CLAIMS

1. Use of a Human human natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes in the manufacture of a medicament for the treatment or prevention of a disorder or a disease associated with/related to/caused by a natural IgM/IgA antibody deficiency (NAD) in a subject, said disorder or disease is selected from the group consisting of a natural antibody deficient infectious, neurodegenerative, metabolic, autoimmuine, and cardiovascular diseases, wherein said human natural IgM and/or IgA antibody is a subgroup of the IgM and/or IgA antibodies repertoire of a subjectderived from IgM and/or IgA enriched plasma pools from healthy individuals, said subgroup essentially consisting of antibodies recognizing oxidized phospholipids and/or oxidation-specific epitopes,
wherein said human natural IgM and/or IgA antibodies contain more than 35% antibodies recognizing oxidized phospholipids and/or oxidation-specific epitopes of the total IgM and/or IgA antibodies.

2. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use in a method of treating or preventing a disorder or a disease associated with/related to/caused by a natural IgM/IgA antibody deficiency (NAD) in a subject.

3. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 2, wherein said natural IgM and/or IgA is derived from IgM and/or IgA enriched plasma pools from healthy individuals.

42. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to claim 2 or 31, wherein said human natural IgM and/or IgA antibody is a subgroup of IgM and/or IgA antibodies derived from IgM and/or IgA enriched plasma pools from healthy individuals, said subgroup essentially consisting of antibodies recognizing oxidized phospholipids and/or oxidation-specific epitopes.

5. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 3 or 4, wherein said disorder or a disease associated with/related to/caused by natural IgM/IgA antibody deficiency (NAD) is a natural antibody deficient

infectious, neurodegenerative, metabolic, autoimmune, or cardiovascular disease.

63. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 3 to 51 or 2, wherein said disorder or a disease associated with/related to/caused by natural IgM/IgA antibody deficiency (NAD) is the virus infection disease COVID-19 caused by the β-Coronavirus SARS-CoV2 or is long COVID-19.

74. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to claim any one of claims 3 1 to 63, wherein said antibody is capable of inhibiting the spreading of a virus from an infected cell to an adjacent second non-infected cell (cell-to-cell spread).

85. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 3 1 to 74, wherein said antibody has an anti-inflammatory activity, preferably the capability of:
reducing the accumulation of free oxidized phospholipids, preferably in infect lungs,
clearing cellular debris in lung tissue,
stimulating IL-10 and/or TGFβ secretion; and/or
neutralizing of pro-inflammatory immune responses triggered by cytokines.

96. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to claim any one of claims 3 1 to 85, wherein said disorder or a disease associated with natural IgM/IgA antibody deficiency (NAD) is an inflammatory disease or a virus infection disease.

107. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to claim 96, wherein said inflammatory disease is selected from the group consisting of infectious diseases mediated by respiratory viruses, preferably COVID19, long COVID-19, influenza, MERS-COV orSARS-COV; infectious diseases caused by bacterial infections mediated by gram positive or gram negative pathogens,

fungi, or parasites; and sterile inflammatory diseases, preferably cardiovascular diseases, atherosclerosis, coronary heart disease, heart attack and stroke, metabolic disorders like diabetes mellitus, neurodegenerative diseases, preferably Alzheimer's Disease, and autoimmune diseases, preferably Systemic Lupus Erythematodes, or Multiple Sclerosis.

118. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to claim 96, wherein said virus infection disease is selected from the group consisting of infections by coronaviruses, preferably SARS-CoV, SARS-CoV-2, MERS); influenza viruses, parainfluenza viruses, respiratory syncytial viruses (RSV), rhinoviruses, adenoviruses, enteroviruses, human metapneumoviruses, herpesviruses, preferably HSV-1, HSV-2, VZV, EBV, HCMV, HHV-6, HHV-7, HHV-8.

129. A pharmaceutical composition, comprising an effective amount of the human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 21 to 11 8, wherein the medicament is a pharmaceutical composition which further comprises and at least one pharmaceutically acceptable excipient.

13. A pharmaceutical composition comprising an effective amount of a human natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes, wherein said human natural IgM and/or IgA antibody is a subgroup of IgM and/or IgA antibodies derived from IgM and/or IgA enriched plasma pools from healthy individuals, said subgroup essentially consisting of antibodies recognizing oxidized phospholipids and/or oxidation-specific epitopes and at least one pharmaceutical excipient.

14. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 2, wherein said antibody is a recombinant human monoclonal natural IgM or IgA antibody.

15. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 14, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-

arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide.

16. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 14 or 15, wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 1, V_HCDR2 comprising SEQ ID NO: 2, V_HCDR3 comprising SEQ ID NO: 3, V_LCDR1 comprising SEQ ID NO: 4, V_LCDR2 comprising SEQ ID NO: 5, and V_LCDR3 comprising SEQ ID NO:6, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide; or

wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 9, V_HCDR2 comprising SEQ ID NO: 10, V_HCDR3 comprising SEQ ID NO: 11, V_LCDR1 comprising SEQ ID NO: 12, V_LCDR2 comprising SEQ ID NO: 13, and V_LCDR3 comprising SEQ ID NO:14, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide.

17. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 16, wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126 of SEQ ID NO: 7 and in positions 1 to 25, 35 to 51, 55 to 90, and 101 to 110 of SEQ ID NO: 8, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide; or

- wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126 of SEQ ID NO: 15 and in positions 1 to 26, 34 to 50, 54 to 89, and 99 to 108 of SEQ ID NO: 16, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide.

18. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 17, wherein said antibody comprises the V_H of SEQ ID NO:7 and the V_L of SEQ ID NO:8 wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide; or
- wherein said antibody comprises the V_H of SEQ ID NO:15 and the V_L of SEQ ID NO:16, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-β peptide.

19. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 18, wherein said disorder or a disease associated with/related to/caused by natural IgM/IgA antibody deficiency (NAD) is a natural antibody infectious, neurodegenerate or cardiovascular disease.

20. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 19, wherein said disorder or a disease associated with/related to/caused by natural IgM/IgA antibody deficiency (NAD) is the virus infection disease COVID-19 caused by the β-Coronavirus SARS-CoV-2 or is long COVID-19.

21. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 20, wherein said antibody is capable of inhibiting the spreading of a virus from an infected cell to an adjacent second non-infected cell (cell-to-cell spread).

22. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 21, wherein said antibody has an anti-inflammatory activity, preferably the capability of:
reducing the accumulation of free oxidized phospholipids, preferably in infected lungs,
clearing cellular debris in lung tissue, and/or
stimulating IL-10 and/or TGFβ secretion and/or neutralizing of pro-inflammatory cytokines.

23. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 22, wherein said disorder or a disease associated with natural IgM/IgA antibody deficiency (NAD) is an inflammatory disease or a virus infection disease.

24. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 23, wherein said inflammatory disease is selected from the group consisting of infectious diseases mediated by respiratory viruses, preferably COVID19, long COVID-19, influenza, MERS-COV orSARS-COV; infectious diseases caused by bacterial infections mediated by gram positive or gram negative pathogens, fungi, or parasites; and sterile diseases, preferably cardiovascular diseases, atherosclerosis, coronary heart disease, heart attack and stroke, metabolic disorders like diabetes mellitus, neurodegenerative diseases, preferably Alzheimer's Disease, and autoimmune diseases, preferably Systemic Lupus Erythematodes, or Multiple Sclerosis.

25. Recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to claim 23, wherein said virus infection disease is selected from the group

consisting of infections by coronaviruses, preferably SARS-CoV, SARS-CoV-2, MERS); influenza viruses, parainfluenza viruses, respiratory syncytial viruses (RSV), rhinoviruses, adenoviruses, enteroviruses, human metapneumoviruses, herpesviruses, preferably HSV-1, HSV-2, VZV, EBV, HCMV, HHV-6, HHV-7, HHV-8.

26. A pharmaceutical composition, comprising an effective amount of the recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 14 to 25 and at least one pharmaceutically acceptable excipient.

27. A human IgM or IgA antibody recognizing and binding to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide,

(a) wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 1, V_HCDR2 comprising SEQ ID NO: 2, V_HCDR3 comprising SEQ ID NO: 3, V_LCDR1 comprising SEQ ID NO: 4, V_LCDR2 comprising SEQ ID NO: 5, and V_LCDR3 comprising SEQ ID NO:6, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 9, V_HCDR2 comprising SEQ ID NO: 10, V_HCDR3 comprising SEQ ID NO: 11, V_LCDR1 comprising SEQ ID NO: 12, V_LCDR2 comprising SEQ ID NO: 13, and V_LCDR3 comprising SEQ ID NO:14, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

(b) wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126 of SEQ ID NO: 7 and in positions 1 to 25, 35 to 51, 55 to 90, and 101 to 110 of SEQ ID NO: 8, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126of SEQ ID NO: 15 and in positions 1 to 26, 34 to 50, 54 to 89, and 99 to 108 of SEQ ID NO: 16, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

(c) wherein said antibody comprises the V_H of SEQ ID NO:7 and the V_L of SEQ ID NO:8 wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises the V_H of SEQ ID NO:15 and the V_L of SEQ ID NO:16, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide.

28. A pharmaceutical composition comprising an effective amount of a human IgM or IgA antibody recognizing and binding to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to

malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide,

(a) wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 1, V_HCDR2 comprising SEQ ID NO: 2, V_HCDR3 comprising SEQ ID NO: 3, V_LCDR1 comprising SEQ ID NO: 4, V_LCDR2 comprising SEQ ID NO: 5, and V_LCDR3 comprising SEQ ID NO:6, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises the complementarity determining regions V_HCDR1 comprising SEQ ID NO: 9, V_HCDR2 comprising SEQ ID NO: 10, V_HCDR3 comprising SEQ ID NO: 11, V_LCDR1 comprising SEQ ID NO: 12, V_LCDR2 comprising SEQ ID NO: 13, and V_LCDR3 comprising SEQ ID NO:14, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

(b) wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126 of SEQ ID NO: 7 and in positions 1 to 25, 35 to 51, 55 to 90, and 101 to 110 of SEQ ID NO: 8, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises an amino acid sequence with at least 70 % sequence identity to the amino acid residues shown in positions 1 to 25, 34 to 50, 59 to 96, and 116 to 126of SEQ ID NO: 15 and in positions 1 to 26, 34 to 50, 54 to 89, and 99 to 108 of SEQ ID NO: 16, wherein said antibody recognizes and binds to to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine,

to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

(c) wherein said antibody comprises the V_H of SEQ ID NO:7 and the V_L of SEQ ID NO:8 wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide; or

wherein said antibody comprises the V_H of SEQ ID NO:15 and the V_L of SEQ ID NO:16, wherein said antibody recognizes and binds to phosphorylcholine exposed by oxidized phosphatidylcholine and/or oxidized 1-palmitoyl-2-arachidonoyl-phosphatidylcholine, to oxidized cardiolipin, to oxidized phosphatidylserine, to malondialdehyde-, 4-hydroxynonenal- and 2-(ω-carboxyethyl)-pyrrole-modified proteins, and/or to oligomeric amyloid-b peptide;

and at least one pharmaceutical excipient.

2910. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 2 1 to 11 9 and 14, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 15 to 25 or pharmaceutical composition for use according to claim 12 or 26,

wherein said human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes or pharmaceutical composition the medicament is to be administered in combination with:

(a) an inhibitor/antagonist of the Angiotensin-Converting-Enzyme (ACE), an inhibitor/antagonist of the Angiotensin-II-type 1 receptor (AT1R) and/or a compound that modulates the expression of the ACE2 receptor; and/or Ang(1-7), AT2R agonists and/or MAS-receptor agonists;

(b) a compound inhibiting/antagonizing/neutralizing ligands of Receptor of Advanced Glycation Endproducts (RAGE) and/or an inhibitor/antagonist of RAGE; and/or

(c) Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) and/or a compound that increases the phagocytic activity of alveolar macrophages (AM), preferably azithromycin.

3011. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 2 1 to 11 9and 14, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 15 to 25 or pharmaceutical composition for use according to claim 12 or 26,
wherein said human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes or pharmaceutical composition the medicament is to be administered in combination with:
an antiviral compound, preferably wherein said antiviral compound is:
remdesivir;
favipiravir;
camostat mesylate;
nafamostat mesylate;
umifenovir; and/or
stronger neo-minophagen C.

3112. Human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes forThe use according to any one of claims 2 1 to 11 9and 14, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes for use according to any one of claims 15 to 25 or pharmaceutical composition for use according to claim 12 or 26,
wherein said human or humanized natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes, recombinant human monoclonal natural IgM and/or IgA antibody recognizing oxidized phospholipids and/or oxidation-specific epitopes or pharmaceutical composition the medicament is to be administered in combination with an immunomodulator, preferably wherein said immunomodulator is:
an anti-PD-1-, anti-PD-L1, anti-CD40-, CD40-Ligand-, ,anti-CSF-1R-, and/or anti-CTLA-4-antibody; and/or

an antibody that binds to cytokines (preferably to IL-6), an antibody that binds to its specific cytokine receptor (preferably to IL-6R), an antibody that binds to chemokine(s) (preferably to CCL2 and CCL5), an antibody that binds to their specific chemokine receptor(s) (preferably to CCR2 and CCR5), and/or synthetic molecules (preferably Maraviroc); and/or
dexamethason.

32. Vaccine comprising a compound that induces the generation of natural IgM and/or IgA antibodies recognizing oxidized phospholipids and/or oxidation-specific epitopes for use in a method of reducing or preventing the clinical signs or disease associated with/related to/caused by natural IgM/IgA antibody deficiency (NAD) in a subject, wherein said vaccine comprises a pharmaceutically acceptable carrier or excipient.

33. Vaccine for use according to claim 32, wherein said vaccine is a Bacillus Calmette-Guérin (BCG) vaccine or pneumococcus tuberculosis vaccine.

34. Vaccine for use according to claims 32 or 33, wherein said Bacillus Calmette-Guérin (BCG) vaccine comprises an attenuated bacterium of *Mycobacterium bovis*.

35. Vaccine for use according to any one of claims 32 to 34, wherein said vaccine is capable of:
stimulating the production of natural IgM specific for oxidized phospholipids and/or oxidation-specific epitopes,
reducing the accumulation of free oxidized phospholipids, preferably in infect lungs,
reducing the accumulation of oxidized phospholipids and/or oxidation-specific epitopes on LDL, preferably in atherosclerotic lesions;
stimulating of IL-10 and/or TGFβ secretion, preferably by alveolar macrophages; and/or
reducing the accumulation of misfolded proteins such as oligomeric amyloid-β, preferably in brain tissues

36. Vaccine for use according any one of claims 32 to 35, wherein said clinical signs or disease associated with natural IgM/IgA antibody deficiency (NAD) is an infection disease.

37. Vaccine for use according to claim 36, wherein said infectious disease is a virus infectious disease.

38. Vaccine for use according to claim 37, wherein said infectious disease is a virus infection disease, preferably wherein said virus infection disease is selected from the group consisting of infections by coronaviruses, preferably SARS-CoV, SARS-CoV-2, MERS); influenza viruses, parainfluenza viruses, respiratory syncytial viruses (RSV), rhinoviruses, adenoviruses, enteroviruses, human metapneumoviruses, herpesviruses, preferably HSV-1, HSV-2, VZV, EBV, HCMV, HHV-6, HHV-7, HHV-8.

39. Vaccine for use according to claim 35 or 38, wherein said virus infection disease is the virus infection disease COVID-19 caused by the β-Coronavirus SARS-CoV2 or is long COVID-19.