Safety and Immunogenicity of mRNA-1403, a Multivalent Norovirus mRNA Vaccine in Healthy Adults:

Interim Results of a Phase 1/2, Randomized, Observer-Blind, Placebo-Controlled, Dose-Ranging Trial

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- **Disclosures**
  - T.S, B.A.B., K.M., W.Y., L.B., T.B., E.L., K.B.C, A.R., M.W., D.F. and J.O. are employees of Moderna, Inc., and may hold stock/stock options in the company.
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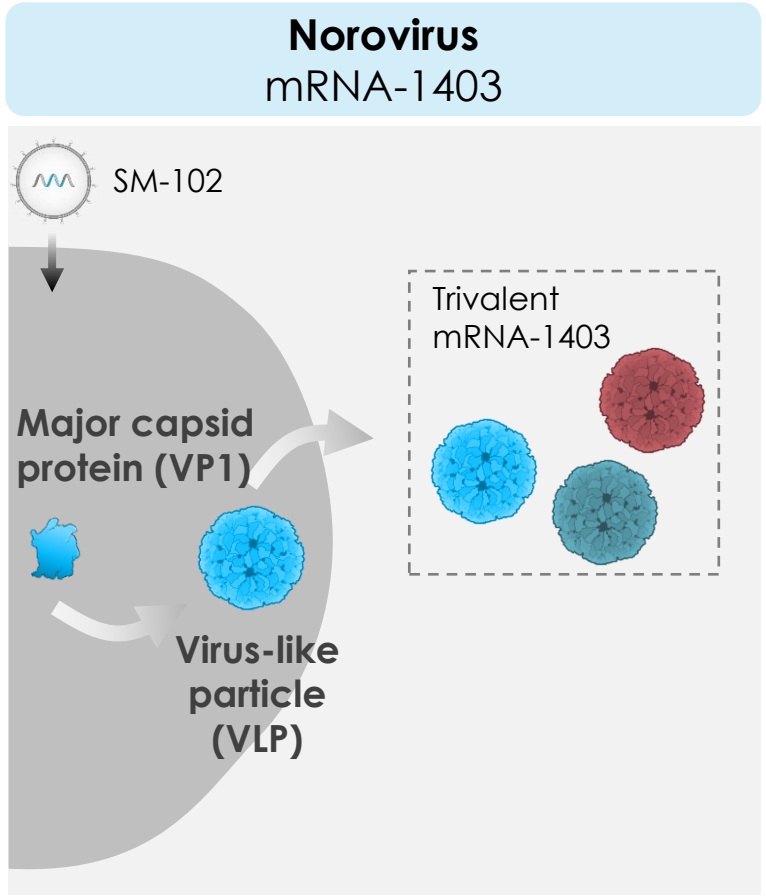
mRNA-1403: mRNA-based multivalent Norovirus (NoV) vaccine

- NoV is the leading cause of acute gastroenteritis (AGE) globally with estimated ~685M cases and 200K deaths annually[1,2]
  - Risk of severe outcomes from NoV is highest in young children and older adults[1,2,3]
- NoV's broad and shifting genotype diversity and limited cross-genotype protection pose challenges to vaccine development[2,3]
  - A multivalent mRNA vaccine could cover the most prevalent genotypes and would be amenable to composition updates to address changes in genotype prevalence[3,4,5]
- mRNA-1403 is a trivalent NoV vaccine candidate using the same LNP technology as Spikevax®/mRESVIA®
  - mRNAs encoding for major capsid protein (VP1) of 3 globally prevalent NoV genotypes GII.4, GI.3 and GII.3
  - Upon expression NoV VP1 self-assembles into VLPs



1. Lopman. Global Burden of Norovirus and Prospects for Vaccine Development. https://www.cdc.gov/norovirus/downloads/global-burden-report.pdf; 2. Mattison et al. Expert Rev Vaccines. 2018; 3. Carlson KB et al npj Vaccines 2024; 4. Cannon et al Emerging Infect. Dis. 2021; 5. Calderwood et al. Clin Infect Dis 2022; LNP, lipid nanoparticle; VLP, virus-like particle

Ongoing Phase 1/2 study in healthy younger and older adults (NCT05992935)

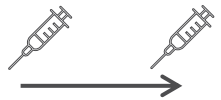
In this ongoing Phase 1/2, randomized, placebo-controlled, observer-blind, dose-ranging study, safety and immunogenicity of mRNA-1403* are being evaluated in healthy adults 18 to 80 years of age

Phase 1*

Healthy adults 18-49 and 60-80 years

mRNA-1403
Low (n=60)
Medium (n=60)
High (n=60)
Highest (n=60)
Highest[a] (n=60)
Placebo (n=30)

[a]Arm received Placebo Day 1 and single injection of 1403 on Day 29



Two i.m. injections, 0,1 month-schedule

Phase 2

Healthy adults 18-59 and 60-80 years

mRNA-1403
Low (n=100)
Medium (n=200)
High (n=200)
Placebo (n=100)

Single i.m. injection

Safety endpoints

- **Solicited** local and systemic **ARs** through 7 days after each injection
- **Unsolicited AEs** through 28 days after each injection
- **MAAEs** through 6 months after last injection
- **SAEs, AESIs, AEs leading to study or vaccine discontinuation** through 12 months after last injection
- **Safety laboratory abnormalities** through 7 days after each injection in a subset (Ph1 only)

Immunogenicity endpoints

- **Serum HBGA-blocking antibody titers** against **vaccine-matched NoV genotypes at 28 days after each injection**
- **Serum NoV VLP-binding antibody levels** against **vaccine-matched NoV genotypes at 28 days after each injection**

Site location(s)
Multiple US sites

*NCT05992935 Ph1 portion is also evaluating a second vaccine candidate, mRNA-1405, which is not the subject of the presentation

i.m., intramuscular; AR, adverse reaction; AE, adverse event; MAAE, medically-attended adverse event; SAE, serious adverse event; AESI, adverse event of special interest; HBGA, histo-blood group antigen; VLP, virus-like particle

Interim results from the ongoing Phase 1/2 study in healthy younger and older adults (NCT05992935)

Interim analyses focused on supporting initiation of a Phase 3 trial to demonstrate safety and efficacy of a single-dose regimen of mRNA-1403 in adults 18 years of age (YOA) and older; presentation will summarize:

- Phase 2 reactogenicity through 7 days (all participants) and humoral immunogenicity through 28 days (in a subset) after a single injection
- Unsolicited adverse events through 8 months after first injection in Phase 1 and through 1 month after single injection in Phase 2

Phase 1

Demographic characteristics in Safety Set*

		18–49 YOA	60–80 YOA
N		188	147
Mean age (SD)		37.2 (7.93)	67.8 (5.33)
Gender (% female)		58.0%	55.1%
Race	White	64.4%	74.1%
	African American	20.2%	24.5%
Ethnicity	Not Hispanic or Latino	80.3%	93.9%

Median duration of follow-up: 240 days from first injection

Phase 2

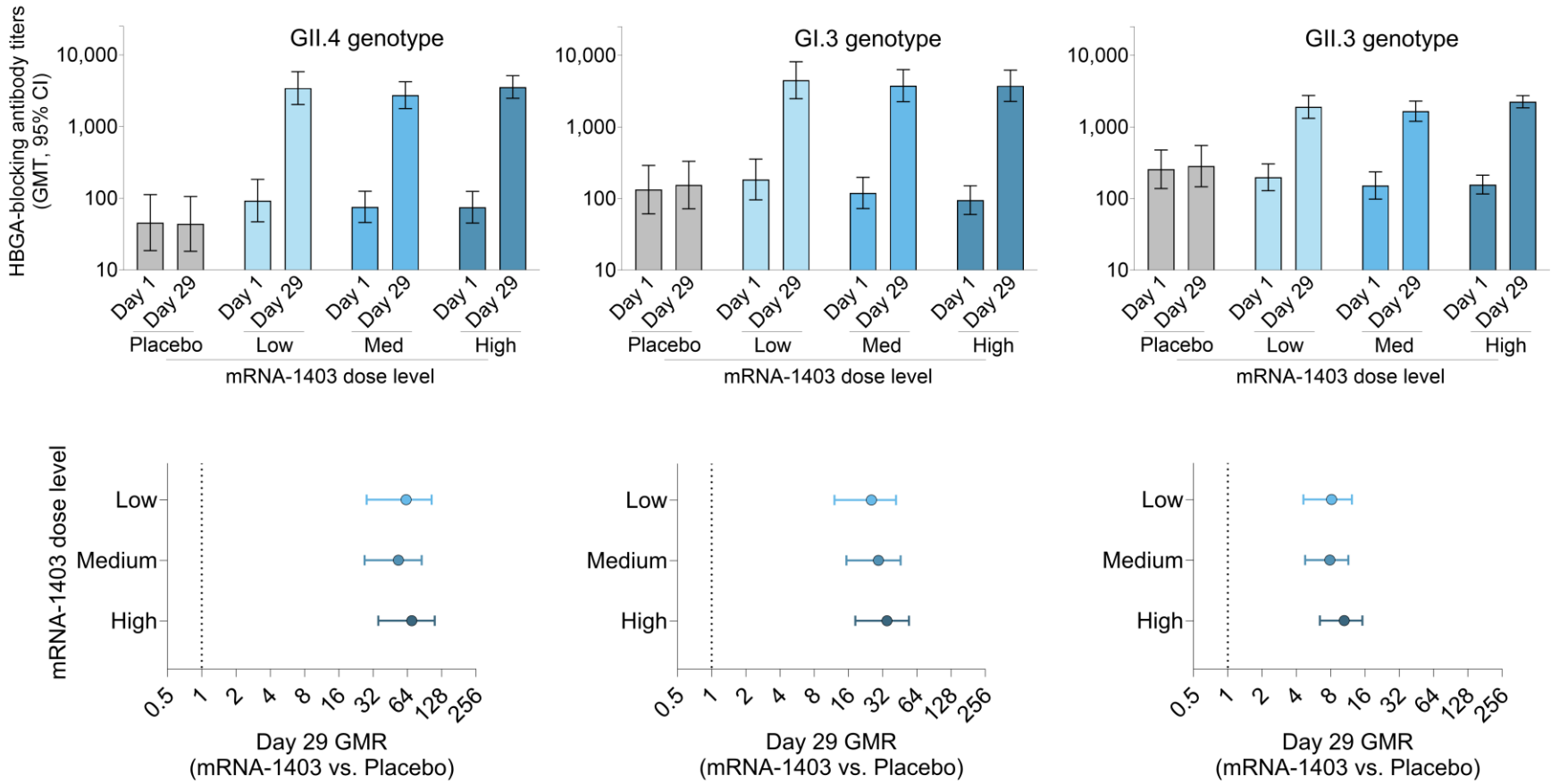
Demographic characteristics in Safety Set*

		18–59 YOA	60–80 YOA
N		335	281
Mean age (SD)		42.8 (11.33)	68.4 (5.66)
Gender (% female)		56.1%	57.3%
Race	White	66.6%	83.3%
	African American	24.5%	13.9%
Ethnicity	Not Hispanic or Latino	77.3%	90.7%

Median duration of follow-up: 36 days from injection

*Safety Set includes all participants who received at least one study injection; YOA, year of age; SD, standard deviation

Immunogenicity of single injection mRNA-1403 in Phase 2: Serum HBGA-blocking antibodies in younger adults (18-59 years of age)



- **A single injection of mRNA-1403 elicited robust HBGA-blocking antibody titers against all three vaccine-matched NoV genogroup I and II genotypes in younger adults across all dose levels**

HBGA, Histo-blood group antigen; NoV, norovirus; GMR, geometric mean ratio
Serum immunogenicity data generated in subset of ~30% of total Phase 2 study cohort

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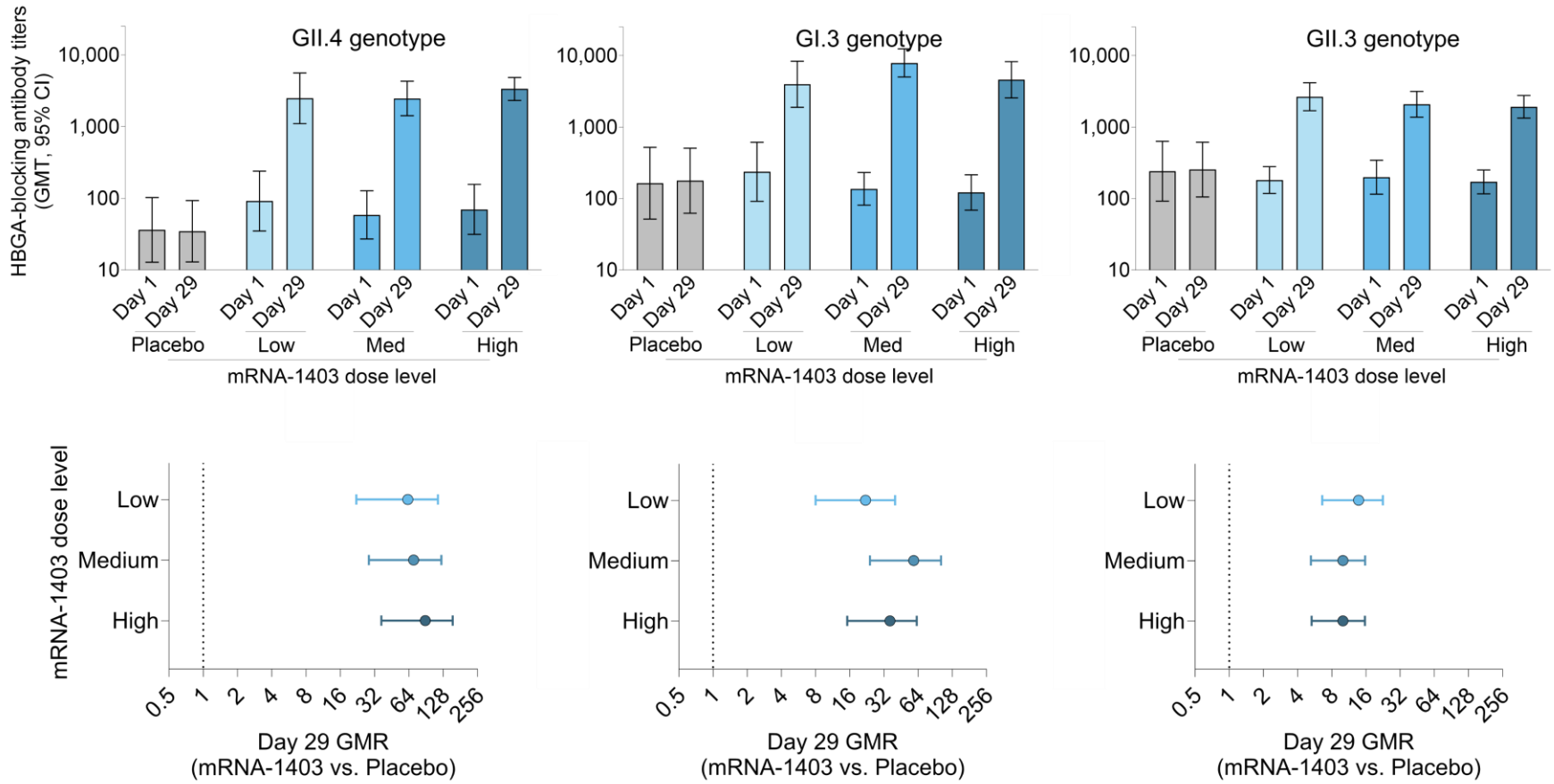
Immunogenicity of single injection mRNA-1403 in Phase 2: Serum HBGA-blocking antibodies in older adults (60-80 years of age)



- **A single injection of mRNA-1403 elicited robust HBGA-blocking antibody titers against all three vaccine-matched NoV genogroup I and II genotypes in older adults across all dose levels (similar to responses elicited in younger adults)**

HBGA, Histo-blood group antigen; NoV, norovirus; GMR, geometric mean ratio
Serum immunogenicity data generated in subset of ~30% of total Phase 2 study cohort

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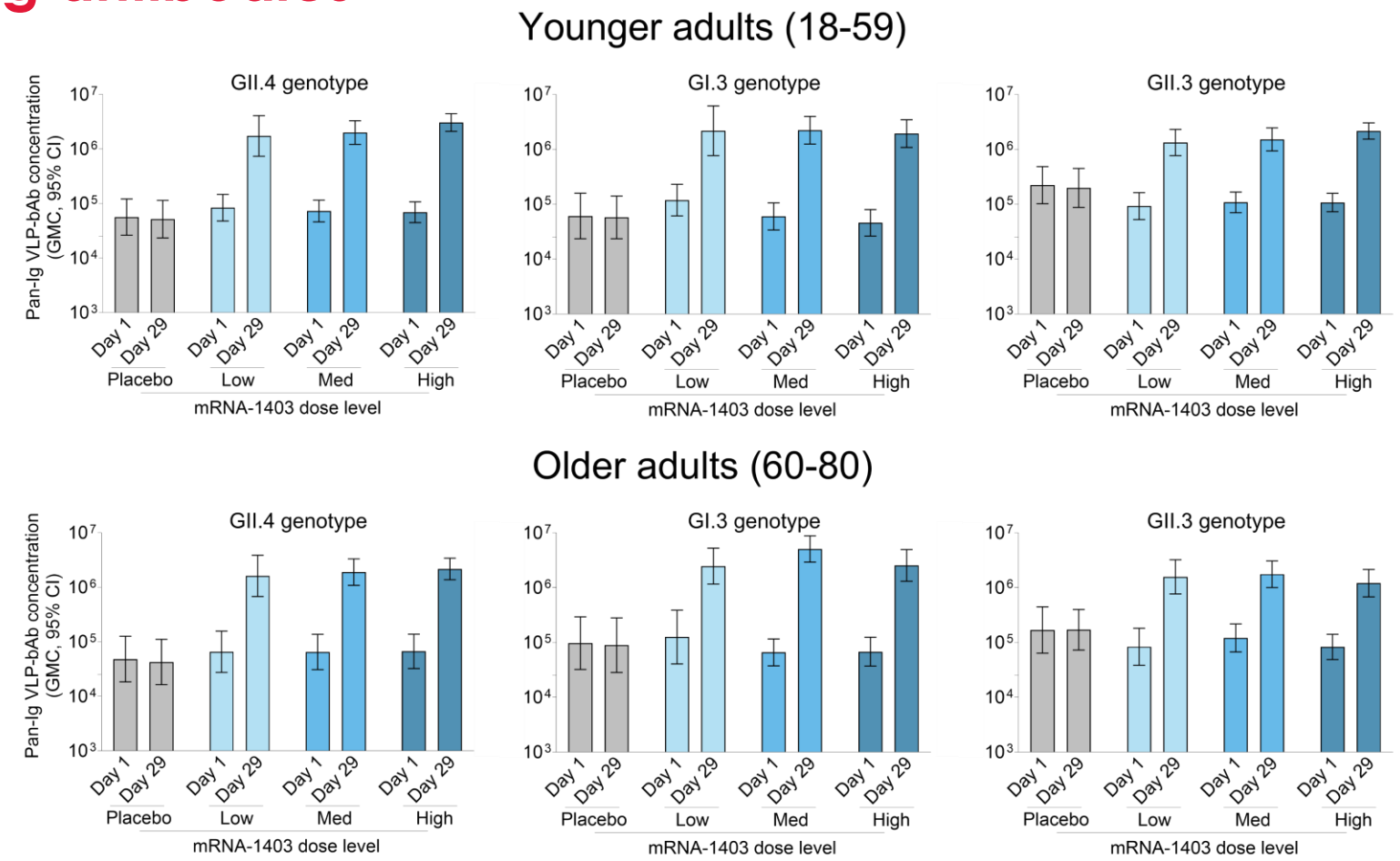
Immunogenicity of single injection mRNA-1403 in Phase 2: Serum VLP-binding antibodies



- **A single injection of mRNA-1403 also elicited robust Pan-Ig NoV VLP-binding antibody levels against vaccine-matched NoV genogroup I and II genotypes in both younger and older adults**

VLP, virus-like particle; Pan-Ig, pan-Immunoglobulin; bAb, binding antibody; NoV, norovirus
Serum immunogenicity data generated in subset of ~30% of total Phase2 study cohort

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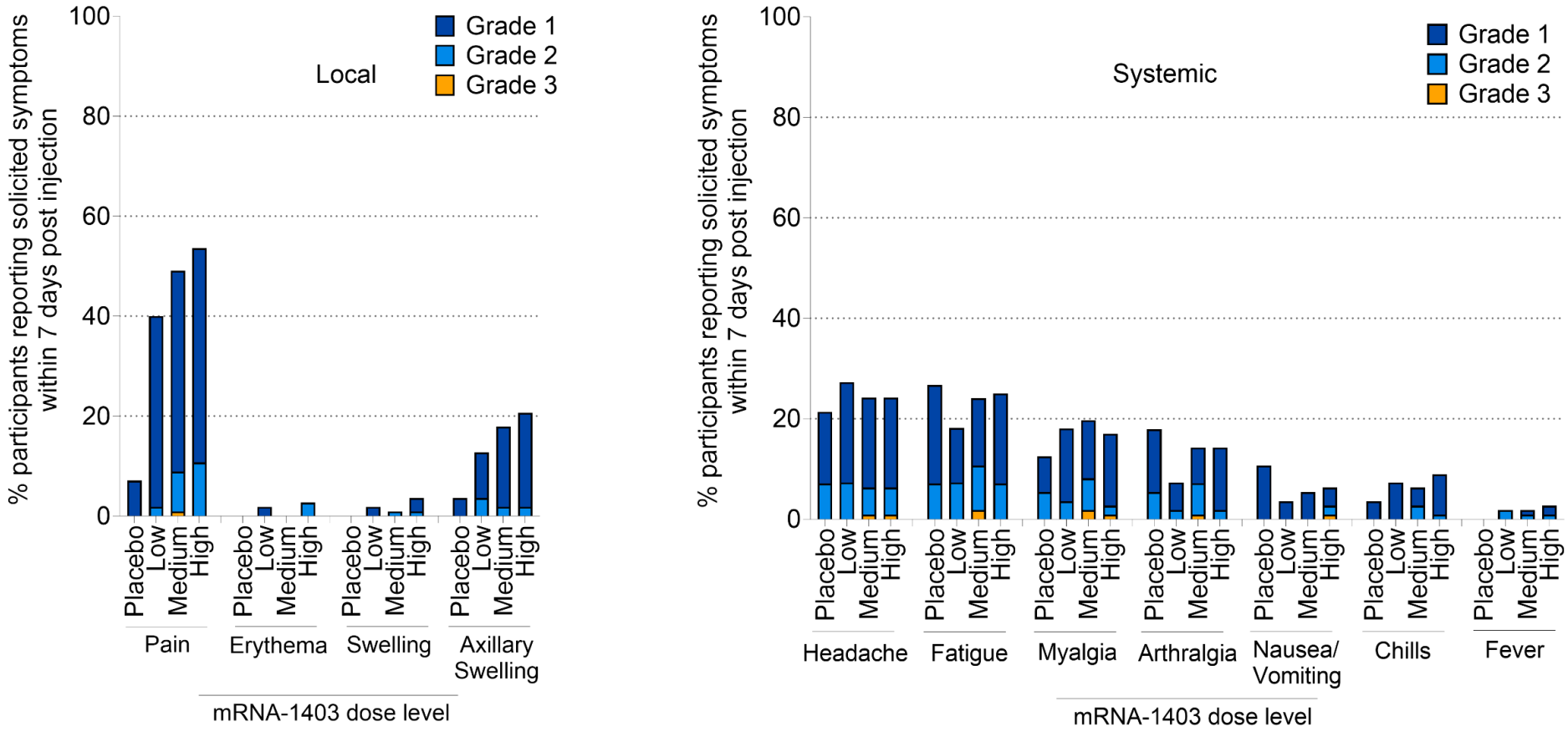
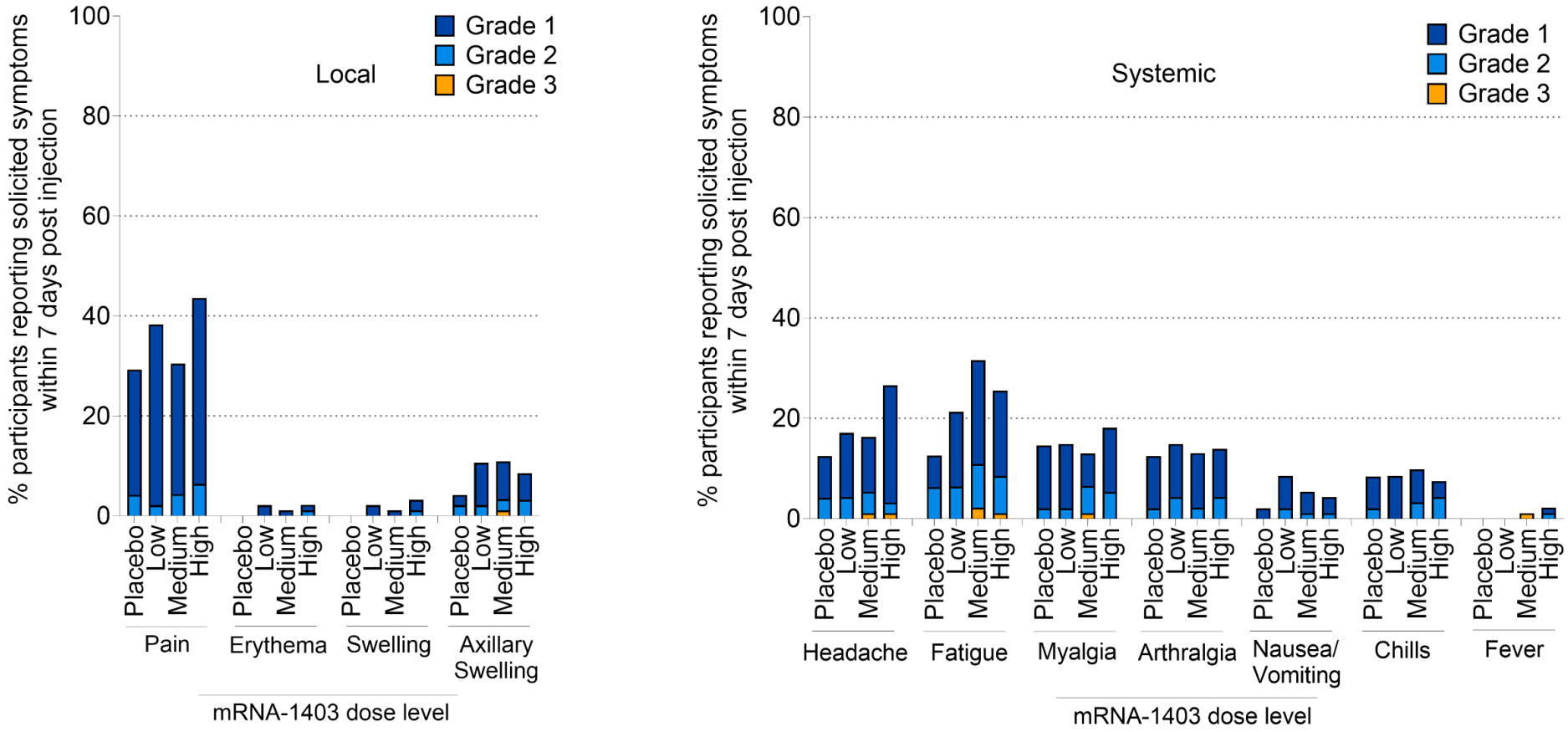
Reactogenicity after single injection of mRNA-1403 in younger adults 18-59 years of age in Phase 2



- **A single injection of mRNA-1403 was well-tolerated across dose levels tested in younger adults**
- **Adverse reactions were mostly Grade 1 or 2 in severity, few Grade 3, no Grade 4 reactions**
- **Median onset within 1 day after mRNA-1403 injection and median duration 2-3 days**

Reactogenicity after single injection of mRNA-1403 in older adults 60-80 years of age in Phase 2



- **A single injection of mRNA-1403 was well-tolerated across dose levels tested in older adults**
- **Adverse reactions were mostly Grade 1 or 2 in severity, few Grade 3, no Grade 4 reactions**
- **Median onset within 2 days after mRNA-1403 injection and median duration 2-3 days**

Summary of unsolicited adverse events across Phase 1 and Phase 2

Phase 1

- **Up to 28 days after any injection**
  - No SAEs, deaths, AESIs or AEs leading to study withdrawal; 1 participant discontinued study injection due to AEs of perioral dermatitis and dermatitis considered injection-related
- **Throughout the study**
  - No deaths or AEs leading to study withdrawal; 1 additional participant discontinued study injection due to AE considered unrelated to injection
  - No SAEs, AESIs, MAAEs or moderate/severe AEs considered related to study injection

Phase 2

- **Up to 28 days after single injection**
  - No deaths, AESIs or AEs leading to study withdrawal
  - No SAEs, MAAEs or severe AEs considered injection-related; injection-related AEs mostly mild, few moderate

- **No safety concerns identified for mRNA-1403 through 8 months of follow-up in Phase 1 and 1 month of follow-up in Phase 2**
- **No clinically meaningful or dose-dependent trends in unsolicited AEs evident among participants who received mRNA-1403 compared to placebo**

AE, adverse event; SAE, serious adverse event; AESI, adverse event of special interest; MAAE, medically-attended adverse event
*AESIs included medical concepts of interest in vaccine safety surveillance per Brighton Collaboration and Safety Platform for Emergency Vaccines: thrombocytopenia, Guillain-Barré-Syndrome, acute disseminated encephalomyelitis, Bell's palsy, seizures, anaphylaxis and myocarditis/pericarditis

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Conclusions

- **Immunogenicity of mRNA-1403 in adults:**
  - A single injection of mRNA-1403 elicited robust serum HBGA-blocking antibody responses against all three NoV vaccine genotypes, across all dose levels evaluated in both younger and older adults
  - Similar findings were observed with serum VLP-binding antibody responses

- **Reactogenicity and safety of mRNA-1403 in adults:**
  - A single injection of mRNA-1403 was well-tolerated and showed a favorable reactogenicity profile across dose levels in both younger and older adults
  - No safety concerns identified through 8 months of follow-up in Ph1 and 1 month of follow-up in Ph2

Available data supported initiation of a Phase 3 study (NCT06592794) evaluating efficacy of a single dose primary schedule of mRNA-1403 in prevention of moderate to severe NoV AGE in adults

HBGA, Histo-blood group antigen; NoV, norovirus; VLP, virus-like particle

Thank you

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