Claims

~~1. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient for prevention or reduction of organ dysfunction or prevention of organ failure in said patient.~~

~~2. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to claim 1, wherein said anti-ADM antibody or said anti-adrenomedullin antibody fragment or said anti-ADM non-Ig scaffold is a non-neutralizing ADM antibody or a non-neutralizing adrenomedullin antibody fragment or a non-neutralizing ADM non-Ig scaffold.~~

~~3. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to claim 1 or 2, wherein said organ is kidney or liver.~~

~~4. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to claim 1 to 3, wherein said organ is heart.~~

~~5. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of the claims 1 to 4, wherein said antibody or fragment or scaffold binds to the N-terminal part (aa 1-21) of adrenomedullin.~~

~~6. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in~~

~~therapy of an acute disease or acute condition of a patient according to any of claims 1 to 5, wherein said antibody or antibody fragment or non-Ig scaffold is monospecific.~~

~~7. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding for use in therapy of an acute disease or acute condition of a patient according any of claims 1 to 6, wherein said antibody or fragment or scaffold exhibits a binding affinitity to ADM of at least 10^{-7} M.~~

~~8. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding for use in therapy of an acute disease or acute condition of a patient according any of claims 1 to 7, wherein said antibody or fragment or scaffold is not ADM-binding Protein 1 (complement factor H).~~

~~9. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 8, wherein said antibody or fragment or scaffold recognizes and binds to the N-terminal end (aa1) of adrenomedullin.~~

~~10. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 9, wherein said antibody or said fragment or scaffold is an ADM stabilizing antibody or fragment or scaffold that enhances the half life (t1/2 half retention time) of adrenomedullin in serum, blood, plasma at least 10 %, preferably at least 50 %, more preferably >50 %, most preferably >100%.~~

~~11. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 10, wherein said antibody or fragment or scaffold blocks the ADM bioactivity not more than 80 %, preferably not more than 50%.~~

~~12. Anti Adrenomedullin (ADM) antibody or an anti ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 11, wherein said disease is selected from the group comprising sepsis, diabetes, cancer, heart failure, and shock.~~

~~13. Anti Adrenomedullin (ADM) antibody or an anti ADM antibody fragment binding to adrenomedullin or anti ADM non Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 12, wherein said disease is not SIRS, sepsis, or septic shock.~~

~~14. Anti Adrenomedullin (ADM) antibody or an anti ADM antibody fragment binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 13, wherein said antibody or fragment is a human monoclonal antibody or fragment that binds to ADM or an antibody fragment thereof wherein the heavy chain comprises the sequences~~

~~SEQ ID NO: 1~~
~~GYTFSRYW~~

~~SEQ ID NO: 2~~
~~ILPGSGST~~

~~SEQ ID NO: 3~~
~~TEGYEYDGFDY~~

~~and wherein the light chain comprises the sequences~~

~~SEQ ID NO:4~~
~~QSIVYSNGNTY~~

~~SEQ ID NO: 5~~
~~RVS~~

SEQ ID NO: 6
FQGSHIPYT.

15. A human monospecific anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to claim 14, wherein said antibody or fragment comprises the sequences:

SEQ ID NO: 7 (AM-VH-C)
QVQLQQSGAELMKPGASVKISCKATGYTFSRYWIEWVKQRPGHGLEWIGEILP
GSGSTNYNEKFKGKATITADTSSNTAYMQLSSLTSEDSAVYYCTEGYEYDGFD
YWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH
SEQ ID NO: 8 (AM-VH1)
QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWISWVRQAPGQGLEWMGRIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH
SEQ ID NO: 9 (AM-VH2-E40)
QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWIEWVRQAPGQGLEWMGRIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH
SEQ ID NO: 10 (AM-VH3-T26-E55)
QVQLVQSGAEVKKPGSSVKVSCKATGYTFSRYWISWVRQAPGQGLEWMGEIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH
SEQ ID NO: 11 (AM-VH4-T26-E40-E55)

QVQLVQSGAEVKKPGSSVKVSCKATGYTFSRYWIEWVRQAPGQGLEWMGEIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHHH

SEQ ID NO: 12 (AM-VL-C)

DVLLSQTPLSLPVSLGDQATISCRSSQSIVYSNGNTYLEWYLQKPGQSPKLLIYR
VSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSHIPYTFGGGTKLE
IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C

SEQ ID NO: 13 (AM-VL1)

DVVMTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLNWFQQRPGQSPRRLIYR
VSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGQGTKL
EIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

SEQ ID NO: 14 (AM-VL2-E40)

DVVMTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLEWFQQRPGQSPRRLIYRVSNRD
SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGQGTKLEIKRTVAAPSV
FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS
LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

16. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of claims 1 to 15, wherein said antibody or fragment or scaffold is a modulating antibody or fragment or scaffold that enhances the half-life (t1/2-half retention time) of adrenomedullin in serum, blood, plasma at least 10 %, preferably at least 50 %, more preferably >50 %, most preferably >100% and that blocks the ADM bioactivity not more than 80 %, preferably not more than 50%.

~~17. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of the claims 1 to 16 to be used in combination with vasopressors *e.g.* catecholamine and/ or fluids administered intravenously.~~

~~18. Anti-Adrenomedullin (ADM) antibody or an anti-ADM antibody fragment binding to adrenomedullin or anti-ADM non-Ig scaffold binding to adrenomedullin for use in therapy of an acute disease or acute condition of a patient according to any of the claims 1 to 16 or a combination according to claim 17 to be used in combination with ADM binding protein and/or further active ingredients.~~

~~19. Pharmaceutical formulation comprising an anti-ADM antibody or anti-ADM antibody fragment or anti-ADM non-Ig scaffold for use in a therapy of an acute disease or acute condition of a patient according to any of claims 1 to 18.~~

~~20. Pharmaceutical formulation for use in therapy of an acute disease or acute condition of a patient according to claim 19, wherein said pharmaceutical formulation is a solution, preferably a ready-to-use solution.~~

~~21. Pharmaceutical formulation for use in therapy of an acute disease or acute condition of a patient according to claim 20, wherein said pharmaceutical formulation is in a freeze-dried state.~~

~~22. Pharmaceutical formulation according to any of claims 19 to 21, wherein said pharmaceutical formulation is administered intra-muscular.~~

~~23. Pharmaceutical formulation according to any of claims 19 to 21, wherein said pharmaceutical formulation is administered intra-vascular.~~

~~24. Pharmaceutical formulation according to claims 19 to 21, wherein said pharmaceutical formulation is administered via infusion.~~

~~25. Pharmaceutical formulation according to claims 19 to 21, wherein said pharmaceutical formulation is to be administered systemically to a patient for prevention or reduction of organ dysfunction or organ failure in a patient having an acute disease or acute condition.~~

~~26. Pharmaceutical formulation according to claims 19 to 21, wherein said pharmaceutical formulation is to be administered systemically via infusion to a patient for prevention or reduction of organ dysfunction or organ failure in a patient having an acute disease or acute condition.~~

1. Use of an anti-Adrenomedullin (ADM) antibody, anti-ADM fragment binding to adrenomedullin or anti-ADM non-Ig protein scaffold binding to adrenomedullin in the manufacture of a medicament for the prevention or reduction of organ dysfunction or the prevention of organ failure in a patient with an acute disease or an acute condition, wherein said antibody, antibody fragment or non-Ig scaffold binds to a region of at least 4 amino acids within the sequence of amino acids 1-42 of mature human ADM as set out in SEQ ID NO: 24.

2. The use of claim 1, wherein said organ is a kidney or liver.

3. The use of claim 1, wherein said organ is a heart.

4. The use of any one of claims 1 to 3, wherein said antibody or fragment or scaffold binds to the N-terminal region of adrenomedullin comprising amino acids 1-21 as set out in SEQ ID NO: 23.

5. The use of any one of claims 1 to 4, wherein said antibody, antibody fragment or non-Ig scaffold is monospecific.

6. The use of any one of claims 1 to 5, wherein said antibody, or antibody fragment or non-Ig scaffold exhibits a binding affiinity to ADM of at least 10^{-7} M.

7. The use of any one of claims 1 to 6, wherein said antibody, antibody fragment or non-Ig scaffold is not ADM-binding-Protein-1 (complement factor H).

8. The use of any one of claims 1 to 7, wherein said antibody, antibody fragment or non-Ig scaffold recognizes and binds to the N-terminal end (aa1) of adrenomedullin.

9. The use of any one of claims 1 to 8, wherein said antibody, antibody fragment or non-Ig scaffold is an ADM stabilizing antibody or fragment or scaffold that enhances the half life (t1/2 half retention time) of adrenomedullin in serum, blood, plasma at least 10 %, at least 50 %, more than 50 % or more than 100%.

10. The use of any one of claims 1 to 9, wherein said antibody, antibody fragment or non-Ig scaffold blocks the ADM bioactivity not more than 80 %, or not more than 50%.

11. The use of any one of claims 1 to 10, wherein said disease is selected from the group consisting of sepsis, diabetes, cancer, heart failure, and shock.

12. The use of any one of claims 1 to 11, wherein said disease is not SIRS, sepsis, or septic shock.

13. The use of any one of claims 1 to 12, wherein said antibody or antibody fragment is a human monoclonal antibody or antibody fragment that binds to ADM or an antibody fragment thereof wherein the heavy chain comprises the sequences

SEQ ID NO: 1
GYTFSRYW

SEQ ID NO: 2
ILPGSGST

SEQ ID NO: 3
TEGYEYDGFDY

and wherein the light chain comprises the sequences

SEQ ID NO:4
QSIVYSNGNTY

SEQ ID NO: 5
RVS

SEQ ID NO: 6
FQGSHIPYT.

14. The use of any one of claims 1 to 13, wherein said antibody, antibody fragment or non-Ig scaffold is a modulating antibody, antibody fragment or non-Ig scaffold that enhances the half life (tl/2 half retention time) of adrenomedullin in serum, blood, plasma at least 10 %, at least 50 %, more than 50 %, or more than 100% and that blocks the ADM bioactivity not more than 80 %, or not more than 50%.

15. The use of any one of claims 1 to 14, wherein said medicament is to be administered in combination with one or more vasopressors and/ or fluids administered intravenously.

16. The use of claim 15, wherein the one or more vasopressors comprises catecholamine.

17. The use of any one of claims 1 to 16, wherein said medicament is to be administered in combination with ADM binding protein and/or further active ingredients.

18. The use of any one of claims 1 to 17, wherein said medicament is to be administered intra-muscularly, intra-vascularly or systemically.

19. The use of claim 1, wherein said medicament is formulated as a solution or in a freeze-dried state.

20. The use of claim 19, wherein said solution is a ready-to-use solution.

21. The use of any one of claims 1, 19 to 20, wherein said medicament is formulated for intra-muscular or intra-vascular administration.

22. The use of any one of claims 1, 19 to 21, wherein said medicament is formulated for administration via infusion.

23. The use of any one of claims 1, 19 to 22, wherein said medicament is formulated for systemic administration.