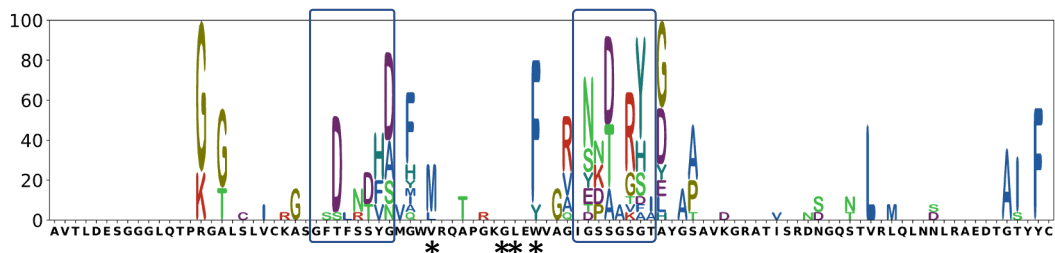


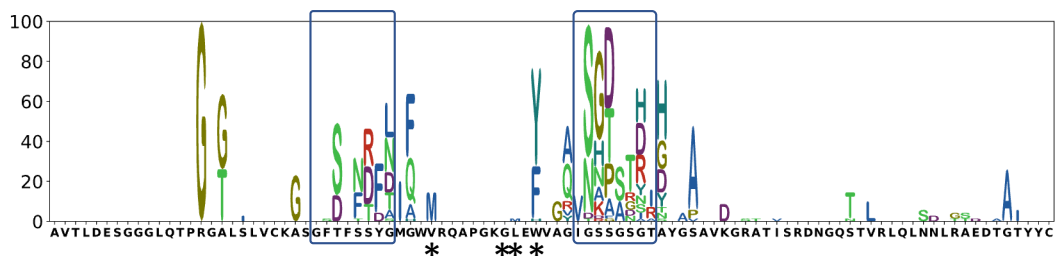
# Supplemental Figure 1.

## Anti-PGRN mAb sequence diversity

### WT VH to PGRN



### sdAb to PGRN



Diversity comparison in VH from WT and sdAbs against human Progranulin.

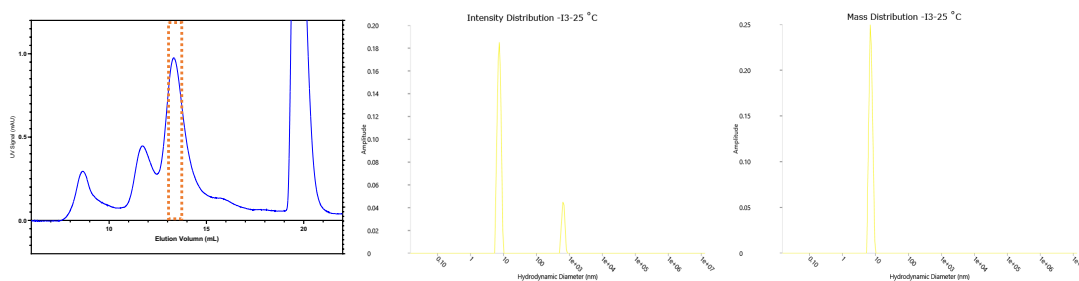
The sequences of VH from normal H+L antibodies (top panel, n=31 mAbs) and sdAb antibodies (bottom panel, n=111 mAbs) from cohorts of PGRN-specific mAbs were aligned and the variation at each position was calculated. The amino acid changes are shown for each residue in the VH sequence (on the X-axis) and the frequency of the changes are indicated by the size of the letters. CDR1 and 2 are indicated by boxes (IMGT definitions). The four hallmark FR2 positions which are changed in camelid VHH are marked with asterisks.

Numbers of clonotypes and singlets in the sdAb and WT cohorts to PGRN:

Sample type	# Filtered seq	# Lineage (clonotype)	# Singlets
WT	31	15	6
sdAb	111	29	19

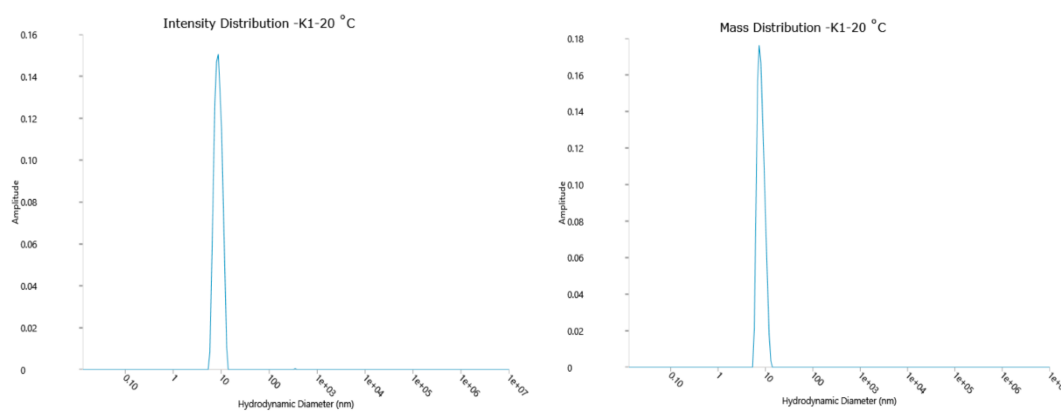
## Supplemental Figure 2: SEC and Dynamic Light Scattering (DLS) results for PGRN and S1

(A) PGRN protein (R&D Systems) was SEC purified in-house and monomeric peak fractions were pooled for kinetics studies (left panel, dashed red box). SEC-purified PGRN was subsequently analyzed by DLS (right panels) to show monodispersity, indicating monomeric state.

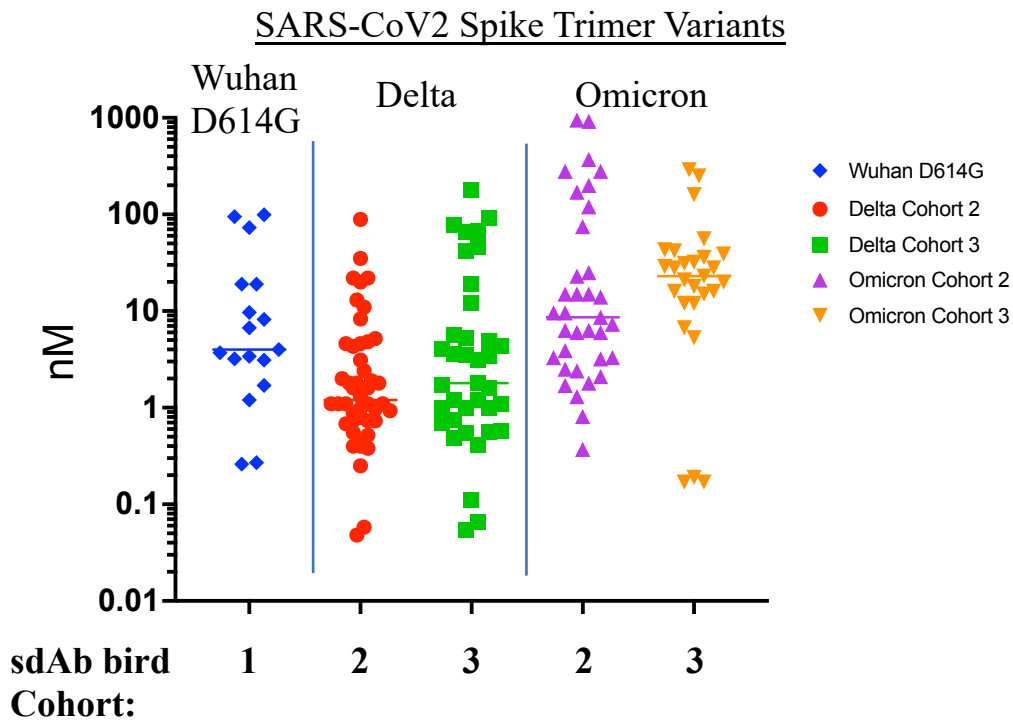


Sample	T (°C)	Z-Ave. Dia. (nm)	Z-Ave. Diff. Co-eff. (m <sup>2</sup> s <sup>-1</sup> )	SD Dia. (nm)	PDI	Fit Var.	Intensity (cps)	Pk 1 Peak Dia. (nm)	Pk 1 Est. Mw (kDa)	Pk 1 Polydispersity (%)	Pk 1 Diff. Coeff. (m <sup>2</sup> s <sup>-1</sup> )	Pk 1 Intensity (%)	Pk 1 Mass (%)
1 mg/ml R&D PGRN, 20 mM HBS	24.99	51.83	9.29E-12	23.73	0.21	0.66	335,787	7.77	80.64	34.8	6.20E-11		100

(B) SARS-CoV2 S1 monomer was analyzed by DLS to show monodispersity of S1 for use in kinetic studies. SEC-MALS data from Acro Biosystems confirm it is monomeric.



# Supplemental Figure 3. Avidity-boosted binding of Cohorts 1, 2 and 3 antibodies to SARS-CoV2 trimers



Binding of antibodies to SARS CoV2 spike trimer variants was measured by SPR. Antibodies were cloned from Cohort 1 (immunized with S1 monomer Wuhan D614G), Cohort 2 (immunized with alternating boosts of Alpha/Beta/Delta trimers), and Cohort 3 (immunized with Delta trimer) birds. Since the antigen is trimeric, avidity effects are produced by cooperative binding by the two arms of the antibody to two protomers in the trimer. Binding to Wuhan and Delta strains were comparable, whereas binding to the Omicron strain was generally weaker.

# Supplemental Table 1. Kinetics Statistics

Antibody Clone	PGRN														
	n	Mean ka (M-1 s-1)	ka Std. Dev.	Mean kd (s-1)	kd Std. Dev.	Mean KD	KD Std. Dev.	Mean Rmax (RU)	Rmax Std. Dev.	Mean Res sd	Std. Dev. Res sd	Mean Expected Rmax (RU)	Expected Rmax Std. Dev.	Mean Specific Activity (%)	Specific Activity Std. Dev.
48324p3.H10	2	9.6E+05	1.8E+02	1.7E-05	5.4E-06	1.8E-11	5.6E-12	1.2E+02	1.7E+01	3	0.05	2.7E+02	1.1E+02	49.1	13.6
48324p3.D08	2	9.3E+05	4.5E+04	2.1E-05	1.8E-06	2.3E-11	2.2E-12	1.3E+02	1.9E+01	3	0.31	2.8E+02	1.1E+02	48.3	12.1
48367p3.D09	2	6.2E+04	3.3E+03	1.3E-05	3.4E-06	2.1E-10	5.5E-11	1.2E+02	2.8E+01	2	0.06	2.2E+02	6.8E+01	54.1	4.1
48367p2.C07	2	4.6E+04	5.9E+02	1.0E-05	8.2E-09	2.2E-10	2.8E-12	1.4E+02	2.7E+01	2	0.12	2.5E+02	1.2E+02	57.8	17.7
48367p2.D11	2	4.6E+05	1.2E+04	2.0E-04	5.3E-06	4.3E-10	1.6E-11	1.4E+02	3.6E+01	3	0.81	N/D	N/D	N/D	N/D
48367p2.G11	2	3.5E+04	2.1E+03	3.3E-05	7.5E-06	9.4E-10	2.2E-10	1.4E+02	2.4E+01	2	0.08	N/D	N/D	N/D	N/D
48324p3.B03	2	1.7E+05	7.1E+03	1.7E-04	5.2E-06	1.0E-09	5.2E-11	1.6E+02	3.4E+01	3	0.20	3.0E+02	1.0E+02	54.6	7.3
48324p3.F09	2	3.5E+05	5.4E+03	6.4E-04	8.7E-05	1.9E-09	2.5E-10	1.3E+02	1.3E+00	3	0.62	2.4E+02	1.2E+02	59.3	27.7
48367p3.D01	2	1.6E+05	1.5E+03	5.8E-04	7.2E-06	3.5E-09	5.4E-11	1.8E+02	3.3E+01	3	0.25	1.6E+02	4.8E+01	114.6	14.2
48367p2.H03	2	6.2E+04	2.1E+03	2.7E-04	3.1E-05	4.3E-09	5.3E-10	1.1E+02	1.4E+01	2	0.03	8.6E+01	1.9E+01	130.3	12.8
48367p2.D07	2	1.1E+05	7.6E+03	9.3E-04	4.6E-05	8.2E-09	6.8E-10	1.4E+02	2.3E+01	4	0.66	N/D	N/D	N/D	N/D
48324p2.E01	1	1.9E+03	0.0E+00	1.8E-05	0.0E+00	9.7E-09	0.0E+00	9.3E+01	0.0E+00	2	0.00	1.4E+02	0.0E+00	66.1	0.0
48324p3.A10	2	1.1E+05	6.3E+02	1.8E-03	6.5E-05	1.6E-08	5.8E-10	1.2E+02	2.0E+01	3	0.17	2.5E+02	1.1E+02	49.8	14.1
48367p2.A12	2	1.8E+05	1.9E+04	3.6E-03	4.8E-04	2.0E-08	3.4E-09	1.1E+02	2.7E+01	4	1.3	2.6E+02	9.9E+01	44.2	6.3
48367p3.F03	2	5.4E+04	1.2E+03	1.9E-03	3.9E-05	3.5E-08	1.1E-09	1.3E+02	1.8E+01	3	0.12	2.5E+02	8.9E+01	54.9	12.0
48367p2.A11	2	4.6E+04	1.3E+01	1.9E-03	4.8E-05	4.0E-08	1.0E-09	1.3E+02	3.2E+01	3	0.28	2.7E+02	1.1E+02	48.4	8.6
48324p2.E07	2	2.3E+03	2.3E+02	1.1E-04	1.0E-05	4.8E-08	6.7E-09	1.1E+02	3.1E+01	2	0.07	2.4E+02	1.1E+02	47.8	8.6
48367p2.B06	2	4.8E+04	3.9E+03	4.4E-03	3.9E-04	9.2E-08	1.1E-08	5.7E+01	1.6E+01	4	0.76	2.7E+02	1.2E+02	22.1	4.1
48324p2.E03	2	1.6E+04	8.8E+03	5.2E-03	2.0E-03	3.5E-07	2.3E-07	5.7E+01	1.5E+01	3	0.02	2.1E+02	8.0E+01	27.5	3.3

Antibody Clone	SARS-CoV2 Spike S1 monomer														
	n	Mean ka (M-1 s-1)	ka Std. Dev.	Mean kd (s-1)	kd Std. Dev.	Mean KD	KD Std. Dev.	Mean Rmax (RU)	Rmax Std. Dev.	Mean Res sd	Std. Dev. Res sd	Mean Expected Rmax (RU)	Expected Rmax Std. Dev.	Mean Specific Activity (%)	Specific Activity Std. Dev.
60396p2.C05	2	7.60E+03	7.90E+01	3.30E-03	1.20E-04	4.30E-07	1.70E-08	5.70E+01	1.40E+01	3	0.26	4.1E+02	6.2E+01	14.4	5.6
60396p1.D01	2	1.20E+05	1.40E+03	7.70E-05	3.00E-06	6.50E-10	2.70E-11	1.10E+02	1.50E+01	2	0.11	3.8E+02	1.3E+01	29.9	4.9
60376p1.B12	2	4.60E+05	1.20E+04	4.10E-03	7.90E-05	9.00E-09	3.00E-10	2.10E+02	9.10E+00	9	0.5	3.1E+02	5.6E+01	71.1	10.1
60396p1.C10	2	3.00E+03	8.90E+02	9.60E-04	1.70E-06	3.50E-07	1.00E-07	6.70E+01	1.90E+01	2	0	3.0E+02	2.5E+01	22.6	4.6
mAb10933	2	1.10E+06	2.20E+04	2.60E-03	5.30E-05	2.50E-09	7.30E-11	1.10E+02	5.10E+01	4	1.6	1.4E+02	1.0E+01	77.5	41.4
mAb10987	1	2.20E+05	0.00E+00	6.50E-03	0.00E+00	2.90E-08	0.00E+00	9.60E+01	0.00E+00	7	0	1.4E+02	0.0E+00	69.6	0.0

Chicken sdAb clones to PGRN (top) and SARS-CoV2 S1 monomer (bottom) were run on SPR and the kinetics statistics are shown. Expected Rmax values are calculated based on surface capture levels (data not shown) of ligands and the ratio of molar masses of (monomeric analyte):(monomeric ligand). Percent specific activity = (100)\*(Experimental Rmax)/(Expected Rmax). Two benchmark IgG antibodies (reference 32) to S1 are also included.