Supplementary Digital Content 4. Five Additional Prespecified Endpoints Used as the Basis of Licensure of Bivalent rLP2086 in the United States: Proportion of Subjects Achieving a ≥4-fold Rise in hSBA Titer and the Proportion of Subjects Achieving a Prespecified Protective hSBA Titer for All 4 MnB Test Strains (composite response) From Baseline to 1 Month After Dose 2 or 3

	Bivalent rLP2086+HPV4		Bivalent rLP2086+Saline	
Immunologic Test	**n[a]/N[b]**	**% (95% CI[c])**	**n[a]/N[b]**	**% (95% CI[c])**
PMB80 [A22]				
1 Month after vaccination 2	566/774	73.1 (69.9, 76.2)	585/788	74.2 (71.0, 77.3)
1 Month after vaccination 3	668/783	85.3 (82.6, 87.7)	681/788	86.4 (83.8, 88.7)
PMB2001 [A56]				
1 Month after vaccination 2	681/736	92.5 (90.4, 94.3)	672/726	92.6 (90.4, 94.4)
1 Month after vaccination 3	705/742	95.0 (93.2, 96.5)	696/730	95.3 (93.6, 96.8)
PMB2948 [B24]				
1 Month after vaccination 2	464/757	61.3 (57.7, 64.8)	477/752	63.4 (59.9, 66.9)
1 Month after vaccination 3	646/775	83.4 (80.5, 85.9)	656/774	84.8 (82.0, 87.2)
PMB2707 [B44]				
1 Month after vaccination 2	354/775	45.7 (42.1, 49.3)	365/770	47.4 (43.8, 51.0)
1 Month after vaccination 3	610/791	77.0 (73.9, 79.9)	636/788	80.7 (77.8, 83.4)
Composite Response				
Before vaccination 1	2/727	0.3 (0.0–1.0)	5/711	0.7 (0.2–1.6)
1 Month after vaccination 2	354/210	49.9 (46.1–53.6)	375/723	51.9 (48.2–55.6)
1 Month after vaccination 3	608/751	81.0 (78.0–83.7)	640/763	83.9 (81.1–86.4)

HPV4=quadrivalent human papillomavirus vaccine; hSBA=serum bactericidal assay using human complement; LLOQ=lower limit of quantitation: 1:16 for PMB80 (A22); 1:8 for PMB2001 (A56), PMB2948 (B24), and PMB2707 (B44).For subjects with a baseline hSBA titer <1:4, a response was defined as an hSBA titer ≥1:16. For subjects with a baseline hSBA titer ≥1:4, a 4-fold response was defined as an hSBA titer ≥4 times the LLOQ or ≥4 times the baseline titer, whichever was higher.

Composite response is defined as an hSBA titer ≥ LLOQ for all four strains.

[a]Subjects with ≥4-fold increase in hSBA titer for the given strain or subjects with observed hSBA titer greater than or equal to the prespecified level for all four test strains (composite response) at the given time point.

[b]Subjects with valid and determinate hSBA titers for the given strain.

[c]Exact 2-sided CI (Clopper and Pearson) based on the observed proportion of subjects.