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Respiratory vaccines

Program Pack

Flu (mRNA-1010)

Seasonal influenza (flu) overview

Seasonal influenza (influenza A and influenza B) occurs seasonally and varies in severity each year, causing respiratory illnesses and placing a substantial burden on healthcare systems

Disease burden

- Worldwide, influenza leads to 3-5M severe cases of influenza and 290-650K influenza-related respiratory deaths annually[1]
- On average, about 8% of the US population experiences symptoms from influenza each year, with 100-710K hospitalizations and 4.9-51K deaths per year[2]
- Peak influenza activity is seen in temperate climates during fall to winter and is reflected in increased outpatient visits, urgent care visits, and hospitalizations
- Influenza A viruses led to >95% of influenza-related hospitalizations in adults in the most recent season[3]

Influenza symptoms & complications

Symptoms


Fever


Cough


Sore throat


Nasal congestion


Fatigue


Vomiting/diarrhea (more common in children)

Complications


Pneumonia (viral and/or bacterial)

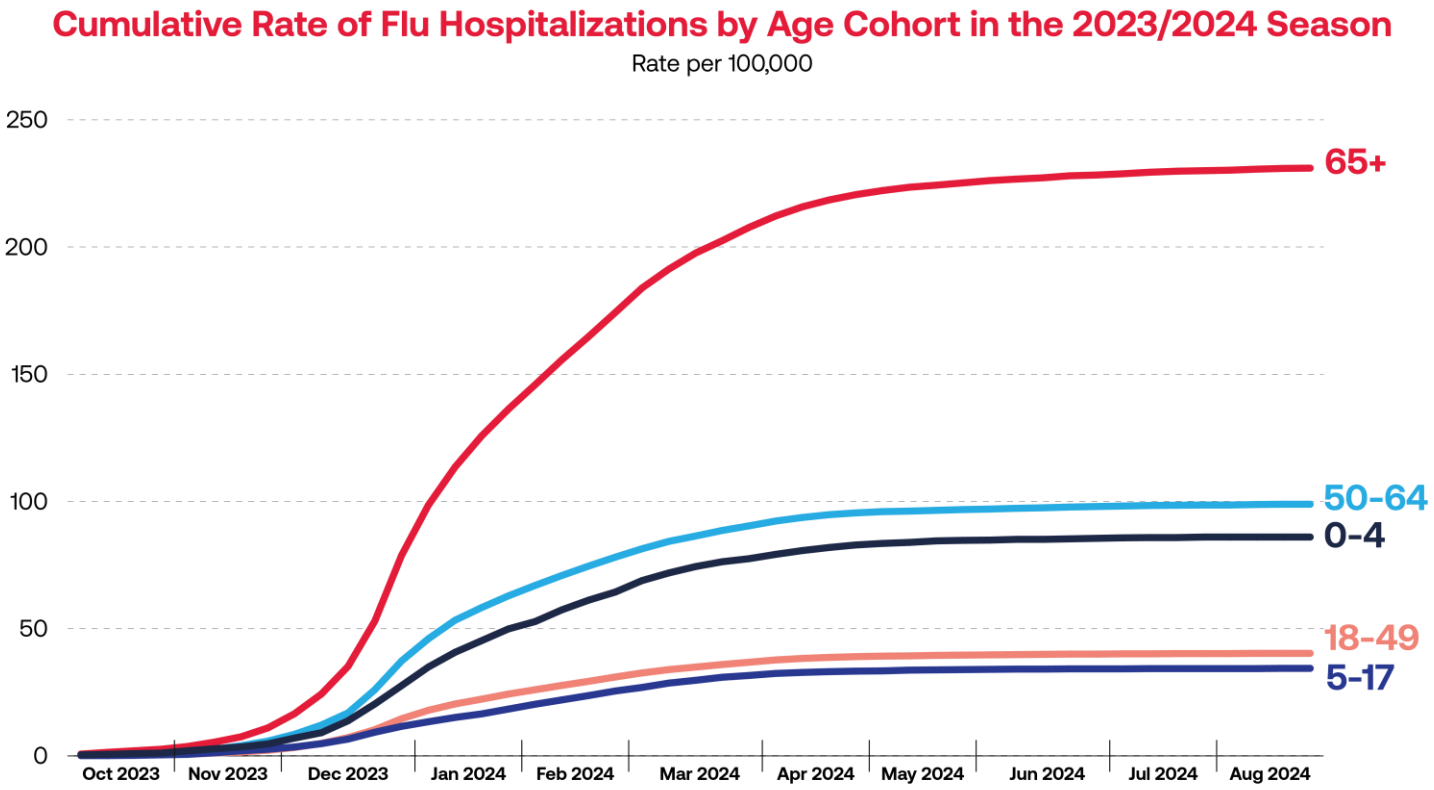

Ear infections


Sinus infections


Exacerbation of chronic conditions (e.g. asthma, heart failure)

1. World Health Organization. Influenza (Seasonal). WHO. 2018. https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)
2. Centers for Disease Control and Prevention. Disease burden of influenza. Available at: https://www.cdc.gov/flu/about/burden/index.html
3. https://www.cdc.gov/flu/weekly/influenza-hospitalization-surveillance.htm

Seasonal influenza causes respiratory illnesses leading to hospitalizations across age groups, especially in older adults



SOURCE: https://www.cdc.gov/flu/weekly/influenza-hospitalization-surveillance.htm

Our mRNA platform will allow us to quickly reformulate based on the current year's strain

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mRNA-1010 Phase 3 P303 study overview

P303 was designed to test the immunogenicity and safety of an optimized composition of mRNA-1010

Design
Randomized, observer-blind, active-controlled study

Participants
2,416 medically stable adults ≥ 18 years old

Vaccination schedule
Single dose of mRNA-1010 or Fluarix

Duration: 6 months
Study participants will be followed for 6 months after study injection

Site locations
Northern hemisphere (United States)

Total N = 2,416
Randomization Ratio = 1:1

mRNA-1010 (50 µg)
N=1227

Fluarix
N=1189

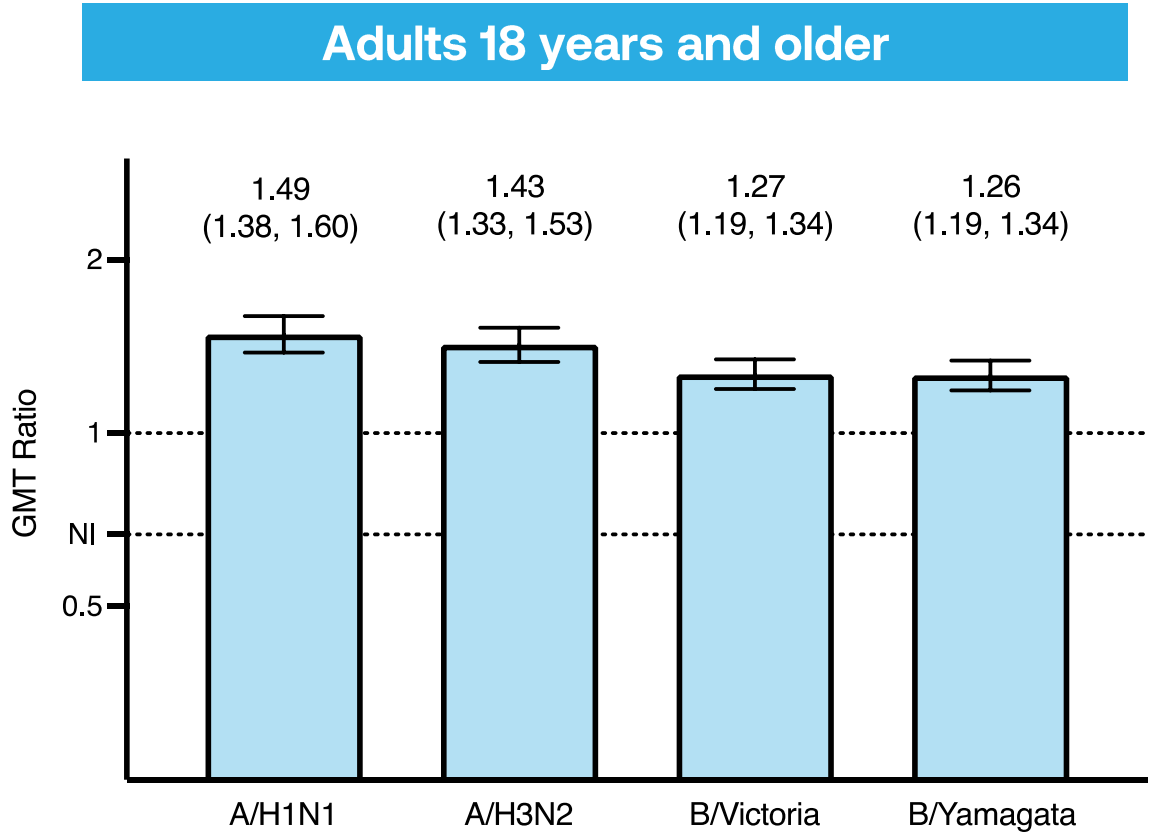
mRNA-1010 met all primary immunogenicity endpoints in P303

Immunogenicity criteria were met for all 8 co-primary endpoints

- GMT ratios
- Seroconversion rates

Higher GMTs and seroconversion rates compared to standard dose influenza vaccine were observed for mRNA-1010 for all four strains in P303 study

Higher immunogenicity relative to standard dose influenza vaccine was consistently observed across age groups



Reported rates of local and systemic reactogenicity after mRNA-1010 compared to standard dose influenza vaccine

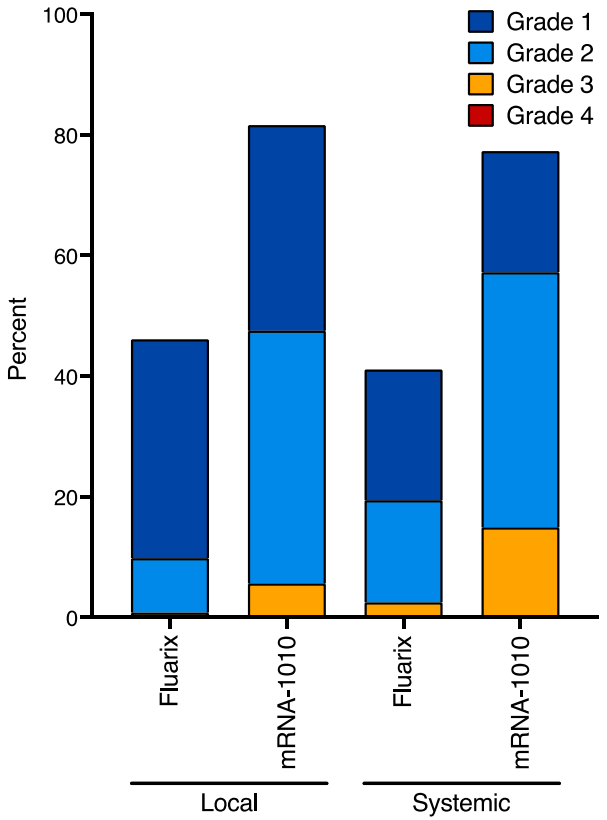
Safety profile was in line with prior clinical studies for mRNA-1010

mRNA-1010 showed an acceptable reactogenicity profile, with the majority of solicited adverse reactions reported as grade 1 or 2 in severity

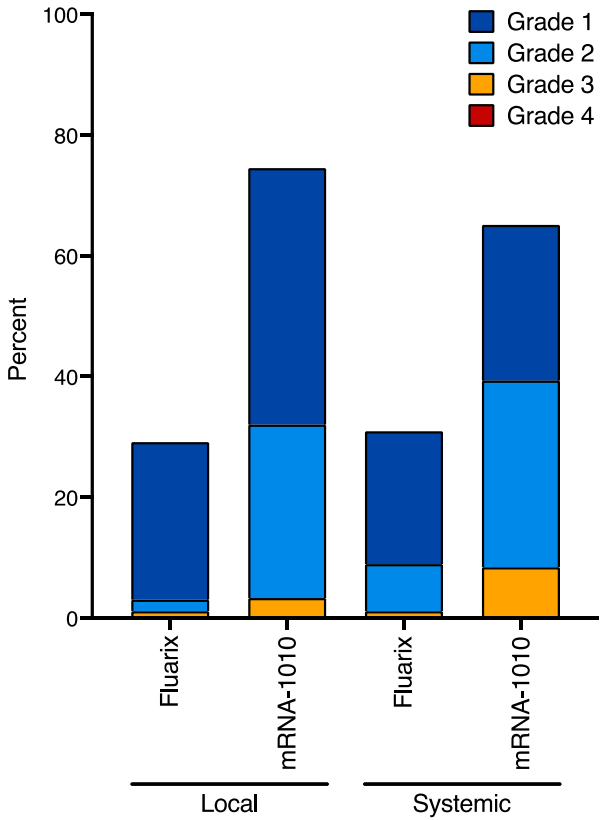
Reactogenicity was higher in mRNA-1010 recipients compared to standard dose influenza vaccine recipients

Reactogenicity in older adults was lower compared to younger age groups

Adults 18 years and older



Adults 65 years and older



mRNA-1010 Phase 3 older adult study overview

Study was designed to test the immunogenicity and safety of an optimized composition of mRNA-1010

Design
Randomized, observer-blind, active control study of optimized mRNA-1010

Participants
3,003 medically stable adults ≥65 years old

Vaccination schedule
Single dose of mRNA-1010 or Fluzone HD

Duration: 6 months
Participants were followed up for 6 months

Site locations
Northern hemisphere (United States)

Total N= 3,003
Randomization Ratio= 1:1

mRNA-1010 (50 µg)
N=1,507

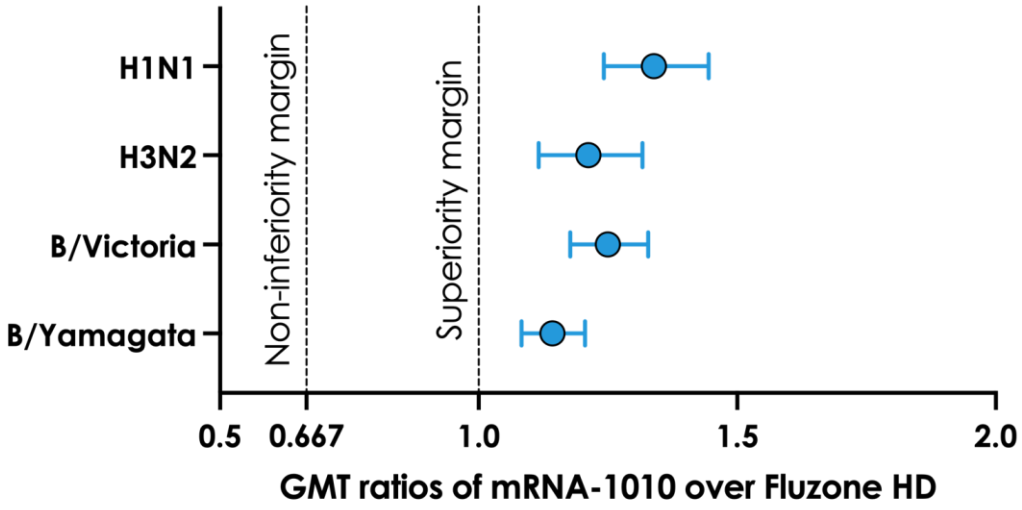
Fluzone HD
N=1,496

8 primary endpoints: GMT and SCR across 4 strains mRNA-1010 vs Fluzone HD

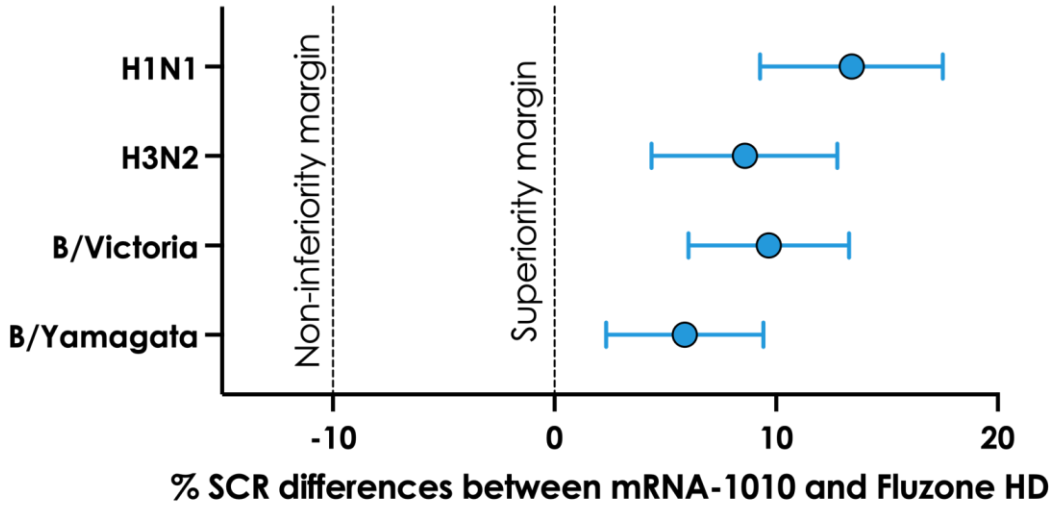
mRNA-1010 met all primary immunogenicity endpoints compared to Fluzone HD in P303

- **Immunogenicity criteria for licensure according to regulatory guidance were met** for all 8 co-primary endpoints
  - GMR
  - Seroconversion rates
- **Superior GMTs and seroconversion rates were observed** for mRNA-1010 for all four strains

GMT ratios



Seroconversion rates

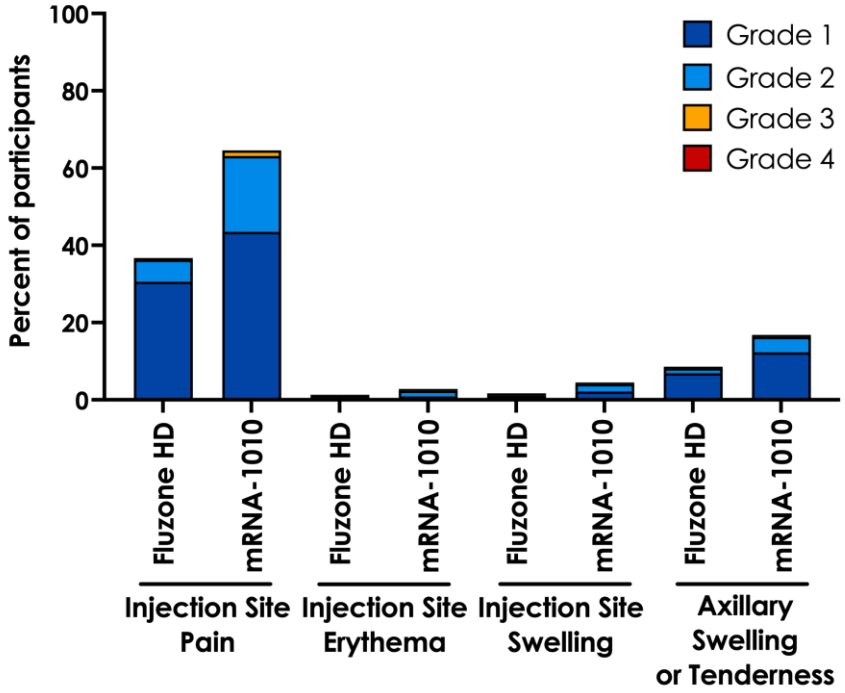


mRNA-1010 met all primary immunogenicity endpoints compared to Fluzone HD in P303

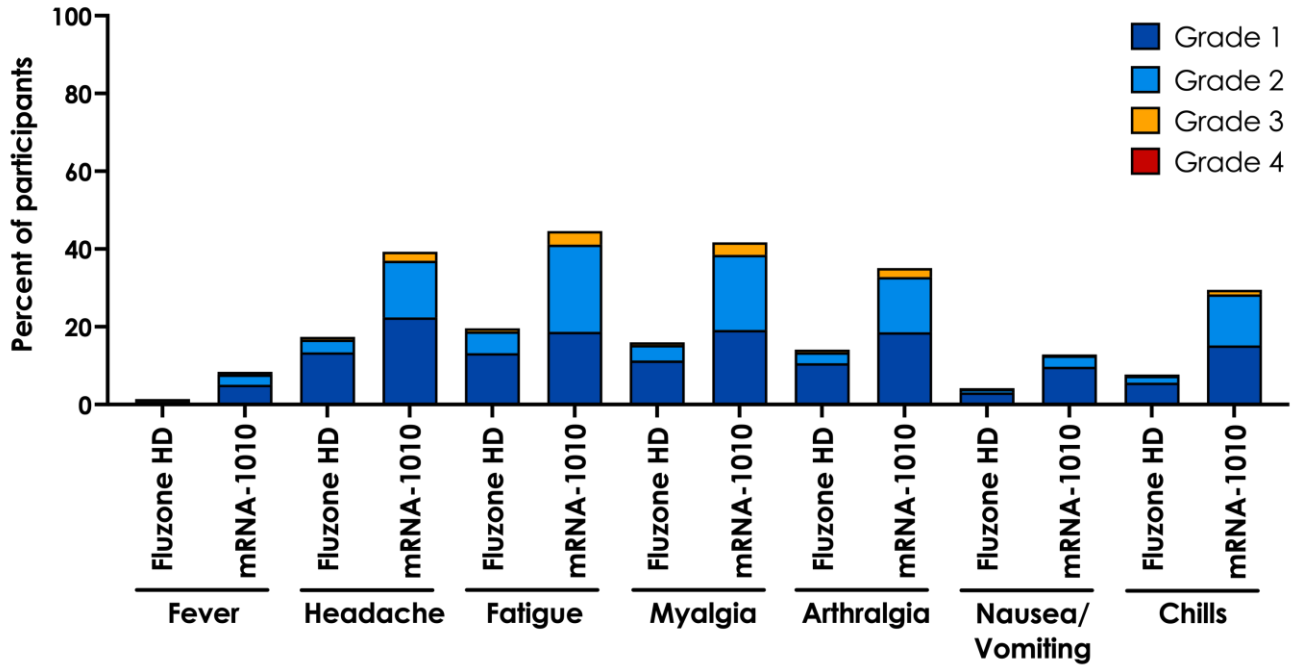
The majority of solicited ARs were grade 1 or grade 2 in severity

- The most common local solicited ARs were injection site pain and axillary swelling; the most common systemic solicited ARs were headache, fatigue, myalgia and arthralgia.

Local Solicited Adverse Reactions



Systemic Solicited Adverse Reactions



mRNA-1010 Phase 3 P303 older adult safety

Unsolicited AEs were reported at similar rates between mRNA-1010 and the active comparator groups

- Profiles were similar based on frequency, severity, seriousness, relatedness as assessed by the investigator, and types of events

No myocarditis/pericarditis events were identified

Rates of SAEs up to end of study were similar between mRNA-1010 and the active comparator

Overall, no safety concerns were identified for mRNA-1010

An acceptable tolerability and safety profile was observed

mRNA-1010 vaccine efficacy study (P304)

Study was designed to test the immunogenicity and safety of an optimized composition of mRNA-1010

Design
Randomized, observer-blind, active control study of optimized mRNA-1010

Participants
~56,000 medically stable adults ≥50 years old across two seasons with ~34,000 in first season

Vaccination schedule
Single dose of mRNA-1010 or Fluarix

Duration:
6 months

Site locations
Northern hemisphere countries

Season 2 study only to commence if success criteria not met in season 1

Season 1	Season 2
Total N= ~34,000	Total N= ~22,000
Randomization Ratio = 1:1	Randomization Ratio = 1:1
mRNA-1010	**mRNA-1010**
N= ~17,000	**N= ~11,000**
Fluarix	**Fluarix**
N= ~17,000	**N= ~11,000**

Primary Endpoint:

- Relative efficacy of mRNA-1010 to an active comparator in preventing protocol-defined influenza like illness caused by any strain confirmed RT-PCR
- Safety and reactogenicity

Flu (mRNA-1010) summary and next steps

Immunogenicity

- Immunogenicity criteria were met for all 8 co-primary endpoints for GMT ratio and seroconversion rates

Reactogenicity / Safety

- Showed an acceptable reactogenicity profile, with the majority of solicited adverse reactions reported as grade 1 or 2 in severity
- No safety concerns were identified for mRNA-1010

Next steps

- Phase 3 vaccine efficacy study readout in summer 2025

Medical and scientific presentations

ESCMID 2025

https://s29.q4cdn.com/435878511/files/doc_presentations/2025/Apr/14/Flu-poster-Durability-of-mRNA-Platform.pdf

ESCMID 2024 (Phase 3 safety & immunogenicity)

https://s29.q4cdn.com/435878511/files/doc_presentations/2024/Apr/29/soens_oral-presentation_eccmid-2024-18.pdf

Forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding: potential market size; Moderna's seasonal influenza vaccine strategy; Moderna's clinical trials; and timing of Phase 3 study. In some cases, forward-looking statements can be identified by terminology such as "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward -looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors include those described in Moderna's most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date referenced on the first page.