Supplementary Material

Table S1. Severity grading scale for local reactions and systemic events.

	Mild	Moderate	Severe
Local reaction			
Pain	Does not interfere with activity	Interferes with activity	Prevents daily activity
Redness	>2.0–5.0 cm	>5.0–10.0 cm	>10 cm
Swelling	>2.0–5.0 cm	>5.0–10.0 cm	>10 cm
Systemic event			
Vomiting	1–2 × in 24 h	>2 × in 24 h	Requires IV hydration
Diarrhea	2–3 loose stools in 24 h	4–5 loose stools in 24 h	≥6 loose stools in 24 h
Headache	Does not interfere with activity	Some interference with activity	Prevents daily routine activity
Fatigue	Does not interfere with activity	Some interference with activity	Prevents daily routine activity
Chills	Does not interfere with activity	Some interference with activity	Prevents daily routine activity
Muscle pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity
Joint pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity

IV=intravenous.

For the fever scale, refer to the key of **Figure 3**.

Table S2. Medical history reported in >2% of participants overall (safety population)

System Organ Class Preferred Term	12–17 Years Old (N[a]=30)	18–55 Years Old (N[a]=174)	>55 Years Old (N[a]=208)	Total (N[a]=412)
Any medical history	26 (86.7)	164 (94.3)	205 (98.6)	395 (95.9)
Cardiac disorders	0	4 (2.3)	28 (13.5)	32 (7.8)
Coronary artery disease	0	0	9 (4.3)	9 (2.2)
Endocrine disorders	1 (3.3)	7 (4.0)	48 (23.1)	56 (13.6)
Hypothyroidism	0	3 (1.7)	37 (17.8)	40 (9.7)
Eye disorders	2 (6.7)	5 (2.9)	60 (28.8)	67 (16.3)
Cataract	0	0	26 (12.5)	26 (6.3)
Myopia	1 (3.3)	4 (2.3)	21 (10.1)	26 (6.3)
Presbyopia	0	0	24 (11.5)	24 (5.8)
Gastrointestinal disorders	0	19 (10.9)	69 (33.2)	88 (21.4)
Gastroesophageal reflux disease	0	14 (8.0)	37 (17.8)	51 (12.4)
Inguinal hernia	0	3 (1.7)	6 (2.9)	9 (2.2)
Hepatobiliary disorders	0	4 (2.3)	15 (7.2)	19 (4.6)
Cholelithiasis	0	2 (1.1)	8 (3.8)	10 (2.4)
Immune system disorders	9 (30.0)	66 (37.9)	64 (30.8)	139 (33.7)
Drug hypersensitivity	3 (10.0)	21 (12.1)	26 (12.5)	50 (12.1)
Food allergy	1 (3.3)	3 (1.7)	5 (2.4)	9 (2.2)
Seasonal allergy	5 (16.7)	47 (27.0)	41 (19.7)	93 (22.6)
Infections and infestations	7 (23.3)	63 (36.2)	88 (42.3)	158 (38.3)
Appendicitis	1 (3.3)	2 (1.1)	11 (5.3)	14 (3.4)
COVID-19	5 (16.7)	60 (34.5)	67 (32.2)	132 (32.0)
Tonsillitis	0	3 (1.7)	6 (2.9)	9 (2.2)

Investigations	5 (16.7)	13 (7.5)	21 (10.1)	39 (9.5)
SARS-CoV-2 test positive	4 (13.3)	5 (2.9)	1 (0.5)	10 (2.4)
Metabolism and nutrition disorders	3 (10.0)	57 (32.8)	137 (65.9)	197 (47.8)
Dyslipidemia	0	4 (2.3)	15 (7.2)	19 (4.6)
Glucose tolerance impaired	0	3 (1.7)	9 (4.3)	12 (2.9)
Hypercholesterolemia	0	8 (4.6)	38 (18.3)	46 (11.2)
Hyperlipidemia	0	6 (3.4)	38 (18.3)	44 (10.7)
Obesity	3 (10.0)	27 (15.5)	37 (17.8)	67 (16.3)
Overweight	0	2 (1.1)	13 (6.3)	15 (3.6)
Type 2 diabetes mellitus	0	9 (5.2)	40 (19.2)	49 (11.9)
Musculoskeletal and connective tissue disorders	4 (13.3)	19 (10.9)	98 (47.1)	121 (29.4)
Arthralgia	1 (3.3)	1 (0.6)	16 (7.7)	18 (4.4)
Arthritis	0	1 (0.6)	8 (3.8)	9 (2.2)
Back pain	0	6 (3.4)	21 (10.1)	27 (6.6)
Osteoarthritis	0	3 (1.7)	44 (21.2)	47 (11.4)
Osteopenia	0	0	14 (6.7)	14 (3.4)
Osteoporosis	0	1 (0.6)	9 (4.3)	10 (2.4)
Spinal osteoarthritis	0	2 (1.1)	8 (3.8)	10 (2.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	11 (6.3)	47 (22.6)	58 (14.1)
Basal cell carcinoma	0	1 (0.6)	9 (4.3)	10 (2.4)
Breast cancer	0	2 (1.1)	12 (5.8)	14 (3.4)
Uterine leiomyoma	0	3 (1.7)	10 (4.8)	13 (3.2)
Nervous system disorders	0	19 (10.9)	44 (21.2)	63 (15.3)
Migraine	0	8 (4.6)	11 (5.3)	19 (4.6)

Psychiatric disorders	7 (23.3)	55 (31.6)	66 (31.7)	128 (31.1)
Anxiety	2 (6.7)	26 (14.9)	27 (13.0)	55 (13.3)
Attention deficit hyperactivity disorder	4 (13.3)	16 (9.2)	1 (0.5)	21 (5.1)
Depression	1 (3.3)	23 (13.2)	29 (13.9)	53 (12.9)
Insomnia	0	9 (5.2)	31 (14.9)	40 (9.7)
Reproductive system and breast disorders	0	19 (10.9)	48 (23.1)	67 (16.3)
Benign prostatic hyperplasia	0	0	15 (7.2)	15 (3.6)
Erectile dysfunction	0	2 (1.1)	11 (5.3)	13 (3.2)
Respiratory, thoracic and mediastinal disorders	5 (16.7)	25 (14.4)	59 (28.4)	89 (21.6)
Asthma	2 (6.7)	12 (6.9)	27 (13.0)	41 (10.0)
Chronic obstructive pulmonary disease	0	1 (0.6)	8 (3.8)	9 (2.2)
Rhinitis allergic	3 (10.0)	6 (3.4)	16 (7.7)	25 (6.1)
Sleep apnea syndrome	0	2 (1.1)	13 (6.3)	15 (3.6)
Skin and subcutaneous tissue disorders	6 (20.0)	18 (10.3)	22 (10.6)	46 (11.2)
Acne	5 (16.7)	6 (3.4)	0	11 (2.7)
Social circumstances	3 (10.0)	8 (4.6)	59 (28.4)	70 (17.0)
Postmenopause	0	3 (1.7)	53 (25.5)	56 (13.6)
Surgical and medical procedures	2 (6.7)	67 (38.5)	121 (58.2)	190 (46.1)
Appendicectomy	1 (3.3)	3 (1.7)	11 (5.3)	15 (3.6)
Caesarean section	0	6 (3.4)	6 (2.9)	12 (2.9)
Cataract operation	0	1 (0.6)	12 (5.8)	13 (3.2)
Cholecystectomy	0	4 (2.3)	12 (5.8)	16 (3.9)
Female sterilization	0	8 (4.6)	6 (2.9)	14 (3.4)
Hysterectomy	0	10 (5.7)	36 (17.3)	46 (11.2)
Skin neoplasm excision	0	2 (1.1)	10 (4.8)	12 (2.9)

Tonsillectomy	0	4 (2.3)	6 (2.9)	10 (2.4)
Vasectomy	0	4 (2.3)	9 (4.3)	13 (3.2)
Wisdom teeth removal	0	10 (5.7)	1 (0.5)	11 (2.7)
Vascular disorders	1 (3.3)	28 (16.1)	117 (56.3)	146 (35.4)
Essential hypertension	1 (3.3)	1 (0.6)	14 (6.7)	16 (3.9)
Hypertension	0	25 (14.4)	92 (44.2)	117 (28.4)

Values are n[b] (%).

[a]Number of participants in the specified group. This value is the denominator for the percentage calculations.

[b]Number of participants with the specified characteristic. Participants with multiple occurrences of the same preferred term are counted only once.

Table S3. Participant demographics of the variant neutralization subset

	Current study: XBB.1.5-adapted BNT162b2 30 µg			Comparator group: BA.4/BA.5-adapted BNT162b2 30 µg		
	18–55 years old (N[a]=20)	**>55 years old (N[a]=20)**	**Total (N[a]=40)**	**18–55 years old (N[a]=20)**	**>55 years old (N[a]=20)**	**Total (N[a]=40)**
Sex, n[b] (%)						
Male	12 (60.0)	7 (35.0)	19 (47.5)	12 (60.0)	7 (35.0)	19 (47.5)
Female	8 (40.0)	13 (65.0)	21 (52.5)	8 (40.0)	13 (65.0)	21 (52.5)
Race, n[b] (%)						
White	18 (90.0)	16 (80.0)	34 (85.0)	17 (85.0)	16 (80.0)	33 (82.5)
Black or African American	2 (10.0)	2 (10.0)	4 (10.0)	1 (5.0)	3 (15.0)	4 (10.0)
Other	0	2 (10.0)	2 (5.0)	1 (5.0)	1 (5.0)	2 (5.0)
Ethnicity, n[b] (%)						
Hispanic/Latino	9 (45.0)	4 (20.0)	13 (32.5)	3 (15.0)	4 (20.0)	7 (17.5)
Age at vaccination (years)						
Mean (SD)	38.0 (10.04)	70.1 (6.51)	54.0 (18.30)	37.9 (9.97)	69.7 (5.95)	53.8 (18.00)
Median (range)	35.5 (25–55)	69.5 (56–82)	55.5 (25–82)	36.0 (25–54)	69.5 (56–81)	55.0 (25–81)
Baseline SARS-CoV-2 status, n[b] (%)						
Positive[c]	20 (100.0)	20 (100.0)	40 (100.0)	20 (100.0)	20 (100.0)	40 (100.0)
Time from last dose of mRNA COVID-19 vaccine[d] to the study vaccination (months[e])						
Mean (SD)	8.8 (1.98)	9.6 (2.04)	9.2 (2.03)	11.0 (1.41)	11.4 (1.16)	11.2 (1.29)
Median (range)	8.3 (5.8–12.0)	10.2 (5.8–11.9)	9.5 (5.8–12.0)	11.3 (7.4–12.8)	11.9 (8.5–12.6)	11.4 (7.4–12.8)
≥5 to <7 months, n[b] (%)	4 (20.0)	4 (20.0)	8 (20.0)	0	0	0
≥7 to <9 months, n[b] (%)	7 (35.0)	2 (10.0)	9 (22.5)	3 (15.0)	1 (5.0)	4 (10.0)
≥9 to ≤12 months, n[b] (%)	9 (45.0)	14 (70.0)	23 (57.5)	13 (65.0)	10 (50.0)	23 (57.5)
>12 months, n[b] (%)	0	0	0	4 (20.0)	9 (45.0)	13 (32.5)
Time from last dose of mRNA COVID-19 vaccine to study vaccination (days)						
Mean (SD)	245.7 (55.35)	269.5 (57.01)	257.6 (56.75)	306.7 (39.39)	318.8 (32.39)	312.7 (36.12)
Median (range)	233.5 (162–	285.0 (162–	265.5 (162–	317.0 (207–	334.5 (239–	320.5 (207–

	336)	333)	336)	359)	354)	359)
BMI, n[b] (%)						
Underweight (<18.5 kg/m^2)	0	1 (5.0)	1 (2.5)	0	0	0
Normal weight (≥18.5–24.9 kg/m^2)	6 (30.0)	6 (30.0)	12 (30.0)	5 (25.0)	3 (15.0)	8 (20.0)
Overweight (≥25.0–29.9 kg/m^2)	9 (45.0)	7 (35.0)	16 (40.0)	8 (40.0)	12 (60.0)	20 (50.0)
Obese (≥30.0 kg/m^2)	5 (25.0)	6 (30.0)	11 (27.5)	7 (35.0)	5 (25.0)	12 (30.0)

Data are for the all-available immunogenicity population. Data for BA.4/BA.5-adapted BNT162b2 are in a comparator group of participants from another study (NCT05472038) who were matched by age, and baseline SARS-CoV-2 status.

BMI=body mass index; NAAT=nucleic acid amplification test; N-binding=SARS-CoV-2 nucleoprotein–binding; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SD=standard deviation.

[a]N was the number of participants in the specified group, or the total sample; this value was the denominator for the percentage calculations.

[b]n was the number of participants with the specified characteristic.

[c]Positive N-binding antibody result at baseline, positive NAAT result at baseline, or medical history of COVID-19.

[d]The inclusion criteria required the participant to have received: ≥3 prior doses of a US-authorized mRNA COVID-19 vaccine with the most recent dose being a US-authorized Omicron BA.4/BA.5–adapted vaccine ≥150 days before study vaccination (current study); 3 or 4 prior doses of 30 µg BNT162b2 with the last dose being 150–365 days before study vaccination (comparator group).

[e]Month was calculated as 28 days.

Figure S1. Serum neutralizing GMTs (95% CIs) before and 7 days after vaccination with XBB.1.5-adapted BNT162b2 30 μg or BA.4/BA.5-adapted BNT162b2 30 μg and GMFRs (95% CIs) from before to 1 week after vaccination to Omicron XBB.1.5 (**a**), EG.5.1 (**b**), and BA.2.86 (**c**). Data for BA.4/BA.5-adapted BNT162b2 are in participants from another study (ClinicalTrials.gov identifier: NCT05472038) who were matched by age, sex, and baseline SARS-CoV-2 status. Data are for the all-available immunogenicity population. Assay results <LLOQ were set to 0.5 × LLOQ. Numbers within the bars are the GMTs. 7d=7 days after vaccination; FFRNT=fluorescent focus reduction neutralization test; GMFR=geometric mean fold rise; GMT=geometric mean titer; LLOQ=lower limit of quantitation; Pre=before vaccination.

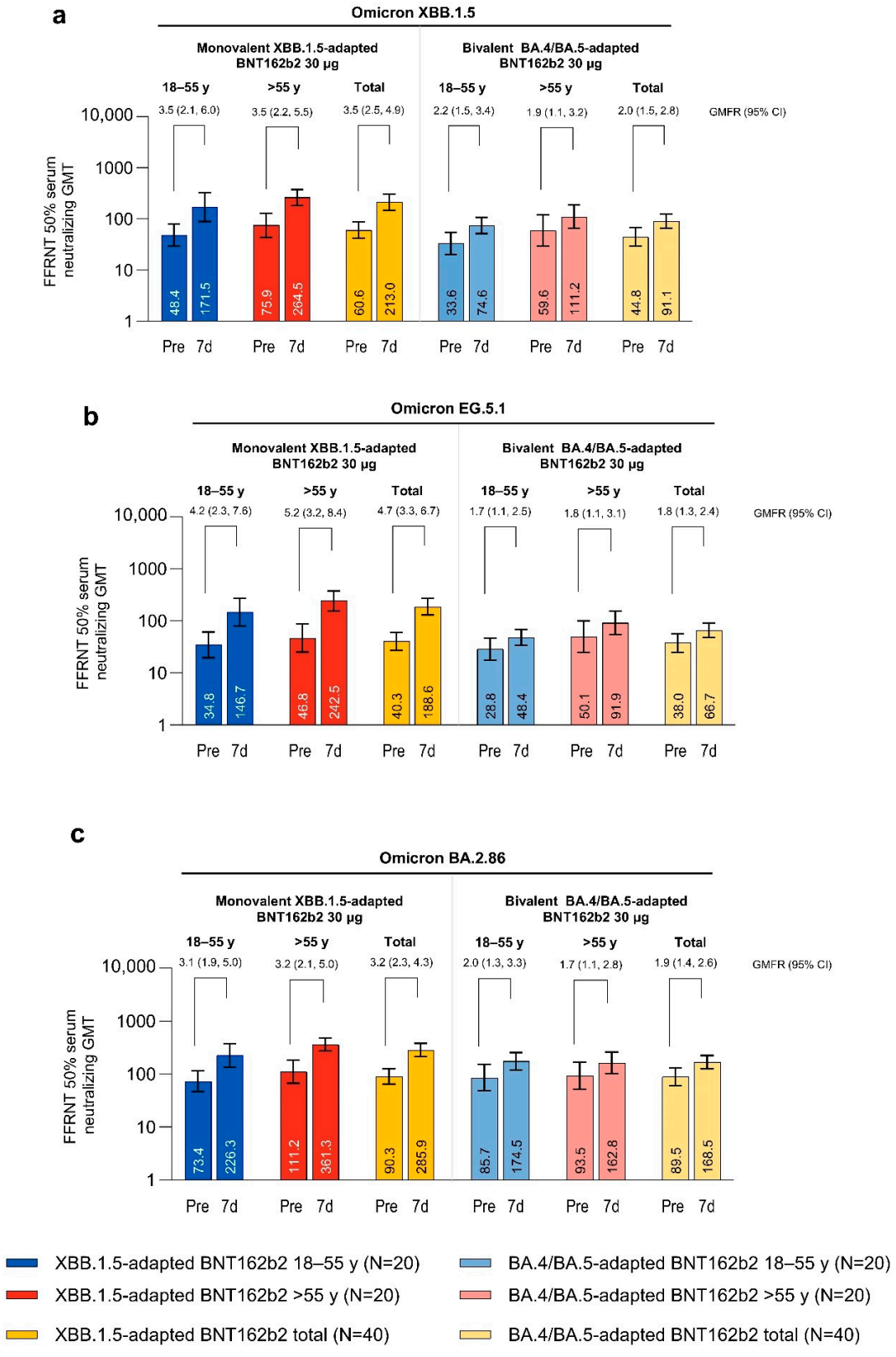
a
Omicron XBB.1.5
Monovalent XBB.1.5-adapted BNT162b2 30 µg
Bivalent BA.4/BA.5-adapted BNT162b2 30 µg
18–55 y
>55 y
Total
18–55 y
>55 y
Total
GMFR (95% CI)
3.5 (2.1, 6.0)
3.5 (2.2, 5.5)
3.5 (2.5, 4.9)
2.2 (1.5, 3.4)
1.9 (1.1, 3.2)
2.0 (1.5, 2.8)
FFRNT 50% serum neutralizing GMT
10,000
1000
100
10
1
48.4
171.5
75.9
264.5
60.6
213.0
33.6
74.6
59.6
111.2
44.8
91.1
Pre 7d
b
Omicron EG.5.1
Monovalent XBB.1.5-adapted BNT162b2 30 µg
Bivalent BA.4/BA.5-adapted BNT162b2 30 µg
18–55 y
>55 y
Total
18–55 y
>55 y
Total
GMFR (95% CI)
4.2 (2.3, 7.6)
5.2 (3.2, 8.4)
4.7 (3.3, 6.7)
1.7 (1.1, 2.5)
1.8 (1.1, 3.1)
1.8 (1.3, 2.4)
FFRNT 50% serum neutralizing GMT
10,000
1000
100
10
1
34.8
146.7
46.8
242.5
40.3
188.6
28.8
48.4
50.1
91.9
38.0
66.7
Pre 7d
c
Omicron BA.2.86
Monovalent XBB.1.5-adapted BNT162b2 30 µg
Bivalent BA.4/BA.5-adapted BNT162b2 30 µg
18–55 y
>55 y
Total
18–55 y
>55 y
Total
GMFR (95% CI)
3.1 (1.9, 5.0)
3.2 (2.1, 5.0)
3.2 (2.3, 4.3)
2.0 (1.3, 3.3)
1.7 (1.1, 2.8)
1.9 (1.4, 2.6)
FFRNT 50% serum neutralizing GMT
10,000
1000
100
10
1
73.4
226.3
111.2
361.3
90.3
285.9
85.7
174.5
93.5
162.8
89.5
168.5
Pre 7d
XBB.1.5-adapted BNT162b2 18–55 y (N=20)
XBB.1.5-adapted BNT162b2 >55 y (N=20)
XBB.1.5-adapted BNT162b2 total (N=40)
BA.4/BA.5-adapted BNT162b2 18–55 y (N=20)
BA.4/BA.5-adapted BNT162b2 >55 y (N=20)
BA.4/BA.5-adapted BNT162b2 total (N=40)

Figure S2. Percentage of participants achieving seroresponse (95% CIs) 1 week after vaccination with XBB.1.5-adapted BNT162b2 30 µg or BA.4/BA.5-adapted BNT162b2 30 µg to Omicron XBB.1.5 (**a**), EG.5.1 (**b**), and BA.2.86 (**c**). Data for BA.4/BA.5-adapted BNT162b2 are in participants from another study (NCT05472038) who were matched by age, sex, and baseline SARS-CoV-2 status. Data are for the all-available immunogenicity population. Seroresponse was defined as achieving a ≥4-fold rise from before study vaccination in FFRNT 50% serum neutralizing titers. If the baseline measurement was <LLOQ, a postvaccination assay result ≥4 × LLOQ was considered a seroresponse. Numbers above the bars are percentages rounded to the nearest full number. FFRNT=fluorescent focus reduction neutralization test; LLOQ=lower limit of quantitation.