

Methods S1: Expression and purification of cilgavimab and tixagevimab in *N. benthamiana* plants.

Variable region sequences for light chain (LC) and heavy chain (HC) of cilgavimab and tixagevimab from literature (Dong et al., 2021) were synthesized by GENEWIZ and were genetically fused to a human kappa constant sequence of the LC and a human gamma IgG1 constant sequence of HC (Lai et al., 2010). LC and HC genes were then cloned into a bean yellow dwarf virus (BeYDV)-based geminiviral vector and transiently expressed in *N. benthamiana* plants by agroinfiltration as described previously (Chen and Lai, 2014).

7D11 mAb were extracted and purified according to published protocols (Jugler et al., 2020). Briefly, mAb-expressing *N. benthamiana* leaves 7 days post infiltration were harvested and homogenized in extraction buffer (1X phosphate-buffered saline, pH 5.2 with 10 mg/mL Na-L-ascorbate, 2mM phenylmethylsulfonyl fluoride, and 1mM ethylenediaminetetraacetic acid). The pH of the homogenate was adjusted to 5.2 and then centrifuged several times. The supernatant was filtered through a 0.2-micron vacuum filter. The clarified protein extract was subsequently subjected to Protein A (MabSelect, Cytiva) chromatography according to the manufacture's protocol prior to further analysis.

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Jugler, C., Joensuu, J. and Chen, Q. (2020) Hydrophobin-Protein A Fusion Protein Produced in Plants Efficiently Purified an Anti-West Nile Virus Monoclonal Antibody from Plant Extracts via Aqueous Two-Phase Separation. *International Journal of Molecular Sciences* **21**, 2140.

Lai, H., Engle, M., Fuchs, A., Keller, T., Johnson, S., Gorlatov, S., Diamond, M.S. and Chen, Q. (2010) Monoclonal antibody produced in plants efficiently treats West Nile virus infection in mice. *Proc. Natl. Acad. Sci. U S A* **107**, 2419-2424.

Variant	pTixagevimab(IC ₅₀)	pCilgavimab (IC ₅₀)
Omicron BA.4.6	90.65 µg/ml	568.30 µg/ml

Table S1. Half-maximal inhibitory concentrations (IC₅₀) of pTixagevimab and pCilgavimab against Omicron BA.4.6 pseudovirus.