CLAIMS

1. Use of an anti-adrenomedullin (ADM) antibody or an anti-adrenomedullin antibody fragment or anti-ADM non-Ig scaffold in the manufacture of a medicament for therapy or prevention of symptoms of illness or for therapy or prevention of an illness characterized by such symptoms in a subject in need thereof wherein said antibody or fragment or scaffold binds to the N-terminal part of ADM (amino acids 1-21; SEQ ID NO:4) or a fragment thereof,
   wherein the symptoms of illness are selected from nausea, headache, muscle aches, back pain, shivering, and/or vomiting, wherein the illness is characterized by an amount of C-reactive protein (CRP) in a sample which is ≥ 10 mg/L, and/or wherein the amount of TNF in a sample is ≥ 50 pg/ml, and/or wherein the amount of bio-ADM in a sample is ≥ 43pg/ml, and/or wherein the mean arterial pressure in said subject in need thereof is decreased.

2. The use according to claim 1, wherein the illness is selected from an inflammatory condition, autoimmune disease, metabolic disease, brain disease, cardiovascular disease and drug-induced disease.

3. The use according to claim 1 or 2, wherein the illness is migraine.

4. The use according to any one of claims 1 to 3, wherein said antibody or antibody fragment or non-Ig scaffold is monospecific.

5. The use according to any one of claims 1 to 4, wherein said antibody or fragment or scaffold exhibits a binding affinity to ADM of at least 10^{-7} M by label-free surface plasmon resonance using a Biacore 2000 system.

6. The use according to any one of claims 1 to 5, wherein said antibody or fragment or scaffold is not ADM-binding-Protein-1 (complement factor H).

7. The use according to any one of claims 1 to 6, wherein said antibody or fragment or scaffold recognizes and binds to the N-terminal end (amino acid 1) of ADM.

8. The use according to any one of claims 1 to 7, wherein said antibody or fragment or scaffold is an ADM stabilizing antibody or fragment or scaffold that enhances the half-life (t1/2 half retention time) of ADM in serum, blood, plasma at least 10 %, preferably at least, 50 %, more preferably > 50 %, most preferably > 100 %.

9. The use according to any one of claims 1 to 8, wherein said antibody or fragment or scaffold blocks the bioactivity of ADM not more than 80 %, preferably not more than 50% using hADM 22-52 as a reference antagonist in CHO-K1 cells expressing human recombinant ADM receptor.

10. The use according to any one of claims 1 to 9, wherein said subject undergoes chemotherapy, treatment with biological biologics, antibiotics, or treatment with anti-viral compounds.

11. The use according to any one of claims 1 to 10, 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:

CDR1: SEQ ID NO: 5
GYTFSRYW

CDR2: SEQ ID NO: 6
ILPGSGST

CDR3: SEQ ID NO: 7
TEGYEYDGFDY

and wherein the light chain comprises the sequences:

CDR1: SEQ ID NO: 8
QSIVYSNGNTY

CDR2:
RVS

CDR3: SEQ ID NO: 9
FQGSHIPYT.

12. The use according to claim 11, wherein said antibody or fragment comprises a sequence as a VH region selected from :

SEQ ID NO: 10 (AM-VH-C)

QVQLQQSGAELMKPGASVKISCKATGYTFSRYWIEWVKQRPGHGLEWIGEILP
GSGSTNYNEKFKGKATITADTSSNTAYMQLSSLTSEDSAVYYCTEGYEYDGFD
YWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH

SEQ ID NO: 11 (AM-VH1)

QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWISWVRQAPGQGLEWMGRIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH

SEQ ID NO: 12 (AM-VH2-E40)

QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWIEWVRQAPGQGLEWMGRIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH

SEQ ID NO: 13 (AM-VH3-T26-E55)

QVQLVQSGAEVKKPGSSVKVSCKATGYTFSRYWISWVRQAPGQGLEWMGEIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH

SEQ ID NO: 14 (AM-VH4-T26-E40-E55)

QVQLVQSGAEVKKPGSSVKVSCKATGYTFSRYWIEWVRQAPGQGLEWMGEIL
PGSGSTNYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKR
VEPKHHHHHH

and comprises a sequence as a VL region selected from :

SEQ ID NO: 15 (AM-VL-C)

DVLLSQTPLSLPVSLGDQATISCRSSQSIVYSNGNTYLEWYLQKPGQSPKLLIYR
VSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDLGVYYCFQGSHIPYTFGGGTKLE
IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C

SEQ ID NO: 16 (AM-VL1)

DVVMTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLNWFQQRPGQSPRRLIYR
VSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGQGTKL
EIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

SEQ ID NO: 17 (AM-VL2-E40)

DVVMTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLEWFQQRPGQSPRRLIYR
VSNRDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGQGTKL
EIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC.

13. The use according to claim 11, wherein said antibody or fragment comprises the following sequence as a heavy chain:

SEQ ID NO: 22

QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWIEWVRQAPGQGLEWIGEILPG
SGSTNYNQKFQGRVTITADTSTSTAYMELSSLRSEDTAVYYCTEGYEYDGFDYW
GQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGA
LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK
SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE
SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK

or a sequence that is > 95% identical thereto,

and comprises the following sequence as a light chain:

SEQ ID NO: 23

DVVLTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLEWYLQRPGQSPRLLIYRVS
NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGGGTKLEIKR
TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESV
TEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

or a sequence that is > 95% identical thereto.

14. Pharmaceutical formulation for use in therapy or prevention of symptoms of illness or for the use in therapy or prevention of an illness characterized by such symptoms in a subject in need thereof comprising an antibody or fragment or scaffold as defined in any one of claims 1 to 13.

15. Use of a pharmaceutical formulation comprising an antibody or fragment or scaffold as defined in any one of claims 1 to 13 in the manufacture of a medicament for therapy or prevention of symptoms of illness or for the use in therapy or prevention of an illness characterized by such symptoms, wherein the symptoms of illness are selected from nausea, headache, muscle aches, back pain, shivering, and/or vomiting, wherein the illness is characterized by an amount of C-reactive protein (CRP) in a sample which is ≥ 10 mg/L, and/or wherein the amount of TNF in a sample is ≥ 50 pg/ml, and/or wherein the amount of bio-ADM in a sample is ≥ 43pg/ml, and/or wherein the mean arterial pressure in said subject in need thereof is decreased.

16. Antibody comprising as a heavy chain:

SEQ ID NO: 22

QVQLVQSGAEVKKPGSSVKVSCKASGYTFSRYWIEWVRQAPGQGLEWIGEILP
GSGSTNYNQKFQGRVTITADTSTSTAYMELSSLRSEDTAVYYCTEGYEYDGFD
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWN
SGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK
KVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

or a sequence that is > 95% identical, preferably > 98%, thereto, and comprises as a light chain:

SEQ ID NO: 23

DVVLTQSPLSLPVTLGQPASISCRSSQSIVYSNGNTYLEWYLQRPGQSPRLLIYR
VSNRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHIPYTFGGGTKLE
IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS
QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C

or a sequence that is > 95% identical, preferably > 98%, thereto.

17. Pharmaceutical composition comprising an antibody according to claim 16.