

METHOD FOR PREVENTION OR TREATMENT OF CORONAVIRUS INFECTION

FIELD OF THE INVENTION

5 The invention is in the field of medical treatment and relates to a method for treating β -coronavirus infections in animals and humans, including Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).

In particular, the present invention relates to methods for prophylactic and/or therapeutic
10 treatment of SARS-CoV-2 by means of mucosal administration, especially intranasal and/or oral inhalation of antibodies against β -coronavirus, in particular SARS-CoV-2.

BACKGROUND OF THE INVENTION

The SARS-CoV-2 virus causes the disease COVID-19 in humans and is widespread having
15 a significant impact on human society. We should expect the SARS-CoV-2 virus and its variants of concern to continue to cause frequent infections, as well as severe disease and death. As of January 2023, the ongoing COVID-19 pandemic caused by SARS-CoV-2, has resulted in more than 6.7 million worldwide deaths since 2019.

20 In recent years, outbreaks of other coronaviruses have caused severe illness and deaths. As scientists develop therapeutic antibodies and vaccines against SARS-CoV-2, the danger remains of future novel variants of SARS-CoV-2 and novel coronaviruses emerging. These novel coronaviruses can lead to morbidity, mortality, and could cause pandemics. It remains vitally important to identify broadly protective therapies that can
25 combat current and emerging coronaviruses in the future.

In addition to SARS-CoV-2, six other coronaviruses are known to cause disease in humans: the betacoronaviruses HCoV-OC43 (human coronavirus OC43), HCoV-HKU1 (human coronavirus HKU1), SARS-CoV (severe acute respiratory syndrome coronavirus)
30 and MERS-CoV (Middle East respiratory syndrome coronavirus). Spillover events, where humans get infected with coronaviruses that circulate in animal reservoirs, are common. Recently, three betacoronaviruses crossed from animals to humans, including SARS-CoV-2 causing serious outbreaks.

Furthermore, two coronaviruses previously linked only to animal infection were recently detected in humans who presented with flu-like symptoms.

Coronaviruses derive their name from their crown-like appearance. Coronaviruses are a large group of viruses that have spike proteins on their surface, resembling crown-like thorns. The antibodies elicited by natural infection or by COVID-19 vaccines used for mass immunization between 2020-2023 primarily target the variable receptor binding domain (RBD) present on these spike proteins.

Structure of the spike protein

Coronavirus infection is a multistep process that involves enzymatic cleavage and rearrangement of the surface spike protein. The spike protein has an S1 subunit with the receptor-binding domain and an S2 subunit involved in fusion of the viral and cell membranes thereby facilitating cell entry.

The viral spike protein of SARS-CoV-2 facilitates viral entry by binding primarily to the angiotensin-converting enzyme 2 (ACE2) receptor on human cells.

The SARS-CoV-2 spike contains two cleavage sites: a furin cleavage site at the boundary of the S1 and S2 subunits, and an S2' site that is highly conserved among different coronaviruses.

S1 subunit

The SARS-CoV-2 spike protein uses the RBD on the S1 subunit to engage the target cell's ACE2 receptor.

The S1 subunit is more accessible and remains the main target of many neutralizing antibodies. The S1 subunit, however, is more genetically variable than the S2 subunit; especially when subjected to the selective pressure from antibodies. This propensity towards genetic variability can lead to viral variants with the predominant changes occurring on the S1 subunit. Changes in the receptor-binding domain in SARS-CoV-2 variants of concern have resulted in frequent reinfections, as protection by the antibodies elicited by previous infection and/or vaccines dramatically reduced.

S2 subunit

The viral spike components essential to infection also involve the structurally complex S2 subunit. The S2 subunit contains dynamic elements essential for fusion with the host cell. Once the receptor has bound, the S1 subunit is discarded and the membrane enzyme
5 transmembrane serine protease 2 (TMPRSS2) or endosomal cathepsins cleave the S2 site.

This cleaving leads to insertion of the fusion peptide into the cell membrane culminating in viral fusion.

10 These S2 subunit elements are less disposed towards genetic variability than the RBD, which so far has been capable of retaining or even increasing binding capabilities to ACE2 despite a variety of mutations.

The S2 domain sites yield poorly accessible targets for novel therapeutics to protect
15 against a wider range of coronaviruses.

The stem helix

The stem helix at the base of the viral spike protein is even more difficult to access than elements on the S2 subunit but historically benefits from better-preserved amino acid
20 sequencing.

Treatments and prevention

Limited options for the viral treatment of SARS-CoV-2 exist in the form of small molecule or antibody antiviral drugs. For prevention of SARS-CoV-2 infection, few interventions
25 exist. Most are non-pharmaceutical interventions such as social distancing and mask wearing. These methods are non-specific, and efficacy largely depends on compliance. Thus, there is a need for different treatments, especially treatments that simultaneously target the multitude of SARS-CoV-2 variants of concern such as, for example, broad-neutralizing antibodies (bnAbs).

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Although treatment of SARS-CoV-2 infection with one, two or more antibodies is a possibility, a treatment comprising a single antibody or combination of antibodies would be considerably more cost-efficient. The currently dominant SARS-CoV-2 Omicron

subvariant BA.5 is resistant to most monoclonal antibody therapeutics. Betacoronaviruses, including SARS-CoV-2, also infect a range of species known to have frequent human contact, thus increasing the risk of zoonotic transfer and new outbreaks with SARS-CoV-2 variants or viruses that previously have not infected humans and for
5 which no therapies exist.

There is therefore an urgent need to develop therapeutic mAbs that broadly target β -coronaviruses, as well as new SARS-CoV-2 variants of concern that are not neutralized by antibodies elicited by immunization and/or natural infection.

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It remains vitally important to identify broadly protective therapies that can combat novel coronaviruses. We have surprisingly developed a novel array of broadly protective antibodies which are disclosed herein.

15 SUMMARY OF THE INVENTION

The inventors have discovered that an antibody having complementarity-determining regions (CDR) as disclosed herein can advantageously be used in the treatment of a coronavirus infection, especially in the prophylactic treatment of coronavirus infection.

20 The inventors have surprisingly established when treating a coronavirus infection, mucosal administration of an antibody having CDRs as disclosed herein is a more potent prophylactic route of administration method compared with intraperitoneal administration.

25 The inventors have surprisingly established when treating a coronavirus infection, intranasal administration of an antibody having CDRs as disclosed herein is a more potent prophylactic route of administration method compared with intraperitoneal administration.

30 Significantly, the mucosal administration method of treatment of the present invention is effective against SARS-Cov-2 and variants of concern and does not require the use of additional antibodies.

A mucosal administration treatment method of the invention is effective even at low dosages and counteracts body weight loss.

Complementarity-determining regions (CDRs)

- 5 Preferably, CDR regions are according to Kabat *et al.*, (1991) as described in Sequences of Proteins of Immunological Interest.

In a preferred embodiment, the invention provides an antibody that comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of
10 SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of
15 SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

- 20 In a preferred embodiment, the invention provides an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of
25 SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of
30 SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the antibody is administered to mucosal epithelium.

In a preferred embodiment, the invention provides a method for the treatment of a coronavirus infection in an individual, the method comprising administering to an

individual in need thereof an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the antibody is administered to mucosal epithelium.

In a preferred embodiment, the invention provides a mucosal composition comprising an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

In a preferred embodiment, the invention provides an antibody for use in a method for treatment of a coronavirus infection in an individual, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising

any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the antibody is administered to mucosal epithelium.

In a preferred embodiment, the invention provides an antibody, or a method or composition comprising the antibody, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising SEQ ID NO: 029, a heavy chain CDR2 region comprising SEQ ID NO: 136, and a heavy chain CDR3 region comprising SEQ ID NO: 256, a light chain variable domain that comprises a light chain CDR1 region comprising SEQ ID NO: 372, a light chain CDR2 region comprising SEQ ID NO: 432, and a light chain CDR3 region comprising SEQ ID NO: 573.

In a preferred embodiment, the invention provides an antibody, or a method or composition comprising the antibody, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region consisting of SEQ ID NO: 029, a heavy chain CDR2 region consisting of SEQ ID NO: 136, and a heavy chain CDR3 region consisting of SEQ ID NO: 256, a light chain variable domain that comprises a light chain CDR1 region consisting of SEQ ID NO: 372, a light chain CDR2 region consisting of SEQ ID NO: 432, and a light chain CDR3 region consisting of SEQ ID NO: 573.

In a preferred embodiment, an antibody is disclosed herein for use in a method for the prophylactic treatment of a coronavirus infection, in an individual, the antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606,

612 to 617, 623 to 628, and wherein between 0.1 mg and 20 mg of the antibody is administered to the mucosa.

In a preferred embodiment, an antibody is disclosed herein for use in a method for the prophylactic treatment of a coronavirus infection, in an individual, the antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, and wherein between 0.1 mg and 20 mg of the antibody is administered intranasally.

In a preferred embodiment, an antibody is disclosed herein for use in a method for the prophylactic treatment of a coronavirus infection, in an individual, the antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, and wherein between 0.1 mg and 20 mg of the antibody is administered by oral inhalation.

In a preferred embodiment, a composition comprising an antibody is disclosed herein, the antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, for use in a method of prevention or treatment of a coronavirus infection, wherein the administration route comprises at least one of pulmonary administration, nasal administration and oropharyngeal administration and wherein the nominal dose of the antibody is between 0.1 mg and 20 mg.

Preferably, an antibody as disclosed herein comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302.

Preferably, an antibody as disclosed herein comprises a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

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Preferably, in a method for treatment of the invention, the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130,

136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302.

5 Preferably, in a method for treatment of the invention, the antibody comprises a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

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In an alternative preferred embodiment, the invention provides an antibody that comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 030 to 034, 039 to 044, 047 to 052, 050 to 054, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 137 to 141, 147 to 152, 132 to 136, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 257 to 261, 286 to 291, 252 to 256, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 373 to 377, 383 to 388, 358 to 362, a light chain CDR2 region comprising any one of SEQ ID NO: 433 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 475 to 479, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 574 to 578, 601 to 606, 612 to 617, 569 to 573.

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Embodiments having > 1 CDRs

25 Preferably, an antibody as disclosed herein comprises a heavy chain variable domain that comprises a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196.

Route of administration

30 In a preferred embodiment, the invention provides an antibody as disclosed herein, or a method or composition comprising the antibody as disclosed herein, wherein the antibody is administered by mucosal administration.

In a preferred embodiment, the invention provides an antibody as disclosed herein, or a method or composition comprising the antibody as disclosed herein, wherein the antibody is administered by intravenous administration.

5 In a preferred embodiment, the invention provides an antibody as disclosed herein, or a method or composition comprising the antibody as disclosed herein, wherein the antibody is administered by at least one of oral inhalation, nasal administration, ocular administration, vaginal administration, rectal administration and oropharyngeal administration.

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In a preferred embodiment, the antibody as disclosed herein is administered intranasally.

Such an antibody is useful for the treatment of coronavirus infection in an individual. Preferably, the method for treatment of coronavirus infection is a method for prophylactic
15 and/or therapeutic treatment of a coronavirus infection. Preferably, the antibody is provided to an individual infected with coronavirus. Preferably, the antibody is provided to the individual prophylactically. Preferably, the antibody is provided to the individual after infection but prior to onset of symptoms.

20 In a preferred embodiment, the disclosure provides a method of treating coronavirus infection in an individual, said method comprising mucosal administration, preferably administering intranasally and/or by oral inhalation, to an individual in need thereof an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044,
25 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372
30 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

In a preferred embodiment, the individual is infected with coronavirus or at risk of coronavirus infection.

In a preferred embodiment, the disclosure provides an antibody as disclosed herein for
5 use in the manufacture of a medicament for use in the treatment of a coronavirus infection.

Clauses

The following numbered clauses each represent preferred embodiments of the invention
10 and are part of the description.

Clause 1:

A method for the treatment of a coronavirus infection in an individual, the method comprising administering to an individual in need thereof an antibody comprising a heavy
15 chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of
20 SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324 , 330 to 335 , 350 to 355 , 372 to 377 , 383 to 388 , 415 to 420 , a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437 , 443 to 448 , 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628,
25 wherein the antibody is administered to the mucosa.

Clause 2:

A mucosal composition comprising an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009,
30 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable

domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324 , 330 to 335 , 350 to 355 , 372 to 377 , 383 to 388 , 415 to 420 , a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437 , 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.

Clause 3:

An antibody for use in a method of prevention or treatment of a coronavirus infection in an individual, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324 , 330 to 335 , 350 to 355 , 372 to 377 , 383 to 388 , 415 to 420 , a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437 , , 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the antibody is administered to mucosa.

Clause 4:

A method, composition or antibody according to any preceding Clause, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising SEQ ID NO: 029, a heavy chain CDR2 region comprising SEQ ID NO: 136, and a heavy chain CDR3 region comprising SEQ ID NO: 256, a light chain variable domain that comprises a light chain CDR1 region comprising SEQ ID NO: 372, a light chain CDR2 region comprising SEQ ID NO: 432, and a light chain CDR3 region comprising SEQ ID NO: 573.

Clause 5:

A method, composition or antibody according to any preceding Clause, wherein the method for treatment of coronavirus virus infection is a method for prophylactic and/or

therapeutic treatment of a coronavirus, preferably wherein the method for treatment is for the prophylactic treatment of a SARS-COV-2 infection.

Clause 6:

- 5 A method, composition or antibody according to any preceding Clause, wherein the antibody comprises a heavy chain variable domain having the sequence of SEQ ID NO:629 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid insertions, deletions, substitutions which are not in the heavy chain CDRs.

10 Clause 7:

A method, composition or antibody according to any preceding Clause, wherein the antibody comprises a light chain variable domain having the sequence of SEQ ID NO:630 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid insertions, deletions, substitutions which are not in the light chain CDRs.

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Clause 8:

A method, composition or antibody according to any preceding Clause, wherein the antibody is an IgG antibody, preferably an IgG1 antibody.

20 Clause 9:

A method, composition or antibody according to any preceding Clause, wherein the antibody is provided to the individual prophylactically.

Clause 10:

- 25 A method, composition or antibody according to any preceding Clause, wherein the administration route comprises at least one of oral inhalation, nasal administration, ocular administration and oropharyngeal administration.

Clause 11:

- 30 A method, composition or antibody according to any preceding Clause, wherein the antibody is administered at least once or at least twice monthly.

Clause 12:

A method, composition or antibody according to any preceding Clause, wherein the antibody is administered to the individual at a dosage of between 0.01 mg and 20 mg.

5 Clause 13:

A composition according to any preceding Clause, comprising an antibody in a single dose unit of between 0.01 mg and 20 mg, preferably between 0.1 mg and 15 mg or preferably 0.5 mg and 10 mg, wherein the antibody is as defined in any one of Clauses 1 to 12.

10 Clause 14:

A composition according to any preceding Clause, wherein the composition is self-administered.

Clause 15:

15 A medicament delivery device comprising a composition according to any preceding Clause.

Dosing

20 Preferably, between 0.01 mg and 20 mg of the antibody is administered to an individual, more preferably between 0.1 mg and 20 mg of the antibody is administered to an individual.

The flat dose, or nominal dose, of the antibody is preferably between 0.01 mg and 17 mg, preferably between 0.011 mg and 16 mg, preferably between 0.012 mg and 15 mg, preferably between 0.013 mg and 14 mg, preferably between 0.014 mg and 13 mg, preferably between 0.015 mg and 12 mg, preferably between 0.016 mg and 11 mg, preferably between 0.017 mg and 10 mg, preferably between 0.018 mg and 9 mg, preferably between 0.020 mg and 8 mg, preferably between 0.023 mg and 7 mg, preferably
25 between 0.025 mg and 6 mg, preferably between 0.030 mg and 5 mg, preferably between 0.040 mg and 4 mg, preferably between 0.050 mg and 3 mg, preferably between 0.075 mg and 2 mg, or preferably between 0.10 mg and 1 mg.
30

The flat dose, or nominal dose, of the antibody is preferably between 0.010 mg and 5.0 mg, preferably between 0.020 mg and 4.5 mg, preferably between 0.030 mg and 4.0 mg, preferably between 0.040 mg and 3.5 mg, preferably between 0.050 mg and 3.0 mg, preferably between 0.060 mg and 2.5 mg, preferably between 0.070 mg and 2.0 mg, preferably between 0.080 mg and 1.5 mg, preferably between 0.090 mg and 1.0 mg, or preferably between 0.100 mg and 0.5 mg.

The flat dose, or nominal dose, of the antibody is preferably between 0.010 mg and 15.0 mg, preferably between 0.020 mg and 14.5 mg, preferably between 0.030 mg and 4.0 mg, preferably between 0.040 mg and 13.5 mg, preferably between 0.050 mg and 13.0 mg, preferably between 0.060 mg and 12.5 mg, preferably between 0.070 mg and 12.0 mg, preferably between 0.080 mg and 11.5 mg, preferably between 0.090 mg and 11.0 mg, or preferably between 0.100 mg and 10.5 mg.

15

The flat dose, or nominal dose, of the antibody to be delivered to a human subject is preferably between 0.1 µg and 10 µg, preferably between 0.2 µg and 9 µg, preferably between 0.3 µg and 8 µg, preferably between 0.4 µg and 7 µg, preferably between 0.5 µg and 6 µg, preferably between 0.6 µg and 5 µg, preferably between 0.7 µg and 4 µg, preferably between 0.8 µg and 3 µg, preferably between 0.9 µg and 2 µg or preferably around 1 µg.

The flat dose, or nominal dose, of the antibody to be delivered to a human subject is preferably between 1 mg and 11 mg, preferably between 2 mg and 12 mg, preferably between 3 mg and 13 mg, preferably between 4 mg and 14 mg, preferably between 5 mg and 15 mg, preferably between 6 mg and 16 mg, preferably between 7 mg and 17 mg, preferably between 8 mg and 18 mg, preferably between 9 mg and 19 mg, or preferably between 10 mg and 20 mg.

The flat dose, or nominal dose, of the antibody to be delivered to a human subject is preferably between 1 mg and 20 mg, preferably between 2 mg and 19 mg, preferably between 3 mg and 18 mg, preferably between 4 mg and 17 mg, preferably between 5 mg and 16 mg, preferably between 6 mg and 15 mg, preferably between 7 mg and 14 mg,

preferably between 8 mg and 13 mg, preferably between 9 mg and 12 mg, or preferably between 10 mg and 11 mg.

5 The flat dose, or nominal dose, of the antibody to be delivered to a human subject is preferably between 11 mg and 20 mg, preferably between 10 mg and 19 mg, preferably between 9 mg and 18 mg, preferably between 8 mg and 17 mg, preferably between 7 mg and 16 mg, preferably between 6 mg and 15 mg, preferably between 5 mg and 14 mg, preferably between 4 mg and 13 mg, preferably between 3 mg and 12 mg, preferably between 2 mg and 11 mg, or preferably between 1 mg and 10 mg.

10

In a preferred embodiment, the disclosure further provides a composition formulated for mucosal administration comprising an antibody as disclosed herein in a single dose unit of between 0.1 mg and 20 mg, preferably between 5 mg and 15 mg or preferably 7.5 mg and 12.5 mg.

15

In a preferred embodiment, the disclosure further provides a composition formulated for intranasal administration comprising an antibody as disclosed herein in a single dose unit of between 0.1 mg and 20 mg, preferably between 5 mg and 15 mg or preferably 7.5 mg and 12.5 mg.

20

In a preferred embodiment, the disclosure further provides a composition formulated for oral inhalation comprising an antibody as disclosed herein in a single dose unit of between 0.1 mg and 20 mg, preferably between 5 mg and 15 mg or preferably 7.5 mg and 12.5 mg.

25 **Timing and intervals**

Preferably, the antibody is administered at least once or at least twice per month.

Preferably, the antibody is administered at least once or at least twice per week.

30 The weekly flat dose, or nominal dose, of the antibody is between 0.010 mg and 17 mg, preferably between 0.011 mg and 16 mg, preferably between 0.012 mg and 15 mg, preferably between 0.013 mg and 14 mg, preferably between 0.014 mg and 13 mg, preferably between 0.015 mg and 12 mg, preferably between 0.016 mg and 11 mg,

preferably between 0.017 mg and 10 mg, preferably between 0.018 mg and 9 mg, preferably between 0.020 mg and 8 mg, preferably between 0.023 mg and 7 mg, preferably between 0.025 mg and 6 mg, preferably between 0.030 mg and 5 mg, preferably between 0.040 mg and 4 mg, preferably between 0.050 mg and 3 mg, preferably between 0.075 mg and 2 mg, or preferably between 0.10 mg and 1 mg.

The weekly flat dose, or nominal dose, of the antibody is between 0.010 mg and 5.0 mg, preferably between 0.020 mg and 4.5 mg, preferably between 0.030 mg and 4.0 mg, preferably between 0.040 mg and 3.5 mg, preferably between 0.050 mg and 3.0 mg, preferably between 0.060 mg and 2.5 mg, preferably between 0.070 mg and 2.0 mg, preferably between 0.080 mg and 1.5 mg, preferably between 0.090 mg and 1.0 mg, or preferably between 0.100 mg and 0.5 mg.

Preferably, the antibody is administered at least once or at least twice per day. Preferably, the antibody is administered daily. Preferably, the antibody is administered twice daily.

Preferably, the daily flat dose, or nominal dose, is between 0.001 mg and 17 mg, preferably between 0.011 mg and 16 mg, preferably between 0.012 mg and 15 mg, preferably between 0.013 mg and 14 mg, preferably between 0.014 mg and 13 mg, preferably between 0.015 mg and 12 mg, preferably between 0.016 mg and 11 mg, preferably between 0.017 mg and 10 mg, preferably between 0.018 mg and 9 mg, preferably between 0.020 mg and 8 mg, preferably between 0.023 mg and 7 mg, preferably between 0.025 mg and 6 mg, preferably between 0.030 mg and 5 mg, preferably between 0.040 mg and 4 mg, preferably between 0.050 mg and 3 mg, preferably between 0.075 mg and 2 mg, or preferably between 0.10 mg and 1 mg.

Framework regions

Preferably, the antibody comprises a heavy chain variable domain having the sequence of SEQ ID NO: 629 and/or a light chain variable domain having the sequence of SEQ ID NO: 630.

Preferably, the heavy chain variable domain of said antibody further comprises a heavy chain framework region FR1 of SEQ ID NO: 631, a heavy chain framework region FR2 of

SEQ ID NO: 632, a heavy chain framework region FR3 of SEQ ID NO: 633, and/or a heavy chain framework region FR4 of SEQ ID NO: 634.

Preferably, said light chain variable domain further comprises a light chain framework region FR1 of SEQ ID NO: 635, a light chain framework region FR2 of SEQ ID NO: 636, a light chain framework region FR3 of SEQ ID NO: 637, and/or a light chain framework region FR4 of SEQ ID NO: 638.

Combination compositions

In a preferred embodiment, we disclose a composition comprising a First binding fragment as disclosed herein and a Second binding fragment, wherein the First fragment comprises a sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the First fragment comprises a sequence comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573. The Second binding fragment comprises a sequence comprising any one of SEQ ID NO.: 639, 640, 641, 642, 643 or SEQ ID NO.: 644. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

In a preferred embodiment, we disclose a composition comprising a First binding fragment as disclosed herein and a Second binding fragment, wherein the First fragment comprises a sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the First fragment comprises any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573. The Second binding fragment comprises a sequence comprising any one of SEQ ID NO.: 645, 646, 647, 648, 649 or SEQ ID NO.: 650.

Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

5

In a preferred embodiment, we disclose a composition comprising a First binding fragment as disclosed herein and a Second binding fragment, wherein the First fragment comprises a sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191
10 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the First fragment comprises a sequence comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573. The Second
15 binding fragment comprises a sequence comprising any one of SEQ ID NO.: 651, 652, 653, 654, 655 or SEQ ID NO.: 656. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

20

In a preferred embodiment, we disclose a composition comprising a First binding fragment as disclosed herein and a Second binding fragment, wherein the First fragment comprises a sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191
25 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the First fragment comprises a sequence comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 and 573. The Second
30 binding fragment comprises a sequence comprising any one of SEQ ID NO.: 657, 658, 659, 660, 661 or SEQ ID NO.: 662. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

Bispecific antibodies

In a preferred embodiment, we disclose a bispecific antibody, wherein the bispecific antibody is capable of binding to the stem helix of a coronavirus. In a preferred
5 embodiment, we disclose a bispecific antibody, wherein the bispecific antibody is capable of binding to the stem helix of SARS-CoV-2.

In a preferred embodiment, we disclose an anti- coronavirus bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix
10 of a coronavirus and a second Fab capable of binding to the fusion peptide of a coronavirus. In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of SARS-CoV-2.

15 In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432 or 573; alternatively wherein the first Fab comprises
20 a sequence comprising any one or more of preferred SEQ ID Numbers: 651, 652, 653, 654, 655 or 656; or alternatively wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 657, 658, 659, 660, 661 to 662, and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 639, 640, 641, 642, 643 to 644; or alternatively wherein the second Fab
25 comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 645, 646, 647, 648, 649 to 650.

In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix
30 of SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432 or 573 and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 639, 640, 641, 642, 643 to 644. Preferably, the fragment is selected from anyone of the group comprising a

full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

5 In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432 or 573 and wherein the second Fab comprises a
10 sequence comprising any one or more of preferred SEQ ID Numbers: 645, 646, 647, 648, 649 to 650. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

15

In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab also capable of binding to the stem helix of SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred
20 SEQ ID Numbers: 029, 136, 256, 372, 432 or 573 and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 651, 652, 653, 654, 655 to 656. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies,
25 tetrabodies and epitope binding fragments thereof.

In a preferred embodiment, we disclose an anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab also capable of binding to the stem helix of SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred
30 SEQ ID Numbers: 029, 136, 256, 372, 432 or 573 and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 657, 658, 659, 660, 661 to 662. Preferably, the fragment is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain

antibodies, scFv, scFv-Fc, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

5 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 029, 136 or 256, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 660, 661, or 662.

10 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 029, 136 or 256, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 642, 643, or 644.

15 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 029, 136 or 256, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 648, 649, or 650.

20 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 029, 136 or 256, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 654, 655, or 656.

25 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 657, 658, or 659, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 372, 432 or 573.

30 In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 639, 640, or 641, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 372, 432 or 573.

In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 645, 646, or 647, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 372, 432 or 573.

5

In a preferred embodiment, we disclose a bispecific antibody comprising a First Fab and a Second Fab, wherein the First Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 651, 652 or 653, and wherein the Second Fab comprises any one or more of sequences shown in preferred SEQ ID Numbers: 372, 432 or 573.

10

The present invention also provides construction, expression, purification methods for a bispecific antibody having a function of binding to the stem helix of SARS-CoV-2, and use of the bispecific antibody in the field of medicine and especially in the prevention and/or treatment of SARS-CoV-2 infections.

15

Clauses

The following numbered clauses each represent preferred embodiments of the invention and are part of the description.

20 Clause 26:

An anti-coronavirus, preferably anti-SARS-CoV-2 bispecific antibody or an antigen binding fragment thereof, having a first Fab capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432 or 573 and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 639, 640, 641, 642, 643 to 644.

Clause 27:

A bispecific antibody or an antigen binding fragment thereof according to Clause 26, comprising a first Fab capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, and a second Fab capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one

or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432 and/or 573 and wherein the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 639, 640, 641, 642, 643 and/or 644.

5 Clause 28:

A bispecific antibody or an antigen binding fragment thereof according to Clauses 26 or 27, comprising a first Fab specifically binding to the stem helix of a coronavirus, preferably SARS-CoV-2, and a second Fab specifically binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, characterized in that:

- 10 a.) the first Fab comprises a heavy chain variable region comprising as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and a light chain variable region comprising as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and
- 15 b.) the second Fab comprises a heavy chain variable region comprising as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 639, a Heavy Chain CDR2 region of SEQ ID NO: 640 and a Heavy Chain CDR3 region of SEQ ID NO: 641 and a light chain variable region comprising as CDRs a Light Chain CDR1 region of SEQ ID NO: 642, a Light Chain CDR2 region of SEQ ID NO: 643 and a Light Chain CDR3 region of SEQ ID NO: 644.

20

Clause 29:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 28, comprising:

- a) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody or an antigen binding fragment thereof, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, and
- 25 b) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody or an antigen binding fragment thereof, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2,
- 30 wherein the constant domains CL and CH1 from the antibody or an antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, are replaced by each other.

Clause 30:

A bispecific antibody or an antigen binding fragment thereof according to Clause 29, wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and the VL domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2 comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 639, a Heavy Chain CDR2 region of SEQ ID NO: 640 and a Heavy Chain CDR3 region of SEQ ID NO: 641 and the VL domain of the antibody or the antigen binding fragment thereof that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 642, a Light Chain CDR2 region of SEQ ID NO: 643 and a Light Chain CDR3 region of SEQ ID NO: 644.

Clause 31:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 28, comprising:

- a) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2; and
- b) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein constant domains CL and CH1 from the antibody that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2 are replaced by each other.

Clause 32:

A bispecific antibody or an antigen binding fragment thereof according to Clause 31,

wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and the VL domain of the antibody capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and

wherein the VH domain of the antibody capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 639, a Heavy Chain CDR2 region of SEQ ID NO: 640 and a Heavy Chain CDR3 region of SEQ ID NO: 641 and the VL domain of the antibody capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 642, a Light Chain CDR2 region of SEQ ID NO: 643 and a Light Chain CDR3 region of SEQ ID NO: 644.

Clause 33:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 28, comprising:

- a) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2; and
- b) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein domains VL-CL and VH-CH1 from the antibody that specifically binds to the fusion peptide of a coronavirus, preferably SARS-CoV-2, are replaced by each other.

Clause 34:

- A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 33, wherein the first Fab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical,

at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 629.

Clause 35:

5 A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 33, wherein the second Fab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid
10 sequences set forth in SEQ ID NO: 663.

Clause 36:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 33, wherein the first Fab comprises a light chain variable region having an amino
15 acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 630.

20 Clause 37:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 33, wherein the second Fab comprises a light chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical,
25 at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 664.

Clause 38:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses
30 26 to 33, wherein the bispecific antibody or an antigen binding fragment thereof is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent

antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

Clause 39:

- 5 A method for the production of a bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38, comprising a) culturing a host cell, comprising an expression vector, comprising a polynucleotide encoding a bispecific antibody or an antibody fragment according to any one of the preceding Clauses under conditions which permit the production of said bispecific antibody or an antigen binding fragment thereof,
10 and b) isolating said bispecific antibody or an antigen binding fragment thereof.

Clause 40:

- A nucleic acid molecule comprising a nucleic acid sequence, wherein the nucleic acid sequence encodes the bispecific antibody or antigen binding fragment thereof, a heavy
15 chain variable region and/or a light chain variable region of the bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38, preferably wherein the nucleic acid molecule is an isolated nucleic acid molecule.

Clause 41:

- 20 A nucleic acid molecule comprising a nucleic acid sequence, wherein the nucleic acid sequence encodes the bispecific antibody or antigen binding fragment thereof, a heavy chain variable region and/or light chain variable region of the bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38 and Clause 40, wherein the nucleic acid sequence comprises at least anyone of:
- 25 (i) a first nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 029, or a first nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 029,
- (ii) a second nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 136, or a second nucleic acid sequence encoding the amino acid sequence having
30 at most 1, 2, 3, 4, or 5 amino acids different from SEQ ID NO. 136,
- (iii) a third nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 256, or a third nucleic acid sequence encoding the amino acid sequence having at most 1, 2 or 3 amino acids different from SEQ ID NO. 256,

- (iv) a fourth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 372, or a fourth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3 or 4 amino acids different from SEQ ID NO. 372,
- (v) a fifth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 432, or a fifth nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 432,
- (vi) a sixth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 573, or a sixth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, or 4 amino acids different from SEQ ID NO. 573,
- (vii) a seventh nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 639, or a seventh nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 639,
- (viii) an eighth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 640, or an eighth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, 4, or 5 amino acids different from SEQ ID NO. 640,
- (ix) a ninth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 641, or a ninth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, or 4 amino acids different from SEQ ID NO. 641,
- (x) a tenth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 642, or a tenth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, or 4 amino acids different from SEQ ID NO. 642,
- (xi) an eleventh nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 643, or an eleventh nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 643, and
- (xii) a twelfth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 644, or a twelfth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, or 3 amino acids different from SEQ ID NO. 644.

Clause 42:

- A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38 for use in a method of treating a coronavirus infection in a subject.

Clause 43:

A composition comprising the bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38.

5 Clause 44:

A composition according to Clause 43 further comprising a second medicament, for simultaneous, separate, or sequential administration.

Clause 45:

10 A composition according to Clause 44, wherein the second medicament comprises a second antibody or antigen binding fragment thereof.

Clause 46:

15 A composition according to Clause 44, wherein the second medicament comprises a bispecific antibody or bispecific antigen binding fragment thereof.

Clause 47:

A composition according to Clause 43, wherein the composition further comprises a pharmaceutically acceptable excipient or carrier.

20

Clause 48:

25 A composition according to Clause 43, for use in inhibiting and /or treating a coronavirus infection in a subject, preferably, a SARS-CoV-1 or SARS-CoV-2 infection in a subject, comprising an effective amount of the bispecific antibody or an antigen binding fragment thereof, nucleic acid molecule, or vector, and optionally a pharmaceutically acceptable excipient or carrier.

Clause 49:

30 The composition of Clause 43, for use as a medicament.

Clause 50:

An inhaler device comprising the composition of Clause 43.

Clause 51:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38, wherein the bispecific antibody or an antigen binding fragment thereof is
5 bivalent.

Clause 52:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 26 to 38, wherein the bispecific antibody or antigen-binding fragment thereof is capable
10 of binding to the stem helix and/or the fusion peptide of at least one of an α -coronavirus, β -coronavirus, γ -coronavirus, and δ -coronavirus, preferably at least an α -coronavirus and/or a β -coronavirus.

Clauses

15 The following numbered clauses each represent preferred embodiments of the invention and are part of the description.

Clause 53:

An anti-coronavirus, preferably anti-SARS-CoV-2 bispecific antibody or an antigen
20 binding fragment thereof, having a first Fab capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432, or 573 and wherein the second Fab comprises a sequence comprising any one or more
25 of preferred SEQ ID Numbers: 645, 646, 647, 648, 649 to 650.

Clause 54:

A bispecific antibody or an antigen binding fragment thereof according to Clause 53, comprising a first Fab capable of binding to the stem helix of a coronavirus, preferably
30 SARS-CoV-2, and a second Fab capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein the first Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 029, 136, 256, 372, 432, and/or 573 and wherein

the second Fab comprises a sequence comprising any one or more of preferred SEQ ID Numbers: 645, 646, 647, 648, 649 and/or 650.

Clause 55:

5 A bispecific antibody or an antigen binding fragment thereof according to Clauses 53 or 54, comprising a first Fab specifically binding to the stem helix of a coronavirus, preferably SARS-CoV-2, and a second Fab specifically binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, characterized in that:

10 a.) the first Fab comprises a heavy chain variable region comprising as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and a light chain variable region comprising as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and

15 b.) the second Fab comprises a heavy chain variable region comprising as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 645, a Heavy Chain CDR2 region of SEQ ID NO: 646 and a Heavy Chain CDR3 region of SEQ ID NO: 647 and a light chain variable region comprising as CDRs a Light Chain CDR1 region of SEQ ID NO: 648, a Light Chain CDR2 region of SEQ ID NO: 649 and a Light Chain CDR3 region of SEQ ID NO: 650.

20 Clause 56:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 55, comprising:

25 a) A light chain comprising VL-CL domains and heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody or an antigen binding fragment thereof, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, and

b) A light chain comprising VL-CL domains and heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody or an antigen binding fragment thereof, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2,

30 wherein constant domains CL and CH1 from the antibody or an antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, are replaced by each other.

Clause 57:

A bispecific antibody or an antigen binding fragment thereof according to Clause 56, wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and the VL domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 645, a Heavy Chain CDR2 region of SEQ ID NO: 646 and a Heavy Chain CDR3 region of SEQ ID NO: 647 and the VL domain of the antibody or the antigen binding fragment thereof that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 648, a Light Chain CDR2 region of SEQ ID NO: 649 and a Light Chain CDR3 region of SEQ ID NO: 650.

Clause 58:

A bispecific antibody, or an antigen binding fragment thereof according to any of Clauses 53 to 55, comprising:

- a) A light chain comprising VL-CL domains and heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2; and
- b) A light chain comprising VL-CL domains and heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein constant domains CL and CH1 from the antibody that is capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2 are replaced by each other.

Clause 59:

A bispecific antibody or an antigen binding fragment thereof according to Clause 58,

wherein the VH domain of the antibody or the antigen binding fragment thereof that is capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 029, a Heavy Chain CDR2 region of SEQ ID NO: 136 and a Heavy Chain CDR3 region of SEQ ID NO: 256 and the VL domain of the antibody capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 372, a Light Chain CDR2 region of SEQ ID NO: 432 and a Light Chain CDR3 region of SEQ ID NO: 573, and

wherein the VH domain of the antibody capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs, a Heavy Chain CDR1 region of SEQ ID NO: 645, a Heavy Chain CDR2 region of SEQ ID NO: 646 and a Heavy Chain CDR3 region of SEQ ID NO: 647 and the VL domain of the antibody capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, comprises as CDRs a Light Chain CDR1 region of SEQ ID NO: 648, a Light Chain CDR2 region of SEQ ID NO: 649 and a Light Chain CDR3 region of SEQ ID NO: 650.

Clause 60:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 55, comprising:

- a) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the stem helix of a coronavirus, preferably SARS-CoV-2; and
- b) A light chain comprising VL-CL domains and a heavy chain comprising VH-CH1-CH2-CH3 domains of an antibody, capable of binding to the fusion peptide of a coronavirus, preferably SARS-CoV-2, wherein domains VL-CL and VH-CH1 from the antibody that specifically binds to the fusion peptide of a coronavirus, preferably SARS-CoV-2, are replaced by each other.

Clause 61:

- A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 60, wherein the first Fab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical,

at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 629.

Clause 62:

5 A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 60, wherein the second Fab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid
10 sequences set forth in SEQ ID NO: 665.

Clause 63:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 60, wherein the first Fab comprises a light chain variable region having an amino
15 acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical, at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 630.

20 Clause 64:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 60, wherein the second Fab comprises a light chain variable region having an amino acid sequence that is at least 90% identical, at least 91% identical, at least 92% identical, at least 93% identical, at least 94% identical, at least 95% identical, at least 96% identical,
25 at least 97% identical, at least 98% identical, or at least 99% identical to the amino acid sequences set forth in SEQ ID NO: 666.

Clause 65:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses
30 53 to 60, wherein the bispecific antibody or antigen binding fragment thereof is selected from anyone of the group comprising a full-length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, scFv-Fc, bi, tri or tetra-valent

antibodies, Bis-scFv, diabodies, triabodies, tetrabodies and epitope binding fragments thereof.

Clause 66:

- 5 A method for the production of a bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 65, comprising a) culturing a host cell, comprising an expression vector, comprising a polynucleotide encoding a bispecific antibody or an antibody fragment according to any one of the preceding Clauses under conditions which permit the production of said bispecific antibody or an antigen binding fragment thereof,
10 and b) isolating said bispecific antibody or an antigen binding fragment thereof.

Clause 67:

- A nucleic acid molecule comprising a nucleic acid sequence, wherein the nucleic acid sequence encodes the bispecific antibody or antigen binding fragment thereof, a heavy
15 chain variable region and/or a light chain variable region of the bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 65, preferably wherein the nucleic acid molecule is an isolated nucleic acid molecule.

Clause 68:

- 20 A nucleic acid molecule comprising a nucleic acid sequence, wherein the nucleic acid sequence encodes the bispecific antibody or antigen binding fragment thereof, a heavy chain variable region and/or light chain variable region of the bispecific antibody or the antigen binding fragment thereof according to any of Clauses 53 to 65 and Clause 67, wherein the nucleic acid sequence comprises at least anyone of:
- 25 (i) a first nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 029, or a first nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 029,
- (ii) a second nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 136, or a second nucleic acid sequence encoding the amino acid sequence having
30 at most 1, 2, 3, 4, or 5 amino acids different from SEQ ID NO. 136,
- (iii) a third nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 256, or a third nucleic acid sequence encoding the amino acid sequence having at most 1, 2 or 3 amino acids different from SEQ ID NO. 256,

- (iv) a fourth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 372, or a fourth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3 or 4 amino acids different from SEQ ID NO. 372,
- (v) a fifth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 432, or a fifth nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 432,
- (vi) a sixth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 573, or a sixth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, or 4 amino acids different from SEQ ID NO. 573,
- (vii) a seventh nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 645, or a seventh nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 645,
- (viii) an eighth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 646, or an eighth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, 4, or 5 amino acids different from SEQ ID NO. 646,
- (ix) a ninth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 647, or a ninth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, 3, 4, or 5 amino acids different from SEQ ID NO. 647,
- (x) a tenth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 648, or a tenth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, or 3 amino acids different from SEQ ID NO. 648,
- (xi) an eleventh nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 649, or an eleventh nucleic acid sequence encoding the amino acid sequence having at most 1 or 2 amino acids different from SEQ ID NO. 649, and
- (xii) a twelfth nucleic acid sequence encoding the amino acid sequence as set forth in SEQ ID NO. 650, or a twelfth nucleic acid sequence encoding the amino acid sequence having at most 1, 2, or 3 amino acids different from SEQ ID NO. 650.

Clause 69:

- A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 65 for use in a method of treating a coronavirus infection in a subject.

Clause 70:

A composition comprising the bispecific antibody and/or an antigen binding fragment thereof according to any of Clauses 53 to 65.

5 Clause 71:

A composition according to Clause 70 further comprising a second medicament, for simultaneous, separate, or sequential administration.

Clause 72:

10 A composition according to Clause 71, wherein the second medicament comprises a second antibody or antigen binding fragment thereof.

Clause 73:

15 A composition according to Clause 71, wherein the second medicament comprises a bispecific antibody or bispecific antigen binding fragment thereof.

Clause 74:

A composition according to Clause 70, wherein the composition further comprises a pharmaceutically acceptable excipient or carrier.

20

Clause 75:

25 A composition according to Clause 70, for use in inhibiting and /or treating a coronavirus infection in a subject, preferably, a SARS-CoV-1 or SARS-CoV-2 infection in a subject, comprising an effective amount of the bispecific antibody or an antigen binding fragment thereof, nucleic acid molecule, or vector, and optionally a pharmaceutically acceptable excipient or carrier.

Clause 76:

The composition of Clause 70, for use as a medicament.

30

Clause 77:

An inhaler device comprising the composition of Clause 70.

Clause 78:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 65, wherein the bispecific antibody or an antigen binding fragment thereof is
5 bivalent.

Clause 79:

A bispecific antibody or an antigen binding fragment thereof according to any of Clauses 53 to 65, wherein the bispecific antibody or antigen binding fragment thereof is capable
10 of binding to the stem helix and/or the fusion peptide of at least one of an α -coronavirus, β -coronavirus, γ -coronavirus, and δ -coronavirus, preferably at least an α -coronavirus and/or a β -coronavirus.

15 DESCRIPTION OF THE DRAWINGS

Figure 1. Survival after lethal challenge - CV3-25.

Kaplan-Meier survival curves of the intraperitoneal prophylactic treatment group. Animals (n=10 per group), treated with a dose titration with the control antibody, CV3-25, at day -1. At day 0, animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A
20 vehicle control group was included (PBS). Lines are nudged relative to the Y-axis to improve visual representation.

Figure 2. Survival after lethal challenge - CV3-25.

Kaplan-Meier survival curves of the intranasal prophylactic treatment group. Animals
25 (n=10 per group, except 15 mg/kg where n=8), treated with a dose titration with the control antibody, CV3-25, at day -1. At day 0, animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Lines are nudged relative to the Y-axis to improve visual representation.

Figure 3. Survival after lethal challenge - Antibody according to the invention.

Kaplan-Meier survival curves of the intraperitoneal prophylactic treatment group. Animals (n=10 per group, except 0.5 mg/kg where n=9), treated with a dose titration with
30

the antibody having heavy chain CDR1 as SEQ ID NO: 029, heavy chain CDR2 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, at day -1. At day 0, animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Lines are nudged relative to the X and Y-axis to improve visual representation.

Figure 4. Survival after lethal challenge – Antibody according to the invention.

Kaplan-Meier survival curves of the intranasal prophylactic treatment group. Animals (n=10 per group), treated with a dose titration with the antibody having heavy chain CDR1 as SEQ ID NO: 029, heavy chain CDR2 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, at day -1. At day 0, animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Lines are nudged relative to the Y-axis to improve visual representation.

Figure 5. Bodyweight change - CV3-25.

Bodyweight change (%) relative to day 0, for the intraperitoneal prophylactic treatment group. Animals (n=10 per group) were treated with a dose titration of the control antibody, CV3-25, at day -1 intranasally. At day 0 animals were infected with $10^{3.5}$ TCI D₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Bars represent the 95% CI. of the mean. If a mouse died / was euthanized during follow-up of the study, the last observed bodyweight was carried forward.

Figure 6. Bodyweight change - CV3-25.

Bodyweight change (%) relative to day 0, for the intranasal prophylactic treatment group. Animals (n=10 per group, except 15 mg/kg where n=8) were treated with a dose titration of the control antibody, CV3-25, at day -1 intranasally. At day 0 animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Bars represent the 95% CI. of the mean. If a mouse died / was euthanized during follow-up of the study, the last observed bodyweight was carried forward.

Figure 7. Bodyweight change - Antibody according to the invention.

Bodyweight change (%) relative to day 0, for the intraperitoneal prophylactic treatment group. Animals (n=10 per group, except 0.5 mg/kg where n=9) were treated with a dose titration of the antibody having heavy chain CDR1 as SEQ ID NO: 029, heavy chain CDR2
5 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, at day -1 intranasally. At day 0 animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Bars represent the 95% CI. of the mean. If a mouse died / was euthanized during follow-up of the study, the last observed
10 bodyweight was carried forward.

Figure 8. Bodyweight change - Antibody according to the invention.

Bodyweight change (%) relative to day 0, for the intranasal prophylactic treatment group. Animals (n=10 per group) were treated with a dose titration of the antibody having heavy
15 chain CDR1 as SEQ ID NO: 029, heavy chain CDR2 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, at day -1 intranasally. At day 0 animals were infected with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta. A vehicle control group was included (PBS). Bars represent the 95% CI. of the mean. If a mouse died / was
20 euthanized during follow-up of the study, the last observed bodyweight was carried forward.

Figure 9. Linear epitope mapping against Spike helix domain of alpha and beta coronaviruses.

25 Grey highlighted amino acids were identified as the epitope where the antibody is binding the Spike protein. Target sequences for the 7 tested strains are aligned by Clustal. *may contain multiple smaller parts of the epitope. Epitope footprints (B) and paratope hotspots (A) for the antibody against the SH domain of SARS-CoV-2. CDR regions for heavy and light chains are indicated.

30

DETAILED DESCRIPTION OF THE INVENTION

For the purpose of clarity and a concise description, features may be described herein as part of the same or separate embodiments, however, it will be appreciated that the disclosure includes embodiments having combinations of all or some of the features

described. References to “method for treatment”, “treatment method”, “antibody for use” and “use of an antibody in the manufacture of a medicament” can be used interchangeably and embodiments disclosed in relation to any one of those aspects also applies in relation to said other aspects. In other words, they all refer to medical treatments involving an
5 antibody as disclosed herein.

Prophylactic treatment

The term ‘**prophylactic treatment**’, as used herein, includes reference to a treatment for preventing infection of an individual with a coronavirus, or preventing symptoms after
10 infection with a coronavirus, or preventing severe symptoms after known infection with a coronavirus with or without symptoms, or preventing hospitalization and death after infection with a coronavirus.

Prevention of an infection is preferably performed by administration of an antibody as
15 disclosed herein prior to coronavirus exposure *i.e.* pre-exposure prophylaxis.

‘Prophylactically’ therefore preferably means prior to virus exposure. Nonetheless, it may also involve administration after infection, for example for reducing the replication or spread, or increasing clearance of the virus *i.e.* post-exposure prophylaxis.

20

Infected individuals may present with no symptoms. Alternatively, infected individuals may present with symptoms.

Preferably, post-exposure prophylaxis involves administering an antibody as disclosed
25 herein after coronavirus exposure to prevent symptomatic disease.

Preferably, post-exposure prophylaxis involves administering an antibody as disclosed herein after coronavirus exposure to prevent severe disease, in particular hospitalization.

30 In a treatment method of the invention, prophylactic treatment involves administration of antibodies against coronavirus at a point in time when the individual is not infected with coronavirus. Preferably, said antibodies bind to a conserved epitope of the spike

protein of a coronavirus virion. In some embodiments, an individual in need thereof is not (yet) infected with coronavirus.

Therapeutic treatment

5 The term '**therapeutic treatment**', as used herein, includes reference to treatment of a viral infection (including coronavirus disease) after viral infection has taken place. A viral infection involves the entry of the body by the virus, and/or the replication of the virus in the body and/or the spreading of the virus to cells, tissues or locations in the body that were previously uninfected. A viral infection may cause one or more disease, but may also
10 be latent, in other words may reside in the body without causing symptoms or disease.

Coronavirus

The term '**coronavirus**', as used herein, includes reference to a positive-sense single-stranded RNA virus belonging to the family of Coronaviridae.

15

Preferably, an antibody as disclosed herein is capable of specifically binding to the stem helix of a coronavirus, in particular SARS-CoV-2.

Preferably, an antibody as disclosed herein is capable of specifically binding to the stem
20 helix of SARS-CoV-2 variants of concern.

Preferably, the antibody as disclosed herein is capable of neutralizing a coronavirus, in particular SARS-CoV-2.

25 Preferably, an antibody as disclosed herein is capable of neutralizing at least one or more, preferably two or more, preferably three or more, preferably four or more, even more preferably five or more coronavirus subtypes.

The phrase "is capable of" as used in, means the ability of an antibody or an antigen-binding fragment thereof as described herein is enough to bind to at least a part of an
30 antigen, such as the stem helix of a coronavirus, in particular SARS-CoV-2 and/or the fusion protein of a coronavirus, in particular SARS-CoV-2. The binding affinity or the binding ability of the antibody and/or the antigen-binding fragment thereof as described

herein can be measured using any methods known by a person skilled in the art. The phrase “is capable of” as used here, encompasses but not limited to the phrase “specifically binding” or “specifically bind to”.

5 **Coronavirus infection**

The term ‘**coronavirus infection**’, as used herein, includes reference to the pathological or non-pathological, preferably pathological, entrance and residence of a coronavirus of any type in a human host. The infecting virus may replicate within the host, its cells or the cells of its microbiome. The infecting virus may or may not cause a disease, for example COVID-19. The infection may or may not be able to be detected by methods for virus infection detection known in the art. The infected individual may or may not be aware of the infection. Typical, but non-exclusive locations of the human body where, for example SARS-CoV-2, may be located in an infected individual, are the respiratory system and/or cells thereof and the cardiovascular system and/or cells thereof. The term ‘coronavirus infection’, as used herein, further includes reference to the entrance and residence of a part of a coronavirus of any type that is able to cause viral replication in a human host. The term ‘**coronavirus infection**’ encompasses symptoms or disease following the infection, e.g. COVID-19. The term ‘coronavirus infection’ encompasses ‘SARS-CoV-2 infection’.

20

Epitope

An “epitope”, as used herein, includes reference to a moiety that is capable of binding to an antibody as disclosed herein with sufficiently high affinity to form a detectable antigen-antibody complex.

25

Individual

The term ‘**individual**’, as used herein, includes reference to a mammal or human that is subject to, or a risk of suffering from viral infection. Infection may take place in any system, tissue or cell belonging to the host, including the host’s microbiome. Coronavirus infection and the disease coronavirus may occur in individuals of all age groups and sexes. Nonetheless, preferably, the individual is a human, in particular an elderly human such as a human that is at least 60, 65, 70, 75, 80, or at least 85 years old, or that has an increased risk of infection because of occupation or living environment. Preferably, the individual is at risk of suffering from severe illness, for example COVID-19, once infected.

In preferred embodiments, the individual has an underlying disease such as (i) a respiratory disease such as asthma, COPD, chronic bronchitis and lung emphysema, (ii) cardiovascular disease such as cardiac arrhythmia or individuals that have received cardiac surgery, (iii) diabetes, (iv) renal failure and/or (v) a disease affecting the immune system, for instance immunocompromised individuals, or higher risk of viral infection because of occupation.

The phrase '**an individual**', as used herein, includes reference to a mammal such as a but not limited to a human that benefits from a specified therapy, for example, the phrase 'an individual' may encompass Non-human primates (NHP).

Preferably, the individual is a mammal, more preferably a human.

Administering and Administration

The terms '**administering**' and '**administration**', as used herein, include reference to the provision of one or more drug and optionally one or more adjuvant with the aim to treat, cure, reduce, or prevent a disease or its symptoms in an individual, or to promote the individual's well-being. Preferred methods of administration of the antibody as disclosed herein include mucosal administration, preferably intranasal administration and oral inhalation.

An individual in need thereof

The phrase '**an individual in need thereof**', as used herein, includes reference to a mammal such as a human that benefits from a specified therapy. A treatment method of the invention may be used prophylactically, the exhibition of symptoms or indications for coronavirus infection are not required. Individuals that are especially in need of the method or antibody for use of the invention, are individuals with an elevated risk of coronavirus infection, individuals with an elevated risk of developing severe symptoms (illness), for example COVID-19, and/or individuals with an elevated risk of dying from COVID-19. The person skilled in the art is aware of the risk factors for an elevated risk of coronavirus infection, an elevated risk of developing severe symptoms of coronavirus infection, and an elevated risk of dying from coronavirus infection.

Antibody

The term '**antibody**', as used herein, includes reference to an intact immunoglobulin, including monoclonal antibodies, such as chimeric, humanized or human monoclonal antibodies, or to a binding molecule comprising an antigen-binding domain (such as heavy chain CDRs 1-3 of a variable domain) of an antibody as disclosed herein or an antibody that competes with an antibody as disclosed herein for specific binding to the binding partner of the immunoglobulin.

In other words, functional fragments of antibodies are also encompassed by the term 'antibody'. Antibodies are generally Y-shaped proteins. Within the antibody, constant domain and variable domains are generally present. The variable domain facilitates antigen binding. An antibody generally comprises two heavy chains and two light chains. Both the heavy chains and the light chains are partially constant and partially variable. Antibodies occur in a few classes: IgA, IgD, IgE, IgG and IgM. Preferably, the antibody of the invention is of the IgG, preferably IgG1, class. Some classes may be further subdivided into subclasses or isotypes. For example, the IgG class is subdivided into the subclasses IgG1, IgG2, IgG3 and IgG4. Preferably, the antibody of the invention is of the IgG, preferably IgG1, class. Antigen-binding regions, or antigen-binding fragments of an antibody, which are encompassed by the term 'antibody' and which are therefore part of the present invention, may include, for example, Fab, F(ab'), F(ab')₂, dAb, Fv, Fd, CDR fragments, diabodies, triabodies, tetrabodies, single-chain antibodies (scFv, scFv-Fc), bivalent single-chain antibodies, single-chain phage antibodies, (poly)peptides that contain at least a fragment of an immunoglobulin that is sufficient to confer specific antigen binding to the (poly)peptide, etc. The above fragments may be produced synthetically or by enzymatic or chemical cleavage of intact immunoglobulins or they may be genetically engineered by recombinant DNA techniques. The methods for production of antibodies and antigen-binding fragments are well-known to a person skilled in the art. The antibody may be conjugated or unconjugated. The antibody may be conjugated, linked, or otherwise physically or functionally associated with an effector moiety or tag, such as inter alia an enzyme, a liposome, a radioactive substance, a fluorophore, a toxic substance. Antibodies may have been stabilized, multimerized, humanized or otherwise manipulated.

Antibodies may be neutralizing, which includes reference to inhibition of a virus as measured by an *in vitro* neutralization assay, for instance in terms of viral host cell entry and/or viral replication. Neutralization can for example be achieved by inhibiting the attachment or adhesion of the virus to the cell surface, or by inhibition of the fusion of viral and cellular membranes following attachment of the virus to the target cell or by inhibiting viral egress from cells. Neutralization does not specify the method of neutralization. Preferably, the antibody is cross-neutralizing, which includes reference to the ability of the antibodies of the invention to bind a set of different molecules, preferably different molecules of different subtypes belonging to the Coronaviridae family.

The term “domain” or “region” as used herein, with reference to a part of an antibody, bispecific antibody, or an antigen binding fragment thereof, can be used interchangeably herein.

The phrase “antigen-binding fragments”, “antigen binding fragments”, “antigen fragment”, “a fragment of an antibody” or “antigen-binding molecule” as used herein, means a protein, polypeptide or molecular complex comprising or consisting of at least one complementarity determining region (CDR) that alone, or in combination with one or more additional CDRs and/or framework regions (FRs), as described herein, is capable of binding to a part of an antigen, including the stem helix of a coronavirus, in particular SARS-CoV-2, and/or the stem helix of a coronavirus, in particular SARS-CoV-2 and its variants of concern. The phrases “antigen-binding fragments”, “antigen binding fragments”, “antigen fragment”, “a fragment of an antibody” or “antigen-binding molecule” as used herein, can be used interchangeably. For instance, the phrase “antigen binding fragments” as used herein is to be used interchangeably with the phrase “antibody fragments” as used herein.

Antibodies comprise complementarity determining regions situated on the variable domains of the heavy chain and the light chain. The CDRs contribute to a large extent to the antigen binding site. Three CDRs can be distinguished, namely CDR1, CDR2 and CDR3. As each CDR can be located on either the light chain or the heavy chain, there are generally six CDRs for each antigen receptor that collectively contact the antigen: the light chain CDR1, the light chain CDR2, the light chain CDR3, the heavy chain CDR1,

the heavy chain CDR2 and the heavy chain CDR3. The CDRs of type CDR3 are the most variable. The CDRs can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured or
5 activated. Epitopes may also consist of or comprise post-translational modifications of proteins. Antibodies of the invention that are of particular interest, are antibodies comprising CDRs that recognize coronavirus antigens, such as the spike protein and in particular the stem helix of the spike protein. The antibody as disclosed herein binds to a conserved epitope in the stem helix at the base of the spike protein of the SARS-CoV-2
10 virion. The epitope of the antibody as disclosed herein uses light and heavy chain CDR loops.

The antibody as disclosed herein can be used in isolated or non-isolated form.

15 Preferably, the compositions of the invention comprise a single anti-coronavirus antibody as disclosed herein.

Preferably, the antibody of the invention as disclosed herein can cross-neutralize coronavirus, in particular SARS-CoV-2.

20

Furthermore, the antibody as disclosed herein can be used alone or in a mixture comprising the antibody (or variant, fragment or bispecific thereof) as disclosed herein, and/or with other antibodies that bind to a coronavirus and have a coronavirus inhibiting effect. In other words, the antibody as disclosed herein can be used in combination, e.g.,
25 as a pharmaceutical composition or co-administration of compositions comprising two or more antibodies that specifically bind coronavirus. For example, antibodies having different, but complementary activities can be combined in a single therapy to achieve a desired therapeutic or prophylactic effect, but alternatively, antibodies having identical activities can also be combined in a single therapy to achieve a desired prophylactic or
30 therapeutic effect. Optionally, the mixture further comprises at least one other therapeutic agent.

Preferably, the antibody as disclosed herein are a bispecific antibody and/or an antigen binding fragment thereof, wherein the bispecific antibody is capable of binding to the stem

helix of a coronavirus and/or capable of binding to fusion peptide of coronavirus. The phrase “capable of binding” encompasses the phrase “specifically binds to”, in other words, an antibody, a bispecific antibody and/or an antigen binding fragment thereof as disclosed herein are that is capable of binding to an epitope may also be capable of binding the other
5 epitopes.

Preferably, the coronavirus as described herein includes SARS-CoV-2 and variants.

The phrase “are replaced by each other”, “are mutually interchanged”, “swap places with
10 each other”, or “are traded for one another” as used herein, includes reference to at least a part of the heavy chain domains of an antibody or an antigen-binding fragment as described herein such as when a CH1 and/or VH, is substituted by at least a part of the light chain domains such as CL and/or VL to which said at least a part of the heavy chain domains are paired, and at the same instant, said at least a part of the light chain domains
15 is substituted by said at least a part of the heavy chain domains. The phrase “are replaced by each other”, “are mutually interchanged”, “swap places with each other”, or “are traded for one another” are to be used interchangeably herein.

20 Preferably, the antibody as disclosed herein is a human antibody.

Framework regions

Antibodies also comprise framework regions, generally four framework regions (FR1, FR2, FR3 and FR4) on each of the variable heavy chain domain and variable light chain
25 domain. The CDRs are situated between the framework regions (preferably in the order FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4) and both the CDRs and framework regions together define a heavy chain variable domain (or region) and light chain variable domain (or region) which may also be referred to as an antigen-binding region or domain.

30

IgG antibody

The term ‘IgG antibody’, as used herein, includes reference to an antibody comprising two antigen-binding sites. IgG is the most common antibody in human serum. Heavy chains

of IgG antibodies are of type γ , which can be subdivided in $\gamma 1$, $\gamma 2$, $\gamma 3$ and $\gamma 4$. Preferably, the antibodies described herein are $\gamma 1$ heavy chains. Light chains of IgG antibodies are of type λ or κ . Preferably, the antibodies described herein are λ light chains.

- 5 Preferably, the antibody is an IgG antibody, preferably an IgG1 antibody.

IgA antibody

The term 'IgA antibody', as used herein, includes reference to an antibody comprising two to four antigen-binding sites. IgA is the most abundant antibody in mucosal secretions.

- 10 An IgA antibody can be produced in monomeric, dimeric or secretory form, with two or four antigen-binding sites, respectively, and can exist as an IgA1 or IgA2 isotype. [Heavy chains of IgA antibodies are of type α , which can be subdivided in $\alpha 1$ and $\alpha 2$. Light chains of IgA antibodies are of type λ or κ .

- 15 Preferably, the antibody is an IgA antibody.

IgM antibody

The term 'IgM antibody', as used herein, includes reference to an antibody comprising ten to twelve antigen-binding sites. An IgM antibody can be produced in pentameric or
20 hexameric form. Heavy chains of IgM antibodies are of type μ . Light chains of IgM antibodies are of type λ or κ .

Preferably, the antibody is an IgM antibody.

Anti-Coronavirus antibody

The term 'anti-coronavirus antibody', as used herein, includes reference to an antibody as disclosed herein, *i.e.* an antibody that can be used in a treatment method of the invention. Preferably, the anti-coronavirus antibody of the invention is able to treat different subtypes of coronavirus.

30

For the avoidance of doubt, the term 'anti-coronavirus antibody', can be used interchangeably with 'coronavirus antibody'.

A composition

In a preferred embodiment, an antibody disclosed herein is the sole active ingredient in a composition administered for treatment, e.g., the antibody is provided in a composition as
5 the sole active ingredient.

In a preferred embodiment, the active ingredients comprise an antibody disclosed herein, e.g., the antibody is provided either as a composition as the sole active ingredient in a composition administered for treatment or in a combination with another antibody.

10

In a preferred embodiment, a first antibody as disclosed herein is provided as a composition in combination with a second antibody, wherein the first antibody comprises a CDR sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to
15 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the first antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573, and
20 the second antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 639, 640, 641, 642, 643 or SEQ ID NO.: 644. Preferably wherein the composition is administered for prophylactic and/or therapeutic treatment.

In a preferred embodiment, a first antibody as disclosed herein is provided as a
25 composition in combination with a second antibody, wherein the first antibody comprises a CDR sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448,
30 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the first antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573, and the second antibody comprises CDR sequences comprising any one or more of SEQ ID NO:

645, 646, 647, 648, 649 or SEQ ID NO.: 650. Preferably wherein the composition is administered for prophylactic and/or therapeutic treatment.

In a preferred embodiment, a first antibody as disclosed herein is provided as a composition in combination with a second antibody, wherein the first antibody comprises a CDR sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the first antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573, and the second antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 651, 652, 653, 654, 655 or SEQ ID NO.: 656. Preferably wherein the composition is administered for prophylactic and/or therapeutic treatment.

In a preferred embodiment, a first antibody as disclosed herein is provided as a composition in combination with a second antibody, wherein the first antibody comprises a CDR sequence comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. More preferably wherein the first antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 029, 136, 256, 372, 432 or 573, and the second antibody comprises CDR sequences comprising any one or more of SEQ ID NO: 657, 658, 659, 660, 661 or SEQ ID NO.: 662. Preferably wherein the composition is administered for prophylactic and/or therapeutic treatment.

Preferably, the composition of the invention is a water-based composition such as an aqueous liquid. Preferably, the composition of the invention further comprises one or more salts, for example sodium chloride. The composition of the invention may further comprise one or more buffering agents, for example sodium acetate. The composition of the invention may further comprise one or more carbohydrates, such as sucrose, or other

active ingredients, such as other antibodies, neuraminidase inhibitors, endonuclease inhibitors, and adjuvants such as oils, cytokines, emulsifiers, or combinations thereof. The pH of the composition of the invention can be between 4 and 8, more preferably the pH is around 5.5. Preferably the pH is around 7.4.

5

Mucosal composition

The term '**mucosal composition**', as used herein, refers to any pharmaceutical formulation that may be topically applied to a mucosal surface and delays or resists the mucosal flushing or removal action.

10

The term '**mucosal composition**', may be used in reference to a route of administration in which an antibody, as disclosed herein, is provided into the nasal cavity, oropharyngeal region or upper respiratory tract, preferably through the nostrils, as part of a prophylactic and/or therapeutic treatment as disclosed herein.

15

Mucosally

The mucosa comprises membranes that line cavities in the human body, covering internal organs, and consist of one or more layers of epithelial cells and loose connective tissue, which may produce **mucus**. The term '**mucosally**', as used herein, may also be referred to as '**mucosal administration**', and includes reference to a route of administration in which a drug is prophylactically and/or therapeutically provided to the **mucosa**, for example, **mucosa found in** the nose, mouth, lungs, vagina, rectum or stomach. The mucous membrane lubricates and protects these organs and cavities from abrasive particles and bodily fluids, as well as invasive pathogens.

20

Preferably, the antibodies of the invention are administered mucosally.

Intranasally

The term '**intranasally**', as used herein, may also be referred to as '**nasal administration**', and includes reference to a route of administration in which a drug is provided into the upper respiratory tract and/or lower respiratory tract, preferably through the nostrils, as part of a prophylactic and/or therapeutic treatment as disclosed herein. Preferably, the administration provides for drug in the nasal cavity. The back section of the nasal cavity

25

is also referred to as the pharynx. Nasal administration preferably provides for delivery of antibodies as disclosed herein in the mucous membrane lining the nasal cavity. Intranasal administration can be performed using, for instance, a nasal spray or nose drops. In some embodiments, the drug is delivered to the nasal cavity via the oral route.

5 For example, RetroNose uses a breath-actuated pressurised metered-dose inhaler (pMDI) to administer drugs through the buccal cavity during the nasal expiratory phase. Such methods allow the drug particles to enter the nasal cavities through the pharynx.

Preferably, the antibodies of the invention are administered intranasally.

10 With intranasal administration, a drug is provided through the nostrils to the upper respiratory tract as part of a prophylactic and/or therapeutic treatment as disclosed herein. Preferably, the administration provides for drug in the nasal cavity. Nasal administration can either be a form of topical administration or systemic administration,

15 as the drugs thus locally delivered can go on to have either local or systemic effects. In the present case, with antibodies as disclosed herein, nasal administration is preferably a form of topical administration.

Intranasal administration as disclosed herein may be done using a medicament in liquid

20 form, preferably in the form of drops or nasal spray. The aqueous liquid may comprise adjuvants. These adjuvants may for example be salts, oils, cytokines, emulsifiers, buffering agents, carbohydrates and combinations thereof. Intranasal administration may also be done using a medicament in solid form, such as powders.

25 **Oral inhalation**

The term 'oral inhalation', as used herein, may also be referred to as 'mouth inhalation', and includes reference to a route of administration in which a drug is provided through the mouth to the upper and/or lower respiratory tract such as lungs, as part of a prophylactic and/or therapeutic treatment of the invention. Oral inhalation may for

30 example be applied for drugs in their powdered form and drugs in the form of liquid droplets or aerosols.

Preferably, the antibodies of the invention are administered by oral inhalation.

With oral inhalation, a drug is provided through the mouth to the respiratory tract, preferably lower respiratory tract such as lungs, as part of a prophylactic and/or therapeutic treatment of the invention. As described further herein, oral inhalation also
5 includes nasal drug delivery (also referred to as nasal drug delivery via the oral route).

Oral inhalation may for example be applied for drugs in their powdered form and drugs in the form of liquid droplets or aerosols. Oral inhalation may include the use of an inhaler. The inhaler may be involved in the achievement of the dose that was determined.
10 The drug that is administered by oral inhalation may reach the lung but may also partially be cleared out by exhalation.

Administration by oral inhalation as disclosed herein may be done using a medicament comprising aerosols in powdered (solid) or liquid form. Powdered aerosols comprising
15 particles smaller than 3 μm in diameter will primarily reach the respiratory region of the lung, and will therefore be absorbed better than larger particles. The medicament may comprise adjuvants. These adjuvants may for example be salts, oils, cytokines, emulsifiers, buffering agents, carbohydrates and combinations thereof.

20 **Oropharyngeal administration**

The term 'oropharyngeal administration', as used herein, may also be referred to as delivery to the part of the pharynx that lies between the soft palate and the hyoid bone and includes reference to a route of administration in which a drug is provided via either the mouth or nasal passages as part of a prophylactic and/or therapeutic treatment.
25 Oropharyngeal administration may, for example, be used for drugs in their powdered form and drugs in the form of liquid droplets or aerosols.

Preferably, the antibodies of the invention are administered by oropharyngeal administration.

30

Prior to

The term 'prior to', as used herein, includes reference to the administration of an antibody before an individual has been exposed to, or is infected with, a coronavirus.

Preferably, the antibody as disclosed is administered to an individual up to 24 hours prior to coronavirus exposure, for example between zero and 24 hours before the individual has been exposed to said coronavirus.

5

Preferably, the antibody as disclosed is administered to an individual up to 48 hours prior to coronavirus exposure, for example between zero and 48 hours before the individual has been exposed to said coronavirus.

- 10 In a preferred embodiment, the antibody is administered 2 days or more prior to coronavirus exposure. In a preferred embodiment, the antibody is administered 3 days or more prior to coronavirus exposure. In a preferred embodiment, the antibody is administered 4 days, or more prior to coronavirus exposure. In a preferred embodiment, the antibody is administered 5 days or more prior to coronavirus exposure. In a preferred
15 embodiment, the antibody is administered 6 days or more prior to coronavirus exposure. In a preferred embodiment, the antibody is administered 7 days or more prior to coronavirus exposure.

Dosage

- 20 The term 'dosage' as used herein, refers to the amount of antibody to be given at a particular time (e.g., over the course of a 24-hour, 12-hour, 30-minute period, etc.). A dose refers to a single dosing episode, whether the dose is a unit dosage form or multiple unit dosage forms taken together (e.g., ingestion of two or more pills, receiving two or more nasal administrations). A dosage includes reference to a pharmaceutical dosage form
25 wherein the medicament is packaged for administration as, e.g., a single-unit dose or multiple-unit dose. A dosage may also be administered as, e.g., one or more drops of an antibody-comprising composition (e.g., nasal drops) or one or more sprays of an antibody-comprising composition (e.g., nasal sprays).

- 30 Preferably, a suitable dosage of an antibody as disclosed herein contains a dose of between 0.01 mg and 20 mg, preferably 0.1 mg and 15 mg, more preferably around 0.5 mg and 10 mg or even around 1 mg, e.g. when the dosage is for intranasal administration. Such dosages are also referred to as "flat dosages" or "nominal dosages" in contrast to dosages based on the weight of the patient. Flat dosages have the advantage that the medicament

can be packaged in a single-unit dose, for example. A single dose of an antibody according to the present invention can provide protection from coronavirus infection for several days and may be provided “on demand” or “as needed”. For example, an individual may administer antibody before leaving the house or before coming into contact with other
5 individuals.

In order to provide long-lasting protection, the antibody may be administered on a regular basis. For example, the antibody is administered once, or at least once per month. In a preferred embodiment, the antibody is administered once, or at least once per week, e.g.,
10 twice weekly. In a preferred embodiment, the antibody is administered once, or at least once per day. As is clear to a skilled person, less antibody may be administered when the antibody is administered more frequently (e.g., daily). In a preferred embodiment, between 0.01 mg to 20 mg of antibody is administered per week (e.g., once or twice weekly or daily). In an exemplary embodiment, between 0.1 mg and 25 mg is administered daily
15 (*i.e.* between 0.7 mg and 175 mg per week). In an exemplary embodiment, 0.5 mg to 3.5 mg is administered daily (*i.e.* between 3.5 mg and 24.5 mg per week).

The invention also provides a composition formulated for intranasal administration and/or oral inhalation comprising an antibody as disclosed herein, preferably in a single
20 dose unit between 0.1 mg to 20 mg, preferably 0.5 mg to 15 mg or preferably 1 mg to 12.5 mg.

Use in a method for treatment

The present invention relates *inter alia* to an antibody as disclosed herein, for use in a
25 method for treatment of coronavirus infection in an individual, more specifically the antibody can be used in a method for the prophylactic and/or therapeutic treatment of coronavirus infection in an individual.

Complementarity-determining regions (CDRs)

30 Preferably, the CDR regions are identified according to Kabat *et al.* (1991) as described in Sequences of Proteins of Immunological Interest.

In a preferred embodiment, the binding interaction of the binding molecules, preferably the antibody, and the stem helix is mediated exclusively by light and heavy chain variable sequences.

- 5 The antibody as disclosed herein may be capable of specifically binding to a coronavirus that is in attenuated or inactivated form or that is viable, and/or in an infective form.

The antibody as disclosed herein is also capable of specifically binding to one or more fragments of the coronavirus.

10

An antibody as disclosed herein comprises a preferred heavy chain CDR1 sequence comprising any one of the following SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070. A CDR comprising the amino acid sequence SEQ ID NO: 029 is especially preferred.

15

An antibody as disclosed herein comprises a preferred heavy chain CDR2 sequence comprising any one of the following SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196. A CDR comprising the amino acid sequence SEQ ID NO: 136 is especially preferred.

20

An antibody as disclosed herein comprises a preferred heavy chain CDR3 sequence comprising any one of the following SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302. A CDR comprising the amino acid sequence SEQ ID NO: 256 is especially preferred.

25

An antibody as disclosed herein comprises a preferred light chain CDR1 sequence comprising any one of the following SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420. A CDR comprising the amino acid sequence SEQ ID NO: 372 is especially preferred.

30

An antibody as disclosed herein comprises a preferred light chain CDR2 sequence comprising any one of the following SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465

to 470, 476 to 481, 508 to 513. A CDR comprising the amino acid sequence SEQ ID NO: 432 is especially preferred.

5 An antibody as disclosed herein comprises a preferred light chain CDR3 sequence comprising any one of the following SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628. A CDR comprising the amino acid sequence SEQ ID NO: 573 is especially preferred.

10 An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a heavy chain framework region FR1 of SEQ ID NO: 631.

An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a heavy chain framework region FR2 of SEQ ID NO: 632.

15 An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a heavy chain framework region FR3 of SEQ ID NO: 633.

An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a heavy chain framework region FR4 of SEQ ID NO: 634.

20

In a preferred embodiment, the heavy chain variable domain of said antibody comprises - a heavy chain framework region FR1 of SEQ ID NO: 631, a heavy chain framework region FR2 of SEQ ID NO: 632, a heavy chain framework region FR3 of SEQ ID NO: 633, and/or a heavy chain framework region FR4 of SEQ ID NO: 634, preferably all said heavy chain
25 heavy chain framework regions FR1 to FR4.

An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a light chain framework region FR1 of SEQ ID NO: 635.

30 An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a light chain framework region FR2 of SEQ ID NO: 636.

An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a light chain framework region FR3 of SEQ ID NO: 637.

5 An antibody as disclosed herein comprises a heavy chain variable domain that further comprises at least a light chain framework region FR4 of SEQ ID NO: 638.

In a preferred embodiment, the light chain variable domain of said antibody comprises - a light chain framework region FR1 of SEQ ID NO: 635, a light chain framework region FR2 of SEQ ID NO: 636, a light chain framework region FR3 of SEQ ID NO: 637, and/or
10 a light chain framework region FR4 of SEQ ID NO: 638, preferably all said light chain framework regions are FR1 to FR4.

Most preferably, an antibody as disclosed herein comprises a heavy chain variable domain having the sequence of SEQ ID NO: 629 and/or a light chain variable domain having the
15 sequence of SEQ ID NO: 630.

In treatment methods of the invention, the heavy chain variable domain (VH) of the antibody is preferably indicated as SEQ ID NO:629. In treatment methods or compositions of the invention, the light chain variable domain (VL) of the antibody is preferably
20 indicated as SEQ ID NO:630. In treatment methods or compositions of the invention, the antibody can be an antibody as disclosed herein, or a binding molecule comprising an antigen-binding domain such as a variable domain (V) thereof.

Preferably, an antibody as disclosed herein comprises a heavy chain variable domain
25 having the sequence of SEQ ID NO:629 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, more preferably having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, substitutions.

Preferably, an antibody as disclosed herein comprises a light chain variable domain
30 having the sequence of SEQ ID NO:630 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10, more preferably having 0, 1, 2, 3, 4 or 5 amino acid insertions, deletions, substitutions.

Preferably, said amino acid insertions, deletions, substitutions in respect of either the heavy chain variable domain and/or the light chain variable domain are not in the CDRs.

SEQUENCES

CDRs and framework regions defined herein are based on the Kabat numbering scheme as described in Sequences of Proteins of Immunological Interest (Kabat *et al.*, 1991).

5 **Heavy chain CDR1 region (SEQ ID NO:001 to SEQ ID NO:076)**

	SEQ ID NO.: 001	FTSY
	SEQ ID NO.: 002	FTSYY
	SEQ ID NO.: 003	FTSYYM
10	SEQ ID NO.: 004	FTSYYMH
	SEQ ID NO.: 005	FTSYYMHW
	SEQ ID NO.: 006	FTSYYMHWV
	SEQ ID NO.: 007	FTSYYMHWVR
	SEQ ID NO.: 008	FTSYYMHWVRQ
15	SEQ ID NO.: 009	FTSYYMHWVRQA
	SEQ ID NO.: 010	GYTFT
	SEQ ID NO.: 011	GYTFTS
	SEQ ID NO.: 012	GYTFTSY
	SEQ ID NO.: 013	GYTFTSYY
20	SEQ ID NO.: 014	GYTFTSYYM
	SEQ ID NO.: 015	GYTFTSYYMH
	SEQ ID NO.: 016	GYTFTSYYMHW
	SEQ ID NO.: 017	GYTFTSYYMHWV
	SEQ ID NO.: 018	GYTFTSYYMHWVR
25	SEQ ID NO.: 019	GYTFTSYYMHWVRQ
	SEQ ID NO.: 020	GYTFTSYYMHWVRQA
	SEQ ID NO.: 021	HWVR
	SEQ ID NO.: 022	HWVRQ
	SEQ ID NO.: 023	HWVRQA
30	SEQ ID NO.: 024	MHWV
	SEQ ID NO.: 025	MHWVR

	SEQ ID NO.: 026	MHWVRQ
	SEQ ID NO.: 027	MHWVRQA
	SEQ ID NO.: 028	SYYM
	SEQ ID NO.: 029	SYYMH
5	SEQ ID NO.: 030	SYYMHW
	SEQ ID NO.: 031	SYYMHWV
	SEQ ID NO.: 032	SYYMHWVR
	SEQ ID NO.: 033	SYYMHWVRQ
	SEQ ID NO.: 034	SYYMHWVRQA
10	SEQ ID NO.: 035	TFTS
	SEQ ID NO.: 036	TFTSY
	SEQ ID NO.: 037	TFTSYY
	SEQ ID NO.: 038	TFTSYYM
	SEQ ID NO.: 039	TFTSYYMH
15	SEQ ID NO.: 040	TFTSYYMHW
	SEQ ID NO.: 041	TFTSYYMHWV
	SEQ ID NO.: 042	TFTSYYMHWVR
	SEQ ID NO.: 043	TFTSYYMHWVRQ
	SEQ ID NO.: 044	TFTSYYMHWVRQA
20	SEQ ID NO.: 045	TSYY
	SEQ ID NO.: 046	TSYYM
	SEQ ID NO.: 047	TSYYMH
	SEQ ID NO.: 048	TSYYMHW
	SEQ ID NO.: 049	TSYYMHWV
25	SEQ ID NO.: 050	TSYYMHWVR
	SEQ ID NO.: 051	TSYYMHWVRQ
	SEQ ID NO.: 052	TSYYMHWVRQA
	SEQ ID NO.: 053	WVRQ
	SEQ ID NO.: 054	WVRQA
30	SEQ ID NO.: 055	YMHW

	SEQ ID NO.: 056	YMHWW
	SEQ ID NO.: 057	YMHWVR
	SEQ ID NO.: 058	YMHWVRQ
	SEQ ID NO.: 059	YMHWVRQA
5	SEQ ID NO.: 060	YTFT
	SEQ ID NO.: 061	YTFTS
	SEQ ID NO.: 062	YTFTSY
	SEQ ID NO.: 063	YTFTSYY
	SEQ ID NO.: 064	YTFTSYYM
10	SEQ ID NO.: 065	YTFTSYYMH
	SEQ ID NO.: 066	YTFTSYYMHW
	SEQ ID NO.: 067	YTFTSYYMHWV
	SEQ ID NO.: 068	YTFTSYYMHWVR
	SEQ ID NO.: 069	YTFTSYYMHWVRQ
15	SEQ ID NO.: 070	YTFTSYYMHWVRQA
	SEQ ID NO.: 071	YYMH
	SEQ ID NO.: 072	YYMHW
	SEQ ID NO.: 073	YYMHWV
	SEQ ID NO.: 074	YYMHWVR
20	SEQ ID NO.: 075	YYMHWVRQ
	SEQ ID NO.: 076	YYMHWVRQA

Heavy chain CDR2 region (SEQ ID NO:077 to SEQ ID NO:196)

25	SEQ ID NO.: 077	EWMGLITPSGDDTYYA
	SEQ ID NO.: 078	EWMGLITPSGDDTYYAQ
	SEQ ID NO.: 079	EWMGLITPSGDDTYYAQR
	SEQ ID NO.: 080	EWMGLITPSGDDTYYAQRF
	SEQ ID NO.: 081	EWMGLITPSGDDTYYAQRFQ
30	SEQ ID NO.: 082	EWMGLITPSGDDTYYAQRFQG
	SEQ ID NO.: 083	EWMGLITPSGDDTYYAQRFQGR

	SEQ ID NO.: 084	EWMGLITPSGDDTYYAQRFQGRV
	SEQ ID NO.: 085	EWMGLITPSGDDTYYAQRFQGRVT
	SEQ ID NO.: 086	EWMGLITPSGDDTYYAQRFQGRVTM
	SEQ ID NO.: 087	EWMGLITPSGDDTYYAQRFQGRVTMT
5	SEQ ID NO.: 088	GDDTYYAQ
	SEQ ID NO.: 089	GDDTYYAQR
	SEQ ID NO.: 090	GDDTYYAQRF
	SEQ ID NO.: 091	GDDTYYAQRFQ
	SEQ ID NO.: 092	GDDTYYAQRFQG
10	SEQ ID NO.: 093	GDDTYYAQRFQGR
	SEQ ID NO.: 094	GDDTYYAQRFQGRV
	SEQ ID NO.: 095	GDDTYYAQRFQGRVT
	SEQ ID NO.: 096	GDDTYYAQRFQGRVTM
	SEQ ID NO.: 097	GDDTYYAQRFQGRVTMT
15	SEQ ID NO.: 098	GLITPSGDDTYYA
	SEQ ID NO.: 099	GLITPSGDDTYYAQ
	SEQ ID NO.: 100	GLITPSGDDTYYAQR
	SEQ ID NO.: 101	GLITPSGDDTYYAQRF
	SEQ ID NO.: 102	GLITPSGDDTYYAQRFQ
20	SEQ ID NO.: 103	GLITPSGDDTYYAQRFQG
	SEQ ID NO.: 104	GLITPSGDDTYYAQRFQGR
	SEQ ID NO.: 105	GLITPSGDDTYYAQRFQGRV
	SEQ ID NO.: 106	GLITPSGDDTYYAQRFQGRVT
	SEQ ID NO.: 107	GLITPSGDDTYYAQRFQGRVTM
25	SEQ ID NO.: 108	GLITPSGDDTYYAQRFQGRVTMT
	SEQ ID NO.: 109	ITPSGDDTYYA
	SEQ ID NO.: 110	ITPSGDDTYYAQ
	SEQ ID NO.: 111	ITPSGDDTYYAQR
	SEQ ID NO.: 112	ITPSGDDTYYAQRF
30	SEQ ID NO.: 113	ITPSGDDTYYAQRFQ

	SEQ ID NO.: 114	ITPSGDDTYYAQRFQG
	SEQ ID NO.: 115	ITPSGDDTYYAQRFQGR
	SEQ ID NO.: 116	ITPSGDDTYYAQRFQGRV
	SEQ ID NO.: 117	ITPSGDDTYYAQRFQGRVT
5	SEQ ID NO.: 118	ITPSGDDTYYAQRFQGRVTM
	SEQ ID NO.: 119	ITPSGDDTYYAQRFQGRVTMT
	SEQ ID NO.: 120	LEWMGLITPSGDDTYYA
	SEQ ID NO.: 121	LEWMGLITPSGDDTYYAQ
	SEQ ID NO.: 122	LEWMGLITPSGDDTYYAQR
10	SEQ ID NO.: 123	LEWMGLITPSGDDTYYAQRF
	SEQ ID NO.: 124	LEWMGLITPSGDDTYYAQRFQ
	SEQ ID NO.: 125	LEWMGLITPSGDDTYYAQRFQG
	SEQ ID NO.: 126	LEWMGLITPSGDDTYYAQRFQGR
	SEQ ID NO.: 127	LEWMGLITPSGDDTYYAQRFQGRV
15	SEQ ID NO.: 128	LEWMGLITPSGDDTYYAQRFQGRVT
	SEQ ID NO.: 129	LEWMGLITPSGDDTYYAQRFQGRVTM
	SEQ ID NO.: 130	LEWMGLITPSGDDTYYAQRFQGRVTMT
	SEQ ID NO.: 131	LITPSGDDTYYA
	SEQ ID NO.: 132	LITPSGDDTYYAQ
20	SEQ ID NO.: 133	LITPSGDDTYYAQR
	SEQ ID NO.: 134	LITPSGDDTYYAQRF
	SEQ ID NO.: 135	LITPSGDDTYYAQRFQ
	SEQ ID NO.: 136	LITPSGDDTYYAQRFQG
	SEQ ID NO.: 137	LITPSGDDTYYAQRFQGR
25	SEQ ID NO.: 138	LITPSGDDTYYAQRFQGRV
	SEQ ID NO.: 139	LITPSGDDTYYAQRFQGRVT
	SEQ ID NO.: 140	LITPSGDDTYYAQRFQGRVTM
	SEQ ID NO.: 141	LITPSGDDTYYAQRFQGRVTMT
	SEQ ID NO.: 142	MGLITPSGDDTYYA
30	SEQ ID NO.: 143	MGLITPSGDDTYYAQ

	SEQ ID NO.: 144	MGLITPSGDDTYYAQR
	SEQ ID NO.: 145	MGLITPSGDDTYYAQRF
	SEQ ID NO.: 146	MGLITPSGDDTYYAQRFQ
	SEQ ID NO.: 147	MGLITPSGDDTYYAQRFQG
5	SEQ ID NO.: 148	MGLITPSGDDTYYAQRFQGR
	SEQ ID NO.: 149	MGLITPSGDDTYYAQRFQGRV
	SEQ ID NO.: 150	MGLITPSGDDTYYAQRFQGRVT
	SEQ ID NO.: 151	MGLITPSGDDTYYAQRFQGRVTM
	SEQ ID NO.: 152	MGLITPSGDDTYYAQRFQGRVTMT
10	SEQ ID NO.: 153	PSGDDTYYA
	SEQ ID NO.: 154	PSGDDTYYAQ
	SEQ ID NO.: 155	PSGDDTYYAQR
	SEQ ID NO.: 156	PSGDDTYYAQRF
	SEQ ID NO.: 157	PSGDDTYYAQRFQ
15	SEQ ID NO.: 158	PSGDDTYYAQRFQG
	SEQ ID NO.: 159	PSGDDTYYAQRFQGR
	SEQ ID NO.: 160	PSGDDTYYAQRFQGRV
	SEQ ID NO.: 161	PSGDDTYYAQRFQGRVT
	SEQ ID NO.: 162	PSGDDTYYAQRFQGRVTM
20	SEQ ID NO.: 163	PSGDDTYYAQRFQGRVTMT
	SEQ ID NO.: 164	SGDDTYYA
	SEQ ID NO.: 165	SGDDTYYAQ
	SEQ ID NO.: 166	SGDDTYYAQR
	SEQ ID NO.: 167	SGDDTYYAQRF
25	SEQ ID NO.: 168	SGDDTYYAQRFQ
	SEQ ID NO.: 169	SGDDTYYAQRFQG
	SEQ ID NO.: 170	SGDDTYYAQRFQGR
	SEQ ID NO.: 171	SGDDTYYAQRFQGRV
	SEQ ID NO.: 172	SGDDTYYAQRFQGRVT
30	SEQ ID NO.: 173	SGDDTYYAQRFQGRVTM

SEQ ID NO.: 174 SGDDTYAQRFGQGRVTMT
SEQ ID NO.: 175 TPGDDTYA
SEQ ID NO.: 176 TPGDDTYAQ
SEQ ID NO.: 177 TPGDDTYAQR
5 SEQ ID NO.: 178 TPGDDTYAQR
SEQ ID NO.: 179 TPGDDTYAQRFG
SEQ ID NO.: 180 TPGDDTYAQRFGG
SEQ ID NO.: 181 TPGDDTYAQRFGQR
SEQ ID NO.: 182 TPGDDTYAQRFGQGRV
10 SEQ ID NO.: 183 TPGDDTYAQRFGQGRVT
SEQ ID NO.: 184 TPGDDTYAQRFGQGRVTM
SEQ ID NO.: 185 TPGDDTYAQRFGQGRVTMT
SEQ ID NO.: 186 WMGLITPGDDTYA
SEQ ID NO.: 187 WMGLITPGDDTYAQ
15 SEQ ID NO.: 188 WMGLITPGDDTYAQR
SEQ ID NO.: 189 WMGLITPGDDTYAQRFG
SEQ ID NO.: 190 WMGLITPGDDTYAQRFG
SEQ ID NO.: 191 WMGLITPGDDTYAQRFGG
SEQ ID NO.: 192 WMGLITPGDDTYAQRFGQR
20 SEQ ID NO.: 193 WMGLITPGDDTYAQRFGQGRV
SEQ ID NO.: 194 WMGLITPGDDTYAQRFGQGRVT
SEQ ID NO.: 195 WMGLITPGDDTYAQRFGQGRVTM
SEQ ID NO.: 196 WMGLITPGDDTYAQRFGQGRVTMT

25 **Heavy chain CDR3 region (SEQ ID NO:197 to SEQ ID NO:302)**

SEQ ID NO.: 197 AGGF
SEQ ID NO.: 198 AGGFD
SEQ ID NO.: 199 AGGFDV
30 SEQ ID NO.: 200 AGGFDVW
SEQ ID NO.: 201 AGGFDVWG

	SEQ ID NO.: 202	AGGFDVWGQ
	SEQ ID NO.: 203	AGGFDVWGQG
	SEQ ID NO.: 204	AGGFDVWGQGT
	SEQ ID NO.: 205	AKMSRA
5	SEQ ID NO.: 206	AKMSRAG
	SEQ ID NO.: 207	AKMSRAGG
	SEQ ID NO.: 208	AKMSRAGGF
	SEQ ID NO.: 209	AKMSRAGGFD
	SEQ ID NO.: 210	AKMSRAGGFDV
10	SEQ ID NO.: 211	AKMSRAGGFDVW
	SEQ ID NO.: 212	AKMSRAGGFDVWG
	SEQ ID NO.: 213	AKMSRAGGFDVWGQ
	SEQ ID NO.: 214	AKMSRAGGFDVWGQG
	SEQ ID NO.: 215	AKMSRAGGFDVWGQGT
15	SEQ ID NO.: 216	CAKMSRA
	SEQ ID NO.: 217	CAKMSRAG
	SEQ ID NO.: 218	CAKMSRAGG
	SEQ ID NO.: 219	CAKMSRAGGF
	SEQ ID NO.: 220	CAKMSRAGGFD
20	SEQ ID NO.: 221	CAKMSRAGGFDV
	SEQ ID NO.: 222	CAKMSRAGGFDVW
	SEQ ID NO.: 223	CAKMSRAGGFDVWG
	SEQ ID NO.: 224	CAKMSRAGGFDVWGQ
	SEQ ID NO.: 225	CAKMSRAGGFDVWGQG
25	SEQ ID NO.: 226	CAKMSRAGGFDVWGQGT
	SEQ ID NO.: 227	GFDV
	SEQ ID NO.: 228	GFDVW
	SEQ ID NO.: 229	GFDVWG
	SEQ ID NO.: 230	GFDVWGQ
30	SEQ ID NO.: 231	GFDVWGQG

	SEQ ID NO.: 232	GFDVWGQGT
	SEQ ID NO.: 233	GGFD
	SEQ ID NO.: 234	GGFDV
	SEQ ID NO.: 235	GGFDVW
5	SEQ ID NO.: 236	GGFDVWG
	SEQ ID NO.: 237	GGFDVWGQ
	SEQ ID NO.: 238	GGFDVWGQG
	SEQ ID NO.: 239	GGFDVWGQGT
	SEQ ID NO.: 240	KMSRA
10	SEQ ID NO.: 241	KMSRAG
	SEQ ID NO.: 242	KMSRAGG
	SEQ ID NO.: 243	KMSRAGGF
	SEQ ID NO.: 244	KMSRAGGFD
	SEQ ID NO.: 245	KMSRAGGFDV
15	SEQ ID NO.: 246	KMSRAGGFDVW
	SEQ ID NO.: 247	KMSRAGGFDVWG
	SEQ ID NO.: 248	KMSRAGGFDVWGQ
	SEQ ID NO.: 249	KMSRAGGFDVWGQG
	SEQ ID NO.: 250	KMSRAGGFDVWGQGT
20	SEQ ID NO.: 251	MSRA
	SEQ ID NO.: 252	MSRAG
	SEQ ID NO.: 253	MSRAGG
	SEQ ID NO.: 254	MSRAGGF
	SEQ ID NO.: 255	MSRAGGFD
25	SEQ ID NO.: 256	MSRAGGFDV
	SEQ ID NO.: 257	MSRAGGFDVW
	SEQ ID NO.: 258	MSRAGGFDVWG
	SEQ ID NO.: 259	MSRAGGFDVWGQ
	SEQ ID NO.: 260	MSRAGGFDVWGQG
30	SEQ ID NO.: 261	MSRAGGFDVWGQGT

	SEQ ID NO.: 262	RAGG
	SEQ ID NO.: 263	RAGGF
	SEQ ID NO.: 264	RAGGFD
	SEQ ID NO.: 265	RAGGFDV
5	SEQ ID NO.: 266	RAGGFDVW
	SEQ ID NO.: 267	RAGGFDVWG
	SEQ ID NO.: 268	RAGGFDVWGQ
	SEQ ID NO.: 269	RAGGFDVWGQG
	SEQ ID NO.: 270	RAGGFDVWGQGT
10	SEQ ID NO.: 271	SRAG
	SEQ ID NO.: 272	SRAGG
	SEQ ID NO.: 273	SRAGGF
	SEQ ID NO.: 274	SRAGGFD
	SEQ ID NO.: 275	SRAGGFDV
15	SEQ ID NO.: 276	SRAGGFDVW
	SEQ ID NO.: 277	SRAGGFDVWG
	SEQ ID NO.: 278	SRAGGFDVWGQ
	SEQ ID NO.: 279	SRAGGFDVWGQG
	SEQ ID NO.: 280	SRAGGFDVWGQGT
20	SEQ ID NO.: 281	YCAKMSRA
	SEQ ID NO.: 282	YCAKMSRAG
	SEQ ID NO.: 283	YCAKMSRAGG
	SEQ ID NO.: 284	YCAKMSRAGGF
	SEQ ID NO.: 285	YCAKMSRAGGFD
25	SEQ ID NO.: 286	YCAKMSRAGGFDV
	SEQ ID NO.: 287	YCAKMSRAGGFDVW
	SEQ ID NO.: 288	YCAKMSRAGGFDVWG
	SEQ ID NO.: 289	YCAKMSRAGGFDVWGQ
	SEQ ID NO.: 290	YCAKMSRAGGFDVWGQG
30	SEQ ID NO.: 291	YCAKMSRAGGFDVWGQGT

	SEQ ID NO.: 292	YYCAKMSRA
	SEQ ID NO.: 293	YYCAKMSRAG
	SEQ ID NO.: 294	YYCAKMSRAGG
	SEQ ID NO.: 295	YYCAKMSRAGGF
5	SEQ ID NO.: 296	YYCAKMSRAGGFD
	SEQ ID NO.: 297	YYCAKMSRAGGFDV
	SEQ ID NO.: 298	YYCAKMSRAGGFDVW
	SEQ ID NO.: 299	YYCAKMSRAGGFDVWG
	SEQ ID NO.: 300	YYCAKMSRAGGFDVWGQ
10	SEQ ID NO.: 301	YYCAKMSRAGGFDVWGQG
	SEQ ID NO.: 302	YYCAKMSRAGGFDVWGQGT

Light chain CDR1 region (SEQ ID NO:303 to SEQ ID NO:420)

15	SEQ ID NO.: 303	ASQSIT
	SEQ ID NO.: 304	ASQSITG
	SEQ ID NO.: 305	ASQSITGR
	SEQ ID NO.: 306	ASQSITGRY
	SEQ ID NO.: 307	ASQSITGRYL
20	SEQ ID NO.: 308	ASQSITGRYLA
	SEQ ID NO.: 309	ASQSITGRYLAW
	SEQ ID NO.: 310	ASQSITGRYLAWY
	SEQ ID NO.: 311	ASQSITGRYLAWYQ
	SEQ ID NO.: 312	ASQSITGRYLAWYQQ
25	SEQ ID NO.: 313	ASQSITGRYLAWYQQK
	SEQ ID NO.: 314	ATLSCRASQSIT
	SEQ ID NO.: 315	ATLSCRASQSITG
	SEQ ID NO.: 316	ATLSCRASQSITGR
	SEQ ID NO.: 317	ATLSCRASQSITGRY
30	SEQ ID NO.: 318	ATLSCRASQSITGRYL
	SEQ ID NO.: 319	ATLSCRASQSITGRYLA

	SEQ ID NO.: 320	ATLSCRASQSITGRYLAW
	SEQ ID NO.: 321	ATLSCRASQSITGRYLAWY
	SEQ ID NO.: 322	ATLSCRASQSITGRYLAWYQ
	SEQ ID NO.: 323	ATLSCRASQSITGRYLAWYQQ
5	SEQ ID NO.: 324	ATLSCRASQSITGRYLAWYQQK
	SEQ ID NO.: 325	CRASQSIT
	SEQ ID NO.: 326	CRASQSITG
	SEQ ID NO.: 327	CRASQSITGR
	SEQ ID NO.: 328	CRASQSITGRY
10	SEQ ID NO.: 329	CRASQSITGRYL
	SEQ ID NO.: 330	CRASQSITGRYLA
	SEQ ID NO.: 331	CRASQSITGRYLAW
	SEQ ID NO.: 332	CRASQSITGRYLAWY
	SEQ ID NO.: 333	CRASQSITGRYLAWYQ
15	SEQ ID NO.: 334	CRASQSITGRYLAWYQQ
	SEQ ID NO.: 335	CRASQSITGRYLAWYQQK
	SEQ ID NO.: 336	ITGR
	SEQ ID NO.: 337	ITGRY
	SEQ ID NO.: 338	ITGRYL
20	SEQ ID NO.: 339	ITGRYLA
	SEQ ID NO.: 340	ITGRYLAW
	SEQ ID NO.: 341	ITGRYLAWY
	SEQ ID NO.: 342	ITGRYLAWYQ
	SEQ ID NO.: 343	ITGRYLAWYQQ
25	SEQ ID NO.: 344	ITGRYLAWYQQK
	SEQ ID NO.: 345	LSCRASQSIT
	SEQ ID NO.: 346	LSCRASQSITG
	SEQ ID NO.: 347	LSCRASQSITGR
	SEQ ID NO.: 348	LSCRASQSITGRY
30	SEQ ID NO.: 349	LSCRASQSITGRYL

	SEQ ID NO.: 350	LSCRASQSITGRYLA
	SEQ ID NO.: 351	LSCRASQSITGRYLAW
	SEQ ID NO.: 352	LSCRASQSITGRYLAWY
	SEQ ID NO.: 353	LSCRASQSITGRYLAWYQ
5	SEQ ID NO.: 354	LSCRASQSITGRYLAWYQQ
	SEQ ID NO.: 355	LSCRASQSITGRYLAWYQQK
	SEQ ID NO.: 356	QSIT
	SEQ ID NO.: 357	QSITG
	SEQ ID NO.: 358	QSITGR
10	SEQ ID NO.: 359	QSITGRY
	SEQ ID NO.: 360	QSITGRYL
	SEQ ID NO.: 361	QSITGRYLA
	SEQ ID NO.: 362	QSITGRYLAW
	SEQ ID NO.: 363	QSITGRYLAWY
15	SEQ ID NO.: 364	QSITGRYLAWYQ
	SEQ ID NO.: 365	QSITGRYLAWYQQ
	SEQ ID NO.: 366	QSITGRYLAWYQQK
	SEQ ID NO.: 367	RASQSIT
	SEQ ID NO.: 368	RASQSITG
20	SEQ ID NO.: 369	RASQSITGR
	SEQ ID NO.: 370	RASQSITGRY
	SEQ ID NO.: 371	RASQSITGRYL
	SEQ ID NO.: 372	RASQSITGRYLA
	SEQ ID NO.: 373	RASQSITGRYLAW
25	SEQ ID NO.: 374	RASQSITGRYLAWY
	SEQ ID NO.: 375	RASQSITGRYLAWYQ
	SEQ ID NO.: 376	RASQSITGRYLAWYQQ
	SEQ ID NO.: 377	RASQSITGRYLAWYQQK
	SEQ ID NO.: 378	SCRASQSIT
30	SEQ ID NO.: 379	SCRASQSITG

	SEQ ID NO.: 380	SCRASQSITGR
	SEQ ID NO.: 381	SCRASQSITGRY
	SEQ ID NO.: 382	SCRASQSITGRYL
	SEQ ID NO.: 383	SCRASQSITGRYLA
5	SEQ ID NO.: 384	SCRASQSITGRYLAW
	SEQ ID NO.: 385	SCRASQSITGRYLAWY
	SEQ ID NO.: 386	SCRASQSITGRYLAWYQ
	SEQ ID NO.: 387	SCRASQSITGRYLAWYQQ
	SEQ ID NO.: 388	SCRASQSITGRYLAWYQQK
10	SEQ ID NO.: 389	SITG
	SEQ ID NO.: 390	SITGR
	SEQ ID NO.: 391	SITGRY
	SEQ ID NO.: 392	SITGRYL
	SEQ ID NO.: 393	SITGRYLA
15	SEQ ID NO.: 394	SITGRYLAW
	SEQ ID NO.: 395	SITGRYLAWY
	SEQ ID NO.: 396	SITGRYLAWYQ
	SEQ ID NO.: 397	SITGRYLAWYQQ
	SEQ ID NO.: 398	SITGRYLAWYQQK
20	SEQ ID NO.: 399	SQSIT
	SEQ ID NO.: 400	SQSITG
	SEQ ID NO.: 401	SQSITGR
	SEQ ID NO.: 402	SQSITGRY
	SEQ ID NO.: 403	SQSITGRYL
25	SEQ ID NO.: 404	SQSITGRYLA
	SEQ ID NO.: 405	SQSITGRYLAW
	SEQ ID NO.: 406	SQSITGRYLAWY
	SEQ ID NO.: 407	SQSITGRYLAWYQ
	SEQ ID NO.: 408	SQSITGRYLAWYQQ
30	SEQ ID NO.: 409	SQSITGRYLAWYQQK

	SEQ ID NO.: 410	TLSCRASQSIT
	SEQ ID NO.: 411	TLSCRASQSITG
	SEQ ID NO.: 412	TLSCRASQSITGR
	SEQ ID NO.: 413	TLSCRASQSITGRY
5	SEQ ID NO.: 414	TLSCRASQSITGRYL
	SEQ ID NO.: 415	TLSCRASQSITGRYLA
	SEQ ID NO.: 416	TLSCRASQSITGRYLAW
	SEQ ID NO.: 417	TLSCRASQSITGRYLAWY
	SEQ ID NO.: 418	TLSCRASQSITGRYLAWYQ
10	SEQ ID NO.: 419	TLSCRASQSITGRYLAWYQQ
	SEQ ID NO.: 420	TLSCRASQSITGRYLAWYQQK

Light chain CDR2 region (SEQ ID NO:421 to SEQ ID NO:513)

15	SEQ ID NO.: 421	ESSR
	SEQ ID NO.: 422	ESSRV
	SEQ ID NO.: 423	ESSRVT
	SEQ ID NO.: 424	ESSRVTG
	SEQ ID NO.: 425	ESSRVTGI
20	SEQ ID NO.: 426	ESSRVTGIP
	SEQ ID NO.: 427	ESSRVTGIPD
	SEQ ID NO.: 428	ESSRVTGIPDR
	SEQ ID NO.: 429	GESS
	SEQ ID NO.: 430	GESSR
25	SEQ ID NO.: 431	GESSRV
	SEQ ID NO.: 432	GESSRVT
	SEQ ID NO.: 433	GESSRVTG
	SEQ ID NO.: 434	GESSRVTGI
	SEQ ID NO.: 435	GESSRVTGIP
30	SEQ ID NO.: 436	GESSRVTGIPD
	SEQ ID NO.: 437	GESSRVTGIPDR

	SEQ ID NO.: 438	LLMYGE
	SEQ ID NO.: 439	LLMYGES
	SEQ ID NO.: 440	LLMYGESS
	SEQ ID NO.: 441	LLMYGESSR
5	SEQ ID NO.: 442	LLMYGESSRV
	SEQ ID NO.: 443	LLMYGESSRVT
	SEQ ID NO.: 444	LLMYGESSRVTG
	SEQ ID NO.: 445	LLMYGESSRVTGI
	SEQ ID NO.: 446	LLMYGESSRVTGIP
10	SEQ ID NO.: 447	LLMYGESSRVTGIPD
	SEQ ID NO.: 448	LLMYGESSRVTGIPDR
	SEQ ID NO.: 449	LMYGE
	SEQ ID NO.: 450	LMYGES
	SEQ ID NO.: 451	LMYGESS
15	SEQ ID NO.: 452	LMYGESSR
	SEQ ID NO.: 453	LMYGESSRV
	SEQ ID NO.: 454	LMYGESSRVT
	SEQ ID NO.: 455	LMYGESSRVTG
	SEQ ID NO.: 456	LMYGESSRVTGI
20	SEQ ID NO.: 457	LMYGESSRVTGIP
	SEQ ID NO.: 458	LMYGESSRVTGIPD
	SEQ ID NO.: 459	LMYGESSRVTGIPDR
	SEQ ID NO.: 460	MYGE
	SEQ ID NO.: 461	MYGES
25	SEQ ID NO.: 462	MYGESS
	SEQ ID NO.: 463	MYGESSR
	SEQ ID NO.: 464	MYGESSRV
	SEQ ID NO.: 465	MYGESSRVT
	SEQ ID NO.: 466	MYGESSRVTG
30	SEQ ID NO.: 467	MYGESSRVTGI

	SEQ ID NO.: 468	MYGESSRVTGIP
	SEQ ID NO.: 469	MYGESSRVTGIPD
	SEQ ID NO.: 470	MYGESSRVTGIPDR
	SEQ ID NO.: 471	RLLMYGE
5	SEQ ID NO.: 472	RLLMYGES
	SEQ ID NO.: 473	RLLMYGESS
	SEQ ID NO.: 474	RLLMYGESSR
	SEQ ID NO.: 475	RLLMYGESSRV
	SEQ ID NO.: 476	RLLMYGESSRVT
10	SEQ ID NO.: 477	RLLMYGESSRVTG
	SEQ ID NO.: 478	RLLMYGESSRVTGI
	SEQ ID NO.: 479	RLLMYGESSRVTGIP
	SEQ ID NO.: 480	RLLMYGESSRVTGIPD
	SEQ ID NO.: 481	RLLMYGESSRVTGIPDR
15	SEQ ID NO.: 482	RVTG
	SEQ ID NO.: 483	RVTGI
	SEQ ID NO.: 484	RVTGIP
	SEQ ID NO.: 485	RVTGIPD
	SEQ ID NO.: 486	RVTGIPDR
20	SEQ ID NO.: 487	SRVT
	SEQ ID NO.: 488	SRVTG
	SEQ ID NO.: 489	SRVTGI
	SEQ ID NO.: 490	SRVTGIP
	SEQ ID NO.: 491	SRVTGIPD
25	SEQ ID NO.: 492	SRVTGIPDR
	SEQ ID NO.: 493	SSRV
	SEQ ID NO.: 494	SSRVT
	SEQ ID NO.: 495	SSRVTG
	SEQ ID NO.: 496	SSRVTGI
30	SEQ ID NO.: 497	SSRVTGIP

	SEQ ID NO.: 498	SSRVTGIPD
	SEQ ID NO.: 499	SSRVTGIPDR
	SEQ ID NO.: 500	VTGI
	SEQ ID NO.: 501	VTGIP
5	SEQ ID NO.: 502	VTGIPD
	SEQ ID NO.: 503	VTGIPDR
	SEQ ID NO.: 504	YGES
	SEQ ID NO.: 505	YGESS
	SEQ ID NO.: 506	YGESSR
10	SEQ ID NO.: 507	YGESSRV
	SEQ ID NO.: 508	YGESSRVT
	SEQ ID NO.: 509	YGESSRVTG
	SEQ ID NO.: 510	YGESSRVTGI
	SEQ ID NO.: 511	YGESSRVTGIP
15	SEQ ID NO.: 512	YGESSRVTGIPD
	SEQ ID NO.: 513	YGESSRVTGIPDR

Light chain CDR3 region (SEQ ID NO:514 to SEQ ID NO:628)

20	SEQ ID NO.: 514	ASSP
	SEQ ID NO.: 515	ASSPP
	SEQ ID NO.: 516	ASSPPT
	SEQ ID NO.: 517	ASSPPTY
	SEQ ID NO.: 518	ASSPPTYT
25	SEQ ID NO.: 519	ASSPPTYTF
	SEQ ID NO.: 520	ASSPPTYTFG
	SEQ ID NO.: 521	ASSPPTYTFGQ
	SEQ ID NO.: 522	ASSPPTYTFGQG
	SEQ ID NO.: 523	ASSPPTYTFGQGT
30	SEQ ID NO.: 524	AVYYCQHFASS
	SEQ ID NO.: 525	AVYYCQHFASSP

	SEQ ID NO.: 526	AVYYCQHFASSPP
	SEQ ID NO.: 527	AVYYCQHFASSPPT
	SEQ ID NO.: 528	AVYYCQHFASSPPTY
	SEQ ID NO.: 529	AVYYCQHFASSPPTYT
5	SEQ ID NO.: 530	AVYYCQHFASSPPTYTF
	SEQ ID NO.: 531	AVYYCQHFASSPPTYTFG
	SEQ ID NO.: 532	AVYYCQHFASSPPTYTFGQ
	SEQ ID NO.: 533	AVYYCQHFASSPPTYTFGQG
	SEQ ID NO.: 534	AVYYCQHFASSPPTYTFGQGT
10	SEQ ID NO.: 535	CQHFASS
	SEQ ID NO.: 536	CQHFASSP
	SEQ ID NO.: 537	CQHFASSPP
	SEQ ID NO.: 538	CQHFASSPPT
	SEQ ID NO.: 539	CQHFASSPPTY
15	SEQ ID NO.: 540	CQHFASSPPTYT
	SEQ ID NO.: 541	CQHFASSPPTYTF
	SEQ ID NO.: 542	CQHFASSPPTYTFG
	SEQ ID NO.: 543	CQHFASSPPTYTFGQ
	SEQ ID NO.: 544	CQHFASSPPTYTFGQG
20	SEQ ID NO.: 545	CQHFASSPPTYTFGQGT
	SEQ ID NO.: 546	FASS
	SEQ ID NO.: 547	FASSP
	SEQ ID NO.: 548	FASSPP
	SEQ ID NO.: 549	FASSPPT
25	SEQ ID NO.: 550	FASSPPTY
	SEQ ID NO.: 551	FASSPPTYT
	SEQ ID NO.: 552	FASSPPTYTF
	SEQ ID NO.: 553	FASSPPTYTFG
	SEQ ID NO.: 554	FASSPPTYTFGQ
30	SEQ ID NO.: 555	FASSPPTYTFGQG

	SEQ ID NO.: 556	FASSPPTYTFGQGT
	SEQ ID NO.: 557	HFASS
	SEQ ID NO.: 558	HFASSP
	SEQ ID NO.: 559	HFASSPP
5	SEQ ID NO.: 560	HFASSPPT
	SEQ ID NO.: 561	HFASSPPTY
	SEQ ID NO.: 562	HFASSPPTYT
	SEQ ID NO.: 563	HFASSPPTYTF
	SEQ ID NO.: 564	HFASSPPTYTFG
10	SEQ ID NO.: 565	HFASSPPTYTFGQ
	SEQ ID NO.: 566	HFASSPPTYTFGQG
	SEQ ID NO.: 567	HFASSPPTYTFGQGT
	SEQ ID NO.: 568	QHFASS
	SEQ ID NO.: 569	QHFASSP
15	SEQ ID NO.: 570	QHFASSPP
	SEQ ID NO.: 571	QHFASSPPT
	SEQ ID NO.: 572	QHFASSPPTY
	SEQ ID NO.: 573	QHFASSPPTYT
	SEQ ID NO.: 574	QHFASSPPTYTF
20	SEQ ID NO.: 575	QHFASSPPTYTFG
	SEQ ID NO.: 576	QHFASSPPTYTFGQ
	SEQ ID NO.: 577	QHFASSPPTYTFGQG
	SEQ ID NO.: 578	QHFASSPPTYTFGQGT
	SEQ ID NO.: 579	SPPT
25	SEQ ID NO.: 580	SPPTY
	SEQ ID NO.: 581	SPPTYT
	SEQ ID NO.: 582	SPPTYTF
	SEQ ID NO.: 583	SPPTYTFG
	SEQ ID NO.: 584	SPPTYTFGQ
30	SEQ ID NO.: 585	SPPTYTFGQG

	SEQ ID NO.: 586	SPPTYTFGQGT
	SEQ ID NO.: 587	SSPP
	SEQ ID NO.: 588	SSPPT
	SEQ ID NO.: 589	SSPPTY
5	SEQ ID NO.: 590	SSPPTYT
	SEQ ID NO.: 591	SSPPTYTF
	SEQ ID NO.: 592	SSPPTYTFG
	SEQ ID NO.: 593	SSPPTYTFGQ
	SEQ ID NO.: 594	SSPPTYTFGQG
10	SEQ ID NO.: 595	SSPPTYTFGQGT
	SEQ ID NO.: 596	VYYCQHFASS
	SEQ ID NO.: 597	VYYCQHFASSP
	SEQ ID NO.: 598	VYYCQHFASSPP
	SEQ ID NO.: 599	VYYCQHFASSPPT
15	SEQ ID NO.: 600	VYYCQHFASSPPTY
	SEQ ID NO.: 601	VYYCQHFASSPPTYT
	SEQ ID NO.: 602	VYYCQHFASSPPTYTF
	SEQ ID NO.: 603	VYYCQHFASSPPTYTFG
	SEQ ID NO.: 604	VYYCQHFASSPPTYTFGQ
20	SEQ ID NO.: 605	VYYCQHFASSPPTYTFGQG
	SEQ ID NO.: 606	VYYCQHFASSPPTYTFGQGT
	SEQ ID NO.: 607	YCQHFASS
	SEQ ID NO.: 608	YCQHFASSP
	SEQ ID NO.: 609	YCQHFASSPP
25	SEQ ID NO.: 610	YCQHFASSPPT
	SEQ ID NO.: 611	YCQHFASSPPTY
	SEQ ID NO.: 612	YCQHFASSPPTYT
	SEQ ID NO.: 613	YCQHFASSPPTYTF
	SEQ ID NO.: 614	YCQHFASSPPTYTFG
30	SEQ ID NO.: 615	YCQHFASSPPTYTFGQ

SEQ ID NO.: 616 YCQHFASSPPTYTFGQG
SEQ ID NO.: 617 YCQHFASSPPTYTFGQGT
SEQ ID NO.: 618 YYCQHFASS
SEQ ID NO.: 619 YYCQHFASSP
5 SEQ ID NO.: 620 YYCQHFASSPP
SEQ ID NO.: 621 YYCQHFASSPPT
SEQ ID NO.: 622 YYCQHFASSPPTY
SEQ ID NO.: 623 YYCQHFASSPPTYT
SEQ ID NO.: 624 YYCQHFASSPPTYTF
10 SEQ ID NO.: 625 YYCQHFASSPPTYTFG
SEQ ID NO.: 626 YYCQHFASSPPTYTFGQ
SEQ ID NO.: 627 YYCQHFASSPPTYTFGQG
SEQ ID NO.: 628 YYCQHFASSPPTYTFGQGT

15 **Heavy chain variable domain (SEQ ID NO: 629)**

QVQLVQSGAEVKKPGASVKVSCQTSGYTFTSYMHWRQAPGQGLEWMGLITPSGD
DTYYAQRFGQGRVTMTRDTSTSPTYMELSSLTSEDVAVYYCAKMSRAGGFVWGQGT
LTVSS

20

Light chain variable domain (SEQ ID NO: 630)

EVVLTQSPGTLSPGERATLSCRASQITGRYLAWYQQKPGQAPRLLMYGESSRVT
GIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQHFASSPPTYTFGQGTKLEIR

25

Heavy chain FR1 region (SEQ ID NO:631)

SEQ ID NO:631 QVQLVQSGAEVKKPGASVKVSCQTSGYTFT

Heavy chain FR2 region (SEQ ID NO:632)

30 SEQ ID NO:632 WVRQAPGQGLEWMG

Heavy chain FR3 region (SEQ ID NO:633)

SEQ ID NO:633 RVTMTRDTSTSPTYMELSSLTSED TAVYYCAK

Heavy chain FR4 region (SEQ ID NO:634)

5 SEQ ID NO:634 WGQGT LVT VSS

Light chain FR1 region (SEQ ID NO:635)

SEQ ID NO:635 EVVLTQSPG TSLSPGERATLSC

10 **Light chain FR2 region (SEQ ID NO:636)**

SEQ ID NO:636 WYQQKPGQAPRLLMY

Light chain FR3 region (SEQ ID NO:637)

SEQ ID NO:637 GIPDRFSGGGSGTDFTLTISRLEPEDFAVYYC

15

Light chain FR4 region (SEQ ID NO:638)

SEQ ID NO:638 FGQGT KLEIR

Heavy chain CDR1 region (SEQ ID NO:639)

20 SEQ ID NO.: 639 DYRIH

Heavy chain CDR2 region (SEQ ID NO: 640)

SEQ ID NO.: 640 RMNPKSGDTNFAQKFQG

25 **Heavy chain CDR3 region (SEQ ID NO: 641)**

SEQ ID NO.: 641 LLIVGGFDPLDDFEV

Light chain CDR1 region (SEQ ID NO: 642)

SEQ ID NO.: 642 SGTSSDVGGYNFVS

30

Light chain CDR2 region (SEQ ID NO: 643)

SEQ ID NO.: 643 EVTKRPS

Light chain CDR3 region (SEQ ID NO: 644)

SEQ ID NO.: 644 SSYGGTNNLL

5

Heavy chain CDR1 region (SEQ ID NO: 645)

SEQ ID NO.: 645 GYAMH

Heavy chain CDR2 region (SEQ ID NO: 646)

10 SEQ ID NO.: 646 VISRDARNKYYADSVKG

Heavy chain CDR3 region (SEQ ID NO: 647)

SEQ ID NO.: 647 LIIPGITEPGSPDALDI

15 **Light chain CDR1 region (SEQ ID NO: 648)**

SEQ ID NO.: 648 RASQDISKWLA

Light chain CDR2 region (SEQ ID NO: 649)

SEQ ID NO.: 649 AASSLQS

20

Light chain CDR3 region (SEQ ID NO: 650)

SEQ ID NO.: 650 QQASSFPWSIT

Heavy chain CDR1 region (SEQ ID NO: 651)

25 SEQ ID NO.: 651 SHYMH

Heavy chain CDR2 region (SEQ ID NO: 652)

SEQ ID NO.: 652 IINPSGSGTAYGQKFQG

30 **Heavy chain CDR3 region (SEQ ID NO: 653)**

SEQ ID NO.: 653 GSGGLFAY

Light chain CDR1 region (SEQ ID NO: 654)

SEQ ID NO.: 654 RASQIVRSNYLA

5 **Light chain CDR2 region (SEQ ID NO: 655)**

SEQ ID NO.: 655 GASSRAT

Light chain CDR3 region (SEQ ID NO: 656)

SEQ ID NO.: 656 LQYDSSPPTYI

10

Heavy chain CDR1 region (SEQ ID NO: 657)

SEQ ID NO.: 657 YFYLH

Heavy chain CDR2 region (SEQ ID NO: 658)

15 SEQ ID NO.: 658 IINPRGDGTRYAQKFQG

Heavy chain CDR3 region (SEQ ID NO: 659)

SEQ ID NO.: 659 GADHGAFDI

20 **Light chain CDR1 region (SEQ ID NO: 660)**

SEQ ID NO.: 660 RASQSVRRNYFA

Light chain CDR2 region (SEQ ID NO: 661)

SEQ ID NO.: 661 DASTRAT

25

Light chain CDR3 region (SEQ ID NO: 662)

SEQ ID NO.: 662 QQYDSSPPMYI

Heavy chain variable domain (SEQ ID NO: 663)

QMQLMQSGAEVKKPGASVTVSCKASGDTFSDYRIHWVRQAPGQGLEWMGRMNPKS
 GDTNFAQKFQGRVTMTRDMSINTAYMTLSGLTFDDTALYYCASLLIVGGFDPLDDFE
 VWGQGTMTVISS

5 **Light chain variable domain (SEQ ID NO: 664)**

QSALTQPPSASGSPGQSVTISCSGTSSDVGGYNFVSWYQHHPGKAPKILIYEVTKRPS
 GVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYGGTNNLLFGGGTKLTVL

Heavy chain variable domain (SEQ ID NO: 665)

10 QVQLVESGGGVVQPGRSLRLSCAASGLTFSGYAMHWVRQAPGKGLEWVAVISRDAR
 NKYYADSVKGRFTISRDNSSKKTVYLEMNSLRVEDTAVYYCAILIPGITEPGSPDALDI
 WGQGTMTVSVSS

Light chain variable domain (SEQ ID NO: 666)

15 DIQMTQSPSSMSASVGDRVITTCRASQDISKWLAWYQQRPGKAPKLLIYAASSLQSGV
 PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQASSFPWSITFGQGTRLEIR

EXAMPLES

20 The monoclonal antibody CV3-25 has shown *in vitro* protection against the original
 Wuhan strain of SARS-CoV-2 binding specifically to the stem helix of SARS-CoV-2, a
 binding region shared with antibodies of the present invention. When administered
 mucosally at lower dosages, CV3-25 affords a lower level of protection when compared to
 its systemic administration. In contrast, however, when antibodies of the present
 25 invention are administered mucosally they afford a greater level of protection as
 demonstrated by the *in vivo* studies presented below.

Example 1: CV3-25

The aim of this study was to assess the pre-exposure efficacy of the monoclonal antibody
 30 CV3-25 following systemic intraperitoneal administration in a SARS-CoV-2 Delta K18
 hACE2 Tg mouse model.

Animals (n=10 per group) were treated with an intraperitoneal dose range of the test CV3-25 (15 to 0.2 mg/kg) or PBS control as vehicle at study day -1. At study day 0, animals were challenged with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta variant.

5 Materials and Methods

The monoclonal antibody CV3-25 was dissolved and diluted with phosphate-buffered saline (PBS), thereby preparing a CV3-25 dilution.

10 The CV3-25 dilution was made up at various concentrations so that 200 µL administrations to the mean weight per cage of the dosing group resulted in CV3-25 doses ranging from 15 mg/kg, 5 mg/kg, 1.7 mg/kg, 0.5 mg/kg to 0.2 mg/kg.

The antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and dilutions were stored at 4°C until usage and the temperature of the storage unit was monitored.

15 The virus strain tested was SARS-CoV-2 Delta variant (Aus/VIC/18440/2021 (B.1.617.2), which has been passed three times through Vero-hSLAM cells.

Animals

20 The animal species used was the SARS-CoV-2 Delta K18 hACE2 Tg (B6.Cg-Tg(K18-ACE2)2PrImn/JArc; Jax™ Stock No.: 034860) mouse model, at a weight of c. 17-26 g on day -9. 60 mice were used at the age of 11-13 weeks on the day of test article administration and were 83.3% female. Ten animals were randomly allocated to 6 treatment groups based on day -9 weights to create groups with comparable mean weight, with 20% males per group, except 15 mg/kg which was exclusively female. All mice were
25 housed in individually ventilated cages (IVCs), with corn cob bedding, tissues or shredded paper as nesting material, a wooden chew block, accessible food pellets and acidic water for animal nourishment and red plastic tunnels. Each cage system holds 3 to 5 mice per cage. All mice were transferred to fresh cages every 14 days. Food and water were inspected daily and topped up as needed.

30 Study design

The dose level of CV3-25 applied in the current example was based on a dose range proven to have prophylactic activity. A total number of 60 mice, 11-13 weeks of age were

transported to the animal facility and allocated to 6 experimental groups according to Table 1 (see below). Mice were given a period of >3 days for acclimatization.

Table 1: Intraperitoneal experimental detail

Test group	Antibody	Admin. route	Dose (mg/kg)	Day of admin.	No. of Animals
15	CV3-25	I.P.	15	-1	10
5	CV3-25	I.P.	5	-1	10
1.7	CV3-25	I.P.	1.7	-1	10
0.5	CV3-25	I.P.	0.5	-1	10
0.2	CV3-25	I.P.	0.2	-1	10
Vehicle	---	I.P.	0	-1	10

5

SARS-CoV-2 Delta K18 hACE2 mice (20% males per group, except 15 mg/kg which was exclusively female) were treated via the Intraperitoneal route of administration with the antibody at a dose between 15 mg/kg and 0.2 mg/kg based upon the average group weight at day -9 adjusted with a 4% average weight gain (based on a subset of the animals weighted at day -1). On Day 0, all mice were challenged with a lethal dose ($10^{3.5}$ TCID₅₀) of the SARS-CoV-2 Delta variant and observed for weight loss and mortality until the end of the study at day 11.

10

Antibody administration

The test antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ upon arrival. The appropriate dose, according to the treatment schedule (Table1), was formulated according to average group weight at day -9 adjusted with a 4% average weight gain (based on a subset of the animals weighted at day -1)

15

Prior to dosing, the material was drawn into a 1 mL syringe with a 26G needle, allowed briefly to warm to room temperature and then administered to each mouse. Mice receive the indicated dose by intraperitoneal administration of 200 μL of antibody solution into the intraperitoneal cavity, mice were scruffed and held inverted at a -45 deg angle for administration (200 μL per mouse).

20

Virus administration

The virus material was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and was defrosted prior to administration. Once defrosted, the material was diluted in sterile PBS corresponding to approximately
5 $10^{3.5}$ TCID₅₀/ 50 μL . As required, the animals were anesthetized by isoflurane (4% v/v with 2 L/min O₂) and each animal received approximately 50 μL (25 μL in each nare) of virus corresponding with approximately $10^{3.5}$ TCID₅₀ by intranasal inoculation. Unused material was frozen at -20°C to -80°C for back titration.

10 Laboratory analysis

Inoculum was back titrated and the dose of the virus administered was verified by titrating replicate samples on Vero cells.

Clinical monitoring

15 General health observations were performed on each animal from the day of arrival until the end of the study at least once daily (during normal servicing procedures). Each animal was weighed daily, beginning at the day of infection (day 0).

Terminal investigations

20 At the end of the study, on day 11, mice were euthanized by cervical dislocation. Gross necropsy was not performed.

Data analysis and statistical methods

Survival proportions at day 11, survival times and change in bodyweight (Area Under the
25 Curve) were compared to the control group using Fisher's exact test, log-rank and Welch's t-test, respectively. All groups were compared to the vehicle (PBS solution) control group. P-values were adjusted according to Bonferroni (for two comparisons to vehicle) followed by a stepwise approach (starting with the highest antibody dose conditionally testing a lower dose if the previous step was statistically significant).

30

Statistical analysis was performed using R and statistical significance was set at $\alpha = 0.05$.

Survival

Prophylactic treatment with ≥ 0.5 mg/kg test antibody provided a statistically significant increase in survival compared to the control group (See Figure 1). The animals that were treated with 0.5 mg/kg test antibody had a 80% survival rate, animals treated with ≥ 1.7 mg/kg had a survival rate of 100%, whereas the survival proportion at day 11 in the control group was 20%. The median survival time of the control group was 6.5 days.

Prophylactic treatment with ≥ 0.5 mg/kg test antibody resulted in a significant improvement in survival time compared to the control group.

Body weight

Change in bodyweight was analyzed using an Area Under the Curve (AUC) analysis in which the last observed body weight was carried forward if a mouse died / was euthanized during the study. The weight per mouse at day 0 was used as baseline and weight change was determined relative to baseline and the net AUC was defined as the summation of the area above and below the baseline using the percentage change per day. Prophylactic treatment with ≥ 0.5 mg/kg test antibody resulted in a significant reduction in weight loss compared to the control group.

Conclusion

In this lethal SARS-CoV-2 Delta K18 hACE2 Tg mouse model, the prophylactic intraperitoneal administration of ≥ 0.5 mg/kg test antibody provides a statistically significant improvement in survival and a reduction in weight loss compared to control, whereas eight out of ten animals in the control group did not survive.

Example 2: CV3-25

The aim of this study was to assess the pre-exposure efficacy of the monoclonal antibody CV3-25 following intranasal administration in a SARS-CoV-2 Delta K18 hACE2 Tg mouse model.

5

Animals (n=10 per group) were treated with an intranasal dose range of the test CV3-25 (15 to 0.2 mg/kg) or PBS control as vehicle on study day -1. At study day 0, animals were challenged with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta variant.

10 Materials and Methods

The monoclonal antibody CV3-25 was dissolved and diluted with phosphate-buffered saline (PBS), thereby preparing a CV3-25 dilution.

The CV3-25-dilution was made up at various concentrations so that 50 µL administrations to the mean weight of the dosing group resulted in CV3-25 doses ranging from 15 mg/kg, 5 mg/kg, 1.7 mg/kg, 0.5 mg/kg to 0.2 mg/kg.

The formulations were stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and the temperature of the storage unit was monitored.

20

The virus strain tested was SARS-CoV-2 Delta variant (Aus/VIC/18440/2021 (B.1.617.2), which had been passed three times through Vero-hSLAM cells.

Animals

25 The animal species used was the SARS-CoV-2 Delta K18 hACE2 Tg (B6.Cg-Tg(K18-ACE2)2PrImn/Jarc; Jax™ Stock No.: 034860) mouse model, at a weight of c. 17-26 g on day -9. 60 mice were used at the age of 11-13 weeks on the day of test article administration and were 83.3% female. Ten animals were randomly allocated to 6 treatment groups, based on day -9 weights to create groups with comparable mean weight, with 20% males per group, except 15 mg/kg which was exclusively female. All mice were housed in individually ventilated cages (IVCs), with corn cob bedding, tissues or shredded paper as nesting material, a wooden chew block, accessible food pellets and
30 acidic water for animal nourishment and red plastic tunnels. Each cage system holds 3 to

5 mice per cage. All mice were transferred to fresh cages every 14 days. Food and water were inspected daily and topped up as needed.

Study design

- 5 The dose level of CV3-25 applied in the current example was extrapolated from a dose range proven to have prophylactic activity intravenously. A total number of 60 mice, 11-13 weeks of age at the time of arrival, were transported to the animal facility and allocated to 6 experimental groups according to Table 2 (see below). Mice were given a period of >3 days for acclimatization.

10

Table 2: Intranasal experimental detail

Test group	Antibody	Admin. Route	Dose (mg/kg)	Day of admin.	No. of Animals
15	CV3-25	I.N.	15	-1	10
5	CV3-25	I.N.	5	-1	10
1.7	CV3-25	I.N.	1.7	-1	10
0.5	CV3-25	I.N.	0.5	-1	10
0.2	CV3-25	I.N.	0.2	-1	10
Vehicle	---	I.N.	0	-1	10

Female SARS-CoV-2 Delta K18 hACE2 mice (20% males per group, except 15 mg/kg which was exclusively female) were treated via the intranasal route of administration with the antibody at a dose between 15 mg/kg and 0.2 mg/kg based upon the average weight at day -9 adjusted with a 4% average weight gain (based on a subset of the animals weighted at day -1). On Day 0, all mice were challenged with a lethal dose ($10^{3.5}$ TCID₅₀) of the SARS-CoV-2 Delta variant and observed for weight loss and mortality until the end of the study at day 11.

20

Antibody administration

The test antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ upon arrival. The appropriate dose, according to the treatment schedule (Table 2), was formulated according to average group

weight at day -9 adjusted with a 4% average weight gain (based on a subset of animals weighted at day -1).

5 Just prior to dosing, the material was drawn into a syringe, allowed briefly to warm to room temperature and then administered to each mouse. Mice were anaesthetized with isoflurane (4% v/v with 2 L/min O₂) for two minutes. The mice were then scruffed and held at a +45 deg angle. 50 µL of compound or vehicle control was then slowly administered to the nares of each mouse (25 µL each nare). The mice were held for an additional 5 to 10 seconds to ensure compound delivery to the lower respiratory tract before being put back
10 into the home box.

Virus administration

The virus material was stored at -80°C ± 10°C and was defrosted prior to administration. Once defrosted, the material was diluted in cold PBS corresponding to approximately 10^{3.5}
15 TCID₅₀/50 µL. As required, the animals were anesthetized with isoflurane (4% v/v with 2 L/min O₂) and each animal received approximately 50µL (25 µL each nare) of virus corresponding with approximately 10^{3.5} TCID₅₀ by intranasal inoculation using a pipette tip. Unused material was frozen at -20°C to -80°C for back titration.

Laboratory analysis

20 Inoculum was returned to the lab and the dose of the virus administered was verified by titrating replicate samples on Vero cells.

Clinical monitoring

25 General health observations were performed on each animal from the day of arrival until the end of the study at least once daily (during normal servicing procedures). Each animal was weighed daily beginning one day prior to infection (day -1).

Terminal investigations

30 At the end of the study, on day 11, mice were euthanized by cervical dislocation. Gross necropsy was not performed.

Data analysis and statistical methods

Two animals in the 15 mg/kg CV3-25 were misdosed (sneezed out part of the antibody volume). These two animals were excluded from the statistical analysis.

- 5 Survival proportions at day 11, survival times and change in bodyweight (Area Under the Curve) were compared to the control group using Fisher's exact test, log-rank and Welch's t-test, respectively. All groups were compared to the vehicle (PBS solution) control group. P-values were adjusted according to Bonferroni (for two comparisons to vehicle) followed by a stepwise approach (starting with the highest antibody dose conditionally testing a
10 lower dose if the previous step was statistically significant).

Statistical analysis was performed using R and statistical significance was set at $\alpha = 0.05$.

Survival

- 15 Prophylactic treatment with ≥ 1.7 mg/kg test antibody provided statistically significant increase in survival compared to control group (See Figure 2). The median survival time of the control group was 6.0 days.

- Prophylactic treatment with ≥ 1.7 mg/kg test antibody resulted in a significant
20 improvement in survival time compared to the control group.

Body weight

- Change in bodyweight was analyzed using an Area Under the Curve (AUC) analysis in which the last observed body weight was carried forward if a mouse died / was euthanized
25 during the study. The weight per mouse at day 0 was used as baseline and weight change was determined relative to baseline and the net AUC was defined as the summation of the area above and below the baseline using the percentage change per day. Prophylactic treatment with ≥ 0.2 mg/kg test antibody resulted in a significant reduction in weight loss compared to the control group.

30

Conclusion

In this lethal SARS-CoV-2 Delta K18 hACE2 Tg mouse model, the prophylactic intranasal administration of ≥ 1.7 mg/kg test antibody provides a statistically significant

improvement in survival and a reduction in weight loss. In contrast, the control group showed 10% survival with a median survival time of 6 days.

Example 3: Antibody according to the invention

5 The aim of this study was to assess the pre-exposure efficacy of a monoclonal antibody according to the invention, having a heavy chain CDR1 as SEQ ID NO: 029, heavy chain CDR2 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, following systemic intraperitoneal administration in a SARS-CoV-2 Delta
10 K18 hACE2 Tg mouse model.

Animals (n=10 per group, except the 0.5 mg/kg group where n=9) were treated with an intraperitoneal dose range of the test antibody described above (10 to 0.2 mg/kg) or PBS control as vehicle at study day -1. At study day 0, animals were challenged with 10^{3.5}
15 TCID₅₀ of SARS-CoV-2 Delta variant.

Materials and Methods

The monoclonal test antibody described above, was buffered in phosphate-buffered saline PBS was diluted to the final concentrations for administration (10 to 0.2 mg/kg in 200 µL).
20 thereby preparing the test antibody dilution.

The test antibody dilution was made up at various concentrations so that 200 µL administrations to a 20 g mouse resulted in test antibody doses ranging from 10 mg/kg, 5 mg/kg, 1.7 mg/kg, 0.5 mg/kg to 0.2 mg/kg.

25

The antibody was stored at -80°C ± 10°C and dilutions were stored at 4°C until usage and the temperature of the storage unit was monitored.

The virus strain tested was SARS-CoV-2 Delta variant (Aus/VIC/18440/2021 (B.1.617.2),
30 which had been passed three times through Vero-hSLAM cells.

Animals

The animal species used was the SARS-CoV-2 Delta K18 hACE2 Tg (B6.Cg-Tg(K18-ACE2)2PrImn/JArc; Jax™ Stock No.: 034860) mouse model, at a weight of c. 16.7-22.4 g at day of viral challenge. 59 mice were used at the age of 7-11 weeks of age and were exclusively female. Ten animals were allocated to 5 treatment groups, and nine animals
 5 to the 0.5 mg/kg group. All mice were housed in individually ventilated cages (IVCs), with corn cob bedding, tissues or shredded paper as nesting material, a wooden chew block, accessible food pellets and acidic water for animal nourishment and red plastic tunnels. Each cage system holds 3 to 5 mice per cage. All mice were transferred to fresh cages every 14 days. Food and water were inspected daily and topped up as needed. Each animal
 10 was weighed daily beginning at the day of infection (day 0).

Study design

The dose level of test antibody applied in the current example was based on the maximal dosing possible for the material stock concentration (4 mg/mL) and based on literature
 15 and previous experience with an anti-S2 antibody (CV3-25) showing protection IP at doses ≥ 0.5 mg/kg. A total number of 59 mice, 7-11 weeks of age, were allocated to 6 experimental groups according to Table 3 (see below). Mice were given a period of > 3 days for acclimatization.

20 **Table 3: Intraperitoneal experimental detail**

Test group	Antibody	Admin. route	Dose (mg/kg)	Day of admin.	No. of Animals
10	As disclosed above.	I.P.	10	-1	10
5		I.P.	5	-1	10
1.7		I.P.	1.7	-1	10
0.5		I.P.	0.5	-1	9
0.2		I.P.	0.2	-1	10
Vehicle	---	I.N.	0	-1	10

Female SARS-CoV-2 Delta K18 hACE2 mice were treated via the intraperitoneal route of administration with the antibody at a dose between 10 mg/kg and 0.2 mg/kg based upon a mouse weight of 20g. On Day 0, all mice were challenged with a lethal dose ($10^{3.5}$ TCID₅₀)

of the SARS-CoV-2 Delta variant and observed for weight loss and mortality until the end of the study at day 12.

Antibody administration

5 The test antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ upon arrival. The appropriate dose, according to the treatment schedule (Table 3), was formulated assuming a weight of 20g per mouse.

Prior to dosing, the material was drawn into a 1 mL syringe with a 26G needle and then
10 administered to each mouse. Mice in the treatment group received the indicated dose by intraperitoneal administration of 200 μL of antibody solution into the intraperitoneal cavity, mice were scruffed and held inverted at a -45° angle for administration (200 μL per mouse). Mice in the vehicle group that received PBS were anaesthetized with isoflurane (4% v/v with 2 L/min O_2) for two minutes. The mice were then scruffed and held
15 at a $+45^{\circ}$ angle. 50 μL of compound or vehicle control was then slowly administered to the nares of each mouse (25 μL each nare). The mice were held for an additional 5 to 10 seconds to ensure compound delivery to the lower respiratory tract before being put back into the home box.

Virus administration

The virus material was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and was defrosted prior to administration, at a titer of $10^{6.3}$ TCID₅₀/mL. Once defrosted, the material was diluted in sterile PBS corresponding to approximately $10^{3.5}$ TCID₅₀/ 50 μL). As required, the animals were anesthetized by isoflurane (4% v/v with 2 L/min O_2) and each animal received
25 approximately 50 μL (25 μL in each nare) of virus corresponding with approximately $10^{3.5}$ TCID₅₀ by intranasal inoculation. Unused material was frozen at -20°C to -80°C for back titration.

Laboratory analysis

30 Inoculum was back titrated and the actual dose of the virus administered was verified by titrating replicate samples on Vero cells.

Terminal investigations

At the end of the study, on day 12, mice were euthanized by cervical dislocation. Gross necropsy was not performed.

5 Data analysis and statistical methods

Survival proportions at day 12, survival times and change in bodyweight (Area Under the Curve) were compared to the vehicle (PBS solution) control group using Fisher's exact test, log-rank and Welch's t-test, respectively. P-values were adjusted according to Bonferroni (for two comparisons to vehicle) followed by a stepwise approach (starting with
10 the highest antibody dose conditionally testing a lower dose if the previous step was statistically significant).

Statistical analysis was performed using R and statistical significance was set at $\alpha = 0.05$.

15 Survival - Intraperitoneal

Prophylactic treatment with ≥ 5 mg/kg test antibody provides statistically significant increase in survival compared to vehicle (See Figure 3). The animals that were treated with 5 and 10 mg/kg of the test antibody had a 90% survival rate, whereas the survival proportion at day 7 in the control group was 0%. The median survival time of the control
20 group was 6.5 days.

Prophylactic treatment with ≥ 1.7 mg/kg test antibody resulted in a significant improvement in survival time.

25 Body weight

Change in bodyweight was analyzed using an Area Under the Curve (AUC) analysis in which the last observed body weight was carried forward if a mouse died / was euthanized during the study. The weight per mouse at day 0 was used as baseline and weight change was determined relative to baseline and the net AUC was defined as the summation of
30 the area above and below the baseline using the percentage change per day. Prophylactic treatment with ≥ 1.7 mg/kg test antibody resulted in a significant reduction in weight loss compared to the control group.

Conclusion

In this lethal SARS-CoV-2 Delta K18 hACE2 Tg mouse model, the prophylactic intraperitoneal administration of ≥ 5 mg/kg test antibody provides significant improvement in survival compared to vehicle and ≥ 1.7 mg/kg a reduction in weight loss
5 whereas all the animals in the control group died.

Example 4: Antibody according to the invention

The aim of this study was to assess the pre-exposure efficacy of a monoclonal antibody according to the invention, having a heavy chain CDR1 as SEQ ID NO: 029, heavy chain
10 CDR2 as SEQ ID NO: 136, heavy chain CDR3 as SEQ ID NO: 256, a light chain CDR1 as SEQ ID NO: 372, a light chain CDR2 as SEQ ID NO: 432, and a light chain CDR3 as SEQ ID NO: 573, following intranasal administration in a SARS-CoV-2 Delta K18 hACE2 Tg mouse model.

15 Animals (n=10 per group) were treated with an intranasal dose range of the test antibody described above (10 to 0.2 mg/kg) or PBS control at study day -1. At study day 0, animals were challenged with $10^{3.5}$ TCID₅₀ of SARS-CoV-2 Delta variant.

Materials and Methods

20 The monoclonal antibody according to the invention was buffered in phosphate-buffered saline PBS was diluted to the final concentrations for administration (10 to 0.2 mg/kg in 50 μ L)

The monoclonal dilution was made up at various concentrations so that 50 μ L
25 administrations to a 20 g mouse resulted in test antibody doses ranging from 10 mg/kg, 5 mg/kg, 1.7 mg/kg, 0.5 mg/kg to 0.2 mg/kg.

The antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and dilutions were stored at 4°C until usage and the temperature of the storage unit was monitored.

30

The virus strain tested was SARS-CoV-2 Delta variant (Aus/VIC/18440/2021 (B.1.617.2)., which had been passed three times through Vero-hSLAM cells.

Animals

The animal species used was the SARS-CoV-2 Delta K18 hACE2 Tg mouse model, at a weight of c. 17.2-21.9 g on the day of test article administration. 60 mice were used at the age of 7-11 weeks and were exclusively female. Ten animals were allocated to 6 treatment groups based on creating groups with similar mean weight and weight variability based on Day -5 weights. All mice were housed in individually ventilated cages (IVCs), with corn cob bedding, tissues or shredded paper as nesting material, a wooden chew block, accessible food pellets and acidic water for animal nourishment and red plastic tunnels. Each cage system holds 3 to 5 mice per cage. All mice were transferred to fresh cages every 14 days. Food and water were inspected daily and topped up as needed. Each animal was weighed daily beginning at the day of infection (Day 0).

Study design

The dose level of the monoclonal antibody applied in the current example was based on the maximal dosing possible for the material stock concentration (4 mg/mL) and based on literature and previous experience with an anti-S2 antibody (CV3-25) showing protection IN at doses ≥ 1.7 mg/kg. A total number of 60 mice, 7-11 weeks of age were transported to the animal facility and allocated to 6 experimental groups according to Table 4 (see below). Mice were given a period of >3 days for acclimatization.

20

Table 4: Intranasal experimental detail

Test group	Antibody	Admin. Route	Dose (mg/kg)	Day of admin.	No. of Animals
10	As disclosed above.	I.N.	10	-1	10
5		I.N.	5	-1	10
1.7		I.N.	1.7	-1	10
0.5		I.N.	0.5	-1	10
0.2		I.N.	0.2	-1	10
Vehicle	---	I.N.	0	-1	10

Female SARS-CoV-2 Delta K18 hACE2 mice were treated via the intranasal route of administration with the antibody at a dose between 10 mg/kg and 0.2 mg/kg based upon

a mouse weight of 20 g. On Day 0, all mice were challenged with a lethal dose ($10^{3.5}$ TCID₅₀) of the SARS-CoV-2 Delta variant and observed for survival and weight loss until the end of the study at day 12.

5 Antibody administration

The test antibody was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ upon arrival. The appropriate dose, according to the treatment schedule (Table 4), was formulated assuming a mouse weight of 20 g.

10 Just prior to dosing, the material was drawn into a 1 mL syringe with a 26G needle, and then administered to each mouse. Mice were anaesthetized with isoflurane (4% v/v with 2 L/min O₂) for two minutes. The mice were then scruffed and held at a +45 deg angle. 50 μL of compound or vehicle control was then slowly administered to the nares of each mouse (25 μL each nare). The mice were held for an additional 5 to 10 seconds to ensure
15 compound delivery to the lower respiratory tract before being put back into the home box.

Virus administration

The virus material was stored at $-80^{\circ}\text{C} \pm 10^{\circ}\text{C}$ and was defrosted prior to administration. Once defrosted, the material was diluted in cold PBS corresponding to approximately $10^{3.5}$ TCID₅₀/ 50 μL . As required, the animals were anesthetized by isoflurane (4% v/v with 2
20 L/min O₂) and each animal received approximately 50 μL (25 μL each nare) of virus corresponding with approximately $10^{3.5}$ TCID₅₀ by intranasal inoculation. Unused material was frozen at -20°C to -80°C for back titration.

25 Laboratory analysis

Inoculum was back titrated and the dose of the virus administered was verified by titrating replicate samples on Vero cells.

Terminal investigations

30 At the end of the study, on day 12, mice were euthanized by cervical dislocation. Gross necropsy was not performed.

Data analysis and statistical methods

Survival proportions at day 12, survival times and change in bodyweight (Area Under the Curve) were compared to the vehicle (PBS solution) control group using Fisher's exact test, log-rank and Welch's t-test, respectively. P-values were adjusted according to Bonferroni (for two comparisons to vehicle) followed by a stepwise approach (starting with the highest antibody dose conditionally testing a lower dose if the previous step was statistically significant).

Statistical analysis was performed using R and statistical significance was set at $\alpha = 0.05$.

Survival - Intranasal

Prophylactic treatment with ≥ 5 mg/kg test antibody provides statistically significant increase in survival compared to vehicle (See Figure 4). The animals that were treated with 5 and 10 mg/kg test antibody had a 80% survival rate, whereas the survival proportion at day 7 in the control group was 0%. The median survival time of the control group was 6.5 days.

Prophylactic treatment with ≥ 0.2 mg/kg test antibody resulted in a significant improvement in survival time.

Body weight

Change in bodyweight was analyzed using an Area Under the Curve (AUC) analysis in which the last observed body weight was carried forward if a mouse died / was euthanized during the study. The weight per mouse at day 0 was used as baseline and weight change was determined relative to baseline and the net AUC was defined as the summation of the area above and below the baseline using the percentage change per day. Prophylactic treatment with ≥ 0.2 mg/kg test antibody resulted in a significant reduction in weight loss compared to the control group.

Conclusion

In this lethal SARS-CoV-2 Delta K18 hACE2 Tg mouse model, the prophylactic intranasal administration of ≥ 5 mg/kg test antibody provides significant improvement in survival and ≥ 0.2 mg/kg a reduction in weight loss compared to vehicle. In contrast, all the animals in the control group had died by day 7.

Example 5: Bi-specific antibody according to the invention

The aim of this intranasal murine study is to assess the pre- and post- exposure efficacy of a bispecific monoclonal antibody in comparison with the parental antibodies, according to the invention, having a first Fab capable of binding to the stem helix of SARS-CoV-2 and a second Fab capable of binding to the fusion peptide of SARS-CoV-2. The first parental antibody ("Parental mAb 1") has the following CDRs as described in SEQ ID Numbers: 029, 136, 256, 372, 432 and 573. The second parental antibody ("Parental mAb 2") has the following CDRs as described in SEQ ID Numbers: 645, 646, 647, 648, 649 to 650. The bi-specific antibody according to the invention has a first Fab that comprises a sequence comprising any one or more of SEQ ID Numbers: 029, 136, 256, 372, 432 or 573; wherein the second Fab comprises a sequence comprising any one or more of SEQ ID Numbers: 645, 646, 647, 648, 649 to 650.

Animals are treated with an intranasal nominal dose (0.001 mg/kg to 15 mg/kg) comprising either Parental mAb 1, or Parental mAb 2, or the bispecific antibody described above or vehicle control at study day -1.

Materials and Methods

The monoclonal parental and bispecific antibodies according to the invention is provided in a sodium acetate buffer (e.g. 20mM Sodium Acetate, 75mM Sodium Chloride, 5% sucrose, pH 5.5) and is diluted to the final concentration for administration ranging from 0.001 mg/kg to 15 mg/kg, administered as 25 µL to 50 µL per nare.

The mice allocated to the control group (Sodium acetate buffer) are administered with vehicle (e.g. 20mM Sodium Acetate, 75mM Sodium Chloride, 5% sucrose, pH 5.5), administered as 25 µL to 50 µL per nare.

All mice receive intranasal challenge with SARS-CoV-2 Delta at day 0.

Animals

The SARS-CoV-2 Delta K18 hACE2 Tg mice are used at a weight of c. 15g to 22g (e.g. 20 g per animal) on commencement of the study. Between 6 and 10 animals are allocated to each treatment group.

Study design

The dose level of the monoclonal and bispecific antibodies applied in the current example is based on the maximal dosing and based upon previous results from efficacy studies in mice with the parental antibodies alone. From the maximal dose of ≤ 15 mg/kg, a 3- or 4- fold dilution curve for each the parental or bispecific antibody is applied.

Table 5: Intranasal experimental detail per antibody

Test group	Antibody	Dose (mg/kg)	Day of admin.	No. of Animals
1	Parental mAb 1 (dose 1)	0.001-15 (e.g. 0.0027, 0.063)	-1	6 – 10
2	Parental mAb 1 (dose 2)	0.001-15 (e.g. 0.106, 0.189)	-1	6 – 10
3	Parental mAb 1 (dose 3)	0.001-15 (e.g. 0.425, 0.567)	-1	6 – 10
4	Parental mAb 1 (dose 4)	0.001-15 (e.g. 1.7)	-1	6 – 10
5	Parental mAb 2 (dose 1)	0.001-15 (e.g. 0.0027, 0.063)	-1	6 – 10
6	Parental mAb 2 (dose 2)	0.001-15 (e.g. 0.106, 0.189)	-1	6 – 10
7	Parental mAb 2 (dose 3)	0.001-15 (e.g. 0.425, 0.567)	-1	6 – 10
8	Parental mAb 2 (dose 4)	0.001-15 (e.g. 1.7)	-1	6 – 10
9	Bispecific mAb (dose 1)	0.001-15 (e.g. 0.007, 0.005)	-1	6 – 10
10	Bispecific mAb (dose 2)	0.001-15 (e.g. 0.027, 0.020)	-1	6 – 10
11	Bispecific mAb (dose 3)	0.001-15 (e.g. 0.106, 0.080)	-1	6 – 10
12	Bispecific mAb (dose 4)	0.001-15 (e.g. 0.425, 0.310)	-1	6 – 10
13	Bispecific mAb (dose 5)	0.001-15 (e.g. 1.7, 1.25)	-1	6 – 10
14	Bispecific mAb (dose 6)	0.001-15	-1	6 – 10

		(e.g. 5.0)		
Vehicle	---	0	-1	6 – 10

The mice are treated via the intranasal route of administration with compositions comprising either parental antibodies or the bispecific antibody at dose ranges between 0.001 and 15 mg/kg. On Day 0, all mice are challenged with a dose of the SARS-CoV-2 and observed for survival and body weight until the end of the study (e.g. Day 10-15).

Antibody administration

The parental monoclonal antibodies or bispecific antibody or vehicle only is administered to each nare (e.g. pipette or spray) according to the treatment schedule (Table 5), using volumes of between 25 µL to 50 µL per nare.

Virus administration

The virus material is defrosted prior to administration. Once defrosted, the material is diluted and each animal received between 25 µL to 50 µL of virus per nare. The mice are infected with between 10^2 and 10^8 TCID₅₀ of SARS-CoV-2 (e.g. $10^{3.5}$ TCID₅₀ of SARS-CoV-2).

Laboratory analysis

Inoculum is returned to the lab and the dose of the virus administered is verified by titrating replicate samples on Vero cells.

Clinical monitoring

General health observations are performed on each animal from the day of arrival until the end of the study at least once daily (during normal servicing procedures). Each animal is weighed daily beginning one day prior to infection (day -1).

Data analysis and statistical methods

Survival proportions and survival times and change in bodyweight (Area Under the Curve) are compared to the corresponding control group using Fisher's exact test, log-rank and Welch's t-test, respectively. All groups are compared to the vehicle control group.

P values are adjusted according to Bonferroni (for three comparisons to vehicle) followed by a stepwise approach within antibody (starting with the highest dose and conditionally testing a lower dose if the previous step was statistically significant).

- 5 Survival dose response curves are fitted for each of the treatments (Parental mAb 1, Parental mAb 2 and Bispecific) and the ED₅₀ is estimated. The efficacy of the bispecific antibody is then compared to the parental antibodies .

Survival

- 10 Prophylactic treatment with Parental mAb 1, Parental mAb 2 or bispecific antibody (as indicated in Table 5) compared to the control group provides statistically significant protection against mortality and a significant improvement in survival time compared to the control group.

Body weight

- 15 Change in bodyweight is analyzed using an Area Under the Curve (AUC) analysis in which the last observed body weight is carried forward if a mouse died/ is euthanized during the study. The weight per mouse at day 0 is used as baseline and weight change is determined relative to baseline with the net AUC defined as the summation of the area
20 above and below the baseline using the percentage change per day.

Prophylactic treatment with the parental or bispecific antibodies (as indicated in Table 5) provides a statistically significant reduction in weight loss, compared to the control group.

Conclusion

- 25 In this SARS-CoV-2 Delta mouse model, the prophylactic intranasal administration of a bispecific antibody (as indicated in Table 5) according to the invention provides significant improvement in survival and a reduction in body weight loss compared with Control
30 Group. The outcome of the combination index is suggestive of at least a comparable, an additive or potentially synergistic effect for the bispecific compared to the parental antibodies.

Example 6: ELISA binding assessment of an antibody according to the invention

The objective of this study was to assess the binding of the antibody against different Corona Spike antigens, a variety of alpha and beta coronaviruses.

5

Binding was tested in an enzyme-linked immunosorbent assay (ELISA). Briefly, a Spike antigen was used to coat the surface of a microwell of an ELISA plate. The antibody was then added in decreasing concentration to the coated and pre-blocked microwell surface in duplicates, attaching to the coated antigen. A detection antibody was added, labeled with horse radish peroxide (HRP), that then generates a colorimetric signal upon addition of the substrate. The readout was optical density and reflects binding. The antibody was assayed in duplicate against a number of alpha and beta coronavirus spike antigens, including but not limited to SARS-CoV-2 Delta, Omicron XBB.1.5 and human coronavirus NL63. The antibody was tested in comparison to other anti-S1 antibodies in the range of 10.0 - 0.000002 nM. Half maximal effective concentration (EC₅₀) was calculated for each antibody on each antigen as an estimate of binding affinity.

15

Table 6: ELISA EC₅₀ values (nM) for the antibody according to invention. N/D = no EC₅₀ value was determined, due to lack of binding.

	CoV-2 Delta	CoV-2 XBB.1.5	NL63
COV30-14	0.00031	0.000057	N/D
Anti-S1 antibody DZIF-10c	6.9	N/D	N/D
Anti-S1 mAb ImdevimAb	0.010	N/D	N/D
Human IgG1 Isotype	N/D	N/D	N/D

20

The ELISA binding assay (Table 6) showed that the antibody according to invention was able to effectively bind all tested Spike antigens from beta coronaviruses, including SARS-CoV-2 Delta and Omicron XBB.1.5. Alpha coronavirus NL63 spike antigen was not bound by the antibody. The anti-S1 antibodies tested only bound the SARS-CoV-2 Delta and not the Omicron mutant, as expected from literature and did not show binding amongst alpha

25

coronavirus NL63. The isotype control antibody did not show any binding to the coronavirus antigens.

Example 7: Affinity binding assessment by MSD of an antibody according to the invention

The objective of this study was to assess relative binding affinity against Spike antigens in a multiplexed way, with very high specificity and low sample input. Therefore, an antibody was tested in a multiplexed assay, Meso Scale Discovery (MSD), which uses electrochemiluminescent labels that were conjugated to detection antibodies. In this assay, up to ten trimeric viral antigens are separately printed onto a spot each well of the plate, allowing for a multiplexed assay readout. The antibody according to the invention bind the viral antigens through Fab-mediated recognition, then an anti-human IgG Sulfo-Tag detection antibody is added, recognizing human IgG Fab. Upon addition of read buffer containing substrate, and running a current through the plate electrodes, an electro- (current) chemi- (buffer substrate) luminescent (light) cascade is initiated which results in light emission. The intensity of emitted light is measured per spot, revealing bound levels of analyte. The antibody was assayed in duplicate against Spike antigens of SARS-CoV-2, SARS-CoV-1, MERS, hCoV NL63, hCoV HKU, hCoV OC43 and hCoV 229E (V-Plex COVID-19 Coronavirus Panel 3 (IgG) Kit cat# K15399U-2) (Table 7), as well as a set of Omicron variants (V-Plex SARS-CoV-2 Panel 34 (IgG) Kit cat# K15690U-2) in a separate assay (Table 8). The antibody was tested in a dilution range starting from 555 ng/ml for the Panel 3 and 10 ng/ml in the Omicron Panel 24 kit. Light emission from the MSD sulfo-tag antibody was quantified with MSD Discovery workbench, calibration curves were used to calculate antibody concentrations, by fitting the raw electrochemiluminescent units (eCLU) from the calibrators to a logistic regression for curve fitting (Sigmoidal, 4PL, $X = \text{conc}$), and the model asymptotes were constrained to the lower limit of detection (LLOQ) and the upper limit of detection (ULOQ). The concentration (ng/ml) corresponding to the midpoint of the dynamic range (ie the range between the lower and upper limit of quantification, LLOQ and ULOQ) was reported.

Table 7: Antibody concentrations corresponding to the midpoint of the dynamic range $(\text{LOQ} + \text{ULOQ})/2$ (ng/ml) for the antibody according to invention against different alpha and beta coronaviruses is shown. N/D = antibody concentration could not be determined.

	SARS-CoV-2	SARS-CoV-1	MERS-CoV	hCoV-OC43	hCoV-HKU1	hCoV-NL63	hCoV-229E	SARS-CoV-2 S1 RBD
COV30-14	0.52	0.26	0.16	3.72	1.85	N/D	N/D	N/D
Anti-S1 mAb DZIF-10c	0.16	N/D	N/D	N/D	N/D	N/D	N/D	0.09
isotype control	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D

The MSD binding array (see Table 7) showed that the antibody according to the invention was able to effectively bind all Spike antigens from beta coronaviruses, including SARS-CoV-2, MERS, HKU1 and OC43. Alpha coronaviruses including 229E and NL63 and SARS-CoV-2 receptor binding domain (RBD) on the S1 part of the Spike were not bound by the antibody. The anti-S1 antibody tested here bound the RBD domain and the wildtype SARS-CoV-2 very well, as expected from literature and did not show binding breadth amongst other tested alpha coronaviruses. This suggests that the antibody according to invention shows efficient binding across all tested beta coronavirus Spikes, while the anti-RBD antibody only bound SARS-CoV-2 Spike and RBD domain. The isotype control antibody did not show any binding to the coronavirus antigens.

Table 8: Antibody concentrations corresponding to the midpoint of the dynamic range $(LOQ+ULOQ)/2$ (pg/ml) for antibody according to the invention against different SARS-CoV-2 Omicron viruses is shown. N/D = antibody concentration could not be determined.

	SARS-CoV-2	SARS-CoV-2 BA.1	SARS-CoV-2 BA.2.7.5	SARS-CoV-2 BA.5	SARS-CoV-2 BF.7	SARS-CoV-2 BN.1	SARS-CoV-2 BQ.1	SARS-CoV-2 BQ.1.1	SARS-CoV-2 XBB.1	SARS-CoV-2 XBB.1.5
COV30-14	540	105	139	155	131	102	168	151	157	154
Anti-S1 mAb DZIF-10c	117	93	81	630	13625	11558	N/D	N/D	N/D	N/D
isotype control	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D

The MSD binding array showed that the antibody according to invention can effectively bind all Omicron variants tested in this assay, at even lower concentrations than SARS-CoV-2 Wuhan (Table 8), therefore retaining activity among the Omicron mutants. The SARS-CoV-2 BA.1 and BN.1 variants were bound at especially low concentrations. While the anti-S1 control antibody bound the SARS-CoV-2 Spike at lower concentrations than the antibody according to invention, the earlier Omicron mutants were only bound at very high concentrations and the later Omicron mutants such as BQ.1 and XBB.1 were not bound. This indicates that the antibody according to invention was able to bind to the latest Omicron mutants while the anti-RBD antibody did not bind these variants. The isotype control antibody did not show any binding to the coronavirus antigens.

Example 8. Live virus neutralization of an antibody according to the invention

The objective of this study was to assess the ability of an antibody to neutralize live corona viruses. The antibody was tested for functional activity in a live virus microneutralization assay against MERS, SARS-CoV-1 and SARS-CoV-2 Wuhan. Briefly, dilution series of an antibody were pre-incubated with the corresponding virus and then added to the respective cell line (Vero: MERS and SARS-CoV-1, SARS-CoV-2: Vero E6 cells) in quadruplicates. After incubation, cells were fixed, stained with an anti-nucleocapsid antibody, and an enzymatically tagged detection antibody was added. Colored precipitate signaling nucleocapsid presence was read out via an Immunospot analyzer and 50% inhibitory concentration (IC_{50}), was reported via the Zielinska method (REF: <https://doi.org/10.1186/1743-422X-2-84>). The antibody was tested for neutralizing activity in the range of 0.025 to 500 $\mu\text{g/ml}$.

Table 9: Live virus neutralization assay. IC₅₀ values in µg/ml are displayed for against three different beta coronaviruses. A pooled convalescent serum from SARS-CoV-2 patients was used as a comparator and SARS-CoV-2 positive control, MN₅₀ titers are shown. N/D = MN₅₀ could not be determined

Live virus neutralization	SARS-CoV-2 Wuhan	SARS-CoV-1	MERS-CoV
COV30-14	25.45	4.95	3.68
SARS-CoV-2 pooled convalescent serum	142.00	N/D	N/D

5

Overall, the antibody according to the invention was able to neutralize the tested viruses SARS-CoV-1, SARS-CoV-2 and MERS-CoV at varying concentrations (see Table 9), with the lowest IC₅₀ concentrations for MERS-CoV. This confirms that the antibody has neutralizing activity across these beta coronaviruses, as indicated by the binding
10 assessments. The convalescent serum was only able to neutralize SARS-CoV-2 Wuhan at high MN₅₀ titers.

Example 9. Pseudovirion neutralization of an antibody according to the invention

15

The objective of this study was to assess the ability of an antibody to neutralize different pseudotyped virus particles. The advantage over a live virus assay was that pseudotyped viruses can be used at a lower biosafety level laboratory and new variants of concern can be produced and tested more rapidly, allowing for broader testing across variants of concern or interest. Briefly, pseudovirions were produced by co-transfecting virus
20 expression plasmids with the pHIV-1NL43 ΔEnv-NanoLuc reporter virus plasmid in HEK293T cells. Then, dilution series of the antibody were pre-incubated with the corresponding pseudovirus and then added to HEK 293T cells expressing ACE2, the entry receptor for SARS-CoV-2, SARS-CoV-1 and NL63. For hCoV 229E, the diluted antibody mixed with virus was added to Huh7 cells which express the aminopeptidase N (APN
25 receptor which facilitates entry of hCoV 229E into host cells. After incubation, cells were washed and lysed to measure the luciferase activity in cell lysates using the Nano-Glo Luciferase Assay System and GloMax system, with a readout of relative light units (RLUs). The 50% inhibitory concentrations (IC₅₀) were determined as the antibody concentration at which infectivity was inhibited by 50% using a four Parameter Logistic

Regression (4PL) curve fit. The bispecific antibody was tested for neutralizing activity in the range of 0.0042 to 250 µg/ml against SARS-CoV-1, SARS-CoV-2 Wuhan, Delta, Omicron BA.4, hCoV NL63 and hCoV 229E.

- 5 Table 10: Pseudovirion neutralization assay. IC₅₀ values in µg/ml were displayed for the anti-stem helix antibody against different alpha and beta coronaviruses. For multiple runs, the geometric mean with the 95% normal range is shown.

	SARS-CoV-1	SARS-CoV-2 Wuhan	SARS-CoV-2 Delta	SARS-CoV-2 BA4	SARS-CoV-2 XBB.1	SARS-CoV-2 BQ.1.1	CoV 229E	CoV NL63
COV30-14	5.887 (5.286-6.556)	0.211 (0.033-1.337)	14.374 (7.194-28.723)	7.601 (3.697-15.626)	9.915 (8.536-11.516)	9.625	>250	>250

- Overall, the antibody was able to neutralize the tested beta viruses SARS-CoV-1, SARS-CoV-2 including variants of concern at varying concentrations (see Table 10), with an overall trend of higher IC₅₀ concentrations for the Omicron variants and Delta. The antibody according to the invention did not neutralize alpha coronaviruses hCoV NL63 and 229E, as expected based on the lack of binding in the MSD binding assessment.

15 Example 10. Epitope mapping

- The goal of this study was to precisely determine the amino acid sequence that the antibody binds to in the Spike protein across different alpha and beta coronaviruses. The method includes mapping of linear epitopes using libraries of overlapping synthetic peptides from the spike protein. Briefly, linear epitopes of the sequence of interest were synthesized directly on a solid chip, generating a library of linear mimics, aiding identification of the correct amino acid sequence of the target antibody. The library of peptides consists of overlapping 15-amino acid fragments, with an overlap of 14 amino acids. Binding of the antibody to each of the synthesized peptide chips was tested in an enzyme-linked immunosorbent assay (ELISA) assay via incubation of the peptide arrays with antibody solutions. After washing, peptide arrays were incubated with an antibody peroxidase conjugate and substrate was added, and the reaction was then stopped using hydrogen peroxide. Color development was measured, and intensity was reported.

The antibody bound the peptide array of alpha and beta coronaviruses in a specific epitope of a 10- 20 amino acids (see Figure 9). The method allowed for a high confidence in the epitope definition, with certain variance in the outer areas of the epitope, indicated by asterisk for the respective strain.

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CLAIMS

1. A method for the treatment of a coronavirus infection in an individual, the method comprising administering to an individual in need thereof an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising
5 any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a
10 light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the
15 antibody is administered to the mucosa.
2. A mucosal composition comprising an antibody comprising a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy
20 chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130, 136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377,
25 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628.
- 30 3. An antibody for use in a method of prevention or treatment of a coronavirus infection in an individual, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising any one of SEQ ID NO: 004 to 009, 015 to 020, 029 to 034, 039 to 044, 047 to 052, 065 to 070, a heavy chain CDR2 region comprising any one of SEQ ID NO: 082 to 087, 103 to 108, 125 to 130,

136 to 141, 147 to 152, 191 to 196, and a heavy chain CDR3 region comprising any one of SEQ ID NO: 210 to 215, 221 to 226, 245 to 250, 256 to 261, 286 to 291, 297 to 302, a light chain variable domain that comprises a light chain CDR1 region comprising any one of SEQ ID NO: 319 to 324, 330 to 335, 350 to 355, 372 to 377, 383 to 388, 415 to 420, a light chain CDR2 region comprising any one of SEQ ID NO: 432 to 437, 443 to 448, 454 to 459, 465 to 470, 476 to 481, 508 to 513, and a light chain CDR3 region comprising any one of SEQ ID NO: 529 to 534, 540 to 545, 573 to 578, 601 to 606, 612 to 617, 623 to 628, wherein the antibody is administered to mucosa.

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4. A method, composition or antibody according to any preceding claim, wherein the antibody comprises a heavy chain variable domain that comprises a heavy chain CDR1 region comprising SEQ ID NO: 029, a heavy chain CDR2 region comprising SEQ ID NO: 136, and a heavy chain CDR3 region comprising SEQ ID NO: 256, a light chain variable domain that comprises a light chain CDR1 region comprising SEQ ID NO: 372, a light chain CDR2 region comprising SEQ ID NO: 432, and a light chain CDR3 region comprising SEQ ID NO: 573.

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5. A method, composition or antibody according to any preceding claim, wherein the method for treatment of coronavirus virus infection is a method for prophylactic and/or therapeutic treatment of a coronavirus, preferably wherein the method for treatment is for the prophylactic treatment of a SARS-COV-2 infection.

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6. A method, composition or antibody according to any preceding claim, wherein the antibody comprises a heavy chain variable domain having the sequence of SEQ ID NO:629 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid insertions, deletions, substitutions which are not in the heavy chain CDRs.

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7. A method, composition or antibody according to any preceding claim, wherein the antibody comprises a light chain variable domain having the sequence of SEQ ID NO:630 having at most 15, preferably 0, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid insertions, deletions, substitutions which are not in the light chain CDRs.

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8. A method, composition or antibody according to any preceding claim, wherein the antibody is an IgG antibody, preferably an IgG1 antibody.
9. A method, composition or antibody according to any preceding claim, wherein the antibody is provided to the individual prophylactically.
10. A method, composition or antibody according to any preceding claim, wherein the administration route comprises at least one of oral inhalation, nasal administration, ocular administration and oropharyngeal administration.
11. A method, composition or antibody according to any preceding claim, wherein the antibody is administered at least once or at least twice monthly.
12. A method, composition or antibody according to any preceding claim, wherein the antibody is administered to the individual at a dosage of between 0.01 mg and 20 mg.
13. A composition according to any preceding claim, comprising an antibody in a single dose unit of between 0.01 mg and 20 mg, preferably between 0.1 mg and 15 mg or preferably 0.5 mg and 10 mg, wherein the antibody is as defined in any one of claims 1 to 12.
14. A composition according to any preceding claim, wherein the composition is self-administered.
15. A medicament delivery device comprising a composition according to any preceding claim.