

**Vaccines and Related Biological Products Advisory  
Committee December 17, 2020 Meeting Presentation -  
Emergency Use Authorization (EUA) Application for  
mRNA-1273**

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# Emergency Use Authorization (EUA) Application for mRNA-1273

**ModernaTX, Inc.**

Vaccines and Related Biological Products Advisory Committee

December 17, 2020

# Introduction

**Tal Zaks, MD PhD**

Chief Medical Officer  
ModernaTX, Inc.



# Seeking EUA Due to Urgent Need for Vaccine Against SARS-COV-2

- Significant morbidity and mortality
  - > 15 million cases and ~300,000 deaths in US<sup>1</sup>
- Unprecedented COVID-19 hardships
  - Direct medical and economic impact
  - Emotional and functional impact
- Moderna has focused on rapid, thorough response to pandemic
  - Close collaboration with NIH on clinical development
  - Transparent sharing of data

1. [https://covid.cdc.gov/covid-data-tracker/#cases\\_casesper100klast7days](https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days)

# mRNA-1273 is Based on Well-Understood mRNA Biology

- mRNA is the blueprint for all protein synthesis
- Uses cell biology to activate immune system
- Inherent safety features
  - Does not self-replicate
  - Does not enter nucleus or integrate into DNA
  - Manufacturing process is cell free and contains no human or animal products, preservatives, or adjuvants

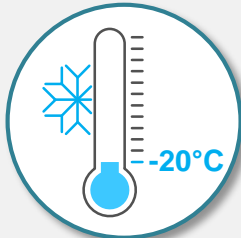
# Clinical Experience with mRNA Infectious Disease Vaccines Since 2015

- 12 Phase 1 and Phase 2 clinical trials
  - 8 viruses prior to SARS-CoV-2
- > 1,700 healthy volunteers enrolled
- Routinely elicited neutralizing antibodies
- No significant safety concerns to date

# mRNA-1273 Shipping, Storage and Administration

## Shipping

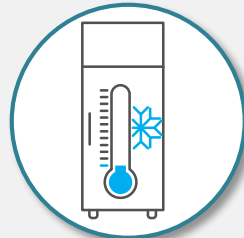
-20°C (-40°C to -15°C)



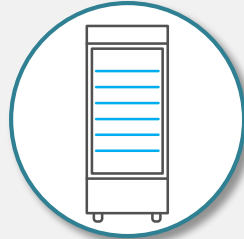
**Able to ship a single carton  
(100 doses)**

## Local Storage Options

(up to the Date of Expiration)



**Freezer**  
-20° C



**Refrigerator**  
5°C  
up to 30 days



**Room Temperature**  
up to 12 hours

**Local transportation under  
controlled condition at 5°C**

## Administration



**Multiple-dose vial  
(10 doses)**

**Use within 6 hours  
after first entry**

**No dilution required**

# Study 301 Data Support Emergency Use Authorization

- Exceed FDA efficacy criteria for BLA
  - VE = 94.1% (89.3%, 96.8%),  $p < 0.0001$
  - Consistency among subgroups
  - Very high efficacy maintained against severe disease
- Safety profile well characterized in > 15,000 vaccine recipients
  - Majority of solicited injection and systemic AEs reported as mild-to-moderate and resolve, occur  $\leq 7$  days of injection



# Moderna Committed to Transparency and Gathering Longer Term Safety Data

- Study 301 will continue to provide safety and effectiveness data
- Will continue to transparently share data
- DSMB will continue to monitor safety
- Will continue to monitor duration of immunity and effectiveness

# Moderna Committed to Collecting Additional Data in a Broader Range of Patients

- Pediatric studies ongoing
- National Cancer Institute collaboration
- Post-authorization active surveillance and safety study
- Global pregnancy registry under development
- Post-authorization effectiveness study

Moderna will continue to collaborate with NIH, FDA, CDC and other agencies

# Agenda

Mechanism of Action

Melissa Moore, PhD  
Chief Scientific Officer, Platform Research  
ModernaTX, Inc.

Efficacy

Jacqueline Miller, MD, FAAP  
Senior Vice President, Therapeutic Area Head, Infectious Disease  
ModernaTX, Inc.

Safety

David Martin, MD, MPH  
Vice President, Pharmacovigilance  
ModernaTX, Inc.

Clinical Perspective

Lindsey Robert Baden, MMSc, MD  
Associate Professor, Brigham and Women's Hospital  
Associate Professor of Medicine, Harvard Medical School  
Director of Clinical Research

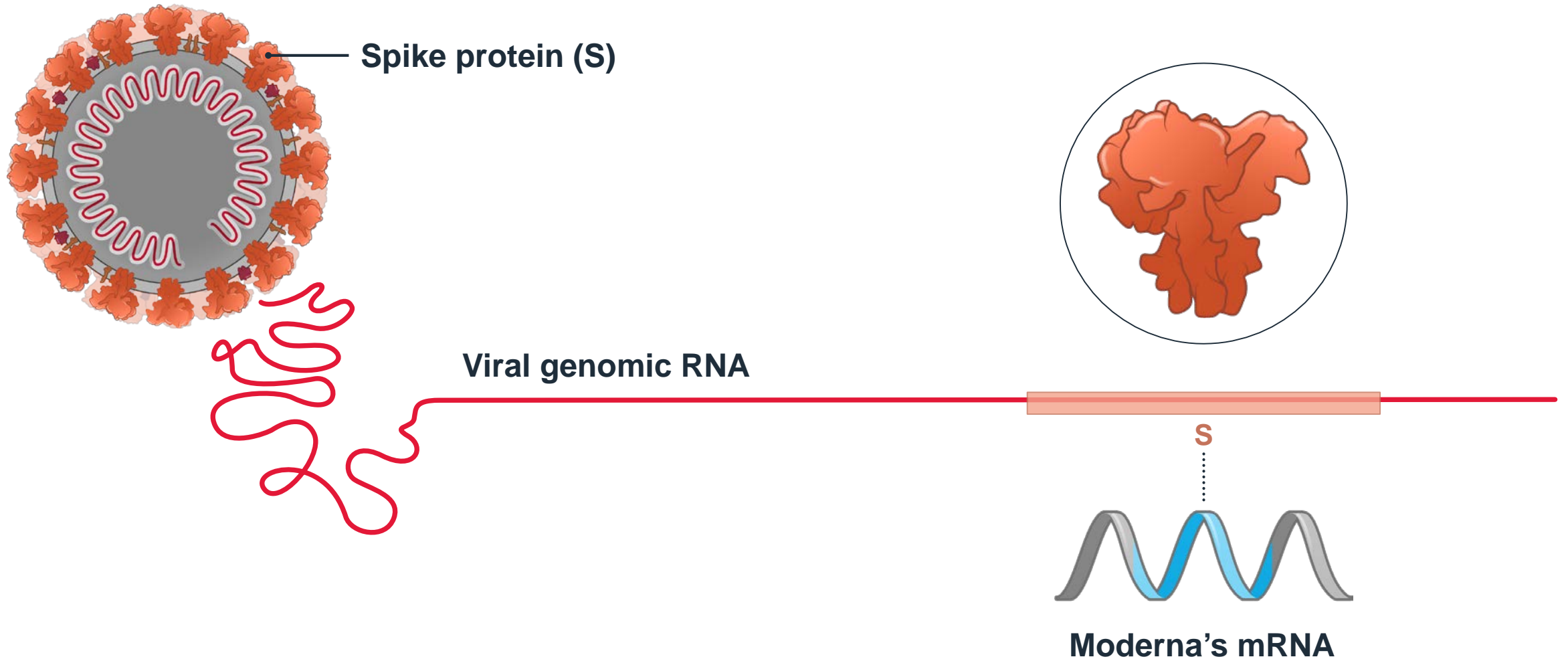
# mRNA Platform and Mechanism of Action of mRNA-1273

**Melissa J. Moore**

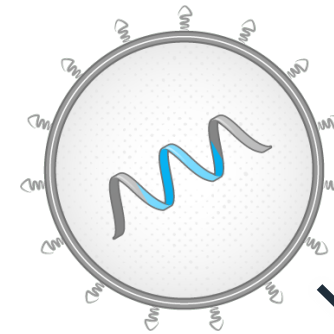
Chief Scientific Officer, Platform Research  
ModernaTX, Inc.



# Our Vaccine Contains an mRNA Encoding the SARS-CoV-2 Spike Protein

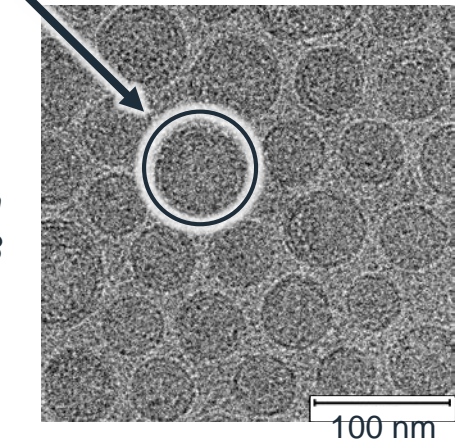


# Our Manufacturing Process Utilizes No Ingredients of Human or Animal Origin

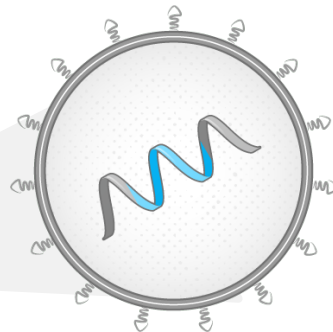


**mRNA in Lipid Nanoparticle (LNP)**

*Electron micrograph of mRNA-1273*



# In the Vial



mRNA-1273

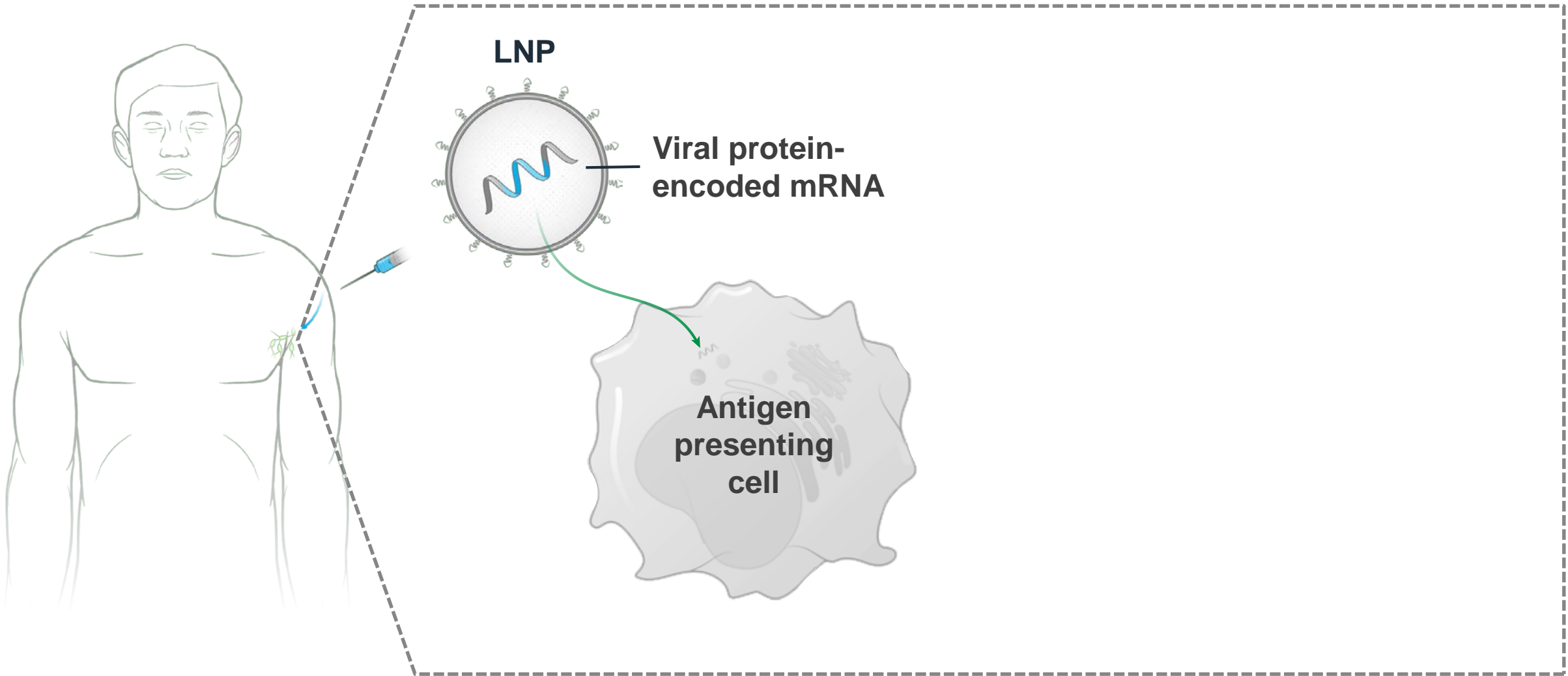
+

*Water*

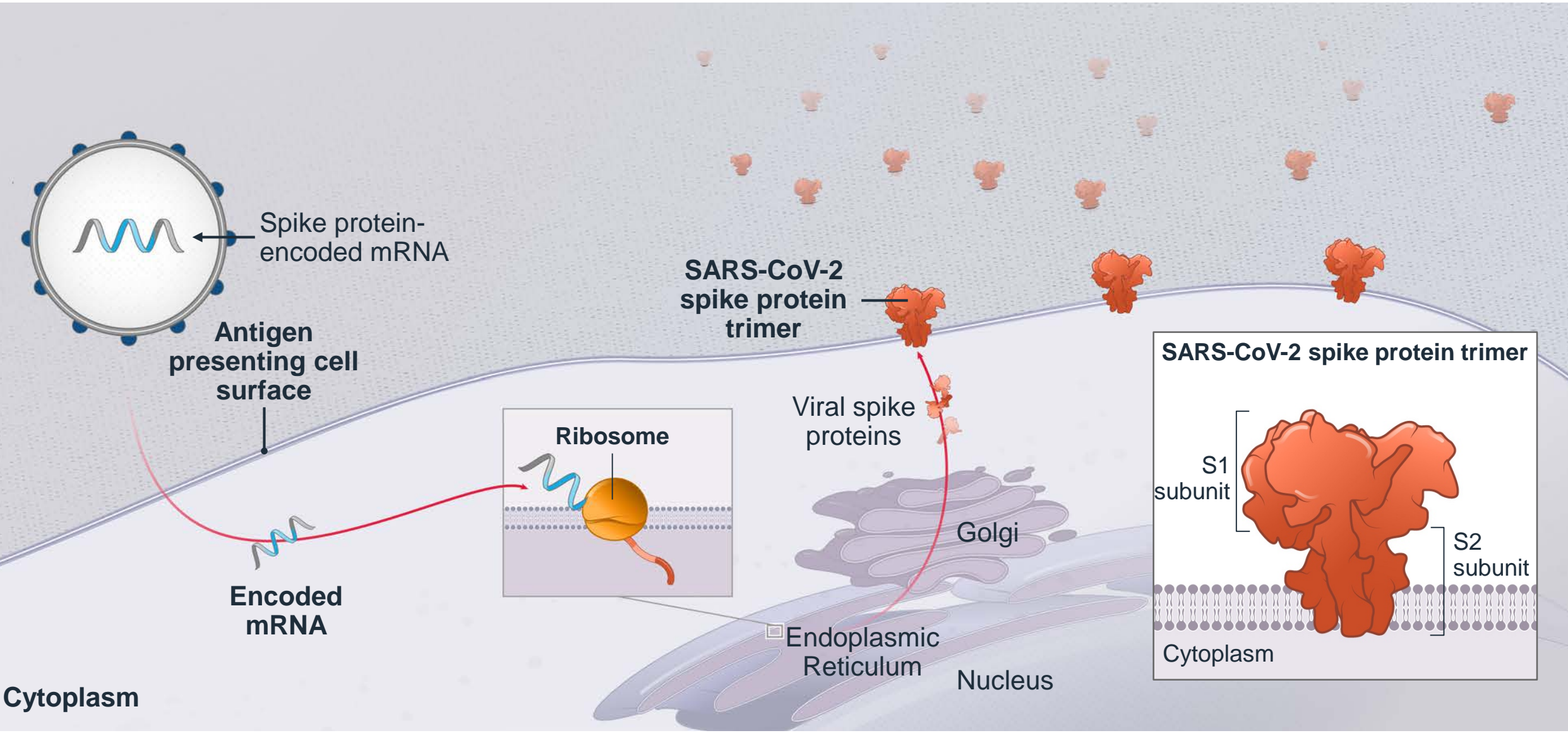
*Sucrose*

*FDA Approved  
Buffers*

- **No preservatives**
- **No antibiotics**
- **No adjuvants**
- **All components rapidly cleared**







Cytoplasm

Spike protein-encoded mRNA

Antigen presenting cell surface

Encoded mRNA

Ribosome

SARS-CoV-2 spike protein trimer

Viral spike proteins

Golgi

Endoplasmic Reticulum

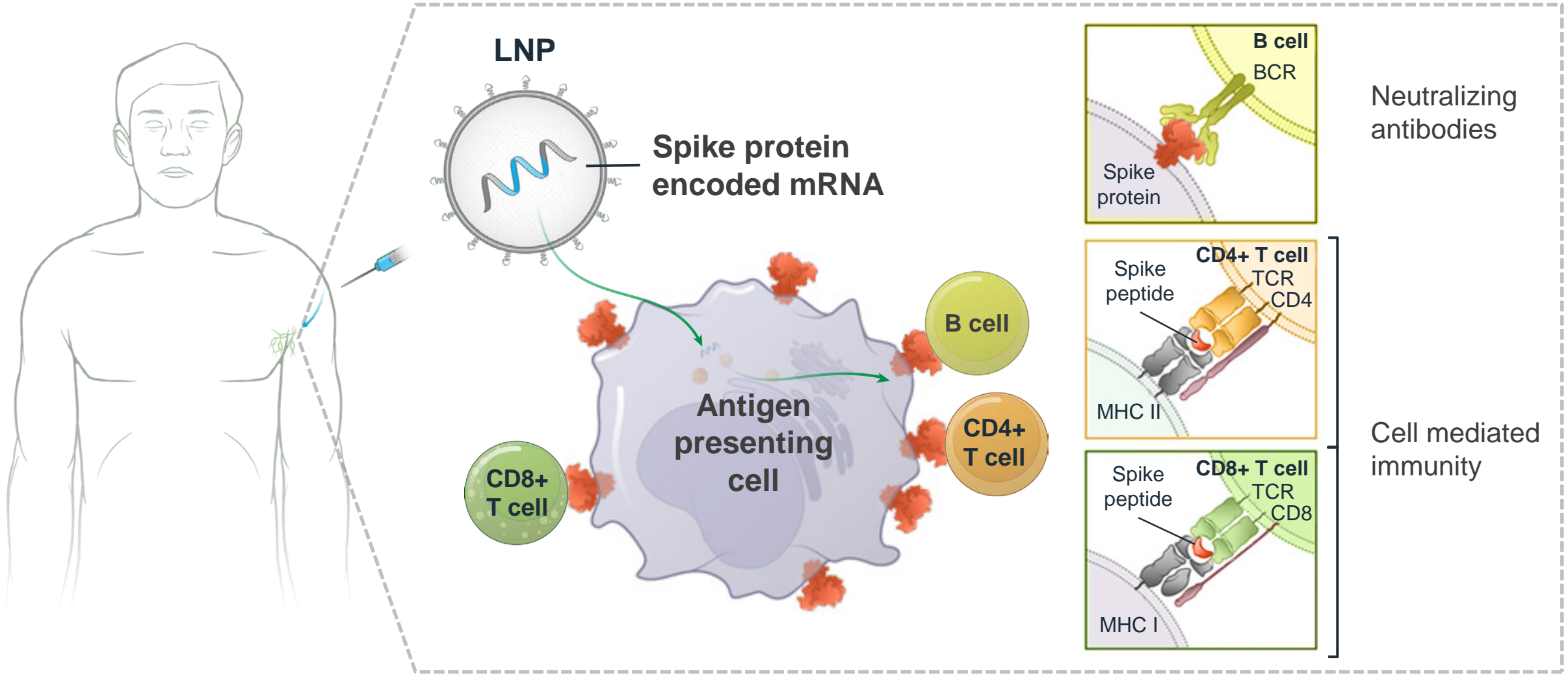
Nucleus

SARS-CoV-2 spike protein trimer

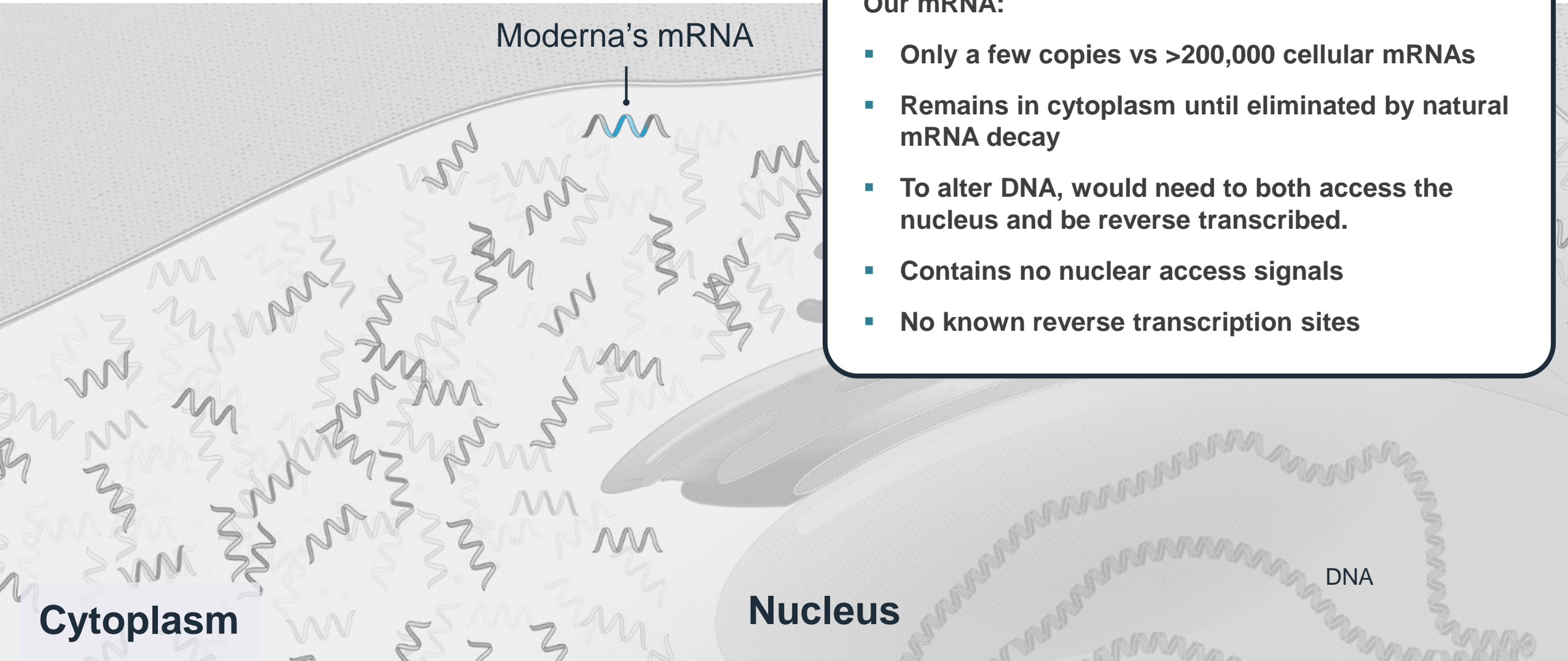
S1 subunit

S2 subunit

Cytoplasm

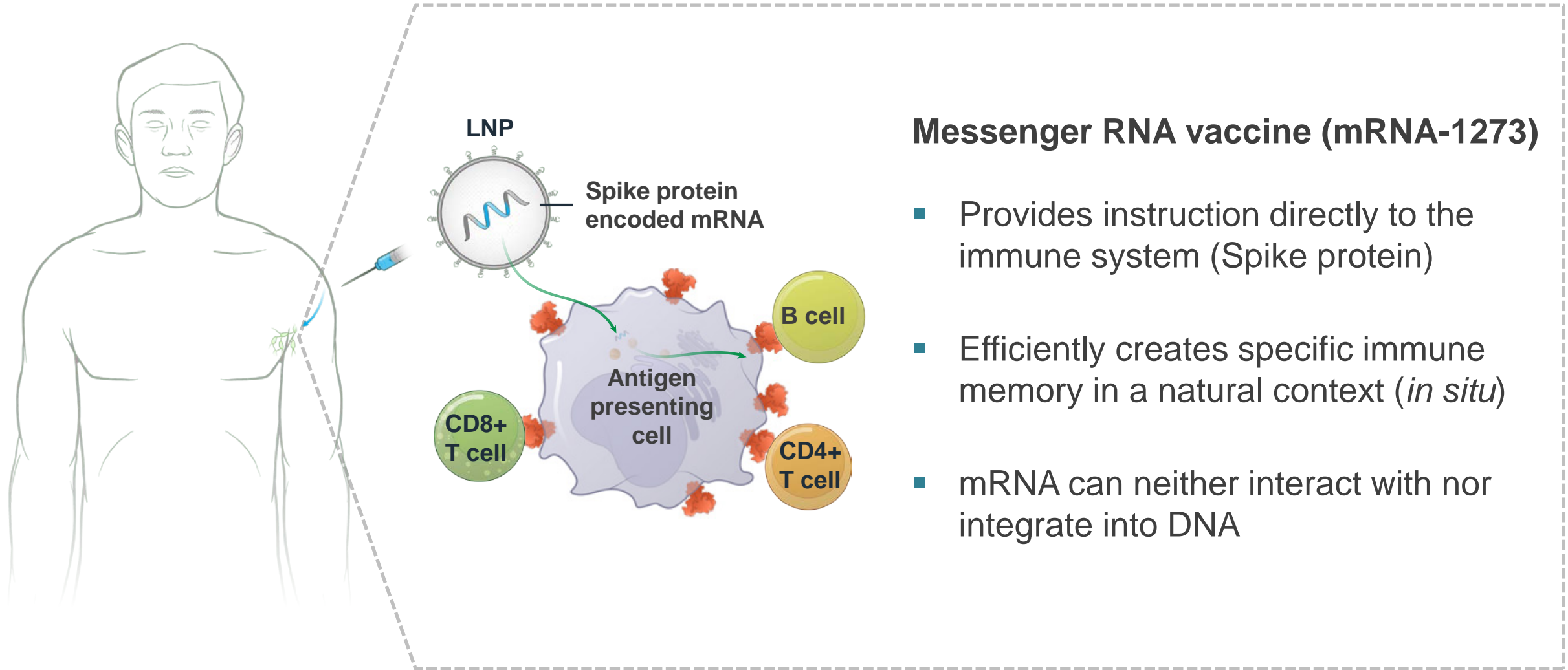


# Our mRNA Vaccine Cannot Alter DNA



## Our mRNA:

- Only a few copies vs >200,000 cellular mRNAs
- Remains in cytoplasm until eliminated by natural mRNA decay
- To alter DNA, would need to both access the nucleus and be reverse transcribed.
- Contains no nuclear access signals
- No known reverse transcription sites



### Messenger RNA vaccine (mRNA-1273)

- Provides instruction directly to the immune system (Spike protein)
- Efficiently creates specific immune memory in a natural context (*in situ*)
- mRNA can neither interact with nor integrate into DNA

# mRNA-1273 Efficacy

**Jacqueline Miller, MD, FAAP**

Senior Vice President, Therapeutic Area Head,  
Infectious Diseases

ModernaTX, Inc.



# mRNA-1273 Non-clinical Results

- Immunogenic
  - Drives robust SARS-CoV-2 specific antibody and Th1-directed CD4+ and CD8+ T-cell responses
- Nonclinical animal challenge studies demonstrate
  - Full protection of mice, hamsters and non-human primates from SARS-CoV-2
  - Does not lead to vaccine-associated enhanced respiratory disease
- No safety concerns identified in developmental and reproductive toxicology study (DART)

# mRNA-1273 Full Development Program Supports the 100- $\mu$ g Dose

**Study 101**  
(Phase 1)  
(N=120)

**Safety and Immunogenicity, and Dose Selection**

**Informed 100 $\mu$ g dose for Phase 2 and 3**

**Study 201**  
(Phase 2)  
(N=600)

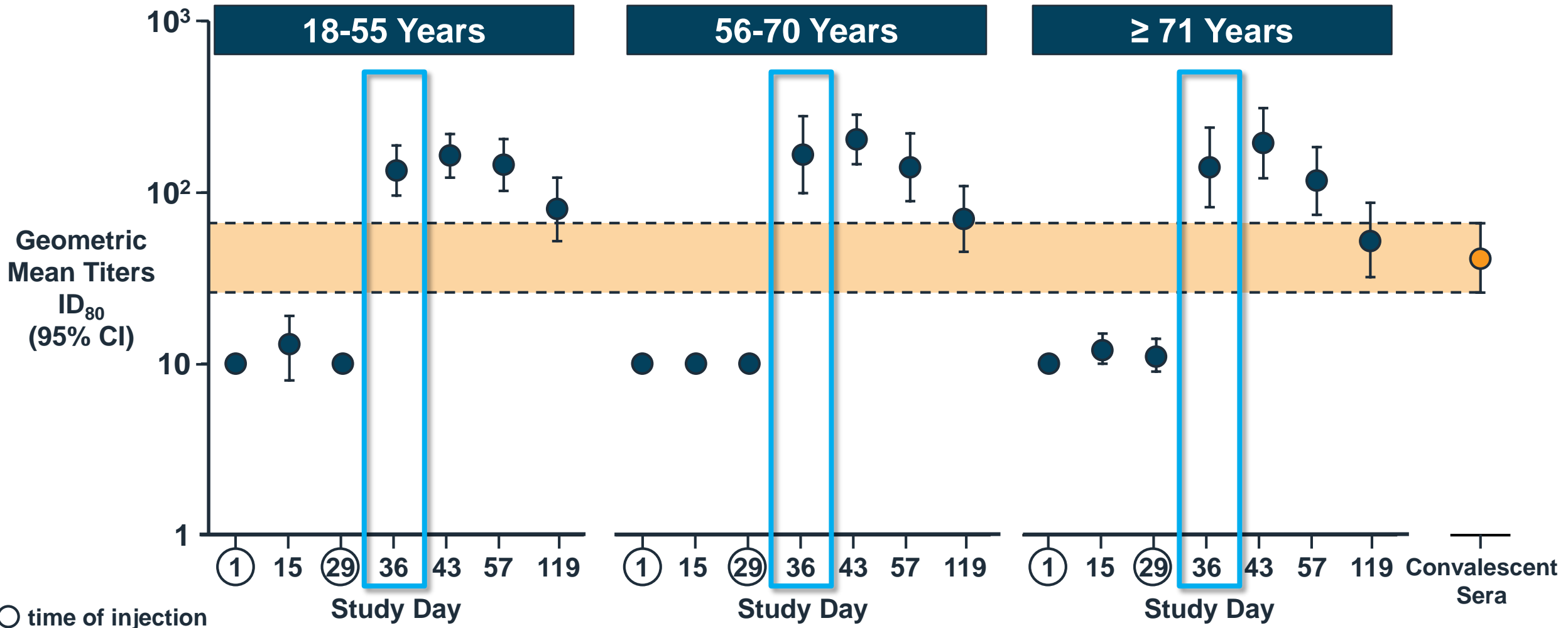
**Safety and Immunogenicity**

**Safety Monitoring Committee safety report**

**Study 301**  
(Phase 3)  
(N=30,420)

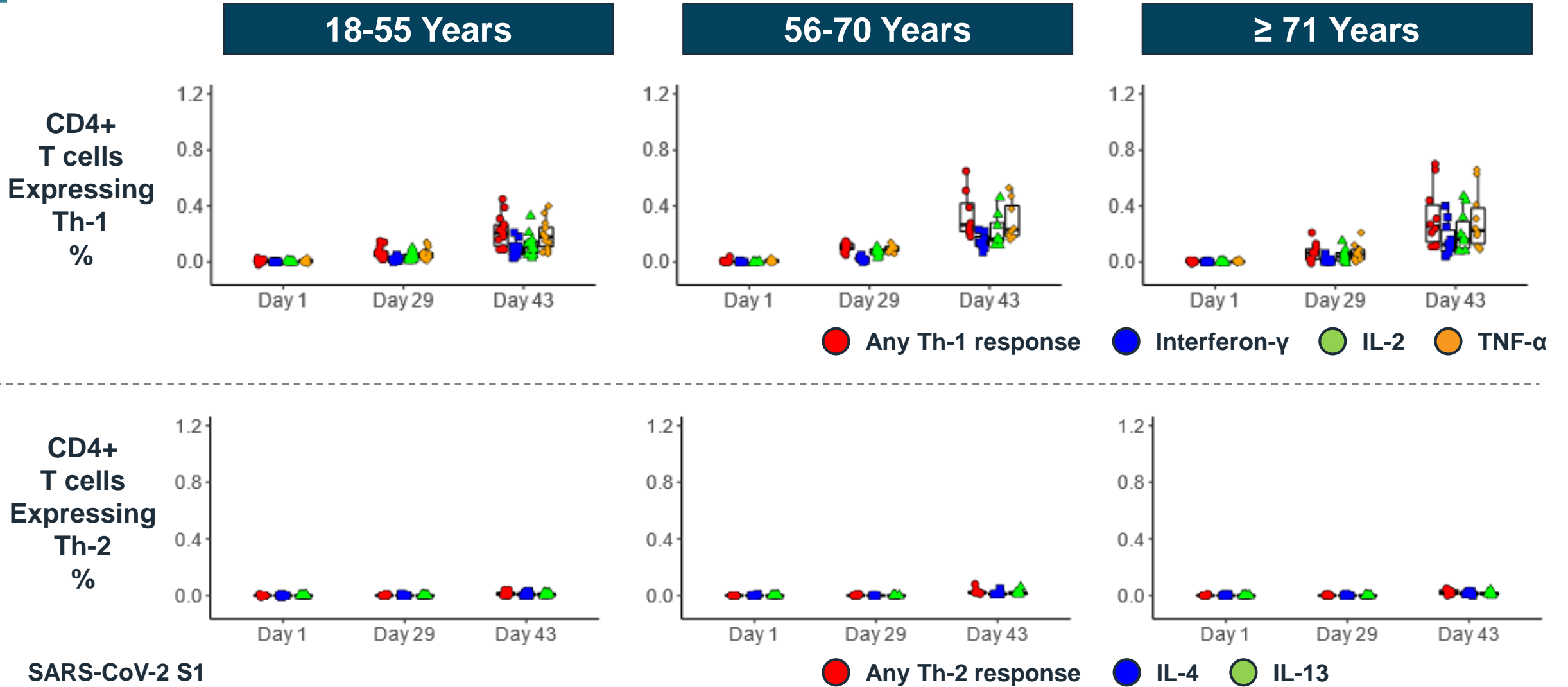
**Efficacy, Safety, Immunogenicity**

# Study 101: mRNA-1273 **100** $\mu\text{g}$ Neutralizes SARS-CoV-2 Across All Age Groups (Pseudovirus Neutralization Assay)



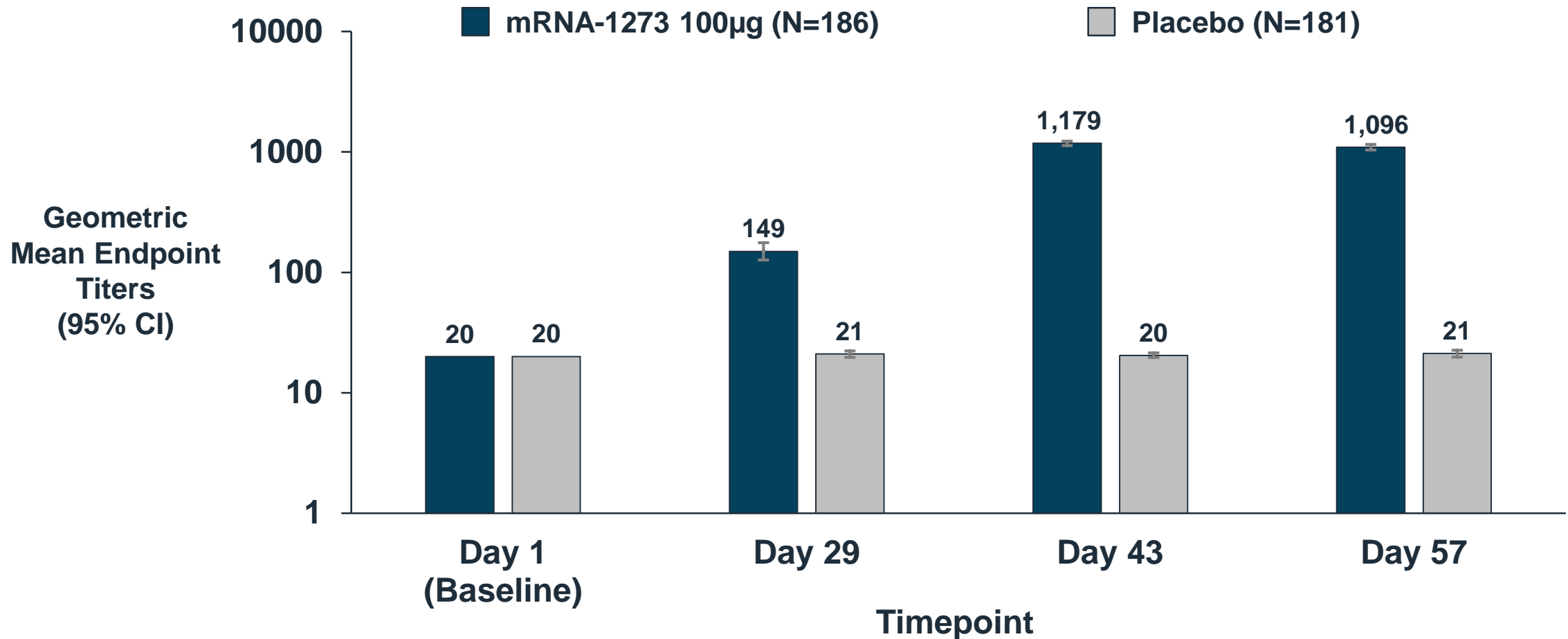


# Study 101: mRNA-1273 Induces CD4+ T-Cell Response at 14 Days Post 2<sup>nd</sup> Dose



# Study 201: mRNA-1273 Induces Neutralizing Antibodies to SARS-CoV-2

*(Per Protocol Set, WT Virus Microneutralization Assay)*



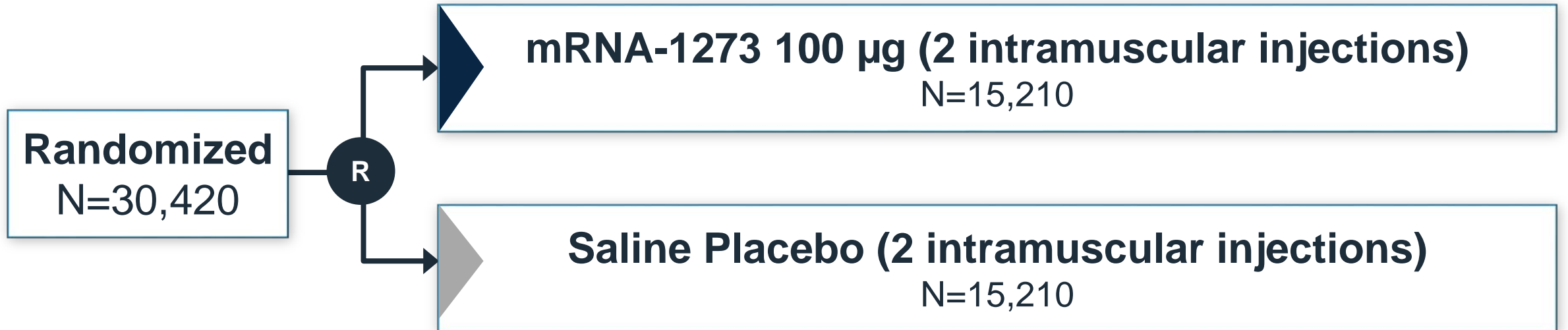
# Summary of Studies 101 and 201 mRNA-1273 Immunogenicity Data

- Neutralizing antibody titers observed in all participants following 2<sup>nd</sup> dose
- GMTs across age strata numerically higher than in pool of convalescent sera
- Neutralizing antibodies persisted for at least 3 months after 2<sup>nd</sup> dose and remained numerically higher than convalescent sera
- Strong Th-1 dominant, CD4+ T-cell response observed
  - Consistent results with preclinical studies

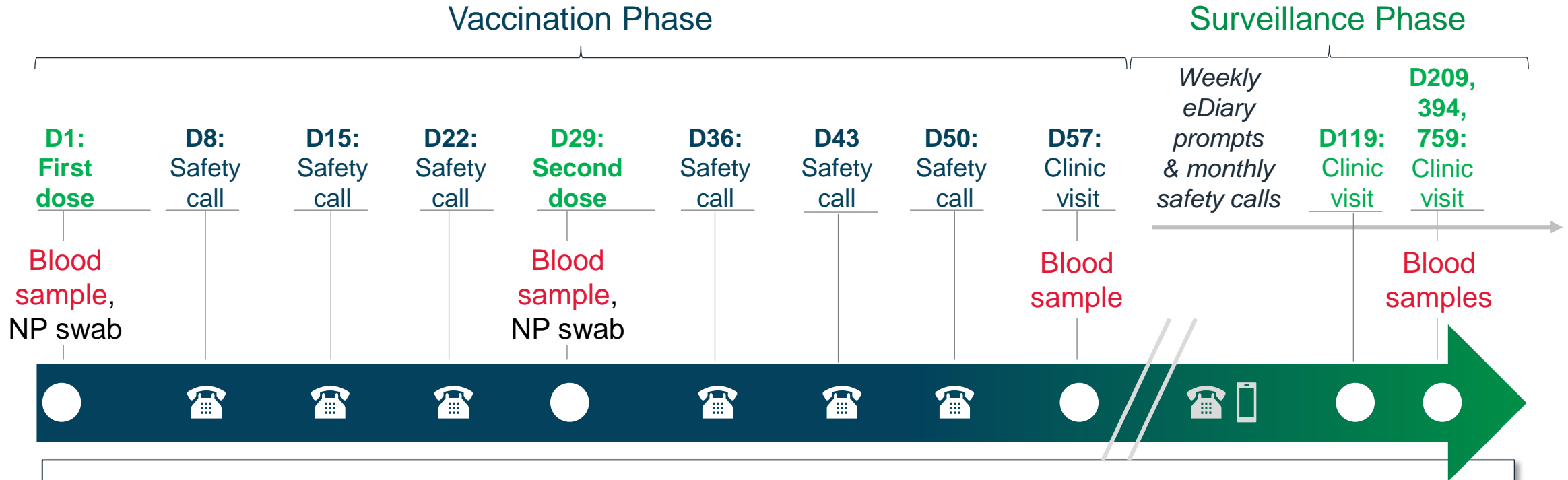


# Study 301

# Study 301: Pivotal, Randomized, Placebo-Controlled Evaluation of Efficacy and Safety



# Study 301: Scheduled Visits and Safety Calls



**COVID-19 active surveillance throughout the study**

**Daily telemedicine visits for participants with COVID-19**

**eDiary captures solicited local and systemic adverse reactions in all participants**

**SAEs and MAAEs captured throughout the study**

# Study 301 Primary and Key Secondary Efficacy Objectives

- Primary Endpoint (Per Protocol Population)
  - Vaccine Efficacy (VE) to prevent COVID-19
  - Primary Hypothesis: Lower limit of 95% confidence interval > 30%
- Secondary Endpoints included VE to prevent:
  - Severe COVID-19
  - Death due to COVID-19
  - COVID-19 using CDC case definition
  - Symptomatic COVID-19 disease occurring after 1<sup>st</sup> dose
  - Asymptomatic SARS-CoV-2 infection

# Study 301 Primary Objective: Case Definition of Symptomatic COVID-19 Disease

- Symptoms
  - $\geq 2$  systemic: fever, chills, myalgia, headache, sore throat, new olfactory and taste disorder(s)
  - OR**
  - $\geq 1$  respiratory: cough, shortness of breath / difficulty breathing, clinical or radiographical evidence of pneumonia

**AND**

- Confirmed SARS-CoV-2 infection via RT-PCR

**Primary analysis: adjudicated cases occurring  $\geq 14$  days after dose 2**



# Study 301 Key Secondary Objective: Case Definition of Severe COVID-19

- Confirmed COVID-19 as per the Primary Endpoint definition, plus any one of the following:
  - Clinical signs indicative of severe systemic illness, RR  $\geq$  30 per minute, HR  $\geq$  125 BPM, SpO<sub>2</sub>  $\leq$  93% on room air at sea level or PaO<sub>2</sub>/FIO<sub>2</sub>  $<$  300 mm Hg
  - Respiratory failure or ARDS, evidence of shock (SBP  $<$  90 mm Hg, DBP  $<$  60 mm Hg or requiring vasopressors)
  - Significant acute renal, hepatic or neurologic dysfunction
  - Admission to ICU or death

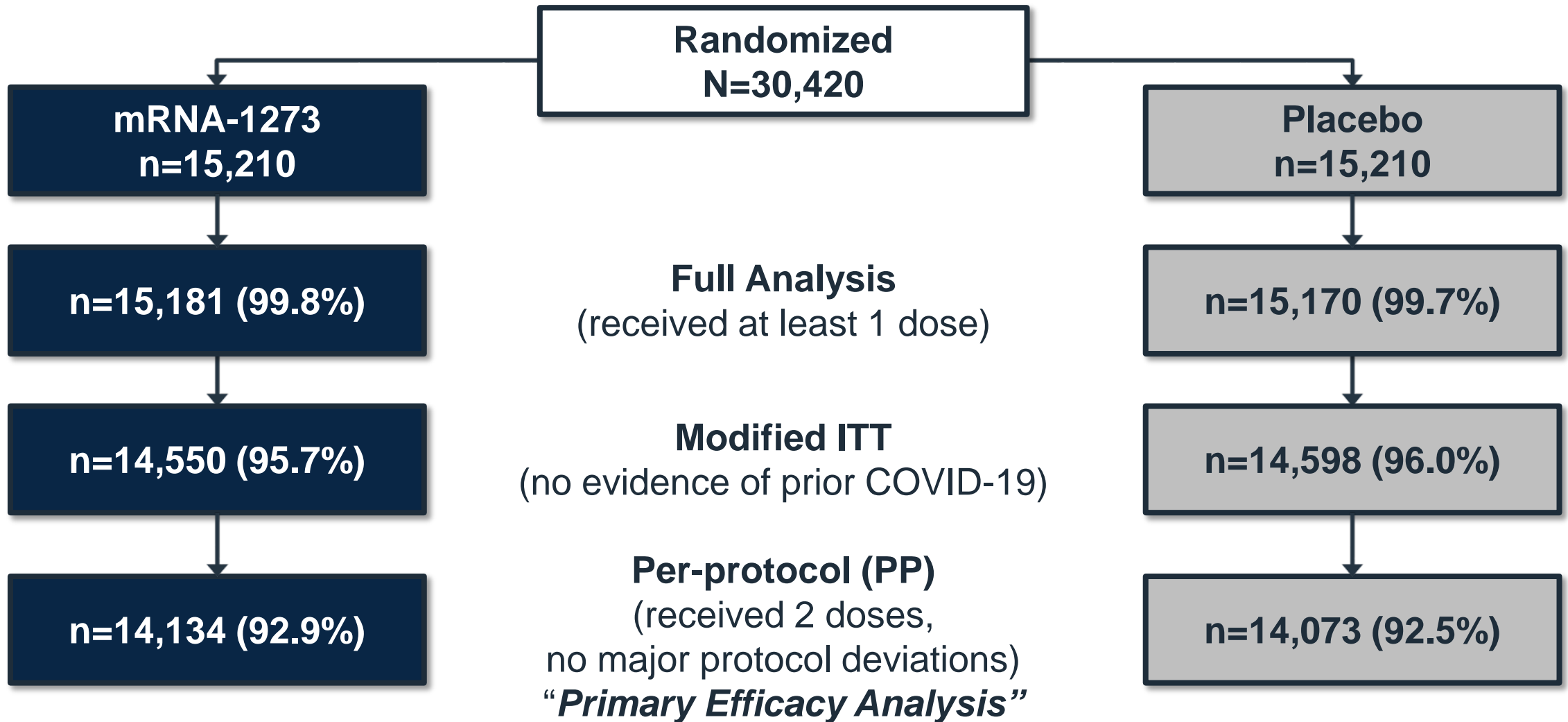
RR: respiratory rate; HR: heart rate; BPM: beats per minute; SpO<sub>2</sub>: oxygen saturation; PaO<sub>2</sub>/FIO<sub>2</sub>: arterial oxygen partial pressure over fractional inspired oxygen; mm Hg: pressure measured by millimeters of mercury; ARDS: acute respiratory distress syndrome; SBP: systolic blood pressure; DBP: diastolic blood pressure; ICU: intensive care unit

# Study 301 Includes an Independent DSMB and Efficacy Endpoint Adjudication Committee

- Independent Data and Safety Monitoring Board (DSMB) chartered by NIH
  - Continuous monitoring for:
    - Vaccine-associated enhanced respiratory disease
    - Any other safety signal
  - Evaluated interim efficacy analysis and alerted Moderna when criteria met
- Independent Efficacy Endpoint Adjudication Committee
  - Reviews potential COVID-19 cases, including laboratory results
  - Determines if case definition for efficacy endpoints were met
  - Confirms case was  $\geq 14$ -days post 2<sup>nd</sup> dose

# Study 301: Disposition of Participants

## *Randomization Set*



# Study 301: Representation of Participants with Risk Factors

## *Full Analysis Set*

	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
<b>Age and health risk for severe COVID-19</b>				
≥ 18 to < 65 without comorbid conditions	8,888	59%	8,886	59%
≥ 18 to < 65 with comorbid conditions	2,530	17%	2,535	17%
≥ 65 with and without comorbid conditions	3,749	25%	3,749	25%
	} 42%		} 42%	

Comorbid conditions included chronic lung disease or moderate to severe asthma, significant cardiac disease, severe obesity, diabetes, liver disease, stable HIV infection

# Study 301: Representative of US Demography

## *Full Analysis Set*

	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
<b>Sex, male</b>	7,923	<b>52%</b>	8,062	<b>53%</b>
<b>Age, years</b>				
<b>Mean (SD)</b>	<b>51 (15.5)</b>		<b>51 (15.6)</b>	
<b>Age group</b>				
<b>≥ 18 to &lt; 65</b>	11,413	<b>75%</b>	11,418	<b>75%</b>
<b>≥ 65</b>	3,768	<b>25%</b>	3,752	<b>25%</b>
<b>Breakdown of ≥ 65 age group</b>				
<b>≥ 65 to &lt; 70</b>	1,905	<b>51%</b>	1,817	<b>48%</b>
<b>≥ 70 to &lt; 75</b>	1,205	<b>32%</b>	1,194	<b>32%</b>
<b>≥ 75 to &lt; 80</b>	467	<b>12%</b>	507	<b>14%</b>
<b>≥ 80</b>	191	<b>5%</b>	234	<b>6%</b>

# Study 301: Representative of US Demography

## *Full Analysis Set*

	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
<b>Race</b>				
White	12,029	79%	11,995	79%
Black or African American	1,563	10%	1,527	10%
Asian	651	4%	731	5%
Multiracial	315	2%	321	2%
American Indian or Alaska Native	112	< 1%	121	< 1%
Native Hawaiian or Other Pacific Islander	35	< 1%	32	< 1%
Other, Not reported, Unknown	476	3%	443	3%
<b>Ethnicity</b>				
Hispanic or Latino	3,121	21%	3,114	21%

# Study 301: 23% of Participants Reported $\geq 1$ Pre-Existing Medical Risk Factor

*Full Analysis Set*

Medical Risk Factor	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
Diabetes	1,435	9%	1,440	9%
Severe obesity (BMI > 40 kg/m <sup>2</sup> )	1,025	7%	1,021	7%
Chronic lung disease	710	5%	744	5%
Significant cardiac disease	752	5%	744	5%
Liver disease	100	< 1%	96	< 1%
HIV	92	< 1%	87	< 1%

# Study 301: Participants with Occupational Risk Factors Under Consideration for Priority Vaccination

## *Full Analysis Set – Primary Efficacy Analysis*

	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
Healthcare workers	3,790	25%	3,831	25%
Educators and students	1,543	10%	1,552	10%
Pastoral, social, or public health workers	533	4%	503	3%
Transportation and delivery services	482	3%	473	3%
Personal care and in-home services	469	3%	469	3%
Manufacturing and production operations	425	3%	421	3%
Emergency response	302	2%	297	2%
Warehouse shipping and fulfillment centers	191	1%	175	1%
Border protection and military personnel	69	0.5%	68	0.4%



# Overview of Confirmed Symptomatic and Severe Cases by Subgroup

*Per Protocol*

Subgroup	N	# of Confirmed COVID-19 Cases	
		Confirmed Symptomatic	Severe
Overall	28,207	196	30
Age and risk			
≥ 18 and < 65 without comorbidities	16,799	126	6
≥ 18 and < 65 with comorbidities	4,273	37	14
≥ 65 with or without comorbidities	7,135	33	10
Participants with comorbidities (all ages)			
Yes	6,373	47	20
No	21,834	149	10
Race and Ethnicity			
Non-Hispanic White	17,939	154	24
Communities of Color	10,220	42	6

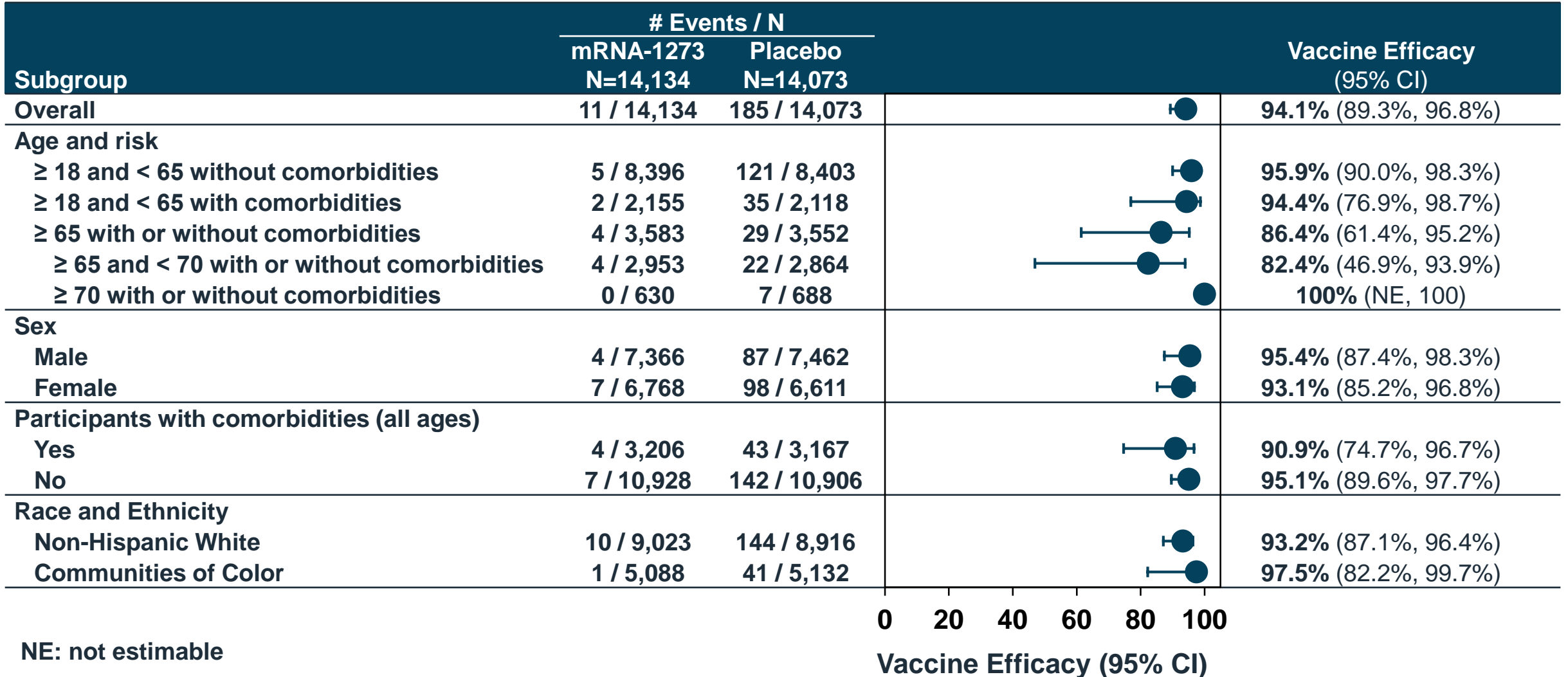
# Study 301: Primary Efficacy Objective Met, VE Against Confirmed, Symptomatic COVID-19 Cases is > 94%

*Per Protocol*

Confirmed, Symptomatic COVID-19 Cases	Interim Analysis		Primary Efficacy Analysis	
	mRNA-1273 N=13,934	Placebo N=13,883	mRNA-1273 N=14,134	Placebo N=14,073
Number of cases, n (%)	5 (< 0.1%)	90 (0.6%)	11 (< 0.1%)	185 (1.3%)
Vaccine efficacy based on hazard ratio (95% CI)	94.5% (86.5%, 97.8%)		94.1% (89.3%, 96.8%)	
p-value	< 0.0001		< 0.0001	
Incidence rate per 1000 person-years	1.8	33.4	3.3	56.5

# Study 301: Subgroup Analyses of Efficacy are Consistent with Primary Analysis

## *Per Protocol – Primary Efficacy Analysis*



# Study 301 Secondary Efficacy Endpoint: Cases of Confirmed Severe COVID-19

*Per Protocol*

Confirmed, Severe COVID-19 Cases	Interim Analysis		Primary Efficacy Analysis	
	mRNA-1273 N=13,934	Placebo N=13,883	mRNA-1273 N=14,134	Placebo N=14,073
Number of cases, n (%)	0 (0%)	11 (< 0.1%)	0 (0%)	30 (0.2%)
Vaccine efficacy based on hazard ratio (95% CI)	100% (NE, 100%)		100% (NE, 100%)	
Incidence rate per 1000 person-years	0	4.1	0	9.1

- One participant death due to COVID-19 in the placebo group
- Given the high efficacy against severe disease, no evidence for vaccine-associated enhanced disease was observed

One potential case of severe disease was reported in the mRNA-1273 group after data cut-off for the primary efficacy analysis, this case has yet to be adjudicated.

NE: not estimable

# Study 301 Secondary Efficacy Endpoint: VE According to CDC Case Definition<sup>1</sup>

*Per Protocol*

CDC Case Definition <sup>1</sup>	Interim Analysis		Primary Efficacy Analysis	
	mRNA-1273 N=13,934	Placebo N=13,883	mRNA-1273 N=14,134	Placebo N=14,073
Number of cases, n (%)	6 (< 0.1%)	121 (0.9%)	11 (< 0.1%)	221 (1.6%)
Vaccine efficacy based on hazard ratio (95% CI)	95.1% (88.9%, 97.8%)		95.1% (91.1%, 97.3%)	
Incidence rate per 1000 person-years	2.2	44.9	3.3	67.6

<sup>1</sup> One clinical symptom from an expanded list and a nasopharyngeal swab positive for SARS-CoV-2 virus

# Study 301 Secondary Endpoint: Symptomatic COVID-19 Cases $\geq$ 14 Days After 1<sup>st</sup> Dose

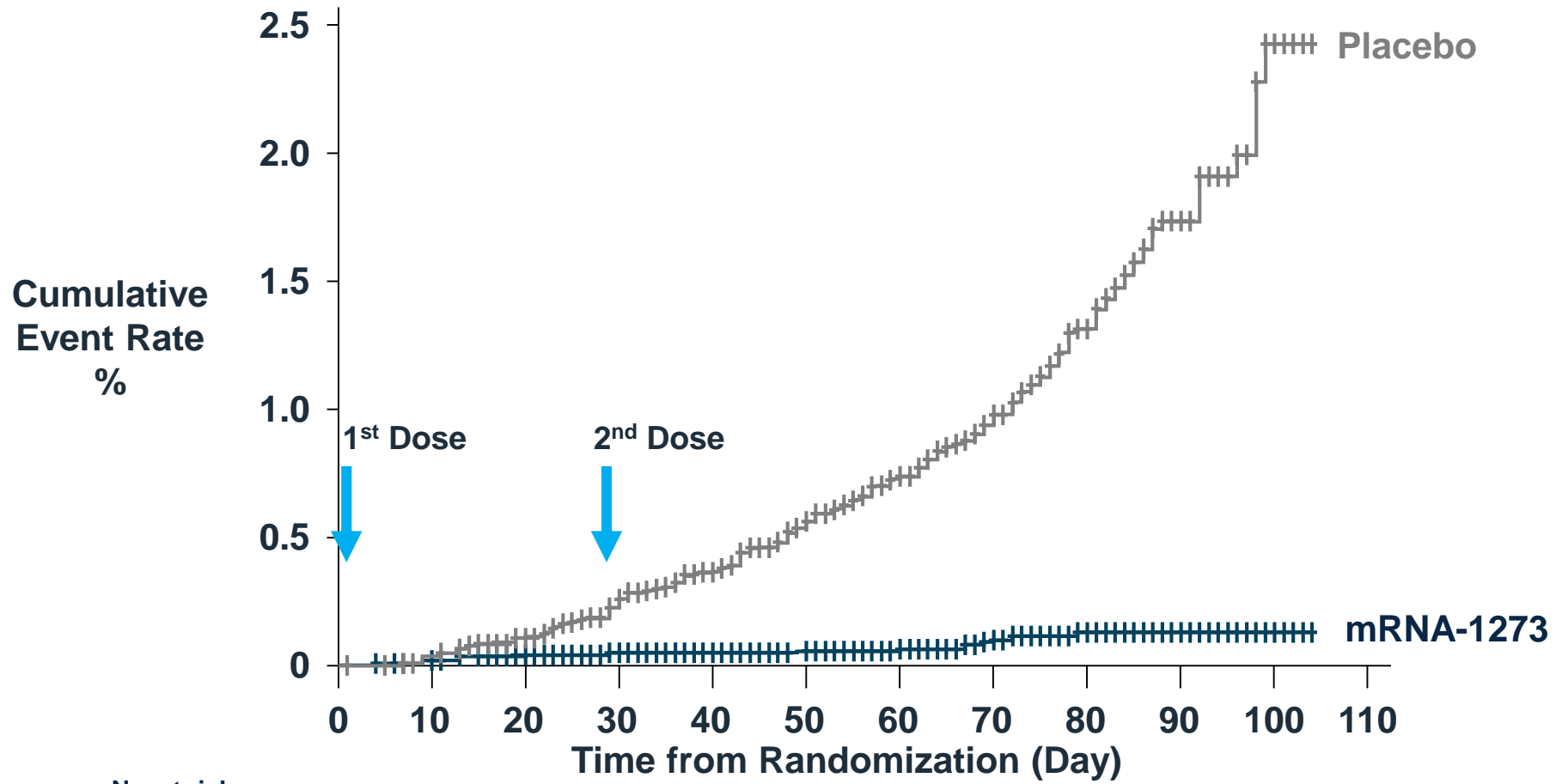
*Per Protocol*

Symptomatic COVID-19 Cases 14 Days After 1 <sup>st</sup> Dose	Interim Analysis		Primary Efficacy Analysis	
	mRNA-1273 N=13,934	Placebo N=13,883	mRNA-1273 N=14,134	Placebo N=14,073
Number of cases, n (%)	6 (< 0.1%)	128 (0.9%)	11 (< 0.1%)	225 (1.6%)
Vaccine efficacy based on hazard ratio (95% CI)	95.4% (89.5%, 98.0%)		95.2% (91.2%, 97.4%)	
Incidence rate per 1000 person-years	2.2	47.5	3.3	68.8

- Not all cases occurring before day-14 post 2nd dose have been adjudicated
- > 96% compliance with 2nd dose

# Kaplan-Meier Estimates of Time to First Occurrence of COVID-19 Starting After Randomization

*mITT - Interim Analysis*



No. at risk	0	10	20	30	40	50	60	70	80	90	100	110
mRNA-1273	14312	14306	13964	13490	12981	12284	10742	8327	5705	2621	583	0
Placebo	14370	14363	14000	13515	12972	12225	10657	8283	5663	2594	586	0

# Study 301: Summary of COVID-19 Cases Within 6 Weeks After Randomization Based on CDC Case Definition<sup>1</sup>

*mITT Population - Interim Analysis*

	mRNA-1273 N=14,550	Placebo N=14,598
	n	n
From randomization to 14 days post 1 <sup>st</sup> dose	5	11
From 14 days post 1 <sup>st</sup> dose to 2 <sup>nd</sup> dose	3	34
From 2 <sup>nd</sup> dose to 14 days post 2 <sup>nd</sup> dose	0	17
<b>Total</b>	<b>8</b>	<b>62</b>

<sup>1</sup> One clinical symptom from an expanded list and a nasopharyngeal swab positive for SARS-CoV-2 virus



# Study 301: Summary of Asymptomatic SARS-CoV-2 Infections as Measured by Scheduled NP Swabs Prior to 2<sup>nd</sup> Dose

## *Per Protocol – Primary Efficacy Analysis*

RT-PCR NP Swab Results	mRNA-1273 N=14,134		Placebo N=14,073	
	n	%	N	%
No documented COVID-19 symptoms between 1 <sup>st</sup> dose and 2 <sup>nd</sup> dose	14	0.1%	38	0.3%

Data suggestive of efficacy for prevention of asymptomatic infection

# Conclusions: mRNA-1273 Efficacy Data

- 94.1% mRNA-1273 efficacy demonstrated in primary analysis on 196 cases
  - Consistent with 94.5% observed in interim analysis on 95 cases
- Primary efficacy hypothesis was met
  - Lower limit of 95% CI was 89.3%, exceeding pre-specified 30% margin
- Reduced severe COVID-19 disease
  - 0 vs 30 cases in mRNA-1273 and placebo groups, respectively
- Other secondary, sensitivity and subgroup analyses support primary efficacy analysis results
- mRNA-1273 offers potential to address the public health crisis of COVID-19

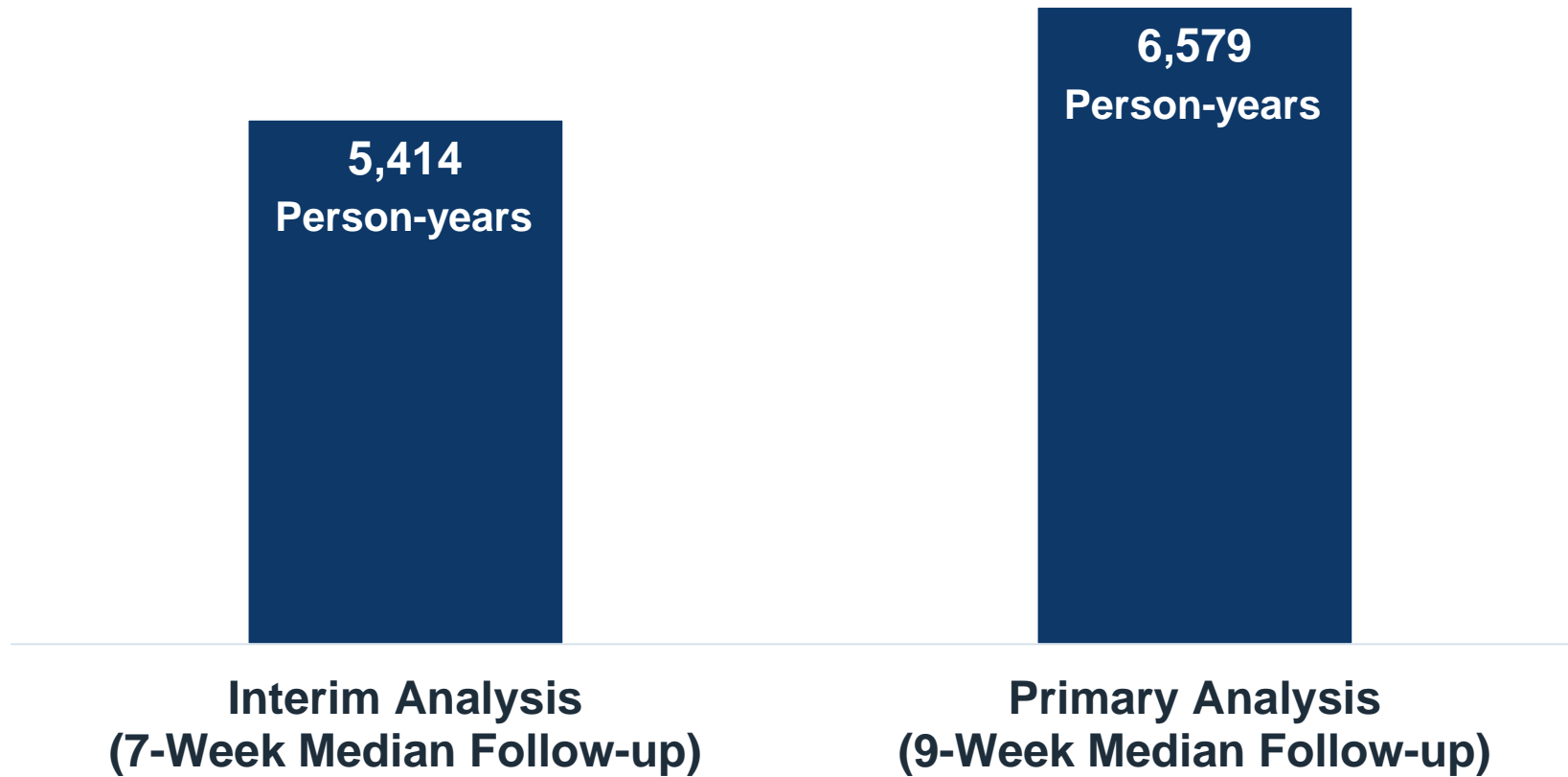
Study 301: mRNA-1273 100 µg Safety  
9-Week Median Follow-up

**David Martin, MD, MPH**

Vice President, Pharmacovigilance  
ModernaTX, Inc.



# Study 301: Primary Analysis Timepoint With 9-Week Median Follow-up



# Study 301: 9-Week Median Exposure Following 2<sup>nd</sup> Dose

*Safety Set, 9-Week Median Follow-up*

Number of Participants	mRNA-1273 N=15,185		Placebo N=15,166	
	n	%	n	%
Received 1 <sup>st</sup> dose	15,185	<b>100%</b>	15,166	<b>100%</b>
Received 2 <sup>nd</sup> dose	14,715	<b>97%</b>	14,613	<b>96%</b>
Completed $\geq$ 28 days since 2 <sup>nd</sup> dose	13,386	<b>88%</b>	13,297	<b>88%</b>
Completed $\geq$ 56 days since 2 <sup>nd</sup> dose	9,406	<b>62%</b>	9,299	<b>61%</b>

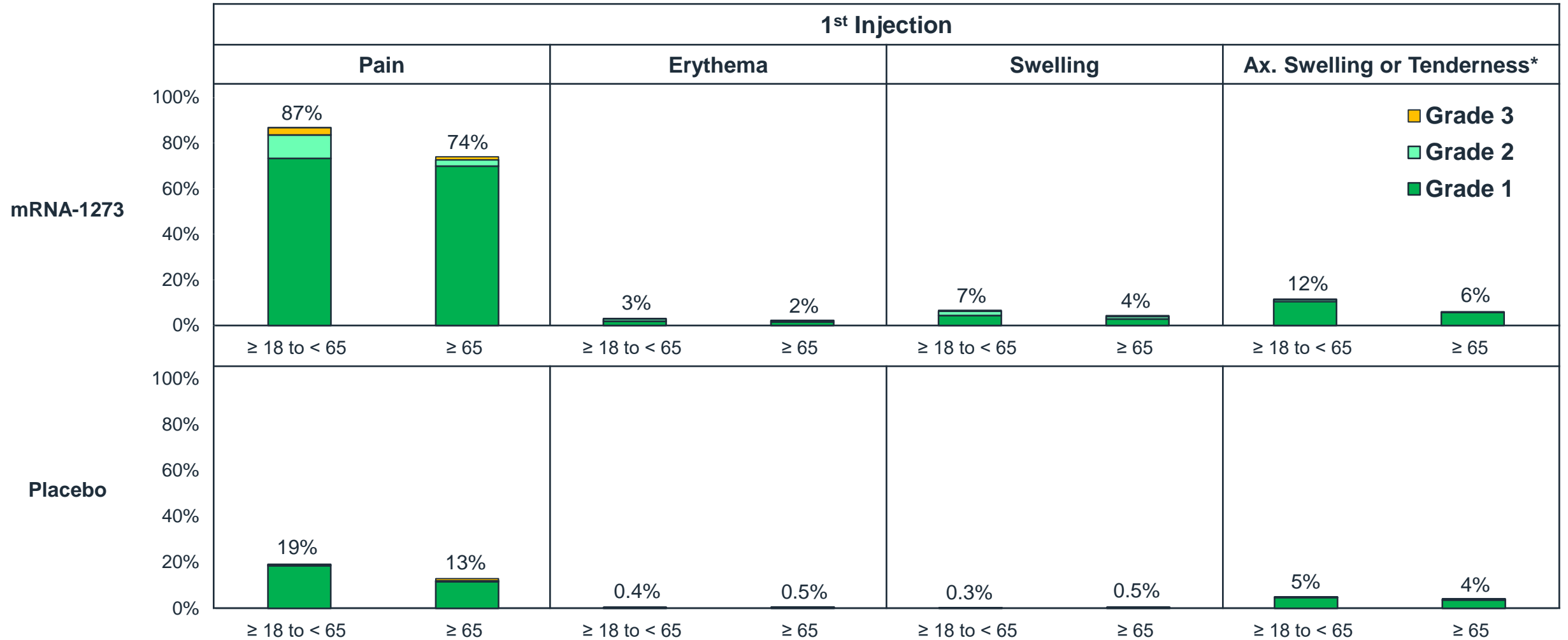


# Solicited Adverse Reactions

**Study 301 Safety Set (N=30,351)**

# Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (1<sup>st</sup> Injection)

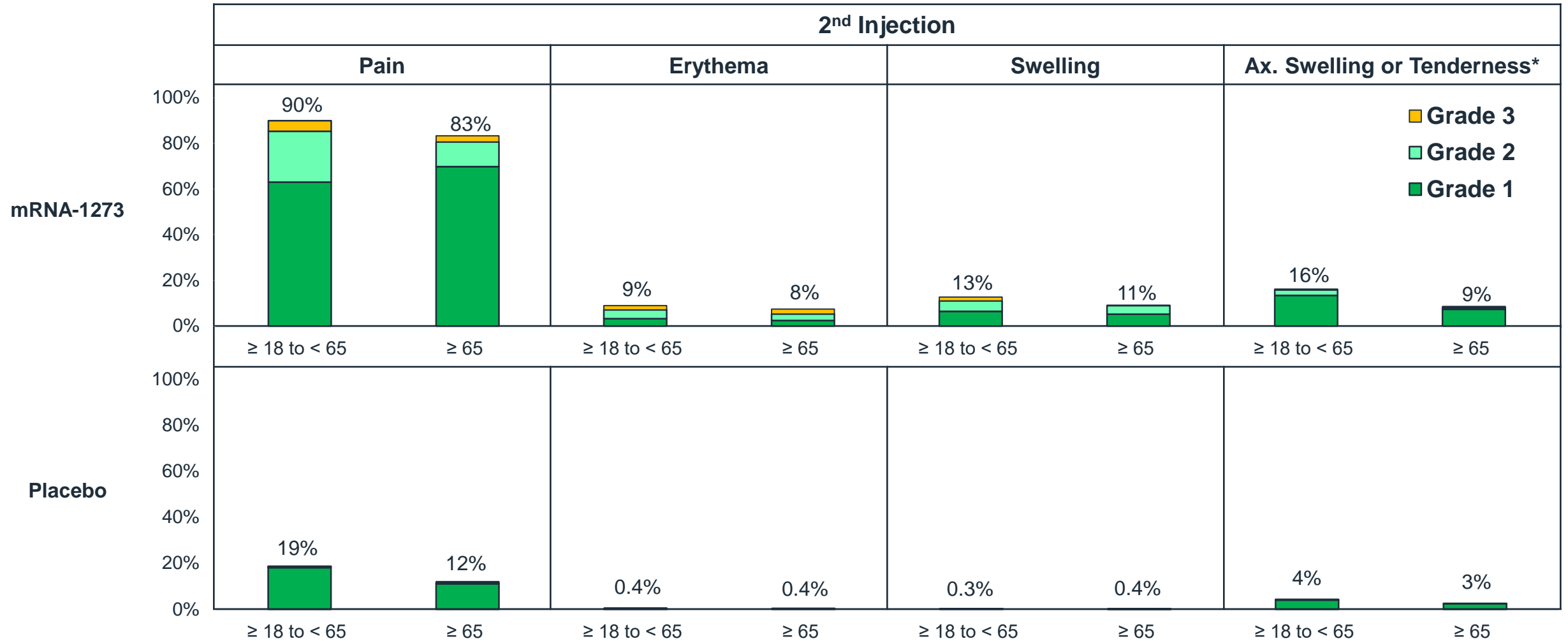
*Safety Set, 9-Week Median Follow-up*



Note: Includes reports within 7 days of either injection. \*Localized axillary swelling or tenderness ipsilateral to the vaccination arm.

# Study 301: Most Solicited Local Adverse Reactions Were Mild-to-Moderate (2<sup>nd</sup> Injection)

*Safety Set, 9-Week Median Follow-up*

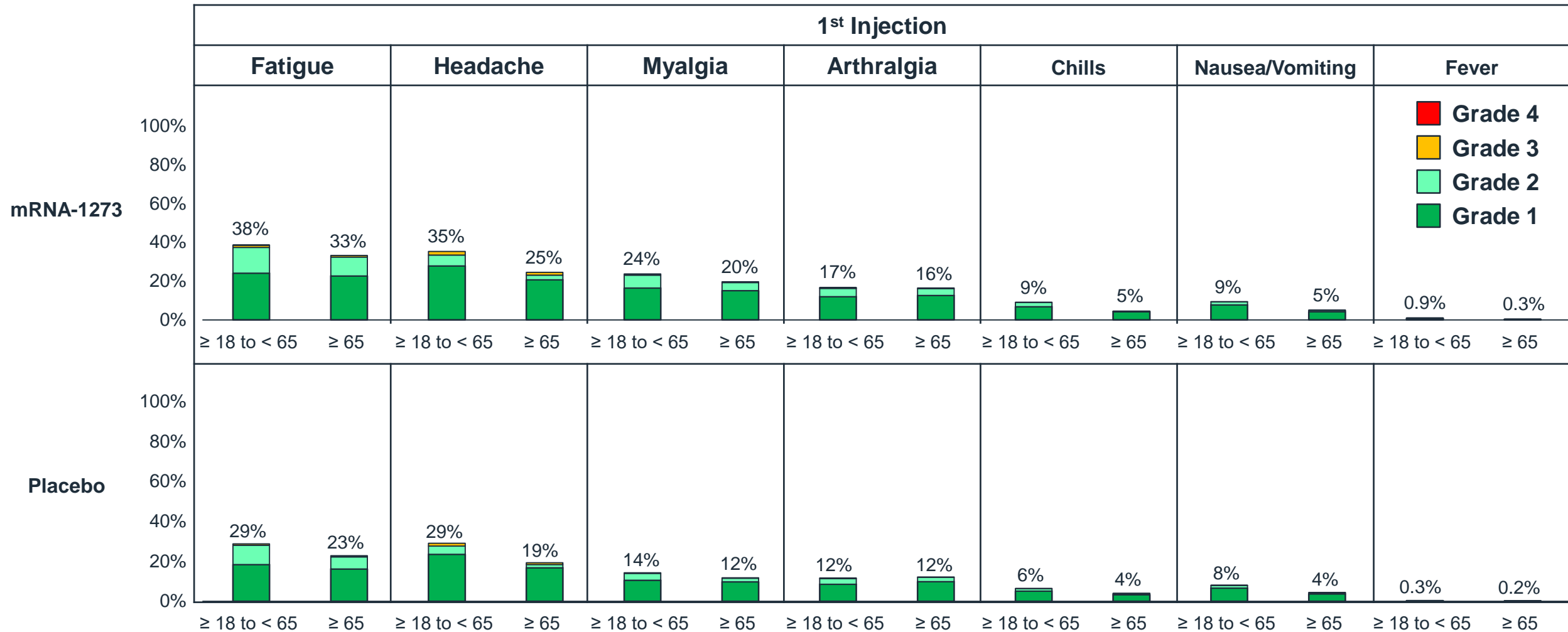


Note: Includes reports within 7 days of either injection. \*Localized axillary swelling or tenderness ipsilateral to the vaccination arm.



# Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (1<sup>st</sup> Injection)

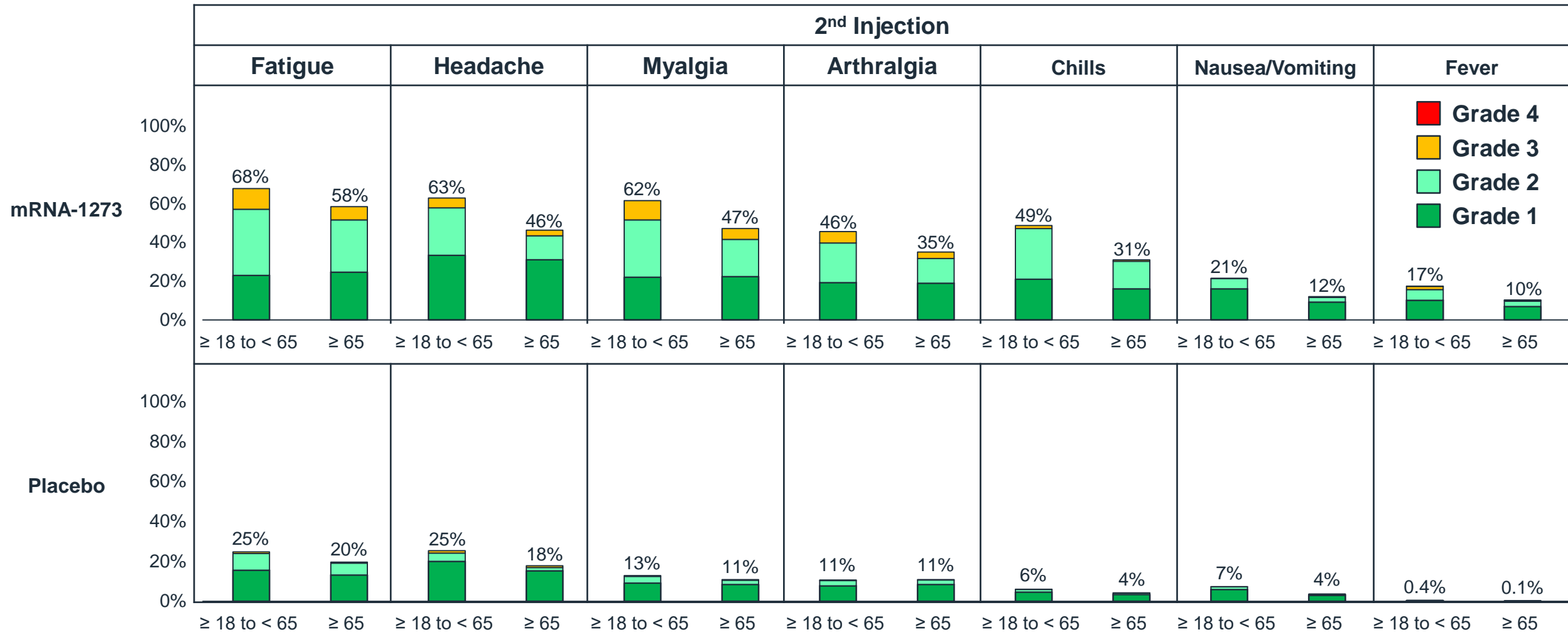
*Safety Set, 9-Week Median Follow-up*



**Note: Solicited Systemic ARs include reports within 7 days of either injection**

# Study 301: Most Solicited Systemic Adverse Reactions Were Mild-to-Moderate (2<sup>nd</sup> Injection)

*Safety Set, 9-Week Median Follow-up*



Note: Solicited Systemic ARs include reports within 7 days of either injection



# Unsolicited Adverse Events

**Study 301 Safety Set (N=30,351)**

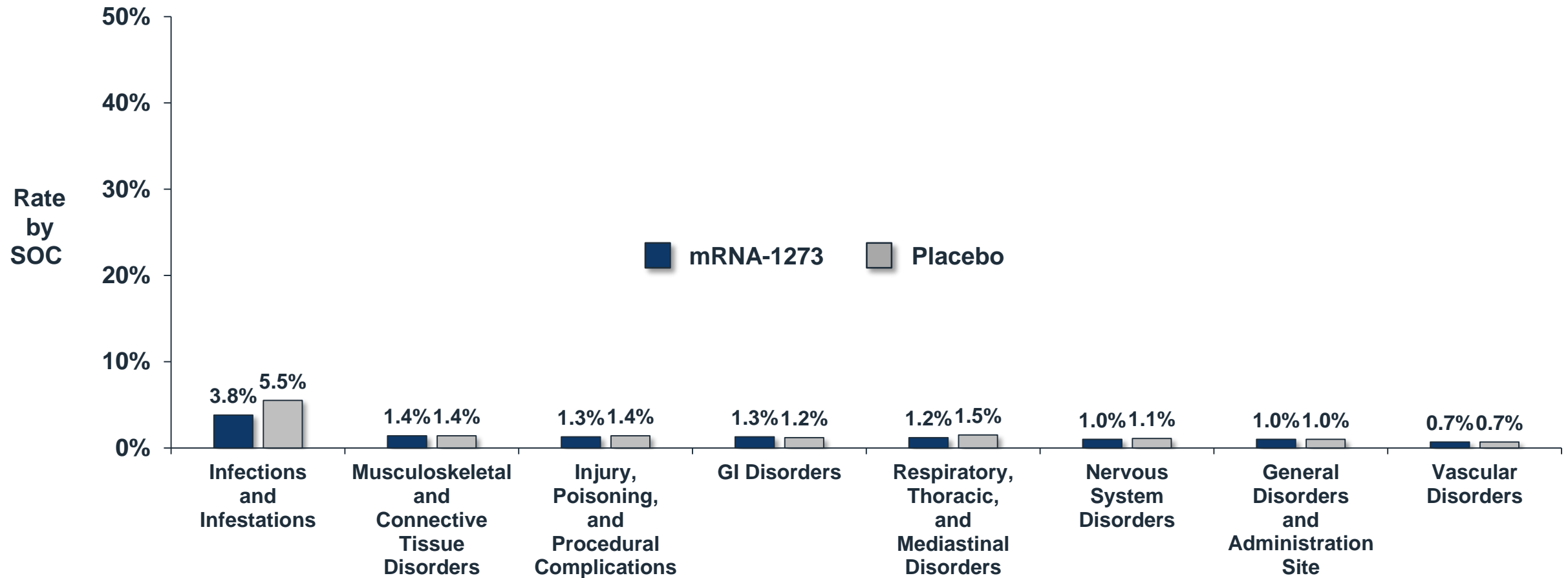
# Study 301: Summary of Unsolicited AEs

*Safety Set, 9-Week Median Follow-up*

Unsolicited Adverse Events	mRNA-1273 N=15,185		Placebo N=15,166	
	n	%	n	%
Any Adverse Event	4,058	27%	3,888	26%
Any Medically-Attended Adverse Event (MAAE)	1,745	11%	1,958	13%
Any Serious Adverse Event (SAE)	147	1%	153	1%
Any death (reported through December 3, 2020)	6	< 0.1%	7	< 0.1%

# Study 301: Rates of Medically-Attended AEs Were Comparable Between Groups

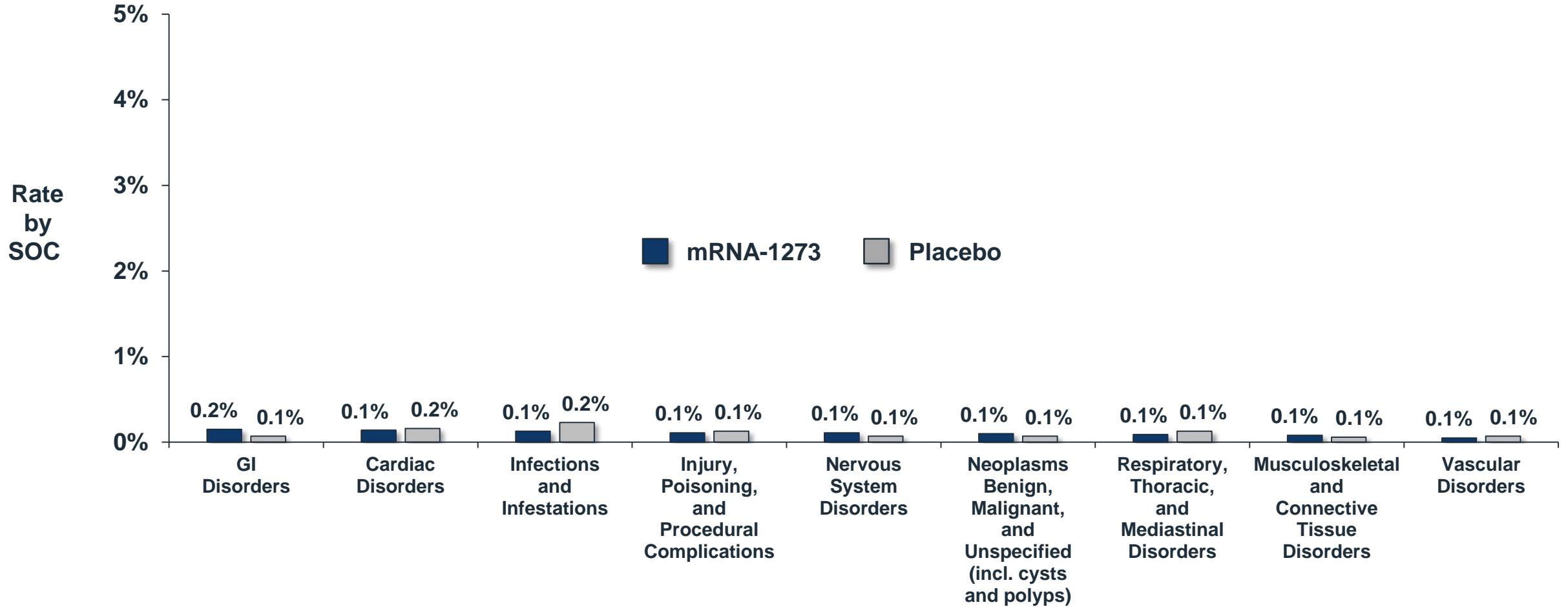
*Safety Set, 9-Week Median Follow-up*



System Organ Class occurring at rate > 0.6%

# Study 301: Rates of SAEs Were Comparable Between Groups

*Safety Set, 9-Week Median Follow-up*



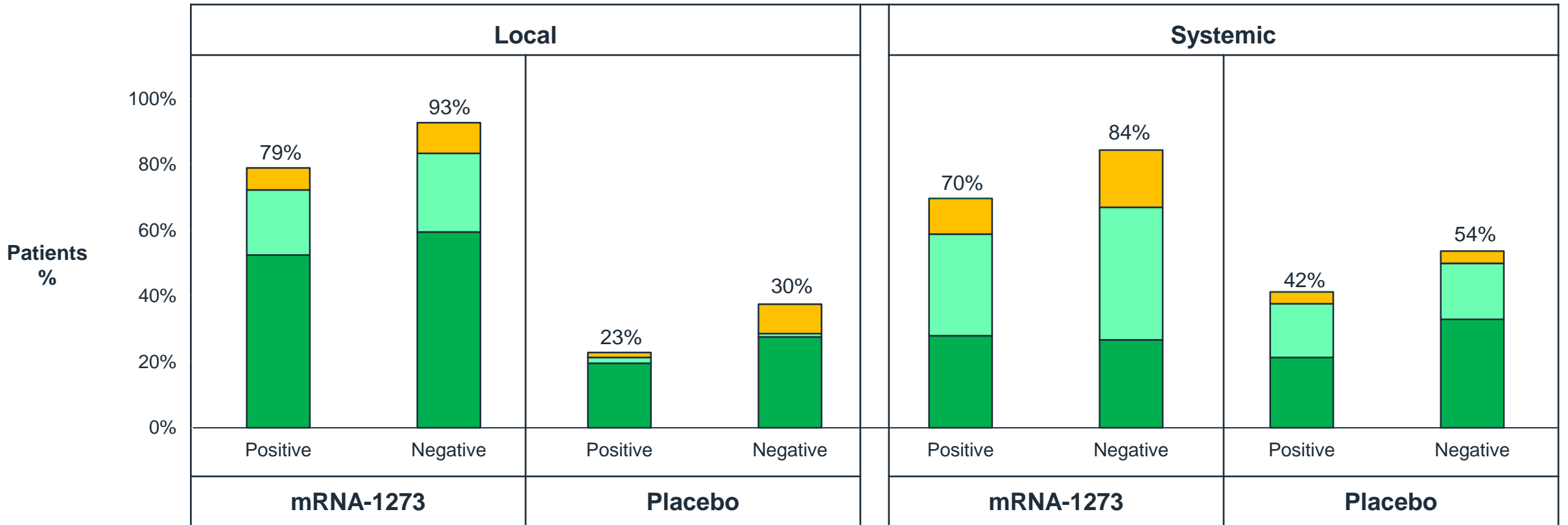
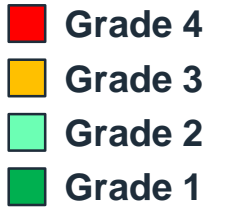
System Organ Class occurring at rate > 0.05%

# Study 301: Deaths Through December 3, 2020

<b>Preferred Term</b>	<b>mRNA-1273 n=6</b>	<b>Placebo n=7</b>	<b>Relationship to Treatment</b>
<b>Abdominal injury (intra-abdominal perforation)</b>	-	1	<b>Not related</b>
<b>Cardio-respiratory arrest</b>	1	1	<b>Not related</b>
<b>Completed suicide</b>	1	-	<b>Not related</b>
<b>COVID-19</b>	-	1	<b>Not related</b>
<b>Head injury</b>	1	-	<b>Not related</b>
<b>Myocardial infarction</b>	1	2	<b>Not related</b>
<b>Multisystem organ failure</b>	1	-	<b>Not related</b>
<b>Not otherwise specified</b>	1	1	<b>Not related</b>
<b>Systemic inflammatory response syndrome (dermatitis bullous)</b>	-	1	<b>Not related</b>

# Study 301: Any Solicited Adverse Reaction by Baseline SARS-CoV-2 Status

*Safety Set, 9-Week Median Follow-up*



Missing baseline SARS-CoV-2 assessment for 288 mRNA-1273 and 235 Placebo participants



# Investigations Unable to Identify Cases Suggestive of mRNA-1273 Anaphylaxis

- No participants excluded for history of anaphylaxis, urticaria, or other significant hypersensitivity
- 2 anaphylactic reactions reported as unsolicited AEs
  - 1 placebo occurring 10 days after 1<sup>st</sup> dose
  - 1 mRNA-1273 occurring 63 days after 2<sup>nd</sup> dose
- Conducted anaphylaxis Standardized MedDRA Query (SMQ), including review of events within 48 hours
  - 0 met Brighton Collaboration Anaphylaxis Case Definition



# Vaccine Safety Monitoring During the EUA

# Integrated US Vaccine Monitoring Developed to Complement USG and other Established Systems

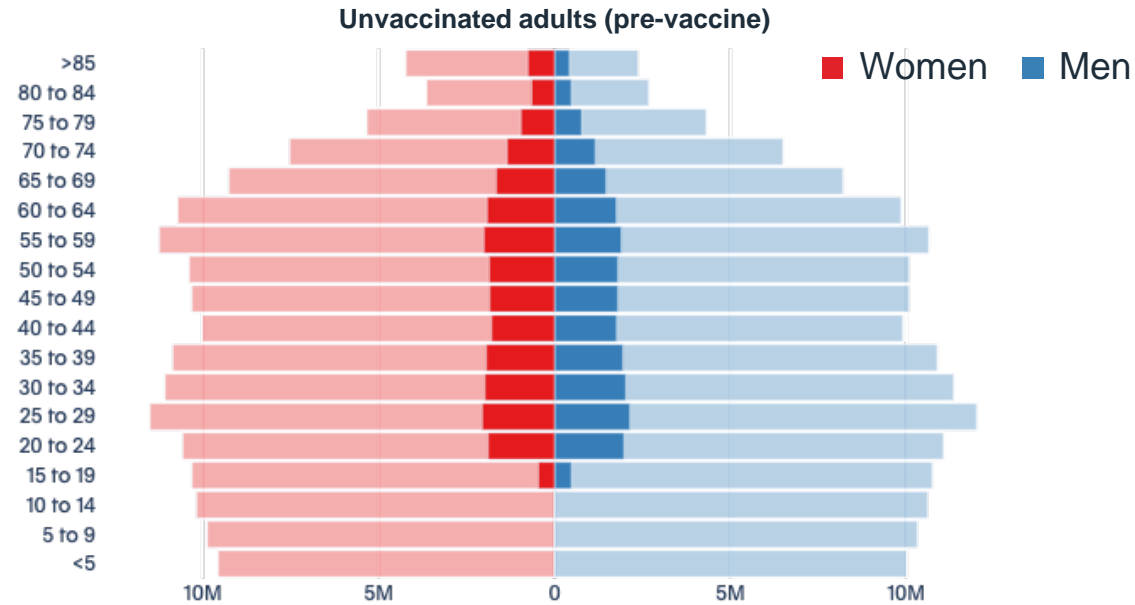
- Address known concerns associated with vaccines by
  - Monitoring AESI in VAERS, other programs and real-world healthcare data
  - Conducting cohort study of pregnant women who receive vaccine
- Monitor long term effectiveness through integrated healthcare system
- Identify and assess new safety signals using
  - Open-ended surveillance of AE reports
  - Real world healthcare claims data

**AESI: adverse event of special interest**

**VAERS: vaccine adverse event reporting system**

# Active Surveillance Program to Complement US Government Systems

## Expected Rates of AESIs Among US adults (pre-vaccination)



Sample closely matches US census population

**45 million US adults**

Closed adjudicated health insurance claims

## Capture Observed Rates of AESIs

**Cohort data updated every 2 weeks to analyze observed over expected AEs**

**Open claims provide early visibility on vaccination**

**Capacity to add new safety signals to the monitoring plan**

**45+ million US adults**

Open and closed health insurance claims linked at the patient level through privacy sparing methods

# Collaboration is Key to Successful Vaccine Safety Monitoring in Global Pandemic

- Moderna Pharmacovigilance and Risk Management Plans being reviewed by FDA and international regulators
- Interface with vaccine safety stakeholders
  - US FDA and CDC and associated advisory committees
  - International regulatory and public health agencies

# Perspective Regarding Placebo Recipients

## Moderna Study 301

Lindsey R Baden, MD  
Brigham and Women's Hospital  
Harvard Medical School



# Disclosures

- Co-PI of the Moderna Study 301, CoVPN 3001 study
  - Funding from NIAID for this activity
  - No funding from Moderna

# A Key Consideration for Study 301 Volunteers

- Their viewpoint – especially given the EUA (12/11) for a SARS-CoV-2 vaccine
  - We must enhance (not undermine) their trust and engagement
  - They are making rapid informed decisions
    - If we make it difficult for them, they will not come back
    - We are asking them for extra visits, blood draws, questionnaires for ~18 months
  - We must provide them information and choice in a timely manner
  - We must ensure equity in volunteer management



# Study 301 Participants Eligible for Vaccination

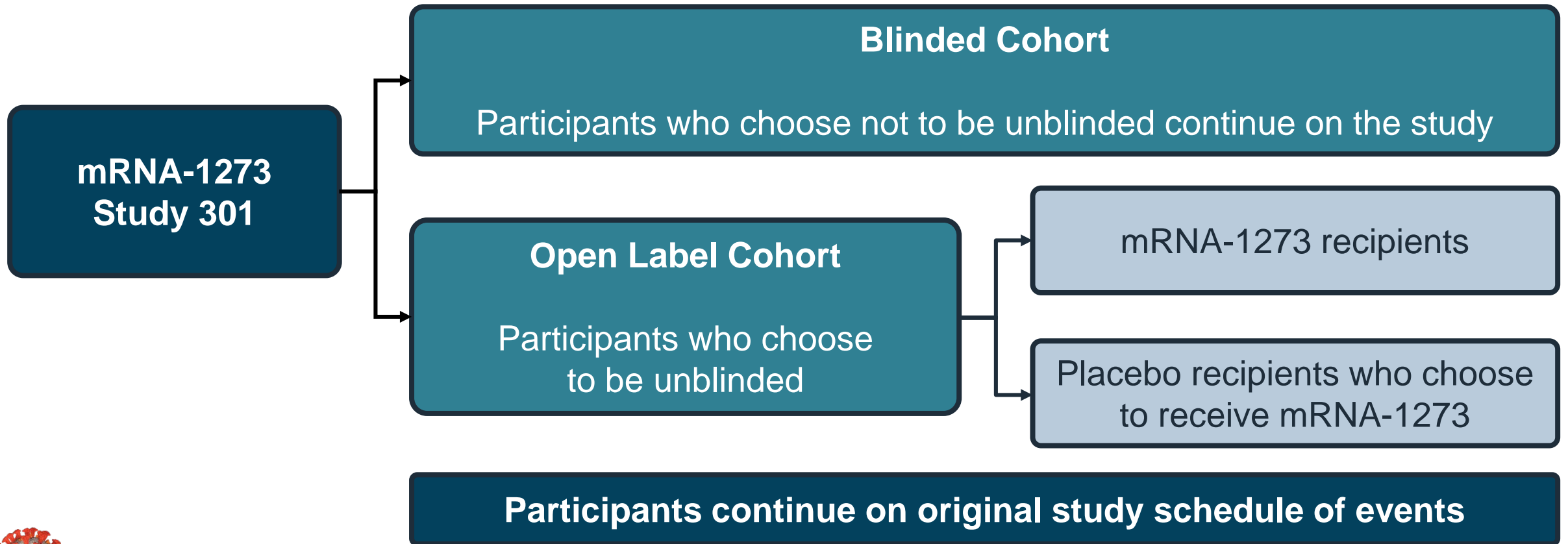
## Based on Current CDC Guidance

- Phase 1a: 7,613 Healthcare workers
- Phase 1b: 7,030 Critical Infrastructure workers
- Phase 1c: 7,520 aged 65+
- Phase 1c: 5,065 aged 18-65 and at risk of severe disease

Clinical study vaccine supplies at sites will otherwise go to waste,  
and can't be used for EUA supply

# Proposed Path Forward

Enables Crossover and Minimizes Loss of Follow-up



# Advantages of Proposed Trial Design

- Benefits Volunteers
  - Not disadvantaged by trial participation
  - Maintains trust and engagement
  - Allows participants to make rapid and informed decisions
  - Ensure equity in volunteer management
- Benefits Society
  - Maintains trial integrity
  - Minimizes loss of follow-up
  - Allows rigorous, continued collection of safety and effectiveness data
  - Supports future BLA submission

Emergency use of the  
MODERNA COVID-19 VACCINE  
for active immunization to prevent  
COVID-**19 in individuals  $\geq$  18 years of age**

**Tal Zaks, MD PhD**

Chief Medical Officer

ModernaTX, Inc.



# Data Support Emergency Use Authorization

- Exceed FDA efficacy criteria for BLA
  - VE = 94.1% (89.3%, 96.8%),  $p < 0.0001$
  - Consistency among subgroups
  - Very high efficacy maintained against severe disease
- Safety profile well characterized in > 15,000 vaccine recipients
  - Majority of solicited injection and systemic AEs reported as mild-to-moderate and resolve, occur  $\leq 7$  days of injection

# Emergency Use Authorization (EUA) Application for mRNA-1273

**ModernaTX, Inc.**

Vaccines and Related Biological Products Advisory Committee

December 17, 2020