NOVAVAX

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NANOFLU PHASE 3 TOPLINE DATA

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NanoFlu Phase 3 clinical trial goals and design

Primary objectives	• To demonstrate the non-inferior immunogenicity of NanoFlu, relative to Fluzone® Quadrivalent, in terms of hemagglutination inhibition (HAI) antibody responses to all vaccine homologous influenza strains at Day 28. • To describe the safety profile of NanoFlu and Fluzone	
Secondary objectives	• To describe the immunogenicity with both egg-propagated virus and wild-type VLP reagents to all four vaccine-homologous influenza strains and to select drifted strains at Day 28. • To describe the immunogenicity in terms of microneutralization (MN) responses to vaccine-homologous and/or antigenically drifted influenza strains at Day 0 and 28 • To describe the quality and amplitude of cell-mediated immune (CMI) responses in a subset of participants	
Design	Randomized, observer-blinded, active-comparator controlled trial	
	Vaccine strains	• WHO-recommended 2019-2020 Northern Hemisphere influenza vaccine strains. A/Brisbane (H1N1); A/Kansas (H3N2); B/Maryland (Victoria); B/Phuket (Yamagata)
	Investigational and comparator vaccines	• Hemagglutinin nanoparticle influenza vaccine, quadrivalent with Matrix-M ™ adjuvant (quad-NIV) [NanoFlu] • Quadrivalent inactivated influenza vaccine (IIV4) [Fluzone]
	Stratification	• History of receipt of 2018-2019 influenza vaccine
	Participants	• 2,650 clinically stable adults ≥65 years of age • Randomized 1:1 (NanoFlu : Fluzone), Single vaccination at Day 0
	Study sites	• 19 U.S. sites
	Length of study participation	• 1 year (safety assessment through 1 year)

NanoFlu Phase 3 clinical trial conclusions

Primary endpoint met: demonstrated immunologic non-inferiority to Fluzone in terms of hemagglutination inhibition (HAI) antibody responses (assayed with *egg-derived virus reagents*) against all four vaccine homologous strains (per CBER criteria).

Statistically significant higher HAI antibody responses (assayed with *wild-type VLP reagents*) compared to Fluzone:

- **24—66% improved Day 28 GMTs against homologous strains**
- **34—41% improved Day 28 GMTs against drifted H3N2 strains**
- **11.4—20.4% increased Day 28 seroconversion rate against homologous strains**
- **14.1—16.8% increased Day 28 seroconversion rate against drifted H3N2 strains**

NanoFlu was well-tolerated

Immunogenicity: Primary endpoint GMT

Egg - based Day 28 HAI GMTs and GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	D28 GMT Ratio	
Assay	Strain	D28 GMT	D28 GMT	(NanoFlu / Fluzone)	95% CI
HAI: EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	49.3	45.0	1.09	(1.03, 1.15)
	A/Kansas/14/2017 (H3N2) (Homologous)	151.5	126.8	1.19	(1.11, 1.27)
	B/Maryland/15/2016 (Vic) (Homologous)	110.7	106.3	1.03	(0.99, 1.07)
	B/Phuket/3073/2013 (Yam) (Homologous)	168.5	133.9	1.23	(1.16, 1.29)

Success: All 95% CI lower bounds are ≥ 0.67

- ✓ GMT ratio success criteria met
- ✓ NanoFlu: 3—23% improved responses using egg-based HAI

Immunogenicity: Primary and secondary GMT endpoints

Egg- or wild-type VLP- based Day 28 HAI GMTs and GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	D28 GMT Ratio	
Assay	Strain	D28 GMT	D28 GMT	(NanoFlu / Fluzone)	95% CI
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	B/Maryland/15/2016 (Vic) (Homologous)	110.7	106.3	1.03	(0.99, 1.07)
	B/Phuket/3073/2013 (Yam) (Homologous)	168.5	133.9	1.23	(1.16, 1.29)
HAI: VLP	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	76.6	62.7	1.24	(1.17, 1.32)
	A/Kansas/14/2017 (H3N2) (Homologous)	153.6	90.7	**1.66**	**(1.53, 1.79)**
	B/Maryland/15/2016 (Vic) (Homologous)	62.8	47.2	1.32	(1.26, 1.39)
	B/Phuket/3073/2013 (Yam) (Homologous)	118.3	78.4	1.47	(1.40, 1.55)

- ✓ NanoFlu: 24—66% improved responses using VLP-based HAI
- ✓ “Superiority” criteria met for homologous H3N2 (66% better)

Immunogenicity: Effect on drifted strains (GMT)

Egg- or wild-type VLP- based Day 28 HAI GMTs and GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	D28 GMT Ratio	
Assay	Strain	D28 GMT	D28 GMT	(NanoFlu / Fluzone)	95% CI
HAI: EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	49.3	45.0	1.09	(1.03, 1.15)
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	B/Maryland/15/2016 (Homologous)	110.7	106.3	1.03	(0.99, 1.07)
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HAI: VLP	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	76.6	62.7	1.24	(1.17, 1.32)
	A/Kansas/14/2017 (H3N2) (Homologous)	153.6	90.7	1.66	(1.53, 1.79)
	B/Maryland/15/2016 (Homologous)	62.8	47.2	1.32	(1.26, 1.39)
	B/Phuket/3073/2013 (Homologous)	118.3	78.4	1.47	(1.40, 1.55)
	A/California (“Drifted” H3N2)	115.0	80.6	1.41	(1.33, 1.50)
	A/Cardiff (“Drifted” H3N2)	63.9	45.4	1.34	(1.27, 1.43)
	A/Netherlands (“Drifted” H3N2)	102.3	74.7	1.38	(1.30, 1.46)
	A/South Australia (“Drifted” H3N2)	98.1	70.4	1.36	(1.28, 1.44)

✓ NanoFlu: 34—41% improved responses on drifted H3N2s using VLP-based HAI

Immunogenicity: Primary endpoint seroconversion

Egg- based Day 28 HAI GMTs and GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	Absolute SCR Difference	
Assay	Strain	SCR	SCR	NanoFlu - Fluzone Quad	95% CI
HAI:EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	22.0% (282/1280)	17.0% (219/1286)	5.0	(1.9, 8.1)
	A/Kansas/14/2017 (H3N2) (Homologous)	41.8% (535/1280)	34.4% (443/1286)	7.3	(3.6, 11.1)
	B/Maryland/15/2016 (Vic) (Homologous)	11.2% (143/1280)	10.7% (137/1286)	0.5	(-1.9, 2.9)
	B/Phuket/3073/2013 (Yam) (Homologous)	31.3% (401/1280)	22.9% (294/1286)	8.5	(5.0, 11.9)

Success:
All 95% CI lower bounds are ≥ -10

- ✓ Seroconversion (SCR) difference success criteria met
- ✓ NanoFlu: 0.5—8.5% increased SCR using egg-based HAI

Immunogenicity: Seroconversion

Egg- or wild-type VLP- based Day 28 HAI GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	Absolute SCR Difference	
Assay	Strain	SCR	SCR	NanoFlu - Fluzone Quad	95% CI
HAI:EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	22.0% (282/1280)	17.0% (219/1286)	5.0	(1.9, 8.1)
	A/Kansas/14/2017 (H3N2) (Homologous)	41.8% (535/1280)	34.4% (443/1286)	7.3	(3.6, 11.1)
	B/Maryland/15/2016 (Vic) (Homologous)	11.2% (143/1280)	10.7% (137/1286)	0.5	(-1.9, 2.9)
	B/Phuket/3073/2013 (Yam) (Homologous)	31.3% (401/1280)	22.9% (294/1286)	8.5	(5.0, 11.9)
HAI:VLP	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	32.7% (419/1280)	21.4% (275/1286)	11.4	(7.9, 14.7)
	A/Kansas/14/2017 (H3N2) (Homologous)	**69.8% (894/1280)**	**49.5% (636/1286)**	**20.4**	**(16.6, 24.1)**
	B/Maryland/15/2016 (Vic) (Homologous)	25.1% (321/1280)	13.5% (173/1286)	11.6	(8.6, 14.6)
	B/Phuket/3073/2013 (Yam) (Homologous)	**35.4% (453/1280)**	**17.7% (228/1286)**	**17.7**	**(14.3, 21.0)**

✓ NanoFlu: 11.4—20.4% increased SCR using VLP-based HAI

Immunogenicity: Seroconversion including drifted strains

Egg- or wild-type VLP- based Day 28 HAI GMTs and GMT ratios (NanoFlu / Fluzone)

		NanoFlu	Fluzone Quad	Absolute SCR Difference	
Assay	Strain	SCR	SCR	NanoFlu - Fluzone Quad	95% CI
HAI:EGG	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	22.0% (282/1280)	17.0% (219/1286)	5.0	(1.9, 8.1)
	A/Kansas/14/2017 (H3N2) (Homologous)	41.8% (535/1280)	34.4% (443/1286)	7.3	(3.6, 11.1)
	B/Maryland/15/2016 (Vic) (Homologous)	11.2% (143/1280)	10.7% (137/1286)	0.5	(-1.9, 2.9)
	B/Phuket/3073/2013 (Yam) (Homologous)	31.3% (401/1280)	22.9% (294/1286)	8.5	(5.0, 11.9)
HAI:VLP	A/Brisbane/02/2018 (H1N1) pdm09 (Homologous)	32.7% (419/1280)	21.4% (275/1286)	11.4	(7.9, 14.7)
	A/Kansas/14/2017 (H3N2) (Homologous)	69.8% (894/1280)	49.5% (636/1286)	20.4	(16.6, 24.1)
	B/Maryland/15/2016 (Vic) (Homologous)	25.1% (321/1280)	13.5% (173/1286)	11.6	(8.6, 14.6)
	B/Phuket/3073/2013 (Yam) (Homologous)	35.4% (453/1280)	17.7% (228/1286)	17.7	(14.3, 21.0)
	A/California ("Drifted" H3N2)	37.1% (475/1280)	20.5% (264/1286)	16.6	(13.1, 20.0)
	A/Cardiff ("Drifted" H3N2)	32.7% (419/1280)	18.6% (239/1286)	14.1	(10.8, 17.5)
	A/Netherlands ("Drifted" H3N2)	38.4% (492/1280)	21.7% (278/1284)	16.8	(13.3, 20.2)
	A/South Australia ("Drifted" H3N2)	34.4% (440/1280)	19.6% (252/1284)	14.7	(11.3, 18.1)

✓ NanoFlu: 14.1—16.8% increased SCR using VLP-based HAI

Topline safety

Safety events (through Day 28)	NanoFlu	Fluzone Quad (SD)
N	**1333**	**1319**
	Counts (%) of Subjects with Events	
Any treatment emergent adverse event (TEAE)	659 (49.4)	551 (41.8)
Any Solicited TEAE	551 (41.3)	420 (31.8)
Local solicited	372 (27.9)	243 (18.4)
Severe local solicited	8 (0.6)	2 (0.2)
Systemic Solicited	369 (27.7)	292 (22.1)
Severe systemic solicited	15 (1.1)	11 (0.8)
Unsolicited TEAE	248 (18.6)	241 (18.3)
Severe unsolicited	23 (1.7)	12 (0.9)
Severe & related unsolicited	10 (0.8)	2 (0.2)
Medically-attended unsolicited	99 (7.4)	104 (7.9)
Serious adverse events (SAEs)	11 (0.8)	5 (0.4)

NanoFlu Phase 3 clinical trial conclusions

Primary endpoint met: demonstrated immunologic non-inferiority to Fluzone in terms of hemagglutination inhibition (HAI) antibody responses (assayed with ***egg-derived virus reagents***) against all four vaccine homologous strains (per CBER criteria).

Statistically significant higher HAI antibody responses (assayed with ***wild-type VLP reagents***) compared to Fluzone:

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