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**Supplemental information**

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**Table S1, Related to Table 1. Properties of monoclonal antibodies isolated from COVID-19 convalescent individual C1.**

| ELISA (OD 450 nm) |                     |               |              |                     |               |              |       |      |      |      |
|-------------------|---------------------|---------------|--------------|---------------------|---------------|--------------|-------|------|------|------|
| Antibody          | V <sub>H</sub> gene | CDR H3 (a.a.) | Identity (%) | V <sub>L</sub> gene | CDR L3 (a.a.) | Identity (%) | Neut. | S2P  | RBD  | Ctrl |
| C1A-A1            | IGHV1-69            | 15            | 99.31        | IGKV3-11            | 11            | 99.64        | -     | 2.46 | 0.26 | 0.00 |
| C1A-A6            | IGHV3-11            | 15            | 98.96        | IGKV1-13            | 9             | 98.92        | +     | 2.55 | 2.81 | 0.00 |
| C1A-A11           | IGHV3-30            | 20            | 99.31        | IGKV1-33            | 9             | 99.28        | +     | 2.87 | 2.85 | 00.0 |
| C1A-B1            | IGHV1-2*02          | 18            | 97.57        | IGKV3-20            | 10            | 98.58        | +     | 2.44 | 0.04 | 0.00 |
| C1A-B3            | IGHV3-53            | 14            | 97.89        | IGKV1-9             | 9             | 98.92        | ++    | 2.66 | 2.94 | 0.00 |
| C1A-B5            | IGHV4-59*11         | 11            | 94.74        | IGKV4-1*01          | 9             | 95.96        | -     | 2.73 | 0.04 | 0.00 |
| C1A-B6            | IGHV1-24            | 14            | 98.61        | IGLV2-8             | 10            | 99.31        | -     | 3.08 | 0.00 | 0.00 |
| C1A-B12           | IGHV3-53            | 14            | 98.6         | IGKV1-9             | 9             | 98.57        | ++    | 2.69 | 2.97 | 0.00 |
| C1A-C1            | IGHV3-23            | 14            | 99.31        | IGKV1-39            | 10            | 100          | ++    | 2.95 | 2.97 | 0.00 |
| C1A-C2            | IGHV3-53            | 14            | 98.6         | IGKV1-9             | 9             | 97.49        | ++    | 2.81 | 2.86 | 0.00 |
| C1A-C4            | IGHV3-53            | 14            | 98.25        | IGKV1-9             | 9             | 97.13        | ++    | 2.89 | 2.85 | 0.00 |
| C1A-C6            | IGHV1-69            | 15            | 98.96        | IGKV3-11            | 11            | 98.92        | -     | 2.58 | 0.02 | 0.01 |
| C1A-C7            | IGHV4-39            | 12            | 99.31        | IGLV2-14            | 10            | 94.79        | -     | 1.04 | 2.08 | 1.37 |
| C1A-C8            | IGHV1-24            | 16            | 99.65        | IGLV3-21            | 12            | 98.57        | -     | 3.02 | 0.00 | 0.00 |
| C1A-C9            | IGHV1-69            | 14            | 97.92        | IGKV1-39            | 8             | 98.92        | +     | 2.99 | 2.93 | 0.00 |
| C1A-C10           | IGHV3-23            | 17            | 98.61        | IGLV2-23            | 12            | 99.65        | +     | 2.75 | 0.04 | 0.00 |
| C1A-D1            | IGHV4-39            | 18            | 91.75        | IGKV1-33            | 9             | 93.19        | -     | 2.06 | 0.30 | 0.05 |
| C1A-D9            | IGHV3-30            | 20            | 98.61        | IGKV2-30            | 10            | 100          | -     | 2.66 | 1.78 | 0.02 |
| C1A-D11           | IGHV1-69            | 14            | 98.26        | IGKV3-11            | 11            | 99.28        | -     | 2.39 | 0.00 | 0.00 |
| C1A-E1            | IGHV3-9*01          | 13            | 89.58        | IGKV1-39            | 10            | 91.04        | -     | 2.70 | 2.82 | 0.00 |
| C1A-E3            | IGHV1-18            | 16            | 98.61        | IGKV1-39            | 5             | 98.92        | +     | 2.74 | 2.86 | 0.00 |
| C1A-E4            | IGHV3-30            | 14            | 97.92        | IGKV3-20            | 9             | 100          | -     | 2.43 | 0.03 | 0.00 |
| C1A-E8            | IGHV3-48            | 21            | 97.22        | IGKV2-28            | 9             | 100          | -     | 2.73 | 0.02 | 0.01 |
| C1A-E9            | IGHV3-30            | 14            | 100          | IGKV3-20            | 9             | 100          | -     | 1.81 | 0.00 | 0.00 |
| C1A-F2            | IGHV3-30-3          | 15            | 99.65        | IGKV2-28            | 8             | 99.66        | -     | 2.25 | 0.01 | 0.00 |
| C1A-F3            | IGHV4-61            | 13            | 98.63        | IGKV1-39            | 10            | 99.28        | -     | 2.40 | 0.07 | 0.01 |
| C1A-F4            | IGHV3-30-3          | 14            | 99.65        | IGKV1-5             | 9             | 99.64        | +     | 2.84 | 2.77 | 0.00 |
| C1A-F7            | IGHV3-15            | 11            | 91.84        | IGKV4-1             | 9             | 93.6         | -     | 2.42 | 0.01 | 0.00 |
| C1A-F10           | IGHV3-53            | 14            | 97.89        | IGKV1-9             | 9             | 98.21        | ++    | 2.98 | 2.69 | 0.00 |
| C1A-F11           | IGHV1-69            | 21            | 89.24        | IGKV1-33            | 8             | 94.98        | -     | 2.39 | 2.37 | 0.00 |
| C1A-F12           | IGHV4-39            | 15            | 90.03        | IGLV1-40            | 11            | 95.49        | -     | 2.62 | 2.78 | 0.01 |
| C1A-G4            | IGHV3-23            | 17            | 99.65        | IGLV2-23            | 11            | 99.65        | -     | 2.57 | 0.00 | 0.00 |
| C1A-G9            | IGHV3-30-3          | 14            | 98.61        | IGKV3-20            | 8             | 100          | -     | 2.46 | 0.01 | 0.00 |
| C1A-G11           | IGHV1-69            | 12            | 97.92        | IGKV1-5             | 9             | 99.28        | -     | 2.75 | 0.01 | 0.00 |
| C1A-G12           | IGHV3-30-3          | 14            | 98.26        | IGKV3-15            | 8             | 98.92        | -     | 2.51 | 0.07 | 0.07 |
| C1A-H5            | IGHV3-53            | 14            | 97.54        | IGKV1-9             | 9             | 97.49        | ++    | 2.69 | 2.67 | 0.00 |
| C1A-H6            | IGHV3-53            | 14            | 98.95        | IGKV1-9             | 9             | 98.21        | ++    | 2.90 | 2.74 | 0.04 |
| C1A-H10           | IGHV3-21            | 18            | 99.31        | IGKV3-15            | 10            | 100          | -     | 2.64 | 0.03 | 0.02 |
| C1A-H11           | IGHV3-30            | 16            | 98.61        | IGLV2-14            | 10            | 99.31        | -     | 2.27 | 0.00 | 0.00 |
| C1A-H12           | IGHV4-39            | 15            | 98.28        | IGKV3-15            | 9             | 99.28        | -     | 2.66 | 0.01 | 0.01 |
| C1B-A3            | IGHV3-30-3          | 14            | 99.65        | IGKV3-11            | 9             | 100          | -     | 2.00 | 0.02 | 0.01 |
| C1B-A5            | IGHV3-30-3          | 14            | 99.65        | IGKV3-20            | 9             | 98.94        | -     | 2.20 | 0.01 | 0.01 |
| C1B-A11           | IGHV3-30-3          | 14            | 98.26        | IGKV3-20            | 9             | 99.29        | -     | 2.35 | 0.28 | 0.00 |

Antibodies highlighted in gray are somatic variants of the same antibody. CDR loop lengths are shown as numbers of amino acids (a.a.). ELISA values are colored in shades of blue according to their magnitude; darker shades are reflective of a stronger signal. S2P: prefusion stabilized version of the SARS-CoV-2 S ectodomain; RBD: receptor-binding domain; Ctrl: negative control protein Lujo virus GP1. Neut: neutralizing activity as shown in Figure S1G. ++ signifies >90% neutralization, and + signifies neutralization not meeting this threshold.

**Table S2, Related to Figure 1. Data collection and refinement statistics**

|   | C1A-B3/RBD <sup>a</sup><br>(PDB 7KFV)                 | C1A-B12/RBD <sup>a</sup><br>(PDB 7KFW)                | C1A-C2/RBD <sup>a</sup><br>(PDB 7KFX) | C1A-F10/RBD <sup>a</sup><br>(PDB 7KFY) |
|---|---|---|---------------------------------------|--|
| <b>Data collection</b>                                |   |   |                                       |  |
| Space group   | <i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub> | <i>P</i> 2 <sub>1</sub> 2 <sub>1</sub> 2 <sub>1</sub> | <i>C</i> 222 <sub>1</sub>             | <i>C</i> 222 <sub>1</sub>              |
| Cell dimensions<br><i>a</i> , <i>b</i> , <i>c</i> (Å) | 84.8, 113.3,<br>268.89                                | 84.8, 113.3, 268.9                                    | 83.5, 149.2, 146.1                    | 85.7, 146.8, 144.6                     |
| $\alpha, \beta, \gamma$ (°)                           | 90.00, 90.00,<br>90.00                                | 90.00, 90.00,<br>90.00                                | 90.00, 90.00,<br>90.00                | 90.00, 90.00,<br>90.00                 |
| Resolution (Å)  | 200-2.77 (2.94-<br>2.77) <sup>b</sup>                 | 200-2.10 (2.23-<br>2.10) <sup>b</sup>                 | 200-2.22 (2.36-<br>2.22) <sup>b</sup> | 200-2.16 (2.29-<br>2.16) <sup>b</sup>  |
| <i>R</i> <sub>sym</sub>                               | 0.38 (3.17) <sup>b</sup>                              | 0.238 (2.01) <sup>b</sup>                             | 0.136 (2.23) <sup>b</sup>             | 0.118 (1.13) <sup>b</sup>              |
| <i>R</i> <sub>pim</sub>                               | 0.11 (1.03) <sup>b,c</sup>                            | 0.095 (0.85) <sup>b,c</sup>                           | 0.062 (1.01) <sup>b,c</sup>           | 0.076 (0.61) <sup>b,c</sup>            |
| <i>I</i> / $\sigma$                                   | 5.4 (0.7) <sup>b</sup>                                | 9.0 (1.4) <sup>b</sup>                                | 6.9 (0.6) <sup>b</sup>                | 6.2 (0.7) <sup>b</sup>                 |
| Completeness (%)                                      | 98.1 (88.6) <sup>b</sup>                              | 98.9 (94.7) <sup>b</sup>                              | 99.1 (97.1) <sup>b</sup>              | 94.0 (89.4) <sup>b</sup>               |
| Redundancy  | 6.9 (6.5) <sup>b</sup>                                | 7.0 (6.4) <sup>b</sup>                                | 3.6 (3.6) <sup>b</sup>                | 2.1 (2.0) <sup>b</sup>                 |
| <b>Refinement</b>                                     |   |   |                                       |  |
| Resolution (Å)  | 133.92-2.79   | 134.44-2.10   | 74.60-2.23                            | 74.04-2.16                             |
| No. reflections                                       | 63645   | 149225  | 44541                                 | 48373                                  |
| <i>R</i> <sub>work</sub> / <i>R</i> <sub>free</sub>   | 0.19/0.23   | 0.18/0.22   | 0.19/0.23                             | 0.19/0.22                              |
| No. atoms   |   |   |                                       |  |
| Protein   | 14414   | 14511   | 4861                                  | 4855                                   |
| Ligand/ion  | 42  | 42  | 14                                    | 14                                     |
| Water   | 400   | 1642  | 325                                   | 532                                    |
| <i>B</i> -factors (Å <sup>2</sup> )                   |   |   |                                       |  |
| Protein   | 88  | 47  | 63                                    | 52                                     |
| Ligand/ion  | 96  | 99  | 103                                   | 101                                    |
| Water   | 66  | 53  | 65                                    | 55                                     |
| R.m.s. deviations                                     |   |   |                                       |  |
| Bond lengths (Å)                                      | 0.008   | 0.008   | 0.008                                 | 0.008                                  |
| Bond angles (°)                                       | 0.980   | 0.970   | 1.000                                 | 1.000                                  |

<sup>a</sup> Numbers of crystals for C1A-B3, C1A-B12, C1A-C2 and C1A-F10 data were 1 each.

<sup>b</sup> Values in parentheses are for the highest-resolution shell.

<sup>c</sup> Values from program *aimless*.

**Table S3, Related to Figures 3 and 4. Human derived SARS-CoV-2 S sequences containing mutations of interest.**

| Virus name                              | PANGO lineage | Accession No.   | S mutations of interest      | Location                  | Collection date | Originating laboratory   | Submitting laboratory  | Authors   |
|---|---------------|-----------------|------------------------------|---------------------------|-----------------|--|--|---|
| hCoV-19/USA/FL-CDC-STM-0000013-F04/2021 | B.1.1.7       | EPI_ISL_884605  | D614G, N501Y, Q493K, Y114del | Florida, United States    | 01/14/2021      | Respiratory Viruses Branch, Centers for Disease Control and Prevention | Respiratory Viruses Branch, Centers for Disease Control and Prevention   | Cook, P.W., Batra, D., Rambo-Martin, B.L., de Feo, E., Antico, J., Tran, C., Tolentino, M., Wickline, S., Gietzen, K., Sickler, B., Liu, J., Allen, E., Febbo, P., Galloway, S., Washington, N.L., White, S., Levan, G., Barret, K.S., Cirulli, E., Bolze, A., Ascencio, A., Rivera-Garcia, C., Cho, R., Nguyen, J., Wang, S., Ramirez, J., Cassens, T., Sandoval, E., Isaksson, M., Lee, W., Becker, D., Laurent, M., Lu, J., Paden, C.R., Tong, S., MacCannell, D.  |
| hCoV-19/Israel/CVL-618ngs/2020          | B.1.362       | EPI_ISL_889024  | D614G, Q493K                 | Israel                    | 12/29/2020      | Israel Central Virology Laboratory                                     | Israel National Consortium for SARS-CoV-2 sequencing   | Neta Zuckerman, Efrat Dahan Bucris, Michal Mandelboim, Dana Bar-Ilan, Oran Erster, Tzvia Mann, Omer Murik, David A. Zeevi, Assaf Rokney, Joseph Jaffe, Eva Nachum, Maya Davidovich Cohen, Ephraim Fass, Gal Zizelski Valenci, Mor Rubinstein, Efrat Rorman, Israel Nissan, Efrat Glick-Saar, Omri Nayshool, Gideon Rechavi, Ella Mendelson, Orna Mor  |
| hCoV-19/Switzerland/BS-42473265/2020    | B.1.160       | EPI_ISL_830854  | D614G, Q493K                 | Basel, Switzerland        | 10/07/2020      | University Hospital Basel, Clinical Virology                           | University Hospital Basel, Clinical Bacteriology   | Tim Roloff, Madlen Stange, Helena MB Seth-Smith, Alfredo Mari, Karoline Leuzinger, Julia Bielicki, Manuel Battegay, Hans Hirsch, Adrian Egli  |
| hCoV-19/Switzerland/BS-42471446/2020    | B.1.160       | EPI_ISL_830843  | D614G, Q493K                 | Basel, Switzerland        | 10/06/2020      | University Hospital Basel, Clinical Virology                           | University Hospital Basel, Clinical Bacteriology   | Tim Roloff, Madlen Stange, Helena MB Seth-Smith, Alfredo Mari, Karoline Leuzinger, Julia Bielicki, Manuel Battegay, Hans Hirsch, Adrian Egli  |
| hCoV-19/England/MILK-11C2FCD/2021       | B.1.1.7       | EPI_ISL_1006449 | D614G, Q493R, N501Y, Y144del | United Kingdom, England   | 01/28/2021      | Lighthouse Lab in Milton Keynes  | Wellcome Sanger Institute for the COVID-19 Genomics UK (COG-UK) Consortium   | The Lighthouse Lab in Milton Keynes and Alex Alderton, Roberto Amato, Sonia Goncalves, Ewan Harrison, David K. Jackson, Ian Johnston, Dominic Kwiatkowski, Cordelia Langford, John Sillitoe on behalf of the Wellcome Sanger Institute COVID-19 Surveillance Team   |
| hCoV-19/USA/CA-CDC-STM-A100413/2021     | B.1.1.7       | EPI_ISL_850699  | D614G, N501Y, Y489H, Y144del | California, United States | 01/07/2021      | Helix / Illumina   | Genomics and Discovery, Respiratory Viruses Branch, Division of Viral Diseases, Centers for Disease Control and Prevention | Peter W. Cook, Dhvani Batra, Ben L. Rambo-Martin Eileen de Feo, Jan Antico, Christine Tran, Matthew Tolentino, Shannon Wickline, Kim Gietzen, Brad Sickler, Jingtao Liu, Eric Allen, Phil Febbo, Summer Galloway, Nicole L. Washington, Simon White, Geraint Levan, Kelly Schiabor Barrett, Elizabeth Cirulli, Alexandre Bolze, Ary Ascencio, Charlotte Rivera-Garcia, Ryan Cho, Jason Nguyen, Sherry Wang, Jimmy Ramirez, Tyler Cassens, Efron Sandoval, Magnus Isaksson, William Lee, David Becker, Marc Laurent, James Lu, Clinton R. Paden, Suxiang Tong, Duncan MacCannell |
| hCoV-19/England/MILK-99469D/2020        | B.1.1.7       | EPI_ISL_552392  | D614G, Y489H                 | United Kingdom, England   | 08/25/2020      | Lighthouse Lab in Milton Keynes  | Wellcome Sanger Institute for the COVID-19 Genomics UK (COG-UK) consortium   | The Lighthouse Lab in Milton Keynes and Alex Alderton, Roberto Amato, Sonia Goncalves, Ewan Harrison, David K. Jackson, Ian Johnston, Dominic Kwiatkowski, Cordelia Langford, John Sillitoe on behalf of the Wellcome Sanger Institute COVID-19 Surveillance Team ( <a href="http://www.sanger.ac.uk/covid-team">http://www.sanger.ac.uk/covid-team</a> )   |
| hCoV-19/England/205261299/2020          | B.1.1.7       | EPI_ISL_754289  | D614G, N501Y, Y144del        | United Kingdom, England   | 12/20/2020      | Respiratory Virus Unit, National Infection                             | COVID-19 Genomics UK (COG-   | PHE Covid Sequencing Team   |

|   |           |                 |  |                            |            |  |  |  |
|---|-----------|-----------------|--|----------------------------|------------|--|--|--|
|   |           |                 |  |                            |            | Service, Public Health England   | UK) Consortium   |  |
| hCoV-19/South Africa/Tygerberg-461/2020 | B.1.351   | EPI_ISL_745186  | D614G, <b>E484K</b> , <b>K417N</b> , <b>N501Y</b> , L242del, A243del, L244del                | South Africa, Western Cape | 12/07/2020 | Wallacedene Clinic Wc WAl  | National Health Laboratory Service (NHLS), Tygerberg   | Susan Engelbrecht, Kayla Delaney, Bronwyn Kleinhans, Houriyah Tegally, Eduan Wilkindon, Gert van Zyl, Wolfgang Preiser, Tulio de Oliveira  |
| hCoV-19/Brazil/AM-20143138FN-R2/2020    | P.1       | EPI_ISL_811149  | D614G, <b>K417T</b> , <b>E484K</b> , <b>N501Y</b>  | Brazil, Amazonas, Manaus   | 12/30/2020 | Laboratorio de Ecologia de Doencas Transmissiv eis na Amazonia, Instituto Leonidas e Maria Deane - Fiocruz Amazonia              | Laboratorio de Ecologia de Doencas Transmissiv eis na Amazonia, Instituto Leonidas e Maria Deane - Fiocruz Amazoni | Valdinete Nascimento, Victor Souza, André Corado, Fernanda Nascimento, George Silva, Ágatha Costa, Debora Duarte, Luciana Gonçalves, Matilde Mejía, Karina Pessoa, Maria Júlia Brandão, Michele Jesus, Felipe Naveca   |
| hCoV-19/England/MILK-F9DBDB/2021        | B.1.429   | EPI_ISL_852237  | D614G, <b>E484K</b> , <b>N501Y</b> , <b>S494P</b>  | United Kingdom, England    | 01/08/2021 | Lighthouse Lab in Milton Keynes  | Wellcome Sanger Institute for the COVID-19 Genomics UK (COG-UK) Consortium   | The Lighthouse Lab in Milton Keynes and Alex Alderton, Roberto Amato, Sonia Goncalves, Ewan Harrison, David K. Jackson, Ian Johnston, Dominic Kwiatkowski, Cordelia Langford, John Sillitoe on behalf of the Wellcome Sanger Institute COVID-19 Surveillance Team  |
| hCoV-19/Mozambique/INS-K008170/2021     | B.1.351   | EPI_ISL_964941  | D614G, <b>K417N</b> , <b>E484K</b> , <b>T478K</b> , <b>N501Y</b> , L242del, A243del, L244del | Africa, Mozambique         | 01/14/2021 | Instituto Nacional de Saude (INS), Mozambique  | KRISP, KZN Research Innovation and Sequencing Platform   | Nalia Ismael, Nadia Siteo, Paulo Arnaldo, Nedio Mabunda, Giandhari J, Pillay S, Emmanuel S, Tegally H, Wilkinson E, de Oliveira T  |
| hCoV-19/Denmark/DCGC-5481/2020          | B.1.1.298 | EPI_ISL_620806  | D614G, <b>N440D</b> , <b>Y453F</b>   | Denmark, Nordjylland       | 09/28/2020 | Department of Virus and Microbiological Special Diagnostics, Statens Serum Institut, Denmark                                     | Albertsen lab, Department of Chemistry and Bioscience, Aalborg University, Denmark                                 | Danish Covid-19 Genome Consortia   |
| hCoV-19/England/MILK-11C2FCD/2021       | B.1.1.7   | EPI_ISL_1006449 | D614G, <b>N501Y</b> , <b>Q493R</b> , Y144del   | United Kingdom, England    | 01/28/2021 | Lighthouse Lab in Milton Keynes  | Wellcome Sanger Institute for the COVID-19 Genomics UK (COG-UK) Consortium   | The Lighthouse Lab in Milton Keynes and Alex Alderton, Roberto Amato, Sonia Goncalves, Ewan Harrison, David K. Jackson, Ian Johnston, Dominic Kwiatkowski, Cordelia Langford, John Sillitoe on behalf of the Wellcome Sanger Institute COVID-19 Surveillance Team  |
| hCoV-19/England/LOND-12E726E/2021       | B.1.1.7   | EPI_ISL_997803  | D614G, <b>F486L</b> , <b>N501Y</b> , Y144del   | United Kingdom, England    | 02/10/2021 | University College London, Great Ormond Street Hospital for Children NHS Foundation Trust, Imperial College Healthcare NHS Trust | COVID-19 Genomics UK (COG-UK) Consortium   | Sergi Castellano, Rachel Williams, Mark Kristiansen, Paola Resende Silva, Sunando Roy, Tony Brooks, Helena Tutill, Paola Niola, Patricia Dyal, Charlotte Williams, Leysa Forrest, Yasmin Panchbhaya, Jacqueline Findlay, Samuel Weeks, Julianne Brown, Kathryn Harris, Paul Randell, James Price, Alison Holmes, Judith Breuer |

Not all S mutations found in the respective sequences are shown. RBD mutations of interest are shown in bold, and NTD deletions relevant to those shown in Figure S7L are shown in regular font. The Y453F<sub>RBD</sub> mutation found in hCoV-19/Denmark/DCGC-5481/2020 is shown because it is a REGN10933 resistance mutation detected in vitro (Baum et al., 2020) and has also been associated with mink-derived SARS-CoV-2 sequences. We gratefully acknowledge the listed authors from the originating laboratories responsible for obtaining the specimens and the submitting laboratories where genetic sequence data were generated and shared through the GISAID Initiative, on which this research is based.

**Table S4, Related to Figures 5 and 6. Summary of the observed effects of S mutations on the activity of monoclonal antibodies and polyclonal serum IgG.**

| S mutations | Effect on monoclonal antibodies  |  | Effect on polyclonal serum IgG    | Additional notes   |
|-------------|--|--|-----------------------------------|--|
|             | Resistance   | Sensitive  |                                   |  |
| N439K       | REGN10987 (with fourteenfold resistance)                                 | All C1A-V <sub>H</sub> 3-53 antibodies, B38, CC12.1, REGN10933               | Modest to no effect in 4/4 donors | Described as a circulating variant with maintained fitness (Thomson et al., 2021)  |
| Q493K       | C1A-V <sub>H</sub> 3-53 antibodies with low RBD affinity, B38, REGN10933 | C1A-V <sub>H</sub> 3-53 antibodies with high RBD affinity, CC12.1, REGN10987 | Resistance in 1/4 donors          | Also described through in vitro resistance mapping efforts (Baum et al., 2020; Weisblum et al., 2020)<br>Observed in other recent human-derived SARS-CoV-2 S sequences (Table S3)  |
| Q493R       | C1A-V <sub>H</sub> 3-53 antibodies with low RBD affinity, B38, REGN10933 | C1A-V <sub>H</sub> 3-53 antibodies with high RBD affinity, CC12.1, REGN10987 | Partial resistance in 1/4 donors  | Also described through in vitro resistance mapping efforts (Baum et al., 2020; Weisblum et al., 2020)<br>Observed in other recent human-derived SARS-CoV-2 S sequences (Table S3)  |
| Day 152*    | All C1A-V <sub>H</sub> 3-53 antibodies, B38, CC12.1, REGN10933           | REGN10987  | Resistance in 4/4 donors tested   | Seven of the eight RBD mutations it contains have been observed in other human-derived SARS-CoV-2 S sequences. The only exception is F486I, although it is similar to F486L, which has been observed (Figure 3B; Table S3) |
| Day 146*    | All C1A-V <sub>H</sub> 3-53 antibodies, B38, CC12.1, REGN10933           | REGN10987 (with fourfold resistance)   | Resistance in 4/4 donors          | All of the RBD mutations it contains have been observed at least individually in other human-derived SARS-CoV-2 S sequences (Figure 3B; Table S3)  |