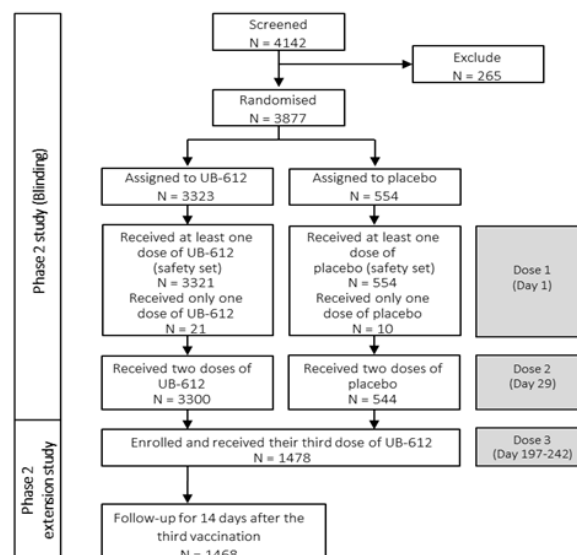


Supplementary Figure 1. Distribution of SARS-CoV-2 Delta variant is being replaced by the Omicron variant (BA.1; BA.1.1.529). The changes overtime in % distribution of SARS-CoV-2 Variants of Concern (VoCs). A. The time points when the five COVID-19 vaccines (Pfizer, Moderna, AZ, j and J and Novavax) were developed and EUA authorized; and the Delta variant that dominated with >95% of all infection cases observed in October 2021; B. The once globally-dominant Delta variant in infectivity is being overtaken and replaced by the heavily-mutated Omicron strain, which constitutes 95% of all infection cases worldwide (80% 21K, BA.1; 15% 21L, BA.2), as of Feb. 13, 2022.



Supplementary Figure 2. Flow of UB-612 phase-2 primary 2-dose series with extension booster. The study design of the Phase-2 primary 2-dose series (100 µg dose; 28 days apart) of UB-612; and the extension study of booster vaccination (NCT04773067) conducted between Oct. 16, 2021 and Apr. 16, 2022. The primary series (n=3875), a total of 1,478 participants (aged at 18-85 years) were enrolled to receive the booster third-dose of 100 µg UB-612.

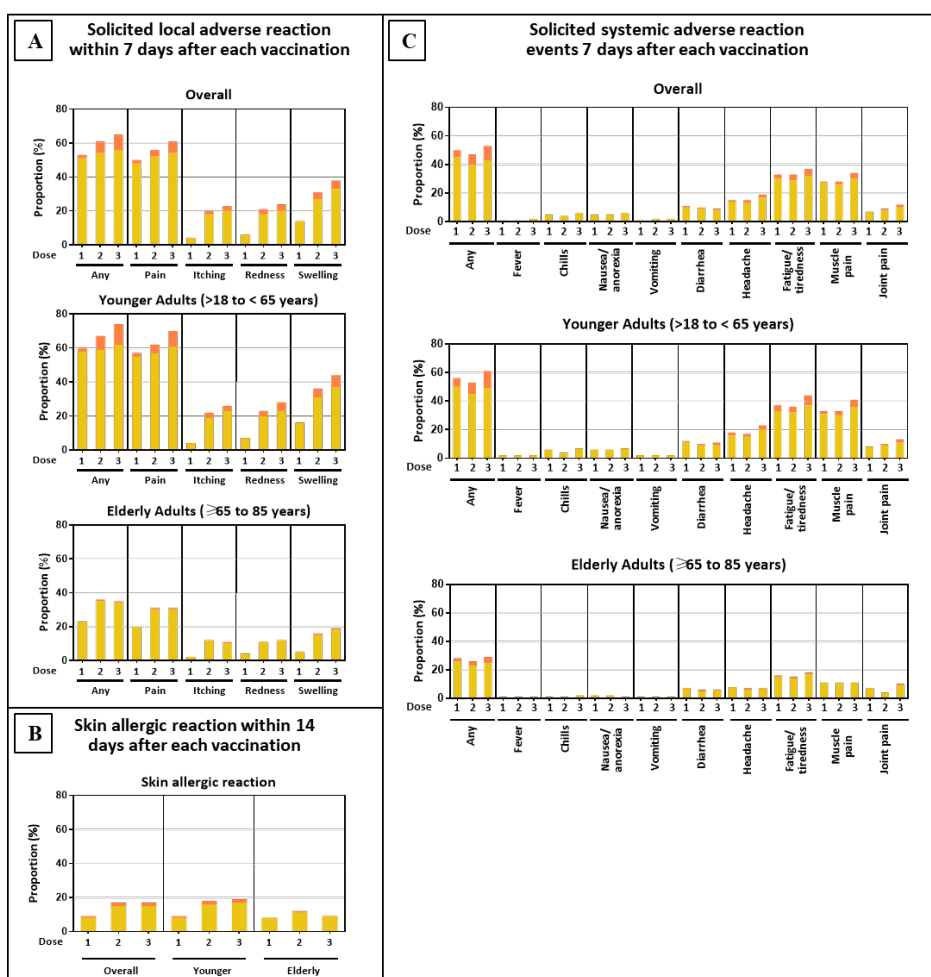
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Table 1. The characteristics of the study participants in the primary and booster series.

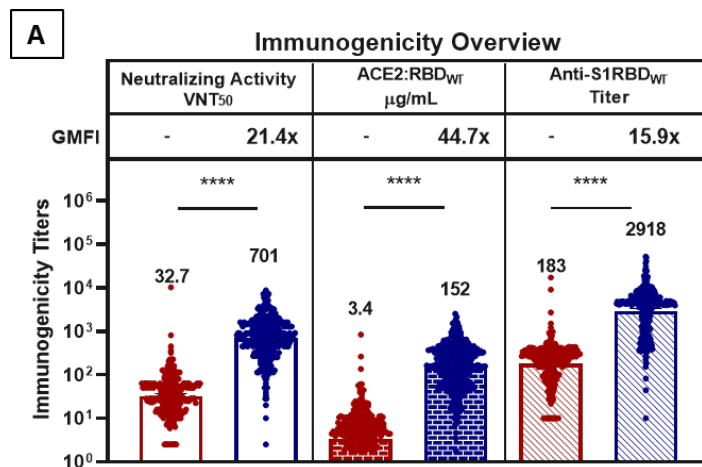
	Participants in primary 2-dose series		Booster	
	UB-612 (N=3321)	Placebo (N=554)	All subjects (N=3875)	UB-612 (N=1478)
Sex-no. (%)				
Male	1686(50.8%)	273(49.3%)	1959(50.6%)	799(54.1%)
Female	1635 (49.2%)	281(50.7%)	1916(49.4%)	679(45.9%)
Age, Mean(SD)	44.9(16.5)	44.4(16.3)	44.8(16.5)	46.1(16.6)
Age-group				
>18 to <65 years	2628(79.1%)	448(80.9%)	3076(79.4%)	1124(76%)
≥65 years	693(20.9%)	106(19.1%)	799(20.6%)	354(24%)
Ethnicity-no. (%)				
Taiwanese	3317(99.9%)	553(99.8%)	3850(99.9%)	1475(99.8%)
Other	4(0.12%)	1(0.18%)	5(0.1%)	3(0.2%)
BMI (kg/m2,Mean(SD)	25.06(4.4)	24.88(4.2)	25.04(4.4)	25.37(4.5)



Supplementary Figure 3. Incidence of adverse effects in the Phase-2 primary 2-dose and extended booster third-dose series. A. Solicited local adverse reaction within 7 days after each vaccination; B. Skin allergic reaction within 14 days after each vaccination; C. Solicited systemic adverse reaction events 7 days after each vaccination (Doses 1 and 2 in the primary series; Dose 3 as a booster). **Note:** (■) Severe; (■) Moderate; (■) Mild.

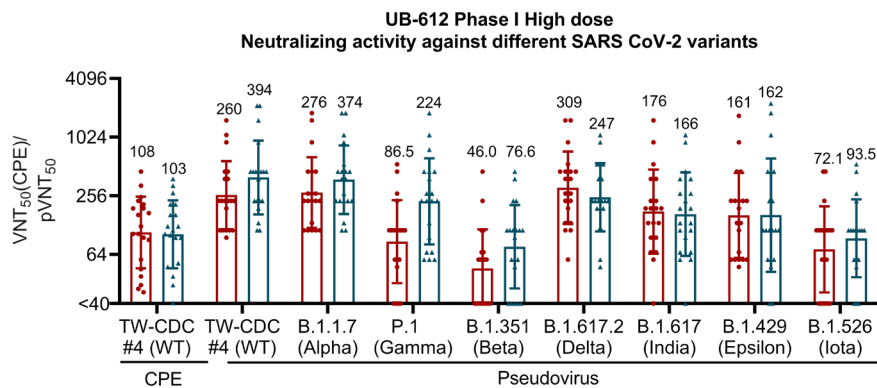
Table 2. Summary of Geometric Mean Titer (GMT) with 95% CI are presented for plots shown in supplementary Figure 4.

Assay	Time Point	n	VNT ₅₀ (Wild-Type) GMT(95%CI)	GMFI (Booster/Pre-Booster)	p value
Live virus	Pre-booster(D220)	302	32.66(28.95-36.84)	21.4	<0.0001
	Booster(D234)	302	700.6(614.4-799)		
ACE2:RBD	Pre-booster(D220)	302	3.399(2.953-3.913)	44.7	<0.0001
	Booster(D234)	302	151.8(131.3-175.4)		
Anti-RBD IgG	Pre-booster(D220)	302	182.6(161.4-206.5)	-	<0.0001

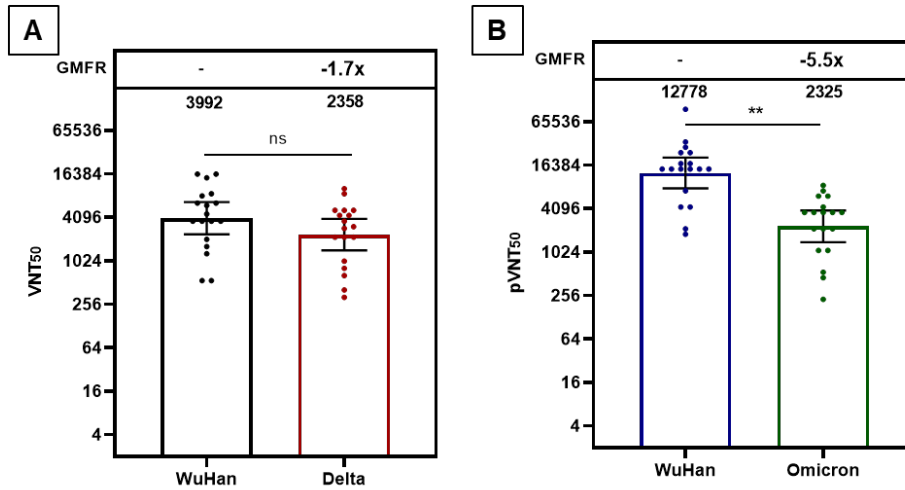


Supplementary Figure 4. Immunogenicity overview (pre and post-booster) on homologous boosting. A. Immunogenicity overview of 302 participants (n=208 for aged 18-65 years; n=94 for aged 65-85 years) received a booster 3rd-dose. The serum samples of 302 participants were collected at the indicted time points, Days 197 to 242 (the pre-booster day) and Days 211 to 256 (14 days post-booster), and tested for neutralizing antibody levels that inhibit 50% of live SARS-CoV-2 wild-type (WT, Wuhan strain), the inhibitory titers against S1-RBD binding to ACE2 by ELISA, and anti-S1-RBD IgG antibody titers by ELISA. The data were expressed as geometric mean titers GMT and 95% CI. Statistical analysis was performed by the Student's t-test (ns p>0.05, **** p<0.0001).

Note: (●) Pre Boost; (●) Booster+14D.



Supplementary Figure 5. Neutralization of different SARS-CoV-2 variants by sera (Day 42 and Day 56) from the Phase-1 primary series. Neutralization titers (Day 42 and Day 56 after UB-612 vaccination) of seropositive vaccinees (n=20) from Phase-1 high dose 100-µg cohort are tested for TW-CDC#4 (WT), variants B.1.1.7 (Alpha), P.1 (Gamma), B.1.429 (Epsilon), B.1.526 (Iota), B.1.351 (Beta) B.1.617 (India), and B.1.617.2 (Delta) variants are presented. Values are indicated as geometric mean titres (GMTs). Neutralization titre <40 was plotted as 20 by the "VNT₅₀" based on live virus CPE assay or "viral-neutralizing titers (pVNT₅₀) based on a pseudovirus assay. The reduction fold for each virus variant relative to wild-type WT (TW-CDC#4) were calculated to be approximately 1.1 for B.1.1.7 (Alpha), 1.8 for P.1 (Gamma), 5.1 for B.1.351 (Beta), 1.6 for B.1.617.2 (Delta), 2.4 for B.1.617 (India), 2.4 for B.1.429 (Epsilon), and 4.2 for B.1.526 (Iota). The reduction fold for the variant strains including VoCs are in the range of 1.0 to 5.0. **Note:** (●) Day 45; (▲) Day 56



Supplementary Figure 6. Viral-neutralizing titers against live SARS-CoV-2 wild type (Wuhan) and Delta variant (VNT₅₀), and pseudo SARS-CoV-2 wild type (Wuhan) and Omicron variant (pVNT₅₀) after the booster third-dose in the Phase-1 trial. Geometric Mean Titers (GMT) at 50% viral-neutralization observed 14 days after the booster third-dose of 100 µg administered at mean Day 286 (Days 255-316) after the primary 2-dose series (Days 0 and 28) of the 196-day Phase-1 trial. A) In the participants of the 100-µg group (n=18) with healthy adults aged at 20-55 years, the post-booster VNT₅₀ titer reached at 3,992 against live SARS-CoV-2 Wuhan wild-type, and at 2,358 against live Delta variant; B) Similarly, unusually high post-booster pVNT₅₀ against Wuhan wild-type pseudovirus at 12,778, and at 2,325 against Omicron variant.

Table 3. Summary of Geometric Mean Titer (GMT) with 95% CI are presented for plots shown in Figure 5.

Assay	Time Point	n	TW_CDC #4 (WT)	TW_CDC#4 (WT)	B.1.1.7 (Alpha)	P.1 (Gamma)	B.1.351 (Beta)	B.1.617.2 (Delta)	B.1.617 (India)	B.1.429 (Epsilon)	B.1.526 (Iota)
VNT ₅₀ GMT (95%CI)	42	20	107.7 (72.4-160.1)	-	-	-	-	-	-	-	-
pVNT ₅₀ GMT (95%CI)	42	20	-	259.9 (178.4-378.7)	276.2 (186.7-408.5)	86.49 (54.61-137)	45.96 (29.86-70.73)	309.1 (206.9-461.7)	176 (110.5-280.2)	160.9 (100.6-257.3)	72.1 (44.76-116.1)
	56	20	-	394 (261.9-592.6)	374 (256.2-546.1)	224.4 (256.2-546.1)	76.61 (48.25-121.6)	246.8 (169.1-360.2)	165.7 (104.4-262.8)	161.8 (86.44-302.9)	93.5 (60.78-143.8)

Table 4. Summary of Geometric Mean Titer (GMT) with 95% CI are presented for plots shown in Figures 6A and 6B.

Assay	n	pVNT ₅₀ (Wild-Type) GMT(95%CI)	pVNT ₅₀ (Omicron) GMT(95%CI)	GMFR(WT/Omicron)	p value
Pseudo virus	18	12778(7821-20873)	2325(1400-3860)	5.5	<0.0001
Assay	n	VNT ₅₀ (Wild-Type) GMT(95%CI)	VNT ₅₀ (Delta) GMT(95%CI)	GMFR(WT/Delta)	p value
Live virus	18	3992(2397-6650)	2358(1426-3900)	1.7	ns

Our youtube video link: <https://youtu.be/Nqea37sHXHc>
Second youtube video link: <https://ubproom.egnyte.com/dl/UtMhbsSj66>