

VH_mouse	EVQLQQSGAELVKPGASVJKLSCASGFNIKE <b>E</b> TY <b>V</b> HVVKQRPEQGLEWIGRID <b>H</b> A <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YDPKFQGKAT <b>V</b> TADTSSN
VH1	QVQLVQSGAEVKKPGASVJKVSKASGFNIK <b>E</b> TY <b>V</b> HVVRQAPGQGLEWMGR <b>I</b> <b>D</b> <b>H</b> <b>A</b> <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YAQKFQGRVTMTRDTSSIS
VH2	QVQLVQSGAEVKKPGASVJKVSKASGFNIK <b>E</b> TY <b>V</b> HVVRQAPGQGLEWMGR <b>I</b> <b>D</b> <b>H</b> <b>A</b> <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YAQKFQGRVTMTRDTSSIS
VH3	QVQLVQSGAEVKKPGASVJKVSKASGFNIK <b>E</b> TY <b>V</b> HVVRQAPGQGLEWMGR <b>I</b> <b>D</b> <b>H</b> <b>A</b> <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YAQKFQGRVTMTRDTSSIS
VH4	QVQLVQSGAEVKKPGASVJKVSKASGFNIK <b>E</b> TY <b>V</b> HVVRQAPGQGLEWMGR <b>I</b> <b>D</b> <b>H</b> <b>A</b> <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YDPKFQGRVT <b>V</b> TADTSSIS
VH5	QVQLVQSGAEVKKPGASVJKVSKASGFNIK <b>E</b> TY <b>V</b> HVVRQAPGQGLEWMGR <b>I</b> <b>D</b> <b>H</b> <b>A</b> <b>I</b> <b>G</b> <b>D</b> <b>S</b> <b>E</b> YDPKFQGRVT <b>V</b> TADTSSIS
humVH_germl	QVQLVQSGAEVKKPGASVJKVSKASGYTFGTYYMHVVRQAPGQGLEWMGRINPNSSGTNYAQKFQGRVTMTRDTSSIS
VH_mouse	TAYLQLS <b>R</b> LTSEDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTTVTVSS
VH1	TAYMELSRLRSDDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTLVTVSS
VH2	TAYMELSRLRSDDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTLVTVSS
VH3	TAYMELSRLRSDDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTLVTVSS
VH4	TAYMELSRLRSDDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTLVTVSS
VH5	TAYMELSRLRSDDTAVYYCARTWGP <b>F</b> <b>F</b> <b>D</b> <b>F</b> WGQGTLVTVSS
hum_VH_germl	TAYMELSRLRSDDTAVYYCAR YFDYWGQGTLVTVSS
VL_mouse	DVVMTQTPLSLPVSILGDQASISCRSSSQLVHS <b>H</b> GNT <b>F</b> LHWYLQKPGQSPK <b>V</b> LIYKVSS <b>S</b> RFSGVPDRFSGSG <b>A</b> GT
VL1	DIVMTQTPLSLSVTPGQPASISCKSSQSLHS <b>H</b> GNT <b>F</b> LYWYLQKPGQSPQLLIY <b>K</b> VSSRFSGVPDRFSGSGSGT
VL2	DIVMTQTPLSLSVTPGQPASISCKSSQSL <b>V</b> HS <b>H</b> GNT <b>F</b> LHWYLQKPGQSPQLLIY <b>K</b> VSSRFSGVPDRFSGSGSGT
VL3	DIVMTQTPLSLSVTPGQPASISCKSSQSLHS <b>H</b> GNT <b>F</b> LYWYLQKPGQSPQ <b>V</b> LIY <b>K</b> VSSRFSGVPDRFSGSGSGT
VL4	DIVMTQTPLSLSVTPGQPASISCKSSQSL <b>V</b> HS <b>H</b> GNT <b>F</b> LYWYLQKPGQSP <b>K</b> VIY <b>K</b> VSSRFSGVPDRFSGSG <b>A</b> GT
humVL_germl	DIVMTQTPLSLSVTPGQPASISCKSSQSLHS <b>D</b> GKTYLYWYLQKPGQSPQ <b>V</b> LIYEVSSRFSGVPDRFSGSGSGT
VL_mouse	DFTLKISRVEAEDLGVYFC <b>S</b> Q <b>S</b> <b>T</b> <b>H</b> <b>V</b> PYTFGGTKLEIK
VL1	DFTLKISRVEAEDVGVYYC <b>S</b> Q <b>S</b> <b>T</b> <b>H</b> <b>V</b> PYTFGGTKLEIK
VL2	DFTLKISRVEAEDVGVYYC <b>S</b> Q <b>S</b> <b>T</b> <b>H</b> <b>V</b> PYTFGGTKLEIK
VL3	DFTLKISRVEAEDVGVYYC <b>S</b> Q <b>S</b> <b>T</b> <b>H</b> <b>V</b> PYTFGGTKLEIK
VL4	DFTLKISRVEAEDVGVYYFC <b>S</b> Q <b>G</b> <b>T</b> <b>H</b> <b>V</b> PYTFGGTKLEIK
humVL_germl	DFTLKISRVEAEDVGVYYCMQGIHLPYTFGGTKLEIK

**Figure S1. Humanization process of VH and VL chains.** Humanized VH (top) and VL (bottom) variable domains. Mutations relative to the closest murine germline (IGHV14-3\*02 IGHJ2\*01, IGKV1-110\*01 IGKJ2\*01) are indicated in red. Mutations in the humanized variable domains relative to the human germline sequence (IGHV1-2\*06 IGHJ4\*01, IGKV2-29\*02 IGKJ2\*01) are indicated in blue.

## In vivo 9-8F2-B11 efficacy in K18-hACE2 mice

The efficacy study was conducted on K18-hACE2 mice, immunocompetent transgenic mice expressing the human form of the ACE2 receptor under the control of the human keratin 18 promoter.

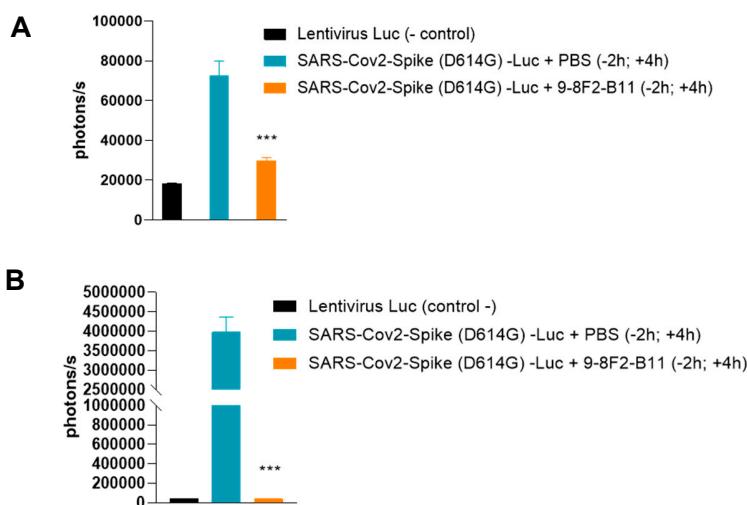
At day 0 the mice (N=3) were anaesthetised by inhalation of isofluorane and infected intranasally with 10 µl/narice of Pseudovirus SARS-CoV2-Spike (D614G)-Luc or with a Lentivirus-Luc used as a negative control for infection (N=3). 2 hours before and 4 hours after infection, the animals were treated with 10 µl/narice of anti-SARS-CoV2 monoclonal antibody 9-8F2-B11 or with PBS (control group for efficacy).

During the course of the study, the clinical signs of the animals were evaluated and their body weight was recorded daily. Since Pseudovirus carries the gene for luciferase, it was possible to monitor the infection by acquisition of the bioluminescence signal produced.

At 48-, 72- and 96-hours post-infection, all animals were analysed using the IVIS 200 Imaging System in order to quantitatively measure the bioluminescence associated with the presence of the pseudo virus.

At 96 hours after infection, after *in vivo* analysis, the animals were sacrificed by asphyxiation and the nasal turbinates and lungs were removed from each.

The explanted organs were also analysed *ex vivo* by IVIS for evaluation of associated bioluminescence.



**Figure S2. 9-8F2-B11 shows high efficacy in neutralizing SARS-CoV-2 in K18-hACE2 mice.** The two graphs show mean values ±SD (photons/s) of the biolumiscence detected in K18-hACE2 mice in both the total body of the animal (**A**) and the turbinates (**B**) at 96h after infection.

