Supplementary Table 1. Comparison of incidence rates of self-reported and clinically confirmed episodes of common infectious diseases over 26 weeks by treatment group and sex.

Syndrome	MALES			FEMALES			
	Rate per 100 person-weeks (episodes/weeks)		IRR* (95% CI)	Rate per 100 person-weeks (episodes/weeks)		IRR* (95% CI)	LRT p-value
	Placebo	Vaccine		Placebo	Vaccine		
Self-reported episodes							
CID	4.32 (41/949)	3.18 (29/911)	0.73 (0.41–1.30)	5.39 (247/4586)	5.31 (261/4917)	0.99 (0.79–1.24)	0.33
CID2	5.01 (52/1038)	4.00 (38/950)	0.79 (0.46–1.36)	5.83 (289/4955)	5.97 (316/5296)	1.02 (0.82–1.23)	0.40
URI	1.48 (15/1016)	1.28 (12/935)	0.86 (0.37–1.95)	1.82 (88/4835)	2.20 (113/5148)	1.20 (0.88–1.63)	0.45
ILI	0.68 (7/1028)	0.85 (8/940)	1.26 (0.42–3.88)	0.98 (48/4895)	0.76 (40/5248)	0.77 (0.49–1.22)	0.42
DIA	3.08 (30/973)	1.61 (15/932)	0.52 (0.24–1.12)	2.94 (140/4759)	2.96 (151/5099)	1.03 (0.76–1.39)	0.11
UFI	0.00 (0/1038)	0.32 (3/947)	ND†	0.26 (13/4942)	0.23 (12/5281)	ND†	ND†
Clinically confirmed episodes							
CID	0.20 (2/988)	0.32 (3/936)	1.58 (0.26–9.43)	0.44 (22/5044)	0.49 (25/5070)	1.13 (0.64–2.02)	0.73
URI	0.10 (1/988)	0.21 (2/936)	2.1 (0.19–23.2)	0.20 (10/5044)	0.26 (13/5070)	1.29 (0.57–3.03)	0.70
ILI	0.00 (0/988)	0.00 (0/936)	ND†	0.08 (4/5044)	0.04 (2/5070)	ND†	ND†
DIA	0.10 (1/988)	0.11 (1/936)	1.04 (0.07–16.7)	0.16 (8/5044)	0.18 (9/5070)	1.12 (0.43–2.99)	0.96
UFI	0.00 (0/988)	0.00 (0/936)	ND†	0.00 (0/5044)	0.02 (1/5070)	ND†	ND†

*Adjusted for cohort as stratification factor in the randomization

† Model fit not valid for syndromes with zero counts in any category of treatment group by sex

CI, confidence intervals; IRR, incidence rate ratio; LRT, likelihood ratio test of significance of interaction term between treatment group and sex

Supplementary Table 2. Comparison of incidence rates of self-reported episodes of common infectious diseases, shown separately for periods in which placebo was vaccine diluent or sterile saline

Syndrome	Rate per 100 person-weeks (episodes/weeks)		Adjusted incidence rate ratio* (95% CI)	p-value
	Placebo	Vaccine		
Self-reported episodes (placebo = diluent)				
CID	5.70 (202/3546)	5.16 (194/3760)	0.89 (0.70–1.14)	0.36
CID2	6.07 (235/3870)	5.87 (237/4040)	0.96 (0.75–1.22)	0.72
URI	1.94 (73/3767)	2.04 (80/3929)	1.05 (0.75–1.46)	0.80
ILI	0.89 (34/3828)	0.80 (32/4001)	0.90 (0.52–1.54)	0.69
DIA	3.23 (119/3685)	2.84 (111/3904)	0.88 (0.62–1.24)	0.44
UFI	0.23 (9/3861)	0.35 (14/4024)	1.47 (0.58–3.85)	0.42
Self-reported episodes (placebo = saline)*				
CID	4.32 (86/1989)	4.64 (96/2068)	1.09 (0.74–1.62)	0.64
CID2	4.99 (106/2123)	5.30 (117/2206)	1.03 (0.70–1.50)	0.89
URI	1.44 (30/2084)	2.09 (45/2154)	1.39 (0.80–2.42)	0.24
ILI	1.00 (21/2095)	0.73 (16/2187)	0.72 (0.37–1.40)	0.34
DIA	2.49 (51/2047)	2.59 (55/2127)	1.06 (0.65–1.73)	0.81
UFI	0.19 (4/2119)	0.05 (1/2204)	ND	ND

*Includes placebo group participants in cohort 202010 who received diluent for their first dose of placebo injection in September 2019, prior to the switch to saline for their second and third doses.

Supplementary Table 3. Occurrence of solicited adverse events over 3 days following each injection, and unsolicited adverse events reported through 4 weeks after first injection, for cohorts/doses for which the placebo used was the vaccine diluent

	Placebo dose			Vaccine dose		
	1	2	3	1	2	3
Solicited adverse events						
No. of respondents	224	169	167	227	170	172
Local reactions, n (%)						
Pain	190 (85)	131 (78)	109 (65)	133 (59)	99 (58)	100 (58)
Erythema	26 (12)	15 (9)	11 (7)	14 (6)	8 (5)	17 (10)
Edema	32 (14)	16 (9)	15 (9)	12 (5)	15 (9)	20 (12)
Pruritus	14 (6)	8 (5)	5 (3)	5 (2)	9 (5)	15 (9)
Induration	12 (5)	5 (3)	2 (1)	9 (4)	4 (2)	12 (7)
Systemic reactions, n (%)						
Fever	9 (4)	0 (0)	2 (1)	7 (3)	4 (2)	1 (1)
Shivering	6 (3)	2 (1)	1 (1)	2 (1)	1 (1)	0 (0)
Faintness	28 (13)	6 (4)	3 (2)	7 (3)	3 (2)	0 (0)
Asthenia	35 (16)	8 (5)	8 (5)	8 (4)	6 (4)	0 (0)
Headache	38 (17)	24 (14)	22 (13)	33 (15)	33 (19)	19 (11)
Dizziness	26 (12)	9 (5)	4 (2)	8 (4)	3 (2)	1 (1)
Arthralgia	16 (7)	8 (5)	7 (4)	7 (3)	7 (4)	2 (1)
Myalgia	76 (34)	37 (22)	22 (13)	51 (22)	29 (17)	17 (10)
Nausea	34 (15)	12 (7)	14 (8)	11 (5)	8 (5)	5 (3)
Abdominal pain	14 (6)	7 (4)	2 (1)	12 (5)	6 (4)	4 (2)
Malaise	48 (21)	18 (11)	11 (7)	18 (8)	26 (10)	9 (5)
Hypersensitivity/allergic reactions, n (%)						
Rash	3 (1)	1 (1)	1 (1)	3 (1)	2 (1)	2 (1)
Urticaria	1 (0.4)	0 (0)	0 (0)	3 (1)	1 (1)	1 (1)
Erythema multiforme	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anaphylaxis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unsolicited adverse events						
No. of participants	232	172	172	231	174	174
Any	18 (8)	8 (5)	7 (4)	5 (2)	3 (2)	3 (2)
Severe	3 (1)	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Serious adverse event (SAE)	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Related to intervention	8 (3)	5 (3)	2 (1)	2 (1)	0 (0)	2 (1)

Supplementary Table 4. Occurrence of solicited adverse events over 3 days following each injection, and unsolicited adverse events reported through 4 weeks after first injection, for cohorts/doses for which the placebo used was sterile saline

	Placebo dose			Vaccine dose		
	1	2	3	1	2	3
Solicited adverse events						
No. of respondents	38	90	92	40	94	92
Local reactions, n (%)						
Pain	9 (24)	20 (22)	14 (15)	16 (40)	49 (52)	44 (48)
Erythema	1 (3)	0 (0)	2 (2)	2 (5)	6 (6)	4 (4)
Edema	1 (3)	1 (1)	0 (0)	2 (5)	3 (3)	2 (2)
Pruritus	1 (3)	1 (1)	2 (2)	1 (3)	3 (3)	3 (3)
Induration	0 (0)	0 (0)	0 (0)	2 (5)	3 (3)	3 (3)
Systemic reactions, n (%)						
Fever	2 (5)	1 (1)	0 (0)	0 (0)	2 (2)	1 (1)
Shivering	0 (0)	2 (2)	0 (0)	0 (0)	1 (1)	0 (0)
Faintness	0 (0)	1 (1)	1 (1)	1 (3)	2 (2)	1 (1)
Asthenia	1 (3)	3 (3)	0 (0)	1 (3)	3 (3)	1 (1)
Headache	7 (18)	7 (8)	6 (6)	4 (10)	6 (6)	6 (6)
Dizziness	0 (0)	1 (1)	0 (0)	1 (3)	3 (3)	2 (2)
Arthralgia	2 (5)	6 (7)	3 (3)	0 (0)	3 (3)	0 (0)
Myalgia	6 (16)	7 (8)	4 (4)	5 (13)	16 (17)	5 (5)
Nausea	4 (11)	2 (2)	1 (1)	1 (3)	3 (3)	3 (3)
Abdominal pain	1 (3)	2 (2)	0 (0)	1 (3)	3 (3)	1 (1)
Malaise	0 (0)	3 (3)	1 (1)	4 (8)	7 (7)	3 (3)
Hypersensitivity/allergic reactions, n (%)						
Rash	0 (0)	0 (0)	1 (1)	2 (5)	2 (2)	0 (0)
Urticaria	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)
Erythema multiforme	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Anaphylaxis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unsolicited adverse events						
No. of participants	40	96	94	43	99	99
Any	1 (3)	3 (3)	1 (1)	1 (2)	1 (1)	1 (1)
Severe	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Serious adverse event (SAE)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Related to intervention	0 (0)	1 (1)	1 (1)	0 (0)	0 (0)	0 (0)