





**Figure 1.** Production of mAbs in C57BL/6 and IFN $\alpha/\beta$  receptor knock-out mice after IDLV-VN04-2 administration in vivo. Groups of 5 C57BL/6 and IFN $\alpha/\beta$  receptor knock-out (IFN $\alpha/\beta$  R KO) mice were given IDLV-VN04-2 (about 400 ng RT/mouse) by the i.n. route of administration. The production of VN04-2 mAb in the serum was measured by ELISA for human IgG at different points post IDLV-VN04-2 administration, as indicated in the figure.



**Figure S2.** Protection from H5N1 IAV challenge at 21 days after IDLV-VN04-2 administration. Groups of 5 BALB/c mice received either IDLV-VN04-2 by the i.n. route (about 160 ng RT/mouse) or were left unimmunized as a control. Mice were then lethally challenged with VNH5N1-PR8 IAV at 21 days after IDLV administration. Weight loss (**a**) and survival (**b**) are shown. Mice with a weight loss of  $\geq$ 20% of their initial body weight were euthanized and counted as dead (Comparison of survival curves, *p* = 0.02, Log-rank Mantel-Cox test).



**Figure S3.** IDLV-VN04-2 does not protect from H5N1 IAV challenge at 30 days after administration. Groups of 5 BALB/c mice received either IDLV-VN04-2 or IDLV-huG1 as a control by the i.n. route (about 250ng RT/mouse), or were left unimmunized. Mice were then lethally challenged with VNH5N1-PR8 IAV at 30 days after IDLV administration. Weight loss (a) and survival (b) are shown. Mice with a weight loss of  $\geq$ 20% of their initial body weight were euthanized and counted as dead. Data representative of two separate experiments are shown (comparison of survival curves *p* = not significant, Log Rank Mantel-Cox test).



**Figure S4**. Combined administration of ILDV-VN04-2 and IDLV-NP protects from H3 IAV challenge Groups of 5 BALB/c mice received IDLV-VN04-2, IDLV-NP or a combination of IDLV-VN04-2 and IDLV-NP by the i.n. route (approximately 300 ng of each vector). Mice left unimmunized were used as a control. Since IDLV-NP is unable to protect after a single administration, mice who had received IDLV-NP alone or in combination received a second dose of this vector 14 days after the first administration. All mice were then lethally challenged with IAV Phil/H3N2 30 days after the initial IDLV administration. Weight loss (**a**) and survival (**b**) are shown. Mice receiving the combination of IDLV-VN04-2 and IDLV-NP, but not IDLV-VN04-2 alone, were protected from challenge, suggesting that IDLV-VN04-2 does not interfere with IDLV-NP-induced protection. (comparison of the survival curves: p = 0.014, Log-rank Mantel-Cox test).