a subject in the manufacture of medicament for preventing or reducing renal damage in a subject suffering from steroid-dependent Immunoglobulin A Nephropathy (IgAN), wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:69.

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. Use of a MASP-2 inhibitory monoclonal antibody or antigen-binding fragment
5 thereof in an amount effective to reduce or prevent proteinuria in a subject in the manufacture of medicament for preventing or reducing renal damage in a subject suffering from steroid-dependent Immunoglobulin A Nephropathy (IgAN), wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof comprises a heavy chain variable region comprising the amino acid sequence set forth as SEQ ID NO:67 and
10 a light chain variable region comprising the amino acid sequence set forth as SEQ ID NO:69.
2. The use of claim 1, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof is to be administered in an amount and for a time effective to achieve at
15 least a 20 percent reduction in 24-hour urine protein excretion as compared to baseline 24-hour urine protein excretion prior to treatment.
3. The use of claim 1, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody, and a human antibody.
4. The use of any of claims 1 to 3, wherein the MASP-2 inhibitory antibody does not
20 substantially inhibit the classical pathway.
5. The use of any of claims 1 to 3, wherein the MASP-2 inhibitory antibody inhibits C3b deposition in 90% human serum with an IC₅₀ of 30 nM or less.
6. The use of claim 1, wherein the human subject has been identified to have steroid-dependent IgAN.
- 25 7. The use of claim 1, wherein the MASP-2 inhibitory antibody or antigen-binding fragment thereof is to be administered in an amount effective to improve renal function.

8. The use of claim 1, wherein the composition is to be administered in an amount sufficient to improve renal function and decrease the corticosteroid dosage in said subject.
9. The use of any of claims 1 to 8, wherein the MASP-2 inhibitory antibody is to be administered subcutaneously, intraperitoneally, intra-muscularly, intra-arterially,
5 intravenously, or as an inhalant.