Phase 1/2 Safety & Immunogenicity of an H5 HA mRNA Pandemic Flu Vaccine

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Presenter’s disclosures



Srinivas Nanduri

is a full-time employee of Sanofi and may hold shares in the company



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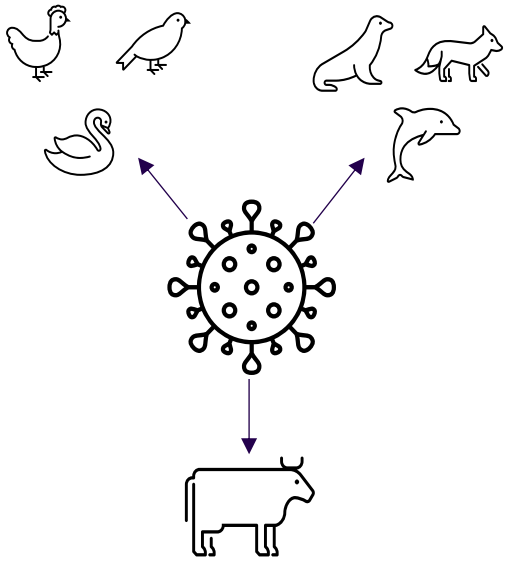
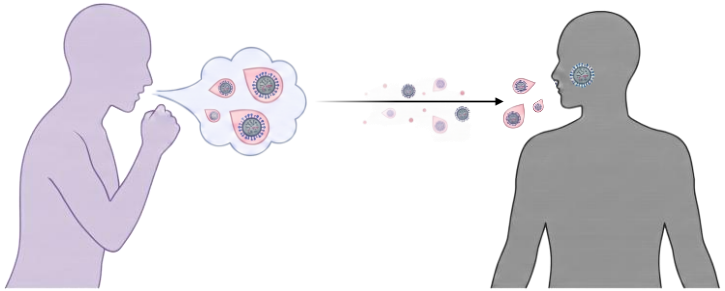
Rapid availability of effective vaccines critical for effective response to a potential H5N1 pandemic

Since 2020, *Clade 2.3.4.4b H5N1 avian influenza A viruses* have caused a panzootic across continents in diverse mammals



Risk for spillover to humans, with possibility of human-to-human transmission and pandemic spread



mRNA-LNP vaccines ideal for pandemic response

- Rapid to manufacture
- Adaptable to new strains quickly
- Antigen design to improve immunogenicity for poorly immunogenic antigens e.g. H5 and other pandemic subtypes

Leveraging structure-based antigen design for pandemic preparedness

Poster P14.112: *Design & development of mRNA vaccine candidate encoding H5-HA for pandemic preparedness*

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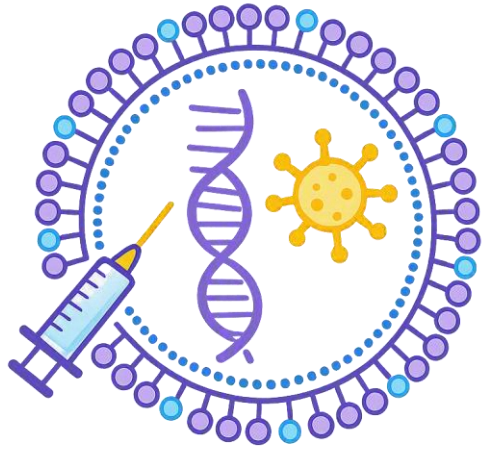
- *Structure-based pre-fusion stabilization* of H5-HA
- *Bioanalytical profile improved over wild-type* with antigen design
- Demonstrated *significantly higher functional antibody titers when compared with wild-type sequence in preclinical studies*
- *Design transferred across diverse H5-HA sequences* for pandemic preparedness



- Study evaluates an mRNA vaccine encoding a structurally optimized H5-HA from the H5N8 A/Astrakhan/3212/2020 strain encapsulated within a lipid nanoparticle

Phase 1/2 study of a *Structurally Designed mRNA Vaccine Candidate* (NCT06907511)

- Randomized, placebo-controlled, modified double-blind, dose-ranging, multi-center study
- 13 sites across the USA



Adults
≥18 years



Two doses 21 days apart of either vaccine (3 dose levels) or placebo

Primary objective

Safety profile

Secondary objective

Immune responses using

Hemagglutination inhibition (HI)

Seroneutralization (SN)

FDA HI thresholds	18-<65	≥65
Minimal lower bound for seroprotection rate – titer ≥1:40	70%	60%
Minimal lower bound for seroconversion rate	40%	30%

*Available from: https://www.fda.gov/files/vaccines,%20blood%20&%20biologics/published/Guidance-for-Industry--Clinical-Data-Needed-to-Support-the-Licensure-of-Pandemic-Influenza-Vaccines.pdf

Key immunogenicity assessment at 21 days following the second dose

Study Arms and Enrolment

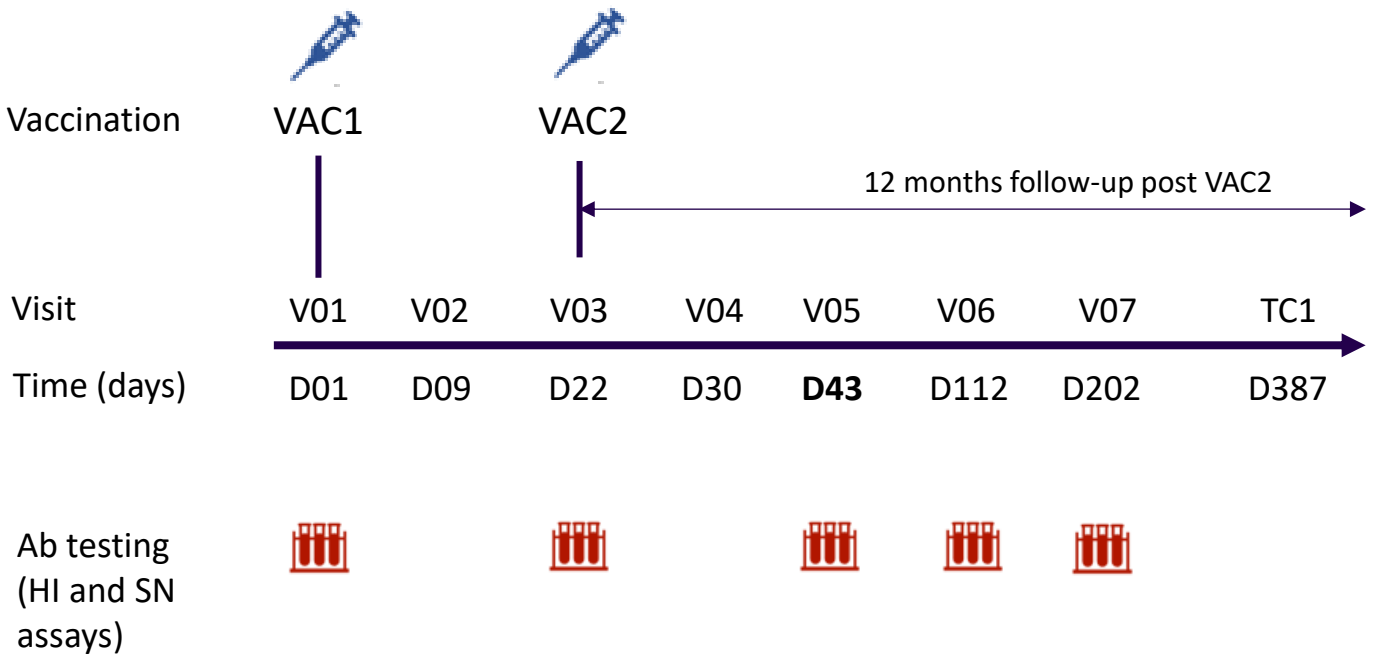
Group		Participants	
		18-<65y	*≥65y*
1	Vx Low dose	30	30
2	Vx Intermediate dose	30	30
3	Vx High dose	30	30
4	Placebo	30	30
	Total	240	

Based on results from an interim analysis

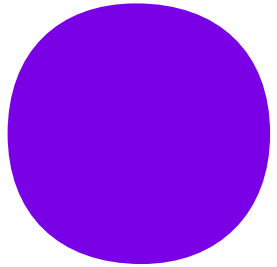
Extension cohort

Group		Participants	
		18-<65y	*≥65y*
1	Vx Low dose	120	120
4	Placebo	120	120
	Total	480	

Graphical Study design



DEMOGRAPHICS



Demographics

Overall, *female preponderance* (55% of enrolled population)

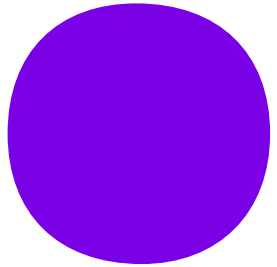
The mean age (± standard deviation [SD])

- *37.7 years (± 11.5) (Group 2) to 48.0 years (± 10.9) (Group 3)* for participants aged 18-64 years
- *69.9 years (± 4.23) (Group 2) to 72.2 years (± 5.43) (Group 3)* for participants aged ≥ 65 years

Most participants were *White* (≥ 56.7% of participants aged 18-64 years and ≥ 72.2% of participants aged ≥ 65 years)

Most participants (≥ 84.0% of participants aged 18-64 years and ≥ 90.0% of participants aged ≥ 65 years) were of *"Not Hispanic or Latino"* ethnicity

SAFETY AND REACTOGENICITY



Safety overview

Safety f/u is ongoing. At time of data analysis, 19 participants (2.6%) reported at least 1 SAE. None of the SAEs were considered as related to the vaccine

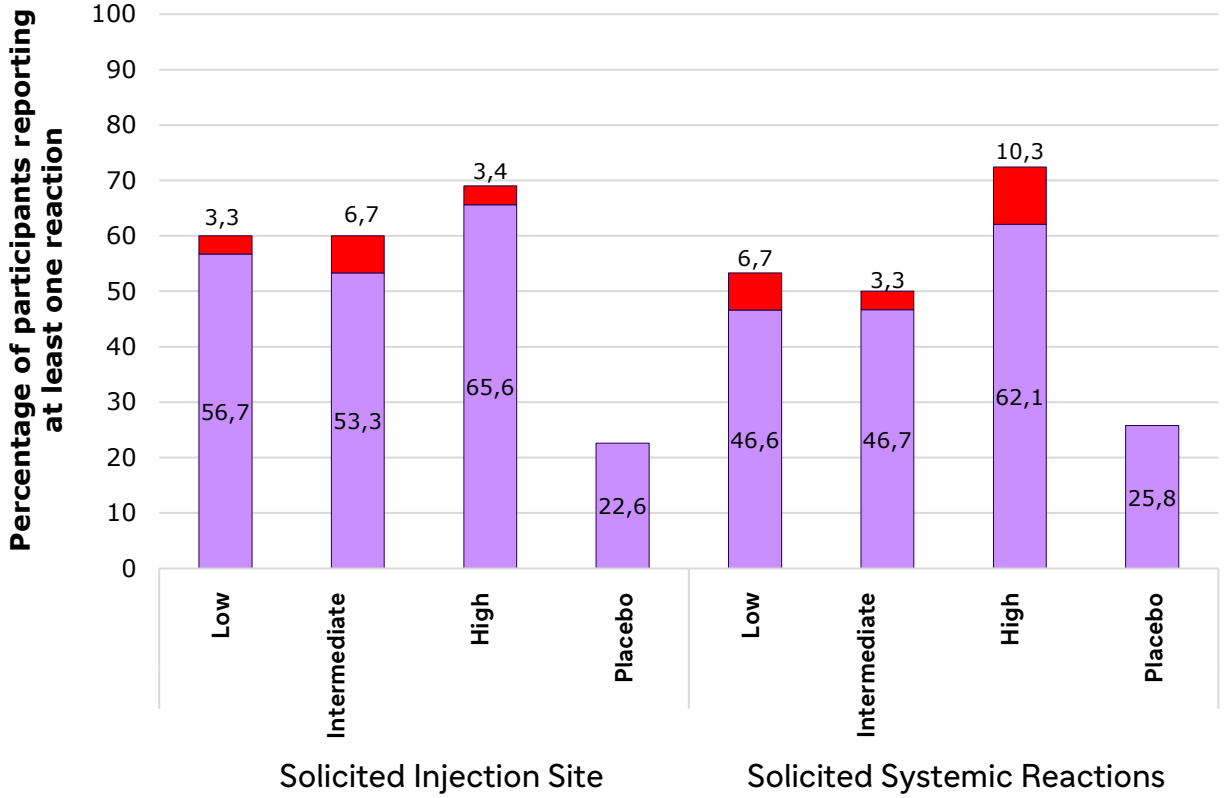
No AESIs reported. One death due to accidental carbon monoxide poisoning - considered unrelated to study intervention

No substantial differences in safety profile was observed between groups

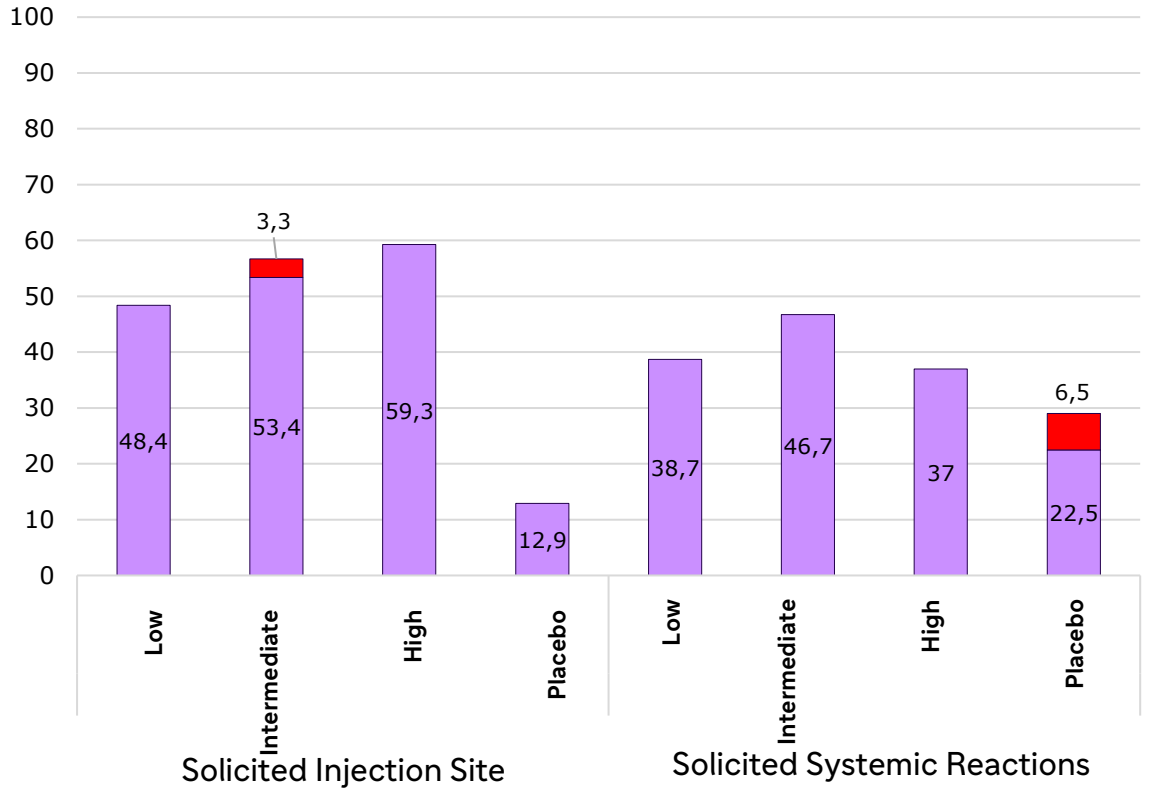
AESI, adverse event of special interest; SAE, serious adverse event

Reactogenicity overview: *Vaccine well tolerated* / Rates of solicited reactions higher in mRNA arms compared with placebo, but *infrequent grade 3 reactions*

Summary of solicited reactions within 7 days after any vaccine injection



18-<65 years

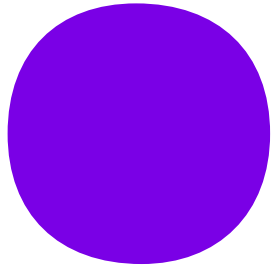


≥65 years

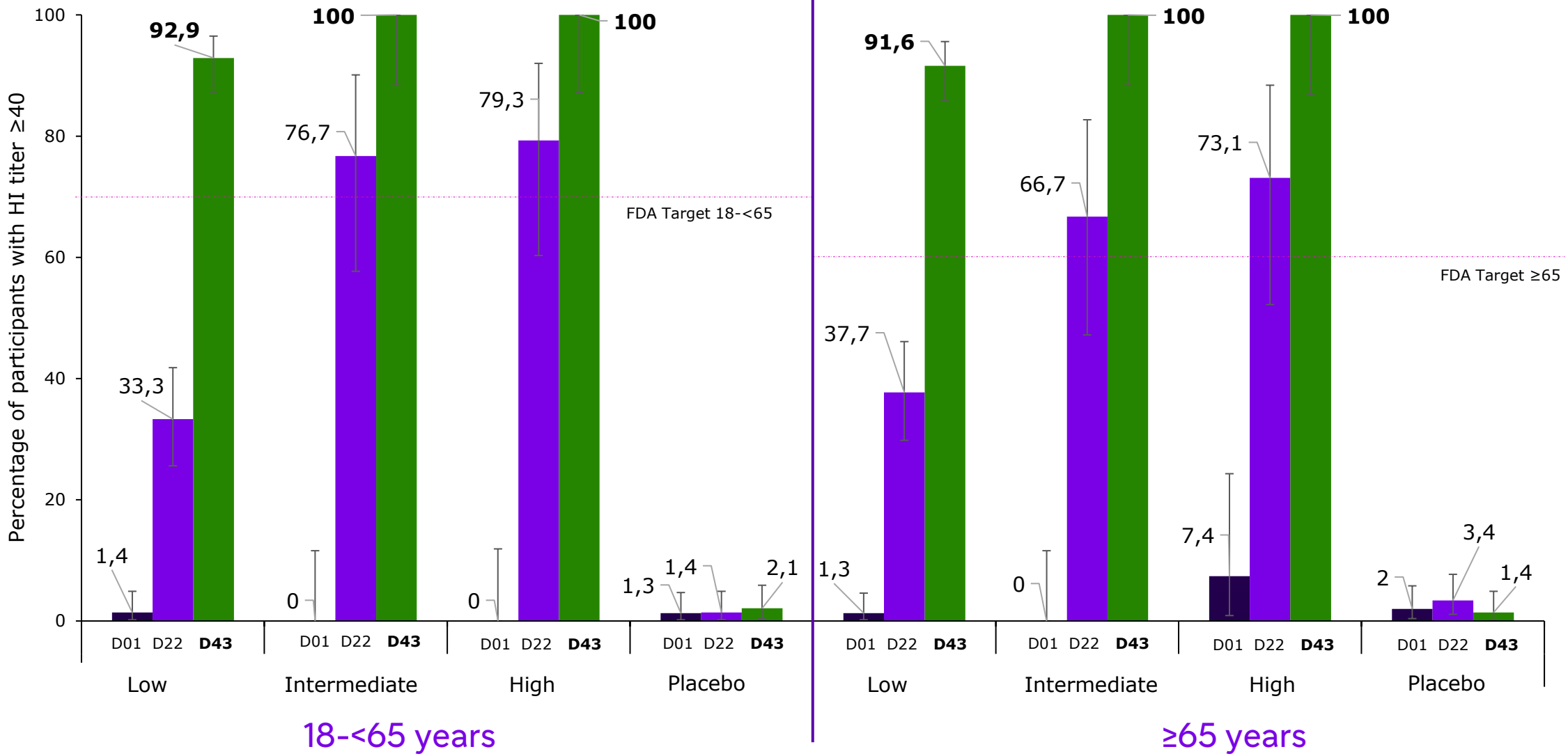
Grade 1 & 2
Grade 3

Results are preliminary and subject to change following study completion and final analysis

IMMUNOGENICITY



At Day 43, HI seroprotection rates exceeded FDA thresholds at all tested dose levels across both age groups



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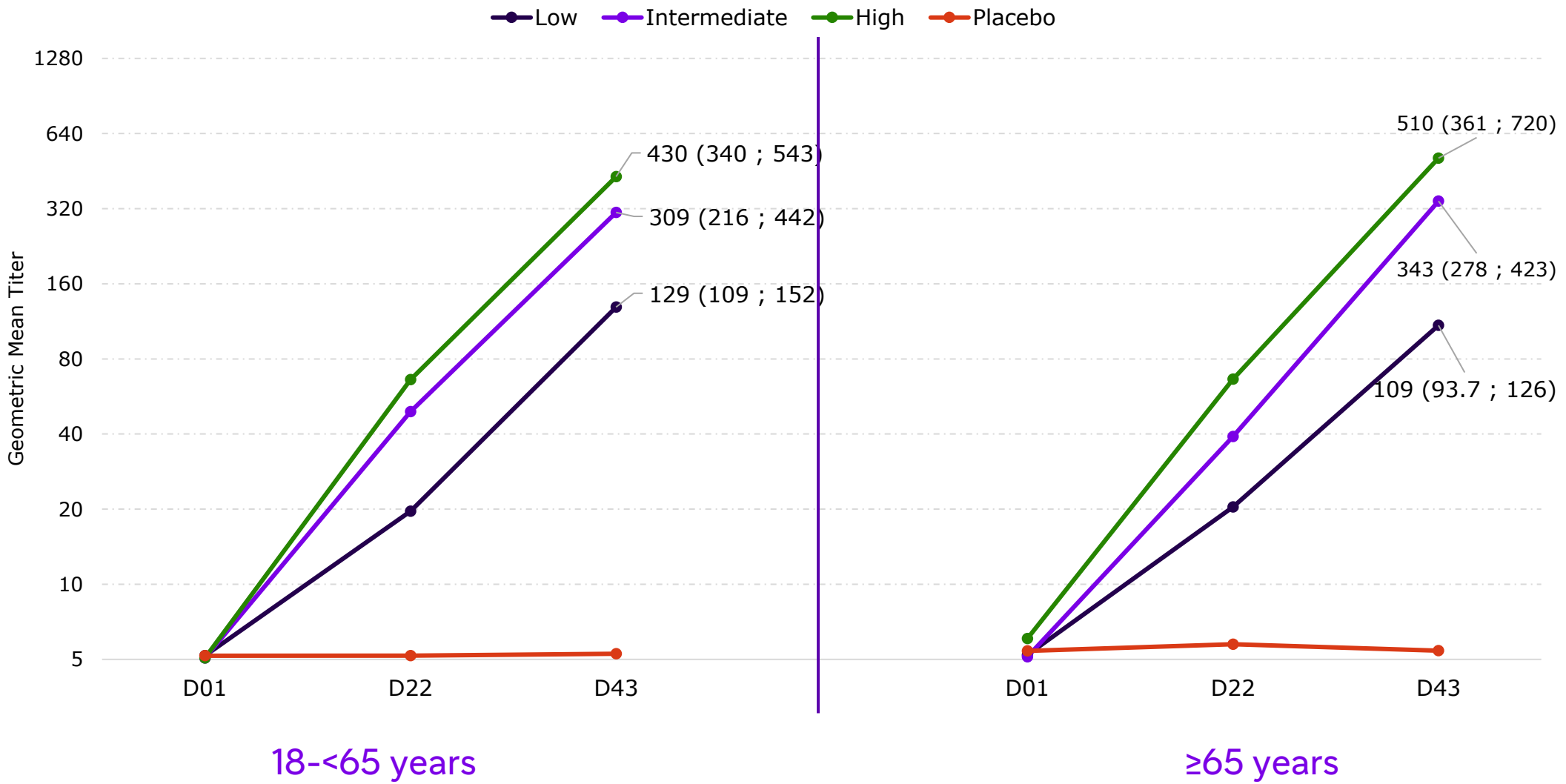
Robust increases in HI GMT from baseline to D43 – Higher titers with increasing dose



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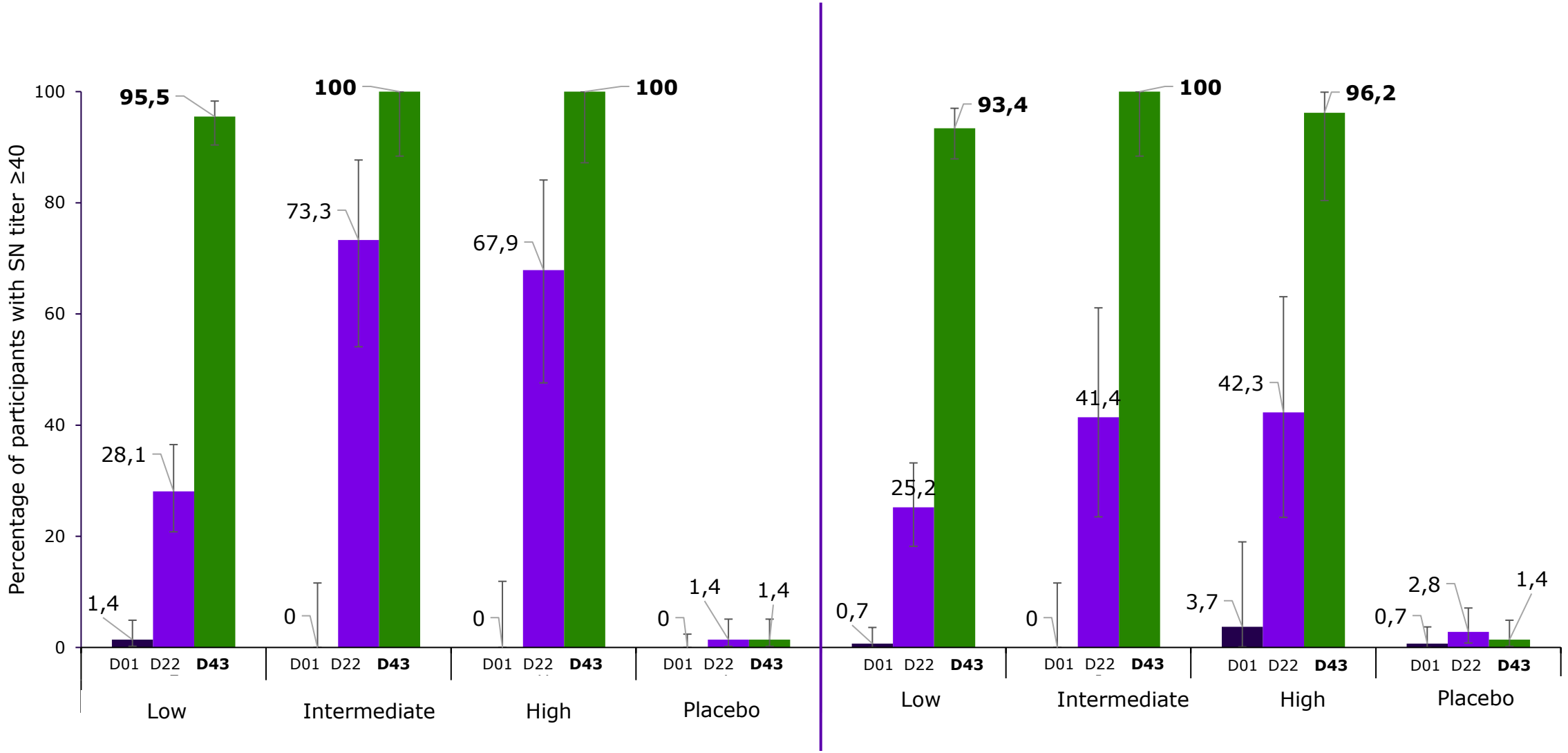
At Day 43, SN titers ≥1:40 observed in ≥93% across all dose groups in both age groups



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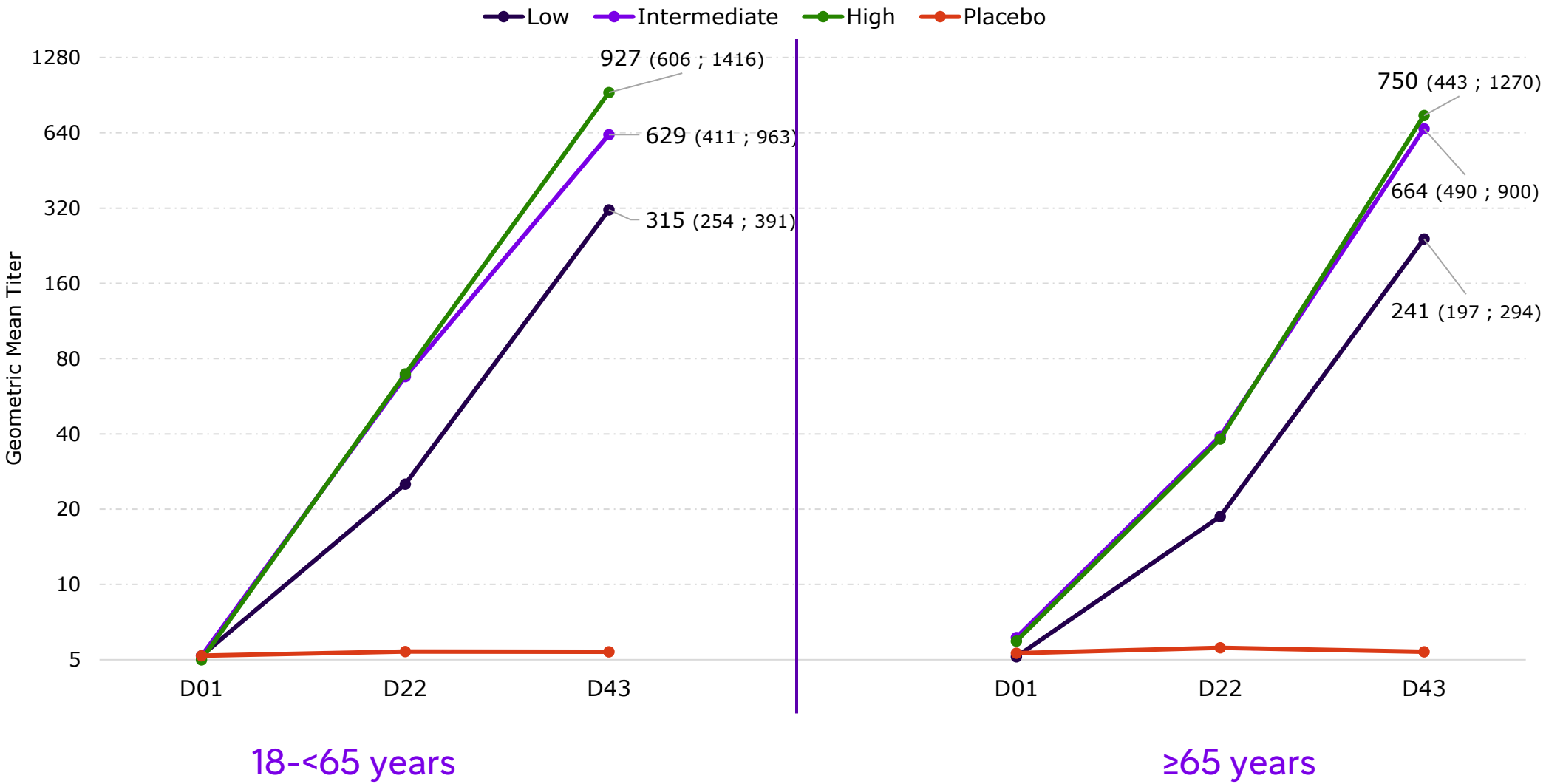
As with HI, *robust increases in SN GMT from baseline to D43* – Higher titers with increasing dose



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Conclusion



Safe & well-tolerated

Infrequent severe solicited reactions. No related severe adverse events



Strong HI response exceeding targets

Seroprotection rate at D43 exceeded FDA criteria in both 18-<65 and ≥ 65 years age groups



Strong neutralizing Ab response

≥ 93% of participants across all dose groups achieved SN titers ≥1:40

The H5 HA mRNA vaccine is a *promising pandemic preparedness vaccine candidate*

Thank you



