Supplemental Table I. Samples sizes used in multivariate analyses

	T1: Pre	T2: 2-4wks_PD1	T3: 2-4wks_PD2	T4: 3-4M_PD2	T5: 2-4wks_PD3	T6: 3-4M_PD3	T7: 2-4wks_PD4	T8: 3-4M_PD4
IgG								
Healthy controls	15	17	21	11	5	6		
IMID pooled	**94**	**112**	**103**	**84**	**52**	**41**	**24**	**19**
Non-TNF IMID	**42**	**59**	**55**	**51**	**29**	**26**	**13**	**11**
Untreated	9	9	9	9	5	6	0	0
Anti-IL17A	3	6	6	6	6	5	4	3
MTX/AZA	3	7	7	4	2	1	1	2
Anti-IL12/23	26	27	23	22	11	11	6	5
Anti-IL23	1	10	10	10	5	3	2	1
TNF IMID	**52**	**53**	**48**	**33**	**23**	**15**	**11**	**8**
Anti-TNF	37	37	34	23	16	9	5	3
Anti-TNF + MTZ/AZA	15	16	14	10	7	6	6	5
Neutralizing (Wild type)								
Healthy controls			21	9	5	6		
IMID pooled			**103**	**79**	**43**	**40**	**16**	**17**
Non-TNF IMID			**55**	**48**	**24**	**25**	**8**	**11**
Untreated			9	9	5	5	0	0
Anti-IL17A			6	5	5	5	3	3
MTX/AZA			7	3	1	1	0	2
Anti-IL12/23			23	22	8	11	4	5
Anti-IL23			10	9	5	3	1	1
TNF IMID			**48**	**31**	**19**	**15**	**8**	**6**
Anti-TNF			34	22	14	9	4	2
Anti-TNF + MTZ/AZA			14	9	5	6	4	4
T cell cytokines								
Healthy controls	14	13	17	8	4	6		
IMID pooled	**85**	**95**	**96**	**75**	**49**	**39**	**25**	**20**
Non-TNF IMID	**36**	**48**	**50**	**46**	**27**	**26**	**14**	**11**
Untreated	9	9	9	9	5	6	0	0
Anti-IL17A	3	5	4	5	6	5	4	3
MTX/AZA	3	5	6	3	1	1	1	2
Anti-IL12/23	20	20	22	21	10	11	7	5
Anti-IL23	1	9	9	8	5	3	2	1
TNF IMID	**49**	**47**	**46**	**29**	**22**	**13**	**11**	**9**
Anti-TNF	36	33	32	20	14	7	5	4
Anti-TNF + MTZ/AZA	13	14	14	9	8	6	6	5

Bolded values represent sums of the rows below (i.e., IMID pooled totals are the sum of Non-TNF IMID and TNF IMID totals).

Abbreviations: AZA: azathioprine; IL: Interleukin; IMID: Immune-Mediated Inflammatory Diseases; M: months; MTX: Methotrexate; PD: Post dose; TNF: Tumor necrosis factor; wks: weeks

Supplemental Table II. Anti-spike and anti-RBD IgG levels and samples outside limits of detection
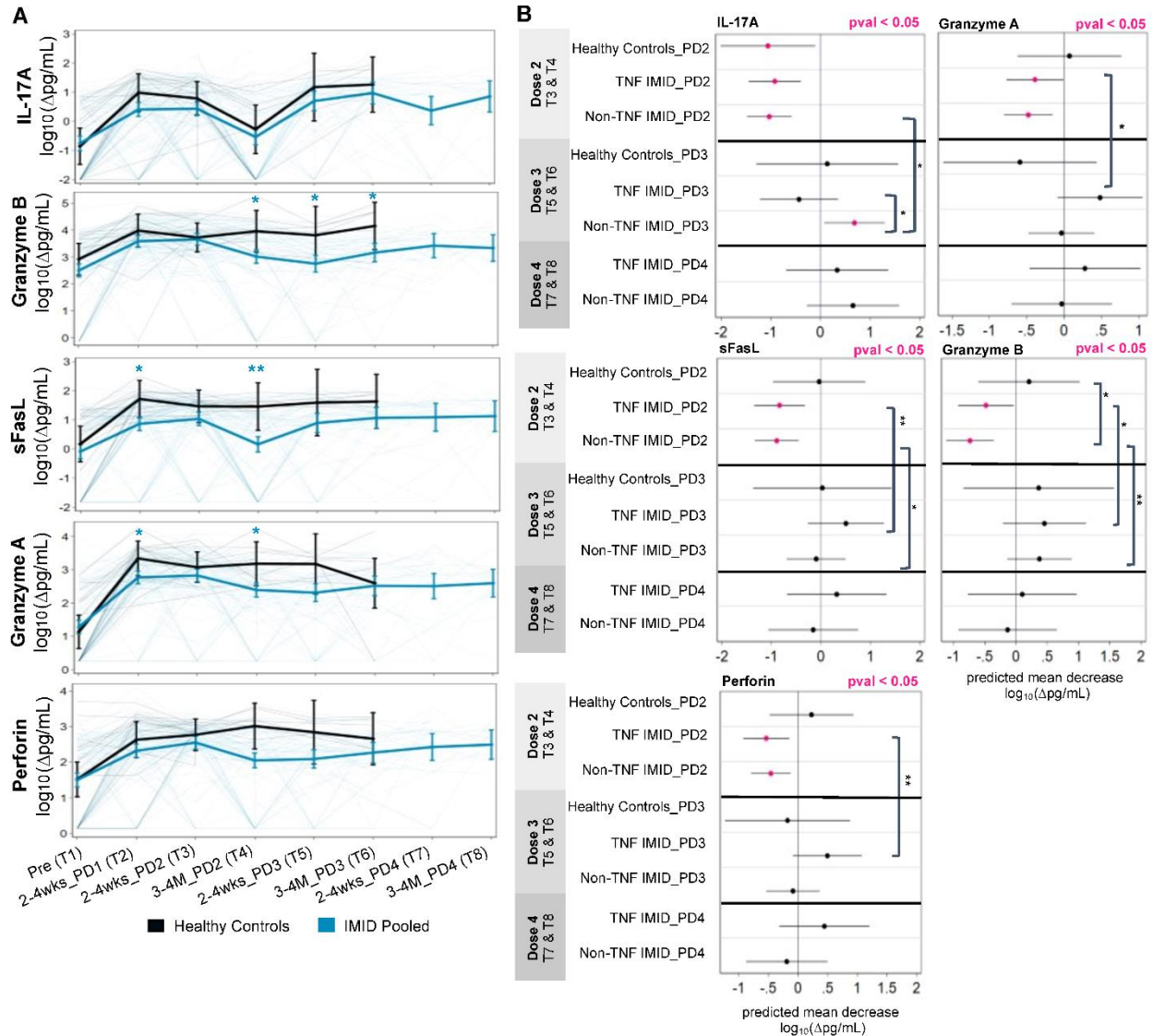
	Spike - $\log_2$(BAU/mL)			RBD - $\log_2$(BAU/mL)		
	Healthy controls	Non-TNF IMID	Anti-TNF	Healthy controls	Non-TNF IMID	Anti-TNF
T1: Pre - N	15	42	52	15	42	52
Median (IQR)	0.8 (-0.8 - 1.5)	0.7 (0.3 - 1.3)	0.8 (0.4 - 1.6)	0.6 (0.6 - 0.6)	0.6 (0.6 - 0.6)	0.6 (0.6 - 0.6)
Upper limit - N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
T2: 2-4wks_PD1 - N	17	59	53	16	58	53
Median (IQR)	8.3 (7.9 - 8.9)	7.6 (6.5 - 8.8)	6.4 (5.4 - 7.2)	7.6 (7.0 - 8.3)	7.2 (6.4 - 7.8)	6.1 (4.8 - 7.1)
Upper limit - N (%)	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
T3: 2-4wks_PD2 - N	21	55	48	21	55	48
Median (IQR)	10.6 (10.6 - 10.6)	10.6 (10.6 - 10.6)	10.5 (9.2 - 10.6)	11.7 (10.6 - 12.1)	12.0 (11.3 - 12.1)	10.5 (9.1 - 11.9)
Upper limit - N (%)	17 (81.0)	45 (81.8)	24 (50.0)	9 (42.9)	25 (45.5)	10 (20.8)
T4: 3-4M_PD2 - N	11	51	33	11	51	33
Median (IQR)	9.7 (9.1 - 10.0)	9.2 (7.9 - 9.7)	5.7 (5.4 - 7.3)	9.5 (9.2 - 10.5)	8.7 (7.5 - 10.1)	6.7 (5.1 - 7.2)
Upper limit - N (%)	0 (0.0)	2 (3.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
T5: 2-4wks_PD3 - N	5	29	23	5	29	23
Median (IQR)	10.6 (10.6 - 10.6)	10.6 (10.5 - 10.6)	10.6 (9.2 - 10.6)	11.6 (11.3 - 11.7)	11.2 (10.4 - 11.8)	10.5 (8.4 - 11.5)
Upper limit - N (%)	5 (100.0)	21 (72.4)	13 (56.5)	1 (20.0)	4 (13.8)	2 (8.7)
T6: 3-4M_PD3 - N	6	26	15	6	26	14
Median (IQR)	10.5 (9.9 - 10.6)	9.6 (9.0 - 10.5)	8.1 (6.1 - 9.2)	10.0 (9.8 - 10.8)	9.3 (8.5 - 10.3)	8.1 (7.2 - 8.6)
Upper limit - N (%)	3 (50.0)	6 (23.1)	1 (6.7)	0 (0.0)	1 (3.8)	0 (0.0)
T7: 2-4wks_PD4 - N		13	11		13	11
Median (IQR)		10.6 (10.6 - 10.6)	9.1 (8.2 - 10.6)		11.0 (10.7 - 11.7)	9.0 (8.6 - 10.4)
Upper limit - N (%)		11 (84.6)	3 (27.3)		2 (15.4)	1 (9.1)
T8: 3-4M_PD4 - N		11	8		11	8
Median (IQR)		9.8 (9.4 - 10.6)	8.6 (6.7 - 9.6)		9.1 (8.5 - 10.7)	7.7 (7.1 - 9.5)
Upper limit - N (%)		4 (36.4)	1 (12.5)		0 (0.0)	0 (0.0)

Abbreviations: BAU/mL: Binding antibody units per milliliter; IMID: Immune-Mediated Inflammatory Diseases; IQR: Inter-quartile range; M: months; PD: Post dose; TNF: Tumor necrosis factor; wks: weeks

Supplemental Table III. Neutralization titers and samples outside limits of detection

	Wild Type Neutralization - Log_{10}(ID50)			Omicron BA.1 Neutralization - Log_{10}(ID50)			Omicron BA.5 Neutralization - Log_{10}(ID50)		
	Healthy controls	Non-TNF IMID	Anti-TNF	Healthy controls	Non-TNF IMID	Anti-TNF	Healthy controls	Non-TNF IMID	Anti-TNF
T3: 2-4wks_PD2 - N	21	55	48						
Median (IQR)	3.6 (3.2 - 3.9)	3.5 (3.3 - 3.9)	2.9 (2.4 - 3.4)						
Upper limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)						
Lower limit – N (%)	0 (0.0)	0 (0.0)	1 (2.1)						
T4: 3-4M_PD2 - N	9	48	31	9	48	31			
Median (IQR)	3.2 (3.0 - 3.2)	2.5 (2.2 - 2.8)	1.6 (0.0 - 2.0)	2.1 (1.3 - 2.2)	1.1 (0.0 - 1.7)	0.0 (0.0 - 0.0)			
Upper limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			
Lower limit – N (%)	0 (0.0)	1 (2.1)	8 (25.8)	1 (11.1)	17 (35.4)	25 (80.6)			
T5: 2-4wks_PD3 - N	5	24	19	5	24	19	5	24	19
Median (IQR)	3.8 (3.6 - 3.9)	3.5 (3.3 - 3.6)	3.6 (2.9 - 3.9)	2.9 (2.8 - 3.3)	2.5 (2.3 - 2.7)	2.5 (0.9 - 3.0)	2.9 (2.6 - 3.1)	2.4 (2.2 - 2.6)	2.2 (1.8 - 2.7)
Upper limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lower limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (21.1)	0 (0.0)	0 (0.0)	1 (5.3)
T6: 3-4M_PD3 - N	6	25	15	6	25	15	6	25	15
Median (IQR)	3.7 (3.4 - 3.9)	3.1 (2.9 - 3.2)	2.7 (2.2 - 3.1)	2.6 (2.5 - 3.1)	2.0 (1.8 - 2.3)	1.6 (0.0 - 1.8)	2.3 (2.2 - 2.6)	1.8 (1.4 - 2.1)	0.0 (0.0 - 1.6)
Upper limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lower limit – N (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (33.3)	0 (0.0)	3 (12.0)	8 (53.3)
T7: 2-4wks_PD4 - N		8	8		8	8		8	8
Median (IQR)		3.6 (3.1 - 3.8)	3.0 (2.2 - 3.5)		2.5 (1.3 - 2.8)	1.2 (1.0 - 2.3)		2.5 (2.0 - 3.0)	1.6 (1.0 - 2.3)
Upper limit – N (%)		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lower limit – N (%)		0 (0.0)	1 (12.5)		1 (12.5)	1 (12.5)		0 (0.0)	1 (12.5)
T8: 3-4M_PD4 - N		11	6		11	6		11	6
Median (IQR)		3.4 (2.9 - 3.6)	2.3 (2.1 - 2.9)		2.2 (1.0 - 2.4)	1.3 (1.2 - 1.6)		2.1 (1.6 - 2.7)	1.2 (0.0 - 1.6)
Upper limit – N (%)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)
Lower limit – N (%)		0 (0.0)	0 (0.0)		1 (9.1)	1 (16.7)		1 (9.1)	2 (33.3)

Abbreviations: ID50: 50% inhibitory dose; IMID: Immune-Mediated Inflammatory Diseases; IQR: Inter-quartile range; M: months; PD: Post dose; TNF: Tumor necrosis factor; wks: weeks

Supplemental Figure 1. Third and forth doses increase the magnitude and durability of T cell cytokine and cytotoxic molecule responses. Timepoints are defined in Table 1. (**A**) Predicted mean T cell cytokines and cytotoxic molecules IL-17A, Granzyme A, Granzyme B, sFasL, Perforin ($\log_{10}(\Delta pg/mL)$) from pre-vaccination to after four doses of vaccine. Mixed-effects linear regression models controlled for age, BMI, and sex (thick colored lines), with an interaction term between timepoint and group. Individual patients are plotted in thin lines. Groupings: healthy controls (black), IMID patients pooled (blue). Mixed-effects linear regression models with an additional control for vaccine type were used to compare IMID pooled vs healthy controls (blue asterisks). (**B**) Predicted mean decrease of cytokine and cytotoxic molecules IL-17A, Granzyme A, Granzyme B, sFasL, and Perforin ($\log_{10}(\Delta pg/mL)$) in healthy controls, TNF IMID, and IMID patients not treated with anti-TNF between 2-4 weeks and 3-4 months after dose 2 (decrease between T3 and T4), after dose 3 (decrease between T5 and T6), and after dose 4 (decrease between T7 and T8). Mixed-effects linear regression models controlled for age, BMI, sex, and vaccine type, with an interaction term between timepoint and group. Mean decrease values that are significant (pval<0.05) are colored in pink. Significant pairwise comparisons are indicated by asterisks and brackets. (**A-B**) Sample sizes are listed in Supplemental Table 1. *p<0.05; **p<0.01; ***p<0.001; Δ: background subtracted; pg/mL: picogram per milliliter; PD: post dose