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<b>Study No.:</b> 113847 (Flu Q-Pan-H1N1-029)
<b>Title:</b> Safety and immunogenicity study of GSK Biologicals' pandemic influenza (H1N1) candidate vaccine (GSK2340274A) in Japanese children aged 6 months to 17 years. GSK2340274A (Flu): GlaxoSmithKline (GSK) Biologicals' A/California/7/2009 (H1N1)v-like vaccine adjuvanted with AS03A.
<b>Rationale:</b> The aim of this study is to assess the immunogenicity and safety of Flu vaccine in Japanese children using different formulations according to age (6 months to 9 years or 10 to 17 years). This summary presents results up to Day 21 based on preliminary data and will be updated when additional data become available. As results are based on preliminary data, the numbers may change when the final data become available.
<b>Phase:</b> II
<b>Study Period:</b> From 27 October 2009 to 15 December 2009 (data lock point Day 21)
<b>Study Design:</b> Open study with two parallel groups.
<b>Centres:</b> 1 centre in Japan.
<b>Indication:</b> Immunization against A/California/7/2009 (H1N1)v-like influenza in children 6 months to 17 years of age.
<b>Treatment:</b> The study groups were as follow: <ul style="list-style-type: none"> <li>Flu [6 months-9 years] Group: Subjects aged from 6 months to 9 years received two doses of Flu vaccine (formulation 1) according to a 0, 21-day schedule. Within this group, enrolment of subjects was stratified by age into two subgroups, from 6 to 35 months and from 3 to 9 years.</li> <li>Flu [10-17 years] Group: Subjects aged from 10 to 17 years received two doses of Flu vaccine (formulation 2) according to a 0, 21-day schedule.</li> </ul> Flu vaccine, regardless of the formulation, was administered intramuscularly in the anterolateral part of the thigh (if the subject was less than 12 months) or in the deltoid region of the arm.
<b>Objectives:</b> <ul style="list-style-type: none"> <li>To assess whether vaccination with two doses of Flu vaccine (formulation 1) results in an immune response to the vaccine-homologous virus that meets or exceeds the U.S. Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER) and the European Medicines Agency (EMA), Committee for Medicinal Products for Human Use (CHMP) guidance targets for pandemic vaccine seroconversion rate (SCR), rate of induction of vaccine-homologous reciprocal HI titres <math>\geq 40</math> (potential seroprotection rate or SPR), and geometric mean fold rise (GMFR) at 21 days after the second dose of Flu vaccine in children aged 6 months to 9 years (Flu [6 months-9 years] Group).</li> <li>To assess whether vaccination with two doses of Flu vaccine (formulation 2) results in an immune response to the vaccine-homologous virus that meets or exceeds the CBER and CHMP guidance targets for pandemic vaccine SCR, SPR, and GMFR at 21 days after the second dose of Flu vaccine in children aged 10 to 17 years (Flu [10-17 years] Group).</li> </ul> <p><i>The CBER Criteria was fulfilled for this study if after dose 2 in Flu [6 months-9 years] Group or Flu [10-17 years] Group :</i></p> <ul style="list-style-type: none"> <li><i>the lower 97.5% confidence interval for SCR was &gt; 40%, and</i></li> <li><i>the lower 97.5% confidence interval for SPR was &gt; 70%</i></li> <p><i>The CHMP Criteria was fulfilled for this study if after dose 2 in Flu [6 months-9 years] Group or Flu [10-17 years] Group :</i></p> <ul style="list-style-type: none"> <li><i>the point estimate for SCR was &gt; 40%, and</i></li> <li><i>the post-vaccination point estimate for SPR was &gt; 70%, and</i></li> <li><i>the point estimate for GMFR was &gt; 2.5.</i></li> </ul> </ul>
<b>Primary Outcome/Efficacy Variable:</b> <ul style="list-style-type: none"> <li>For the humoral immune response in terms of vaccine H1N1 HI antibodies against A/California/7/2009 (H1N1)v-like virus, the following parameters were calculated with 97.5% confidence intervals (CIs).</li> </ul> <p><i>Observed variable:</i></p> <ul style="list-style-type: none"> <li>- H1N1 HI antibodies on Day 42<sup>#</sup></li> <p><i>Derived variable:</i></p> <ul style="list-style-type: none"> <li>- Geometric Mean Titres (GMTs) of H1N1 HI antibodies;</li> <li>- SCR* on Day 42<sup>#</sup>;</li> <li>- SPR** on Day 42<sup>#</sup>;</li> <li>- GMFR*** on Day 42<sup>#</sup>.</li> </ul> </ul>

\*SCR is defined as the percentage of vaccinees that have either a pre-vaccination titre < 1:10 and a postvaccination titre  $\geq$  1:40, or a pre-vaccination titre  $\geq$  1:10 and at least a 4-fold increase in post-vaccination titre.

\*\*SPR is defined as the percentage of vaccinees with a serum HI titre  $\geq$  1:40 that usually is accepted as indicating protection.

\*\*\*GMFR, also called seroconversion factor (SCF), is defined as the fold increase in serum HI GMTs post-vaccination compared to pre-vaccination.

# At the time of writing this summary, data were available up to Day 21 only. This summary will be updated when additional results become available.

#### **Secondary Outcome/Efficacy Variable(s):**

##### *Immunogenicity*

• For the humoral immune response in terms of H1N1 HI antibodies against A/California/7/2009 (H1N1)v-like virus, the following parameters were calculated with 95% CIs:

##### *Observed variable:*

- H1N1 HI antibodies on Day 0, Day 21, Day 42<sup>#</sup> and at Day 182<sup>#</sup>.

##### *Derived variable:*

- GMTs and seropositivity rates;
- SCRs;
- SPRs;
- GMFRs

The same analyses as above were performed in each age stratum.

• For the humoral immune response in terms of neutralising antibodies against A/California/7/2009 (H1N1)v-like virus, the following parameters were calculated with 95% CIs:<sup>§</sup>

##### *Observed variable:*

- Serum neutralising antibody titres on Day 0, Day 21, Day 42 and Day 182.

##### *Derived variable:*

- GMTs and seropositivity rates;
- VRRs\*;

\*VRR is defined as the percentage of vaccinees that have a four-fold increase between pre- and postvaccination titres.

##### *Safety:*

- Percentage, intensity and relationship to vaccination of solicited local and general signs and symptoms during a 7-day follow-up period, i.e., day of vaccination and six subsequent days after each vaccination on Day 0 and Day 21. #
- Percentage, intensity and relationship to vaccination of unsolicited adverse events (AEs) during a 21-day follow-up period after the first vaccination and during a 63-day follow-up period after the second vaccination. #
- Occurrence of medically attended events (MAEs), potential Immune-Mediated Diseases (pIMDs), serious adverse events (SAEs) and relationship to vaccination during the entire study period. #
- The number and percentage of subjects with normal or abnormal values of biochemical and haematological parameters on Day 0, Day 7 and Day 42.<sup>§</sup>

# At the time of writing this summary, data were available up to Day 21 only. This summary will be updated when additional results become available.

<sup>§</sup>Not available at the time of writing this summary.

#### **Statistical Methods:**

Analyses were performed on the Total Vaccinated cohort that included all vaccinated subjects.

The analyses were performed on preliminary data.

##### *Analysis of immunogenicity:*

The analysis of immunogenicity was done as a descriptive analysis of the humoral immune response.

For the humoral immune response in terms of H1N1 HI antibodies, the following parameters were calculated (with 97.5% CIs):

- Seropositivity rates and GMTs of H1N1 HI antibody titres at Day 0 and Day 21.
- SCR at Day 21.
- SPR at Day 0 and Day 21.
- GMFR at Day 21.

##### *Analysis of safety:*

The incidence of solicited local and general symptoms occurring during 7 days after the first vaccination was tabulated with exact 95% CI for each treatment group and for all age strata, then per age stratum. The same calculation was performed for symptoms of any intensity and those with intensity of Grade 3, as well as for solicited general events with relationship to vaccination. All solicited local AEs were assessed as causally related.

The percentage of subjects with at least one report of an unsolicited AE classified by Medical Dictionary for Regulatory

<p>Activities (MedDRA) Preferred Term up to 21 days after the first dose of vaccine was tabulated for each treatment group. The same tabulation was performed for grade 3 unsolicited AEs and for unsolicited AEs that were assessed by the investigator as related to vaccination.</p> <p>SAEs, MAEs and pIMDs were collected and summarized up to Day 21.</p> <p>Subjects were stratified into the following subgroups of age: from 6 to 35 months, from 3 to 5 years, from 6 to 9 years, and from 10 to 17 years for solicited general symptoms, MAEs, pIMDS, unsolicited AE and SAE.</p>										
<p><b>Study Population:</b> Healthy male or female Japanese children aged between 6 months to 17 years of age at the time of first vaccination, inclusive. Female subjects of childbearing potential had to practice adequate contraception for 30 days prior to vaccination, to have a negative pregnancy test and to continue such precautions during the entire treatment period and for 2 months after completion of the vaccination series. Written informed consent was obtained from the subject's parent(s) or Legally Acceptable Representative(s) of the subject prior to study entry. Whenever possible, an assent was also obtained from the subject.</p>										
<b>Number of Subjects:</b>				<b>Flu [6 months-9 years] Group</b>				<b>Flu [10-17 years] Group</b>		
				<b>6-35 months</b>		<b>3 to 9 years</b>				
Planned, N				10		20		30		
Randomised, N (Total Vaccinated cohort)				30		30		30		
Completed, n (%) at Day 21				29 (96.7)		30 (100)		30 (100)		
Total Number Subjects Withdrawn, n (%)				1 (3.3)		0 (0.0)		0 (0.0)		
Withdrawn due to Adverse Events n (%)				TBC		TBC		TBC		
Withdrawn due to Lack of Efficacy n (%)				Not Applicable		Not applicable		Not applicable		
Withdrawn for other reasons n (%)				TBC		TBC		TBC		
<b>Demographics</b>				<b>Flu [6 months-9 years] Group</b>				<b>Flu [10-17 years] Group</b>		
N (Total Vaccinated cohort)				30				30		
Females: Males				16:14				18:12		
Mean Age (SD)				49.0 months (27.66)				13.2 years (2.64)		
Asian - japanese heritage, n (%)				30 (100)				30 (100)		
TBC: To be completed. Data not available.										
<b>Primary Efficacy Results:</b> Not available										
<b>Secondary Outcome Variable(s):</b> Seropositivity rates and GMTs for HI antibodies (Total Vaccinated cohort; for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)										
				<b>≥ 1:10</b>				<b>GMT</b>		
						<b>95% CI</b>				<b>95% CI</b>
<b>Antibody</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>value</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PRE	10	0	0.0	0.0	30.8	5.0	5.0	5.0
		PI(D21)	10	10	100	69.2	100	154.6	96.2	248.3
<p>GMT = geometric mean antibody titre calculated on all subjects  N = number of subjects with available results  n/% = number/percentage of subjects with titre within the specified range  95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  PRE= pre-vaccination at Day 0  PI(D21)= post-vaccination at Day 21</p>										
<b>Secondary Outcome Variable(s):</b> Seropositivity rates and GMTs for HI antibodies (Total Vaccinated cohort; for subjects of the Flu [6 months-9 years] Group aged 3 years-9 years)										
				<b>≥ 1:10</b>				<b>GMT</b>		
						<b>95% CI</b>				<b>95% CI</b>
<b>Antibody</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>	<b>value</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PRE	20	4	20.0	5.7	43.7	6.9	5.0	9.7
		PI(D21)	19	19	100	82.4	100	252.4	188.9	337.2
<p>GMT = geometric mean antibody titre calculated on all subjects  N = number of subjects with available results  n/% = number/percentage of subjects with titre within the specified range  95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit  PRE= pre-vaccination at Day 0  PI(D21)= post-vaccination at Day 21</p>										
<b>Secondary Outcome Variable(s):</b> Seropositivity rates and GMTs for HI antibodies (Total Vaccinated cohort, for subjects										

of the Flu [10 years-17 years] Group)										
						≥ 1:10		GMT		
						95% CI		95% CI		
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL
Flu A/CAL/7/09.HA1 Ab	Flu [10-17 years]	PRE	30	18	60.0	40.6	77.3	15.7	9.8	25.2
		PI(D21)	30	30	100	88.4	100	363.6	261.9	504.8
GMT = geometric mean antibody titre calculated on all subjects N = number of subjects with available results n/% = number/percentage of subjects with titre within the specified range 95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit PRE= pre-vaccination at Day 0 PI(D21)= post-vaccination at Day 21										
<b>Secondary Outcome Variable(s):</b> Seroconversion rate (SCR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)										
						SCR				
						95% CI				
Strain	Group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PI(D21)	10	10	100	69.2	100			
Seroconversion defined as: - For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination - For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= post-vaccination at Day 21										
<b>Secondary Outcome Variable(s):</b> Seroconversion rate (SCR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-9 years)										
						SCR				
						95% CI				
Strain	Group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PI(D21)	19	19	100	82.4	100			
Seroconversion defined as: - For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination - For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= post-vaccination at Day 21										
<b>Secondary Outcome Variable(s):</b> Seroconversion rate (SCR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group aged)										
						SCR				
						95% CI				
Strain	Group	Timing	N	n	%	LL	UL			
Flu A/CAL/7/09.HA1 Ab	Flu [10-17 years]	PI(D21)	30	28	93.3	77.9	99.2			
Seroconversion defined as: - For initially seronegative subjects, antibody titre ≥ 1:40 after vaccination - For initially seropositive subjects, antibody titre after vaccination ≥ 4 fold the pre-vaccination antibody titre N = Number of subjects with pre- and post-vaccination results available n/% = Number/percentage of seroconverted subjects 95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit PI(D21)= post-vaccination at Day 21										
<b>Secondary Outcome Variable(s):</b> Seroprotection rates (SPR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)										
						SPR				
						95% CI				
Strain	Group	Timing	N	n	%	LL	UL			

Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PRE	10	0	0.0	0.0	30.8
		PI(D21)	10	10	100	69.2	100
<p>N = Number of subjects with available results  n/% = Number/percentage of seroprotected subjects (HI titre <math>\geq</math> 1:40)  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PRE= pre-vaccination at Day 0  PI(D21)= post-vaccination at Day 21</p>							
<b>Secondary Outcome Variable(s):</b> Seroprotection rates (SPR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-9 years)							
				<b>SPR</b>			
				<b>95% CI</b>			
<b>Strain</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/09.HA1 Ab	Flu [6 months-9 years]	PRE	20	1	5.0	0.1	24.9
		PI(D21)	19	19	100	82.4	100
<p>N = Number of subjects with available results  n/% = Number/percentage of seroprotected subjects (HI titre <math>\geq</math> 1:40)  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PRE= pre-vaccination at Day 0  PI(D21)= post-vaccination at Day 21</p>							
<b>Secondary Outcome Variable(s):</b> Seroprotection rates (SPR) for HI antibodies (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)							
				<b>SPR</b>			
				<b>95% CI</b>			
<b>Strain</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
Flu A/CAL/7/09.HA1 Ab	Flu [10-17 years]	PRE	30	8	26.7	12.3	45.9
		PI(D21)	30	30	100	88.4	100
<p>N = Number of subjects with available results  n/% = Number/percentage of seroprotected subjects (HI titre <math>\geq</math> 1:40)  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PRE= pre-vaccination at Day 0  PI(D21)= post-vaccination at Day 21</p>							
<b>Secondary Outcome Variable(s):</b> Seroconversion factor (SCF) for HI antibody titre at each post-vaccination time point (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)							
				<b>SCF</b>			
				<b>95% CI</b>			
<b>Vaccine strain</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>Value</b>	<b>LL</b>	<b>UL</b>	
Flu A/CAL/7/09.HA1 Ab (1/DIL)	Flu [6 months-9 years]	PI(D21)	10	30.9	19.2	49.7	
<p>N = Number of subjects with pre- and post-vaccination results available  SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PI(D21)= post-vaccination at Day 21</p>							
<b>Secondary Outcome Variable(s):</b> Seroconversion factor (SCF) for HI antibody titre at each post-vaccination time point (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-9 years)							
				<b>SCF</b>			
				<b>95% CI</b>			
<b>Vaccine strain</b>	<b>Group</b>	<b>Timing</b>	<b>N</b>	<b>Value</b>	<b>LL</b>	<b>UL</b>	
Flu A/CAL/7/09.HA1 Ab (1/DIL)	Flu [6 months-9 years]	PI(D21)	19	35.7	24.5	52.1	
<p>N = Number of subjects with pre- and post-vaccination results available  SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PI(D21)= post-vaccination at Day 21</p>							
<b>Secondary Outcome Variable(s):</b> Seroconversion factor (SCF) for HI antibody titre at each post-vaccination time point (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)							
				<b>SCF</b>			
				<b>95% CI</b>			

Vaccine strain	Group	Timing	N	Value	LL	UL
Flu A/CAL/7/09.HA1 Ab (1/DIL)	Flu [10-17 years]	PI(D21)	30	23.2	14.7	36.6
<p>N = Number of subjects with pre- and post-vaccination results available  SCF = Seroconversion Factor or geometric mean ratio (mean[log10(POST/PRE)])  95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit  PI(D21)= post-vaccination at Day 21</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)						
			<b>Flu [6 months-9 years] Group</b>			
			<b>95 % CI</b>			
Symptom	Intensity	N	n	%	LL	UL
Pain	Any	10	6	60.0	26.2	87.8
	Grade 3	10	0	0.0	0.0	30.8
Redness	Any	10	0	0.0	0.0	30.8
	> 100 mm	10	0	0.0	0.0	30.8
Swelling	Any	10	3	30.0	6.7	65.2
	> 100 mm	10	0	0.0	0.0	30.8
<p>N= number of subjects with the documented dose  n/= number/percentage of subjects reporting at least once the symptom  95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  Any= occurrence of any local symptom regardless of intensity grade  Grade 3 pain= cried when limb was moved/spontaneously painful</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-5years)						
			<b>Flu [6 months-9 years] Group</b>			
			<b>95 % CI</b>			
Symptom	Intensity	N	n	%	LL	UL
Pain	Any	14	13	92.9	66.1	99.8
	Grade 3	14	1	7.1	0.2	33.9
Redness	Any	14	0	0.0	0.0	23.2
	> 100 mm	14	0	0.0	0.0	23.2
Swelling	All	14	2	14.3	1.8	42.8
	> 100 mm	14	0	0.0	0.0	23.2
<p>N= number of subjects with the documented dose  n/= number/percentage of subjects reporting at least once the symptom  95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  Any= occurrence of any local symptom regardless of intensity grade  Grade 3 pain= cried when limb was moved/spontaneously painful</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 years-9 years)						
			<b>Flu [6 months-9 years] Group</b>			
			<b>95 % CI</b>			
Symptom	Intensity	N	n	%	LL	UL
Pain	Any	6	5	83.3	35.9	99.6
	Grade 3	6	0	0.0	0.0	45.9
Redness	Any	6	1	16.7	0.4	64.1
	> 100 mm	6	0	0.0	0.0	45.9
Swelling	Any	6	2	33.3	4.3	77.7
	> 100 mm	6	0	0.0	0.0	45.9
<p>N= number of subjects with the documented dose  n/= number/percentage of subjects reporting at least once the symptom  95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  Any= occurrence of any local symptom regardless of intensity grade  Grade 3 pain= Pain that prevents normal activity</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-						

vaccination period (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)						
			Flu [10-17 years] Group			
			95 % CI			
Symptom	Intensity	N	n	%	LL	UL
Pain	Any	30	30	100	88.4	100
	Grade 3	30	3	10.0	2.1	26.5
Redness	Any	30	7	23.3	9.9	42.3
	> 100 mm	30	0	0.0	0.0	11.6
Swelling	Any	30	14	46.7	28.3	65.7
	> 100 mm	30	1	3.3	0.1	17.2

N= number of subjects with the documented dose  
n/%= number/percentage of subjects reporting at least once the symptom  
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  
Any= occurrence of any local symptom regardless of intensity grade  
Grade 3 pain= Pain that prevents normal activity

**Secondary Outcome Variable(s):** Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)

Flu [6 months-9 years] Group						
			95 % CI			
Symptom	Intensity/ Relationship	N	n	%	LL	UL
Drowsiness	Any	10	1	10.0	0.3	44.5
	Grade 3	10	0	0.0	0.0	30.8
	Related	10	1	10.0	0.3	44.5
Irritability	Any	10	3	30.0	6.7	65.2
	Grade 3	10	1	10.0	0.3	44.5
	Related	10	3	30.0	6.7	65.2
Loss of appetite	Any	10	1	10.0	0.3	44.5
	Grade 3	10	0	0.0	0.0	30.8
	Related	10	1	10.0	0.3	44.5
Temperature/(Axillary)	≥ 37.5°C	10	0	0.0	0.0	30.8
	≥ 39°C	10	0	0.0	0.0	30.8
	Related	10	0	0.0	0.0	30.8

N= number of subjects with the documented dose  
n/%= number/percentage of subjects reporting at least once the symptom  
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  
Any= occurrence of any general symptom, regardless of intensity grade or relationship with vaccination  
Grade 3 Drowsiness and Irritability = general symptom that prevented normal activity  
Grade 3 Loss of appetite = Not eating at all  
Related= general symptom assessed by the investigator as causally related to the study vaccination

**Secondary Outcome Variable(s):** Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3years-5years)

Flu [6 months-9 years] Group						
			95 % CI			
Symptom	Intensity/ Relationship	N	n	%	LL	UL
Drowsiness	Any	14	4	28.6	8.4	58.1
	Grade 3	14	0	0.0	0.0	23.2
	Related	14	4	28.6	8.4	58.1
Irritability	Any	14	3	21.4	4.7	50.8
	Grade 3	14	0	0.0	0.0	23.2
	Related	14	3	21.4	4.7	50.8
Loss of appetite	Any	14	4	28.6	8.4	58.1
	Grade 3	14	0	0.0	0.0	23.2
	Related	14	3	21.4	4.7	50.8
Temperature/(Axillary)	≥ 37.5°C	14	3	21.4	4.7	50.8
	≥ 39°C	14	0	0.0	0.0	23.2

	Related	14	3	21.4	4.7	50.8
<p>N= number of subjects with the documented dose  n/%= number/percentage of subjects reporting at least once the symptom  95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  Any= occurrence of any general symptom, regardless of intensity grade or relationship with vaccination  Grade 3 Drowsiness and Irritability = general symptom that prevented normal activity  Grade 3 Loss of appetite = Not eating at all  Related= general symptom assessed by the investigator as causally related to the study vaccination</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6years-9years)						
				<b>Flu [6 months-9 years] Group</b>		
				<b>95 % CI</b>		
<b>Symptom</b>	<b>Intensity/ Relationship</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
Fatigue	Any	6	1	16.7	0.4	64.1
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Gastrointestinal	Any	6	1	16.7	0.4	64.1
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Headache	Any	6	2	33.3	4.3	77.7
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Joint pain at other location	Any	6	0	0.0	0.0	45.9
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Muscle aches	Any	6	0	0.0	0.0	45.9
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Shivering	Any	6	1	16.7	0.4	64.1
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	1	16.7	0.4	64.1
Sweating	Any	6	0	0.0	0.0	45.9
	Grade 3	6	0	0.0	0.0	45.9
	Related	6	0	0.0	0.0	45.9
Temperature/(Axillary)	≥ 37.5°C	6	2	33.3	4.3	77.7
	≥ 39°C	6	0	0.0	0.0	45.9
	Related	6	1	16.7	0.4	64.1
<p>N= number of subjects with the documented dose  n/%= number/percentage of subjects reporting at least once the symptom  95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit  Any= occurrence of any general symptom, regardless of intensity grade or relationship with vaccination  Grade 3= general symptom that prevented normal activity  Related= general symptom assessed by the investigator as causally related to the study vaccination</p>						
<b>Secondary Outcome Variable(s):</b> Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)						
				<b>Flu [10-17 years] Group</b>		
				<b>95 % CI</b>		
<b>Symptom</b>	<b>Intensity/ Relationship</b>	<b>N</b>	<b>n</b>	<b>%</b>	<b>LL</b>	<b>UL</b>
Fatigue	Any	30	11	36.7	19.9	56.1
	Grade 3	30	1	3.3	0.1	17.2
	Related	30	10	33.3	17.3	52.8
Gastrointestinal	Any	30	3	10.0	2.1	26.5
	Grade 3	30	0	0.0	0.0	11.6
	Related	30	3	10.0	2.1	26.5
Headache	Any	30	12	40.0	22.7	59.4

	Grade 3	30	0	0.0	0.0	11.6
	Related	30	11	36.7	19.9	56.1
Joint pain at other location	Any	30	5	16.7	5.6	34.7
	Grade 3	30	0	0.0	0.0	11.6
	Related	30	4	13.3	3.8	30.7
Muscle aches	Any	30	7	23.3	9.9	42.3
	Grade 3	30	0	0.0	0.0	11.6
	Related	30	7	23.3	9.9	42.3
Shivering	Any	30	7	23.3	9.9	42.3
	Grade 3	30	0	0.0	0.0	11.6
	Related	30	6	20.0	7.7	38.6
Sweating	Any	30	2	6.7	0.8	22.1
	Grade 3	30	1	3.3	0.1	17.2
	Related	30	1	3.3	0.1	17.2
Temperature/(Axillary)	≥ 37.5°C	30	4	13.3	3.8	30.7
	≥ 39°C	30	1	3.3	0.1	17.2
	Related	30	3	10.0	2.1	26.5

N= number of subjects with the documented dose

n/%= number/percentage of subjects reporting at least once the symptom

95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Any= occurrence of any general symptom, regardless of intensity grade or relationship with vaccination

Grade 3= general symptom that prevented normal activity

Related= general symptom assessed by the investigator as causally related to the study vaccination

**Secondary Outcome Variable(s):** Percentage of subjects reporting the occurrence of medically attended events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)

<b>Most frequent MAEs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 10</b>
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Subjects with any MAE(s), n (%)	4 (40.0)
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----- *	1 (10.0)
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Conjunctivitis	1 (10.0)
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Ocular hyperaemia	1 (10.0)
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Bronchitis	1 (10.0)
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Nasopharyngitis	2 (20.0)
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\*AE not yet classified by MedDRA Preferred Term

**Secondary Outcome Variable(s):** Percentage of subjects reporting the occurrence of medically attended events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-5 years)

<b>Most frequent MAEs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 14</b>
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Subjects with any MAE(s), n (%)	1 (7.1)
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----- *	1 (7.1)
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\*AE not yet classified by MedDRA Preferred Term

**Secondary Outcome Variable(s):** Percentage of subjects reporting the occurrence of medically attended events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 years-9 years)

<b>Most frequent MAEs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 6</b>
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Subjects with any MAE(s), n (%)	1 (16.7)
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Cough	1 (16.7)
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**Secondary Outcome Variable(s):** Percentage of subjects reporting the occurrence of medically attended events within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)

<b>Most frequent MAEs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [10-17 years] Group N = 30</b>
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Subjects with any MAE(s), n (%)	2 (6.7)
Bronchitis	1 (3.3)
Influenza	1 (3.3)
<b>Secondary Outcome Variable(s):</b> Percentage of subjects reporting the occurrence of potential Immune-Mediated Diseases (pIMDs) within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)	
<b>Most frequent pIMDs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 10</b>
Subjects with any pIMD(s), n (%)	0 (0.0)
<b>Secondary Outcome Variable(s):</b> Percentage of subjects reporting the occurrence of potential Immune-Mediated Diseases (pIMDs) within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-5 years)	
<b>Most frequent pIMDs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 14</b>
Subjects with any pIMD(s), n (%)	0 (0.0)
<b>Secondary Outcome Variable(s):</b> Percentage of subjects reporting the occurrence of potential Immune-Mediated Diseases (pIMDs) within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 years-9 years)	
<b>Most frequent pIMDs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 6</b>
Subjects with any pIMD(s), n (%)	0 (0.0)
<b>Secondary Outcome Variable(s):</b> Percentage of subjects reporting the occurrence of potential Immune-Mediated Diseases (pIMDs) within the 21-day (Days 0-20) post-vaccination period (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)	
<b>Most frequent pIMDs (occurring within Day 0-20 following vaccination)</b>	<b>Flu [10-17 years] Group N = 30</b>
Subjects with any pIMD(s), n (%)	0 (0.0)
<b>Safety results:</b> Number (%) of subjects with unsolicited adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)	
<b>Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 10</b>
Subjects with any AE(s), n (%)	8 (80.0)
Subjects with grade 3 AE(s), n (%)	1 (10.0)
Subjects with related AE(s), n (%)	7 (70.0)
----- *	1 (10.0)
Conjunctivitis	1 (10.0)
Eye discharge	1 (10.0)
Ocular hyperaemia	1 (10.0)
Diarrhoea	2 (20.0)
Bronchitis	1 (10.0)
Nasopharyngitis	2 (20.0)
Crying	1 (10.0)
Cough	1 (10.0)
Rhinorrhoea	2 (20.0)
Sneezing	1 (10.0)
*AE not yet classified by MedDRA Preferred Term Grade 3= event that prevented normal activity Related= event assessed by the investigator as causally related to the study vaccination	
<b>Safety results:</b> Number (%) of subjects with unsolicited adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3years-5years)	
<b>Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 14</b>
Subjects with any AE(s), n (%)	5 (35.7)
Subjects with grade 3 AE(s), n (%)	1 (7.1)
Subjects with related AE(s), n (%)	4 (28.6)

-----*	1 (7.1)
Eye discharge	1 (7.1)
Vomiting	1 (7.1)
Pyrexia	1 (7.1)
Insomnia	1 (7.1)
Cough	1 (7.1)
Rhinorrhoea	1 (7.1)
Pruritus	1 (7.1)
*AE not yet classified by MedDRA Preferred Term Grade 3= event that prevented normal activity Related= event assessed by the investigator as causally related to the study vaccination	
<b>Safety results:</b> Number (%) of subjects with unsolicited adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6years-9years)	
<b>Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)</b>	<b>Flu [6 months-9 years] Group N = 6</b>
Subjects with any AE(s), n (%)	1 (16.7)
Subjects with grade 3 AE(s), n (%)	0 (0.0)
Subjects with related AE(s), n (%)	1 (16.7)
Pyrexia	1 (16.7)
Cough	1 (16.7)
Grade 3= event that prevented normal activity Related= event assessed by the investigator as causally related to the study vaccination	
<b>Safety results:</b> Number (%) of subjects with unsolicited adverse events (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)	
<b>Most frequent adverse events - On-Therapy (occurring within Day 0-20 following vaccination)</b>	<b>Flu [10-17 years] Group N = 30</b>
Subjects with any AE(s), n (%)	9 (30.0)
Subjects with grade 3 AE(s), n (%)	2 (6.7)
Subjects with related AE(s), n (%)	7 (23.3)
Axillary pain	2 (6.7)
Bronchitis	1 (3.3)
Influenza	1 (3.3)
Cough	1 (3.3)
Dysphonia	1 (3.3)
Epistaxis	1 (3.3)
Oropharyngeal pain	1 (3.3)
Rhinitis allergic	1 (3.3)
Rhinorrhoea	1 (3.3)
Eczema	1 (3.3)
Urticaria	1 (3.3)
Grade 3= event that prevented normal activity Related= event assessed by the investigator as causally related to the study vaccination	
<b>Safety results:</b> Number (%) of subjects with serious adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 months-35 months)	
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>	
<b>All SAEs</b>	<b>Flu [6 months-9 years] Group N = 10</b>
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Flu [6 months-9 years] Group N = 10</b>
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Safety results:</b> Number (%) of subjects with serious adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 3 years-5 years)	
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>	
<b>All SAEs</b>	<b>Flu [6 months-9 years] Group</b>

	<b>N = 14</b>
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Flu [6 months-9 years] Group</b> <b>N = 14</b>
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Safety results:</b> Number (%) of subjects with serious adverse events (Total Vaccinated cohort, for subjects of the Flu [6 months-9 years] Group aged 6 years-9 years)	
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>	
<b>All SAEs</b>	<b>Flu [6 months-9 years] Group</b> <b>N = 6</b>
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Flu [6 months-9 years] Group</b> <b>N = 6</b>
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Safety results:</b> Number (%) of subjects with serious adverse events (Total Vaccinated cohort, for subjects of the Flu [10 years-17 years] Group)	
<b>Serious adverse event, n (%) [n considered by the investigator to be related to study medication]</b>	
<b>All SAEs</b>	<b>Flu [10-17 years] Group</b> <b>N = 30</b>
Subjects with any SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]
<b>Fatal SAEs</b>	<b>Flu [10-17 years] Group</b> <b>N = 30</b>
Subjects with fatal SAE(s), n (%) [n assessed by the investigator as related]	0 (0.0) [0]

**Conclusion:**

The first dose of either vaccine formulation elicited immune responses in children 6 months to 17 years of age that exceeded regulatory authority criteria for pandemic influenza vaccine immunogenicity. As of twenty-one days after the first vaccination, at least one unsolicited AE was reported for 8 (80.0%) subjects aged 6-35 months, 5 (35.7%) subjects aged 3-5 years, 1 (16.7%) subject aged 6-9 years and 9 (30.0%) subjects aged 10-17 years. No SAE was reported up to Day 21.

**Publications:** None

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