# Moderna's Respiratory Vaccines: hMPV/PIV3 vaccine (mRNA-1653)

*Last program update: February 24, 2022*

| Modality | Program | ID # | Preclinical development | Phase 1 | Phase 2 | Phase 3 | Commercial | Moderna rights |
|---|---|---|---|---|---|---|---|---|
| Adults | COVID-19 vaccine | mRNA-1273/Spikevax® | | | | | | Worldwide |
| | | mRNA-1273.351 | Beta variant | | | | | Worldwide |
| | | mRNA-1273.617 | Delta variant | | | | | Worldwide |
| | | mRNA-1273.211 | Beta variant + wild-type | | | | | Worldwide |
| | | mRNA-1273.213 | Beta + Delta variant | | | | | Worldwide |
| | | mRNA-1273.529 | Omicron variant | | | | | Worldwide |
| | | mRNA-1273.214 | Omicron + wild-type | | | | | Worldwide |
| | | mRNA-1283 | Next generation (2-5 °C) | | | | | Worldwide |
| Prophylactic vaccines | Flu vaccine | mRNA-1010 | | | Phase 3 prep | | | Worldwide |
| | | mRNA-1011 | | | | | | Worldwide |
| | | mRNA-1012 | | | | | | Worldwide |
| | | mRNA-1020 | | | | | | Worldwide |
| | | mRNA-1030 | | | | | | Worldwide |
| | COVID + Flu vaccine | mRNA-1073 | | | | | | Worldwide |
| | Older adults RSV vaccine | mRNA-1345 | | | | | | Worldwide |
| Adolescents & Pediatrics | COVID-19 vaccine (adolescents) | mRNA-1273 | TeenCOVE | | | | | Worldwide |
| | COVID-19 vaccine (pediatrics) | mRNA-1273 | KidCOVE | | | | | Worldwide |
| | Pediatric RSV vaccine | mRNA-1345 | | | | | | Worldwide |
| | Pediatric hMPV + PIV3 vaccine | mRNA-1653 | Phase 1b | | | | | Worldwide |
| | Pediatric RSV + hMPV vaccine | mRNA-1365 | | | | | | Worldwide |



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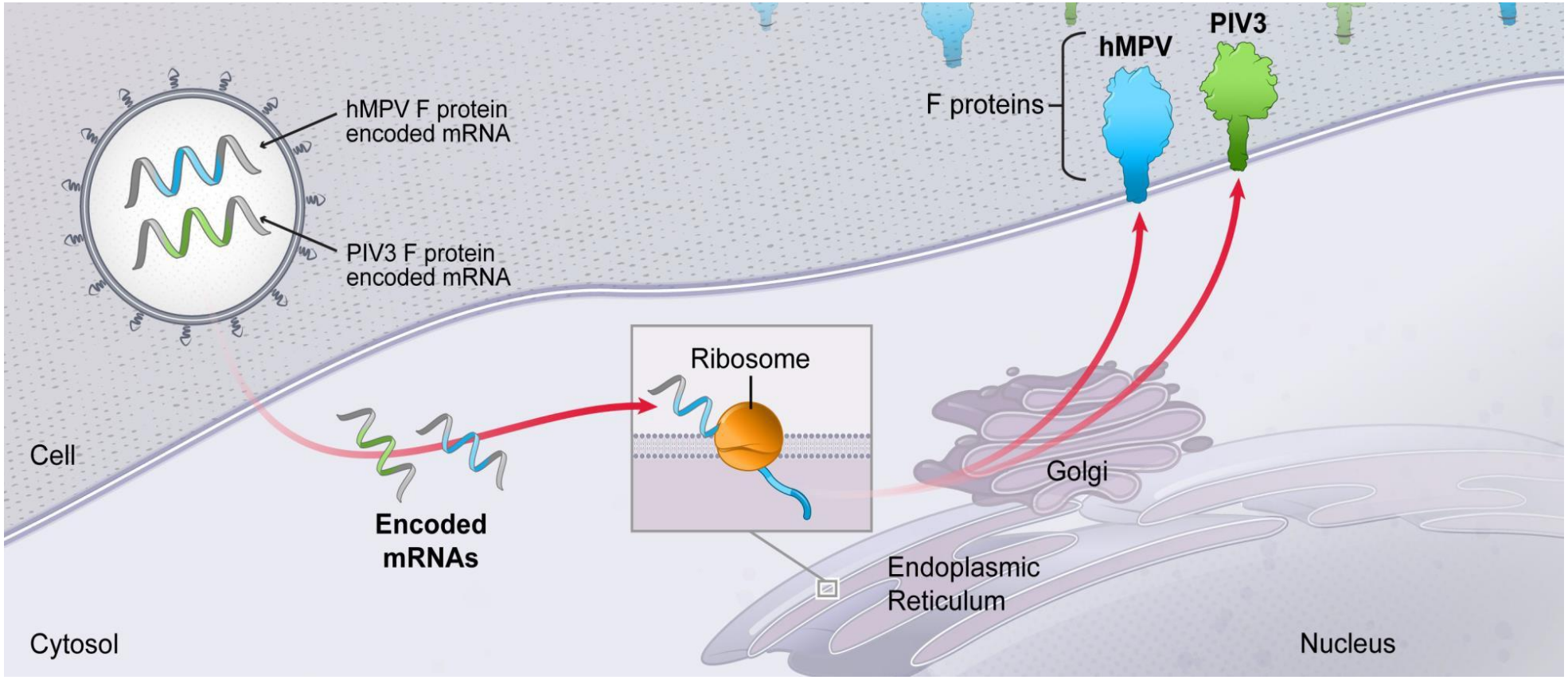
# hMPV/PIV3 vaccine (mRNA-1653) combines mRNAs encoding antigens from two different viruses



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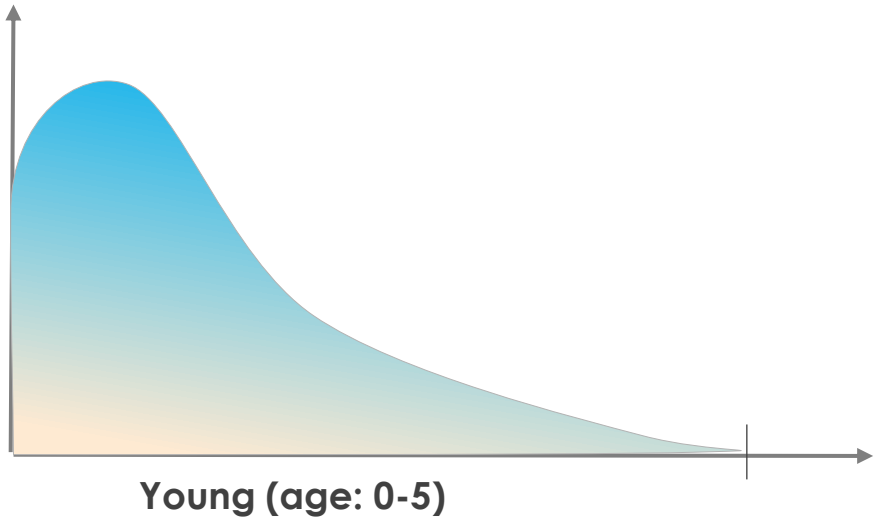
# Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) represent a high unmet need in young children

**Burden of hMPV/PIV3**
*(illustrative)*




Most hMPV or PIV3-associated hospitalizations in children occur under 2 years old

Hospitalization rates in children < 5 years old in the U.S.:

- hMPV: 1.2 per 1,000
- PIV3: 0.5 per 1,000

hMPV/PIV3 infection sequelae:

- High fever
- Otitis media
- Thick nasal discharge
- Breathing difficulties, coughing
- Croup
- Pneumonia
- Bronchiolitis



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# hMPV/PIV3 vaccine (mRNA-1653) Phase 1b fully enrolled

## Overview

- To evaluate the safety and immunogenicity of mRNA-1653 when administered to adults and to children 12-59 months of age with serologic evidence of prior exposure to hMPV and PIV3

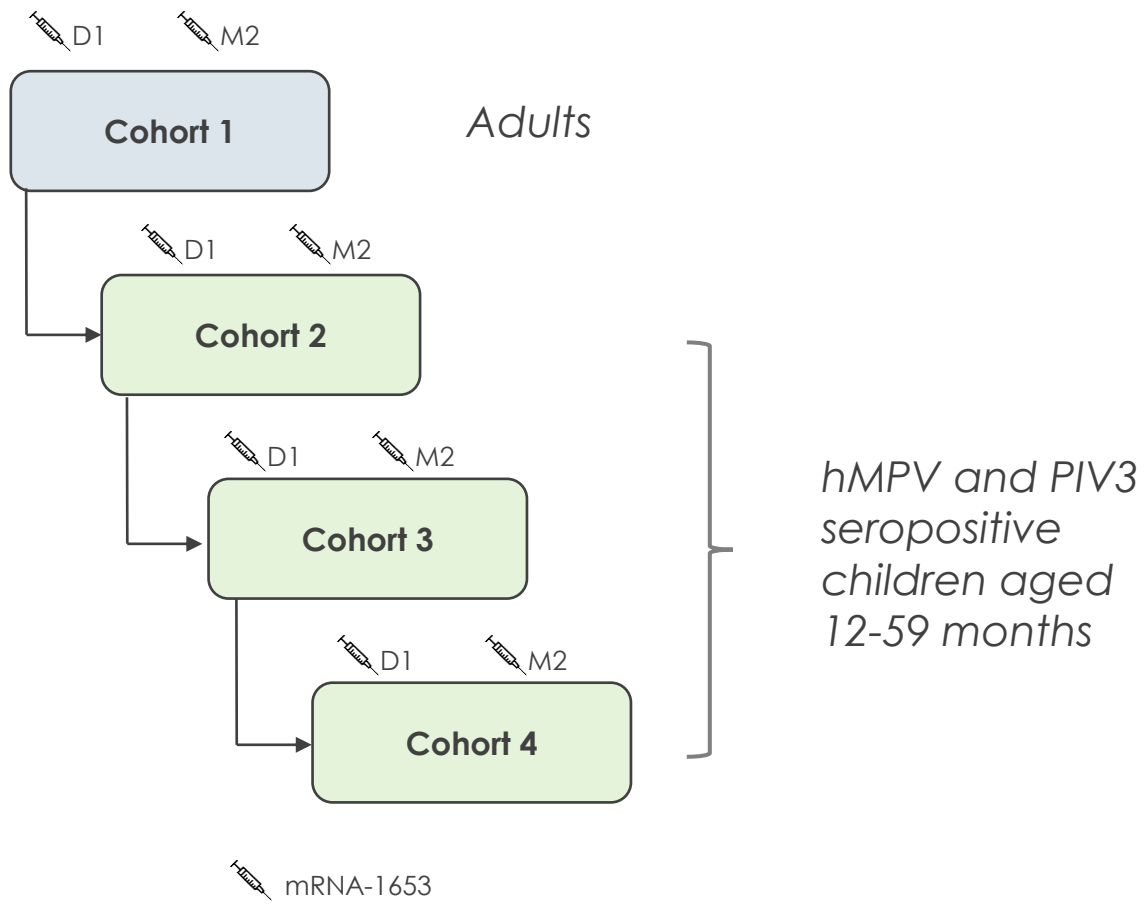
## Outcome Measures

- Safety and immunogenicity
  - Neutralizing antibodies against hMPV and PIV3

## Trial progress

- Interim data from the adult cohort in this study corroborated the data shared in 2019 from our first Phase 1 study (hMPV and PIV3 neutralization titers were boosted ~6X and ~3X baseline, respectively)
- Recent interim data also show that mRNA-1653 boosts hMPV and PIV3 titers in seropositive children

## Phase 1 trial design



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# Preclinical and Phase 1 clinical data



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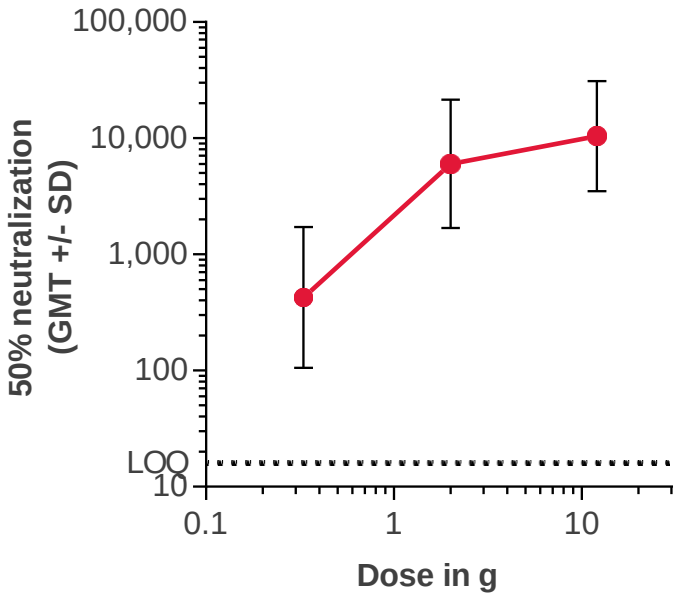
# hMPV/PIV3 vaccine (mRNA-1653)

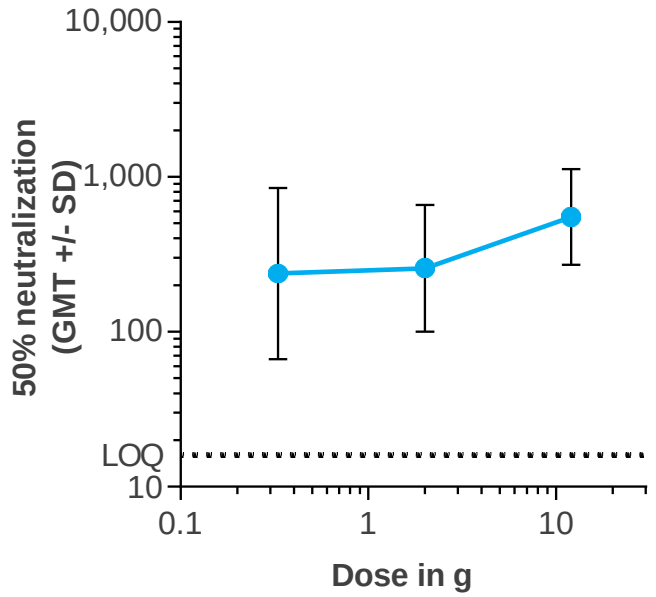
## *Preclinical data – combo vaccine generates neutralizing titers against each virus*

*Species:*
**Mouse**

**hMPV neutralizing titers with hMPV/PIV3 mRNA vaccine**




**PIV3 neutralizing titers with hMPV/PIV3 mRNA vaccine**




**Pre-clinical studies of hMPV and PIV3 combination vaccine demonstrated ability to generate robust neutralizing antibody titers. In separate experiments in NHP (not shown) vaccination conferred protection against hMPV or PIV3 viral challenge**



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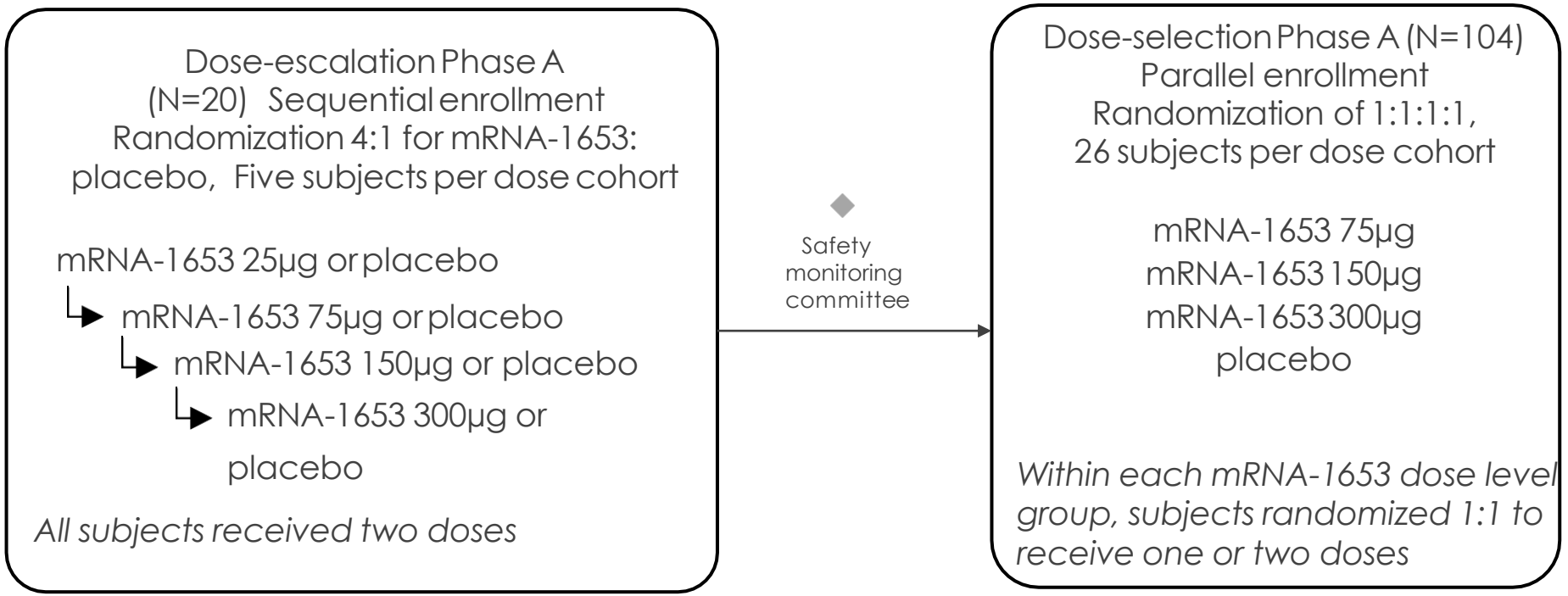
# hMPV/PIV3 vaccine (mRNA-1653)

## *Preclinical data – combo vaccine generates neutralizing titers against each virus*

### Key Objectives

- Evaluate safety and immunogenicity through 12 months after the second vaccination
- Select optimal dose and vaccination schedule for further clinical development

*Dosing schedule: Day 1 and month 1*



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# hMPV/PIV3 vaccine (mRNA-1653)

## *Phase 1 in healthy adults; Interim results, through 1 month*

**Unsolicited Adverse Events, Through 28 Days After Each Vaccination Exposed Set**

| Dose Level (µg) | 25 | 75 | | 150 | | 300 | | Placebo |
|---|---|---|---|---|---|---|---|---|
| Dose Schedule | 2-dose | 1-dose | 2-dose | 1-dose | 2-dose | 1-dose | 2-dose | |
| N | 4 | 13 | 17 | 13 | 17 | 13 | 17 | 30 |
| ≥ 1 event | 3 (75.0) | 3 (23.1) | 5 (29.4) | 4 (30.8) | 5 (29.4) | 6 (46.2) | 7 (41.2) | 5 (16.7) |
| ≥ 1 *related* event | 0 | 0 | 1 (5.9) | 1 (7.7) | 3 (17.6) | 3 (23.1) | 3 (17.6) | 0 |
| ≥ 1 Grade 3+ event | 0 | 0 | 0 | 0 | 0 | 1 (7.7) | 2 (11.8) | 0 |
| ≥ 1 *related* Grade 3+ event | 0 | 0 | 0 | 0 | 0 | 1 (7.7) | 2 (11.8) | 0 |
| ≥ 1 SAE | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ≥ 1 medically-attended event | 0 | 1 (7.7) | 1 (5.9) | 0 | 0 | 5 (38.5) | 3 (17.6) | 0 |
| ≥ 1 AESI | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ≥ 1 AE leading to withdrawal | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

*Reported as number of subjects reporting event (% of subjects reporting event)*
*N = number of subjects enrolled in the specified treatment group; SAE = serious adverse events; AESI = adverse events of special interest*

## Safety and tolerability

- mRNA-1653 was found to be generally well tolerated at all dose levels
- No serious adverse events (SAEs), adverse events of special interest, or adverse events leading to withdrawal were reported
- Injection site pain was the most commonly reported solicited adverse event and grade 3 adverse event



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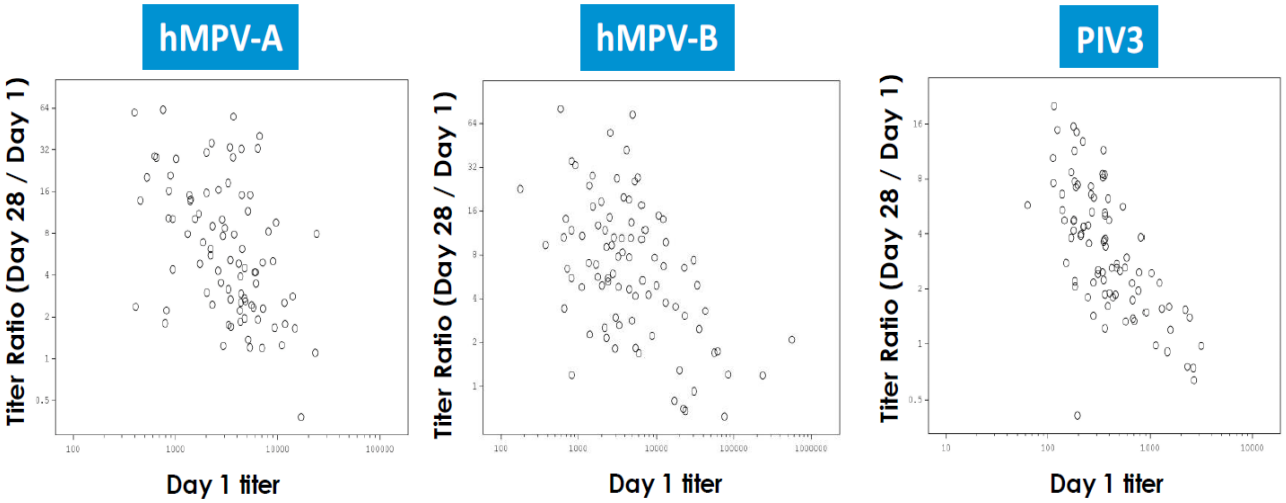
# hMPV/PIV3 vaccine (mRNA-1653)

## *Phase 1 in healthy adults; Interim results, through 1 month*

**Relationship Between Baseline Titer and Response to First mRNA-1653 Vaccination (Day 28 / Day 1 Titer Ratio)**




- mRNA-1653 tended to induce a greater boost in neutralizing antibody in subjects with lower baseline titers
- 1 month after a single vaccination, hMPV and PIV3 neutralization titers were ~6x and ~3x baseline, respectively

**Geometric Mean Titer Ratio Day 28 / Day 1**

| | total mRNA N=90 | Placebo N= 28 |
|---|---|---|
| **hMPV-A** | 6.04 | 1.00 |
| **hMPV-B** | 6.33 | 1.04 |
| **PIV3** | 3.24 | 1.03 |



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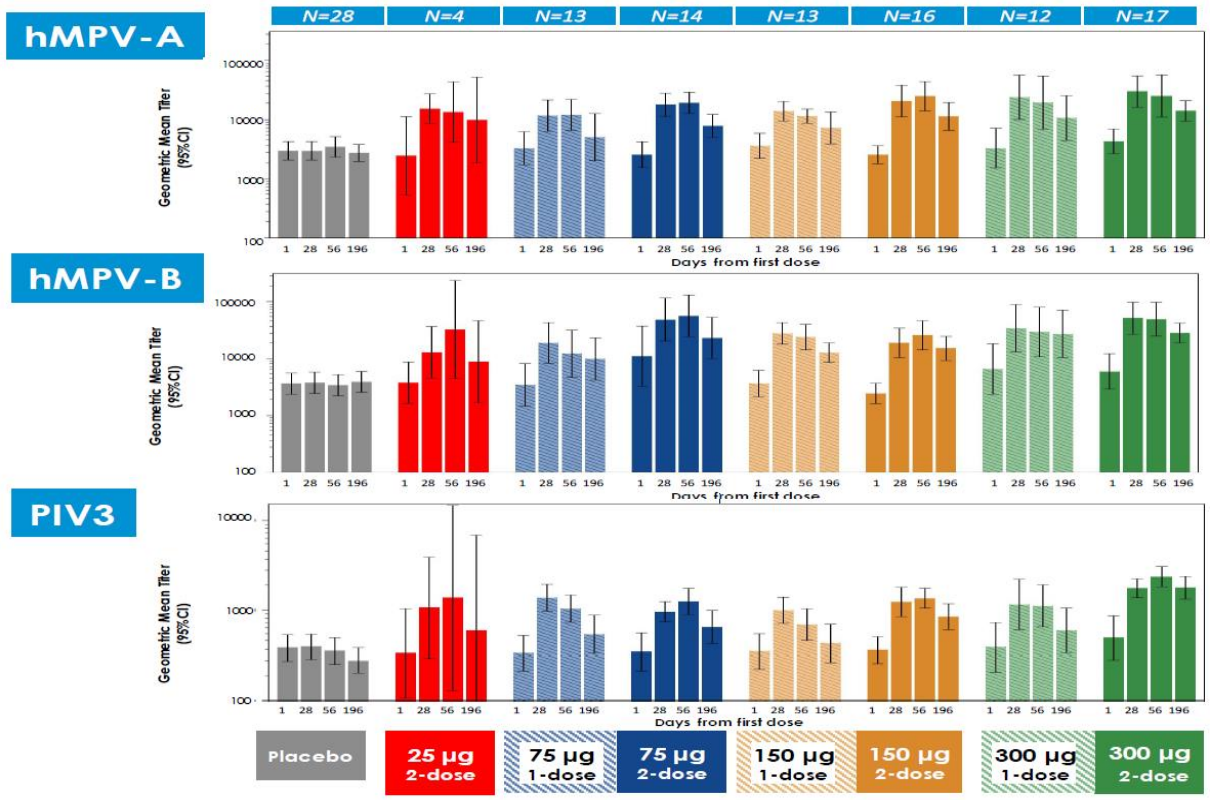
# hMPV/PIV3 vaccine (mRNA-1653)

## *Phase 1 in healthy adults; Interim results, through 7 months*

**Neutralizing Antibody Titers Through Day 196 by Dose Level and Regimen**




## Immunogenicity

- Single vaccination boosted serum neutralization titers against hMPV and PIV3 at all dose levels tested
- Second vaccination did not further boost antibody titers, suggesting a single vaccination was sufficient to achieve a plateau in neutralizing antibodies in this pre-exposed population
- Second interim data show antibody titers remained above baseline at all dose levels at 7 months after vaccination



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# hMPV/PIV3 vaccine (mRNA-1653)

## *Phase 1 in healthy adults; Summary interim results, through 7 months*

### Safety and tolerability

- mRNA-1653 was found to be generally well tolerated at all dose levels
- No serious adverse events (SAEs), adverse events of special interest, or adverse events leading to withdrawal were reported
- Injection site pain was the most commonly reported solicited adverse event and grade 3 adverse event

### Immunogenicity

- Single vaccination boosted serum neutralization titers against hMPV and PIV3 at all dose levels tested mRNA-1653 was found to be generally well tolerated at all dose levels
- Neutralizing antibodies against hMPV and PIV3 present at baseline in all subjects, consistent with prior exposure to both viruses
- 1 month after a single vaccination, hMPV and PIV3 neutralization titers ~6x and ~3x baseline, respectively
- Second vaccination did not further boost antibody titers, suggesting a single vaccination was sufficient to achieve a plateau in neutralizing antibodies in this pre-exposed population
- Second interim data show antibody titers remained above baseline at all dose levels at 7 months after vaccination



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