

CLAIMS

1. A fusion protein comprising a first part comprising a fragment of human
5 ACE2 or a variant of said fragment, said human ACE2 having the amino acid sequence according to SEQ ID No. 1, and a second part comprising the Fc portion of human IgG4 or a variant of the Fc portion of human IgG4, said Fc portion of human IgG4 having the amino acid sequence according to SEQ ID No. 5, wherein the first part and the second part are linked by the amino acid sequence according to SEQ ID No. 4.

10 2. Fusion protein according to claim 1, wherein the fragment of human ACE2 consists of the amino acid sequence according to SEQ ID No. 2.

3. Fusion protein according to claim 1, wherein the fragment of human ACE2 is
15 the extracellular domain of ACE2 consisting of the amino acid sequence according to SEQ ID No. 3.

4. Fusion protein according to claim 1, having the amino acid sequence according to any one of SEQ ID Nos. 6 to 9.

20 5. A fusion protein comprising a first part comprising a fragment of human ACE2 consisting of the amino acid sequence according to SEQ ID No. 2 or a variant of said fragment, and a second part comprising the Fc portion of human IgG or a variant of the Fc portion of human IgG.

25 6. Fusion protein according to claim 5, wherein the IgG is IgG1 or IgG4.

7. Fusion protein according to claim 5, wherein the IgG is IgG4 and the first part and the second part are linked by the amino acid sequence according to SEQ ID No. 4.

30 8. Fusion protein according to claim 5, wherein the IgG is IgG1 and the first part and the second part are linked by the amino acid sequence according to SEQ ID No. 15.

9. Fusion protein according to claim 5, having the amino acid sequence
35 according to any one of SEQ ID Nos. 6, 8, 10 or 12.

10. A fusion protein comprising a first part comprising a fragment of human ACE2 or a variant of said fragment, said human ACE2 having the amino acid sequence according to SEQ ID No. 1, and a second part comprising the Fc portion of human IgG2 or

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IgG3 or a variant of the Fc portion of human IgG1, IgG2 or IgG3, wherein the fusion protein has reduced binding to FcγRIIIa compared to a fusion protein comprising the same first part and a second part comprising the Fc portion of wild-type human IgG1.

5 11. Fusion protein according to claim 10, wherein the fusion protein has essentially the same binding to FcRn compared to a fusion protein comprising the same first part and a second part comprising the Fc portion of wild-type human IgG1.

10 12. Fusion protein according to claim 10 or 11, wherein the variant of the Fc portion of human IgG1 comprises the amino acid substitutions L3A and L4A in the sequence according to SEQ ID No. 16.

15 13. Fusion protein according to any one of claims 10 to 12, wherein the fragment of human ACE2 consists of the amino acid sequence according to SEQ ID No. 2.

15 14. Fusion protein according to any one of claims 10 to 12, wherein the fragment of human ACE2 is the extracellular domain of ACE2 consisting of the amino acid sequence according to SEQ ID No. 3.

20 15. Fusion protein according to any one of claims 1 to 14 wherein the variant of the human ACE2 fragment is an enzymatically inactive variant of human ACE2.

25 16. Fusion protein according to claim 15, wherein the enzymatically inactive variant of human ACE2 comprises a H374N and a H378N mutation, the numbering referring to SEQ ID No. 1.

30 17. Fusion protein according to any one of claims 1 to 16, wherein the variant of the human ACE2 fragment comprises an amino acid substitution at leucine 584, the numbering referring to SEQ ID No. 1.

30 18. Fusion protein according to any one of claims 1 to 17, wherein the variant of the human ACE2 fragment comprises at least one amino acid substitution at at least one residue selected from lysine 619, arginine 621, lysine 625, arginine 697, lysine 702, arginine 705, arginine 708, arginine 710 and arginine 716, the numbering referring to SEQ ID No. 1.

35 19. Fusion protein according to any one of claims 1 to 18, wherein the variant of the human ACE2 fragment comprises amino acid substitutions at lysine 619, arginine 621,

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lysine 625, arginine 697, lysine 702, arginine 705, arginine 708, arginine 710 and arginine 716, the numbering referring to SEQ ID No. 1.

20. Fusion protein according to any one of claims 1 to 18, wherein the variant of
5 the human ACE2 fragment comprises a S645C mutation, the numbering referring to SEQ ID No. 1.

21. Nucleic acid molecule comprising a nucleic acid sequence encoding the
10 fusion protein according to any one of claims 1 to 20.

22. Expression vector comprising the nucleic acid molecule according to claim
21.

23. Host cell comprising the nucleic acid molecule according to claim 21 or the
15 expression vector according to claim 22.

24. Method for producing the fusion protein according to any one of claims 1 to
20, comprising culturing the host cell according to claim 23 in a suitable culture medium.

25. Fusion protein according to any one of claims 1 to 20 for medical use.

26. Fusion protein according to any one of claims 1 to 20 for use in preventing
and/or treating an infection with a coronavirus binding to ACE2.

27. Fusion protein for use according to claim 26, wherein the coronavirus
25 binding to ACE2 is selected from the group consisting of SARS, SARS-CoV-2 and NL63,
preferably it is SARS-CoV-2.

28. Fusion protein for use according to claim 26 or 27, wherein the fusion protein
30 is to be administered in combination with an anti-viral agent.

29. Fusion protein for use according to claim 28, wherein the anti-viral agent is
selected from the group consisting of remdesivir, arbidol HCl, ritonavir, lopinavir, darunavir,
ribavirin, chloroquin and derivatives thereof, nitazoxanide, camostat mesilate, tocilizumab,
35 siltuximab, sarilumab and baricitinib phosphate.

30. Fusion protein according to any one of claims 1 to 20 for use in treating
hypertension (including high blood pressure), congestive heart failure, chronic heart failure,
acute heart failure, contractile heart failure, myocardial infarction, arteriosclerosis, kidney

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failure, renal failure, Acute Respiratory Distress Syndrome (ARDS), Acute Lung Injury (ALI), chronic obstructive pulmonary disease (COPD), pulmonary hypertension, renal fibrosis, chronic renal failure, acute renal failure, acute kidney injury, inflammatory bowel disease and multi-organ dysfunction syndrome.

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31. Pharmaceutical composition comprising an effective amount of the fusion protein according to any one of claims 1 to 20 and a pharmaceutically acceptable carrier or excipient.

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32. Pharmaceutical composition according to claim 31, further comprising an anti-viral agent.