

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

**Moderna, Inc.**

Vaccines and Related Biological Products Advisory Committee  
Day, Month 2020

# Introduction

**Tal Zaks, MD PhD**

Chief Medical Officer  
Moderna, 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 animal products, preservatives, or adjuvants
- Clinical experience with mRNA infectious disease vaccines since 2015

# **mRNA-1273 Codes for SARS-CoV-2 Spike Protein**

- SARS-CoV-2 spike protein is immunogenic, activating humoral and cellular immunity
- SARS-CoV-2 spike-based vaccines are protective in animal models
- Neutralizing antibodies against SARS-CoV-2 spike proteins are protective

# mRNA-1273 Shipping, Storage and Administration

## Shipping

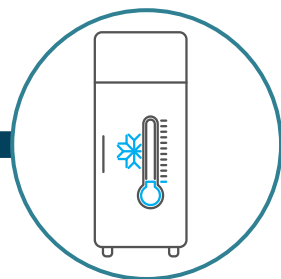
-25° to -15°C



**Full or partial pallets**  
(up to 115,200 doses)

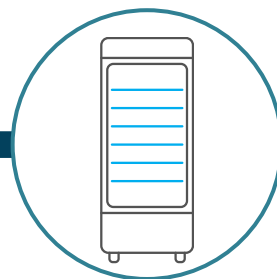
## Freezer

-25° to -15°C  
(up to 6 months)



## Refrigerator

2-8°C  
(up to 30 days)



## Administration

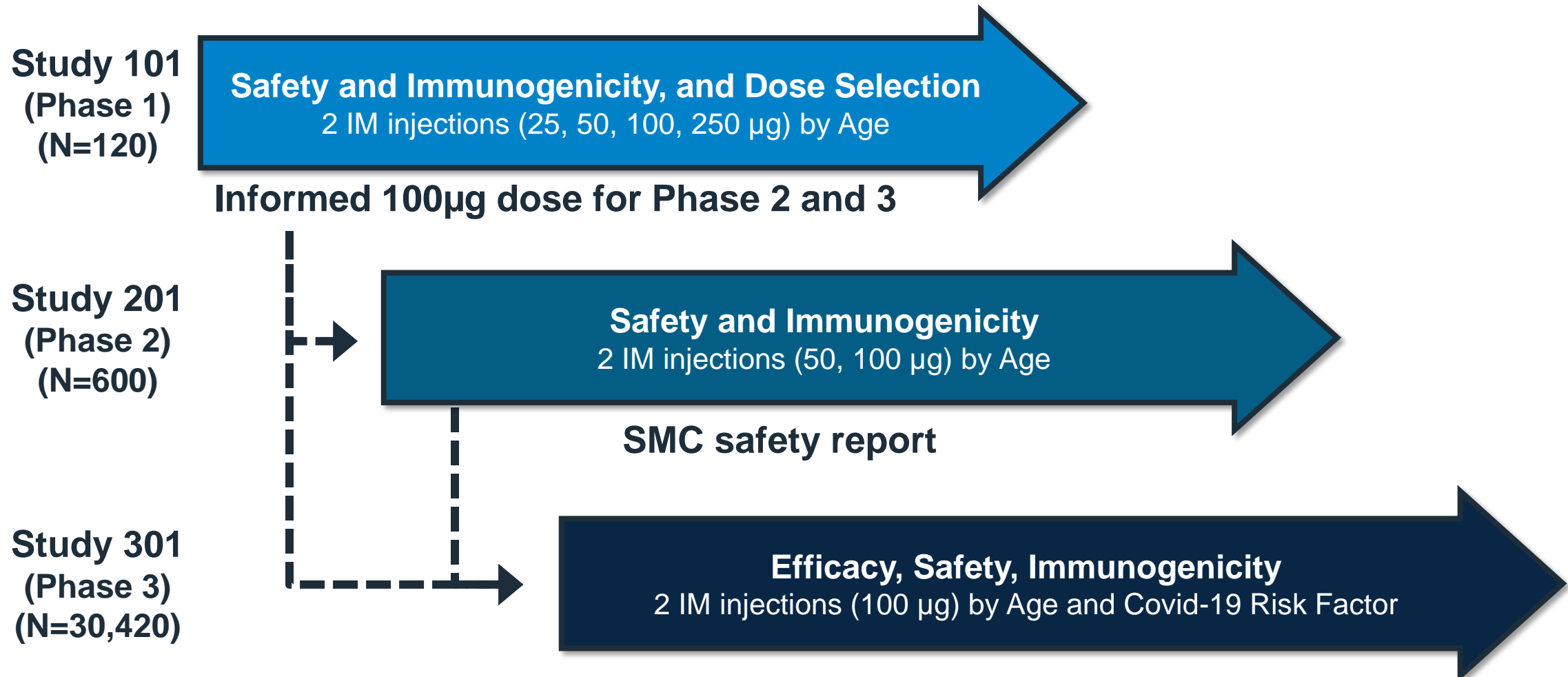
15 to 25°C  
(up to 12 hours)



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

**No dilution  
required**

# Clinical Development Program Designed in Consultation with FDA, NIH, BARDA and OWS



# Pivotal Study 301 Followed FDA Guidance for Powering and Enrollment

- Similar requirements for BLA and EUA
- Prespecified case-driven efficacy assessments
  - Interim Analysis based on 95 cases (7-week median follow up)
  - Primary Efficacy Analysis based on 196 cases (8-week median follow up)
- Stratification used to support adequate enrollment of important sub-groups
- Independent NIH-appointed DSMB



# Study 301 Data Support Emergency Use Authorization

- Exceed FDA efficacy criteria for BLA
  - VE = 94.1% (89.3%, 96.8%),  $p < 0.0001$
  - Very high efficacy maintained against severe disease
  - Consistency among subgroups
- No evidence of increased risk for enhanced disease
- Safety profile well characterized by > 15,000
  - 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  
Moderna, Inc.

## Efficacy

### **Jacqueline Miller, MD, FAAP**

Senior Vice President, Therapeutic Head, Infectious Disease  
Moderna, Inc

## Safety

### **David Martin, MD, MPH**

Vice President, Pharmacovigilance  
Moderna, 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

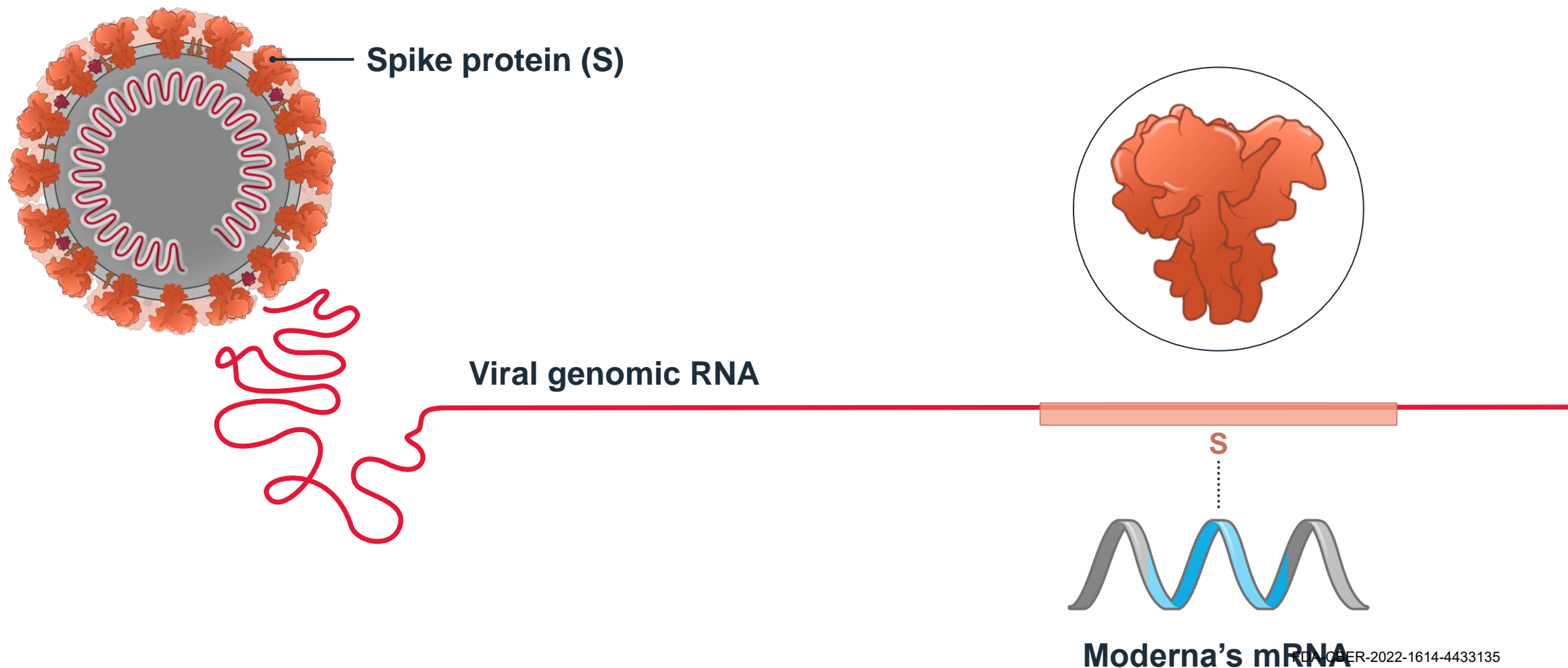
# **mRNA Platform and Mechanism of Action of mRNA-1273**

**Melissa J. Moore**

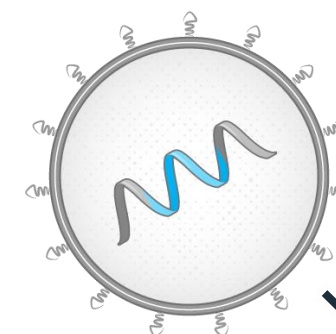
Chief Scientific Officer, Platform Research  
Moderna, Inc



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

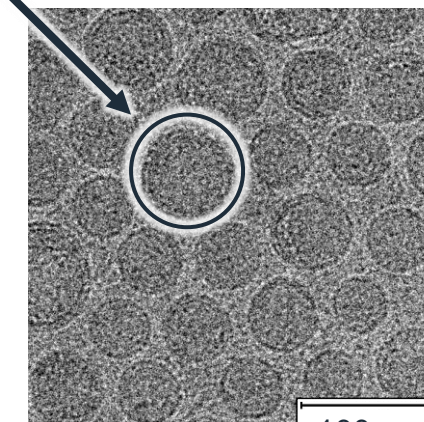


# Our Manufacturing Process Utilizes No Ingredients of Human or Animal Origin



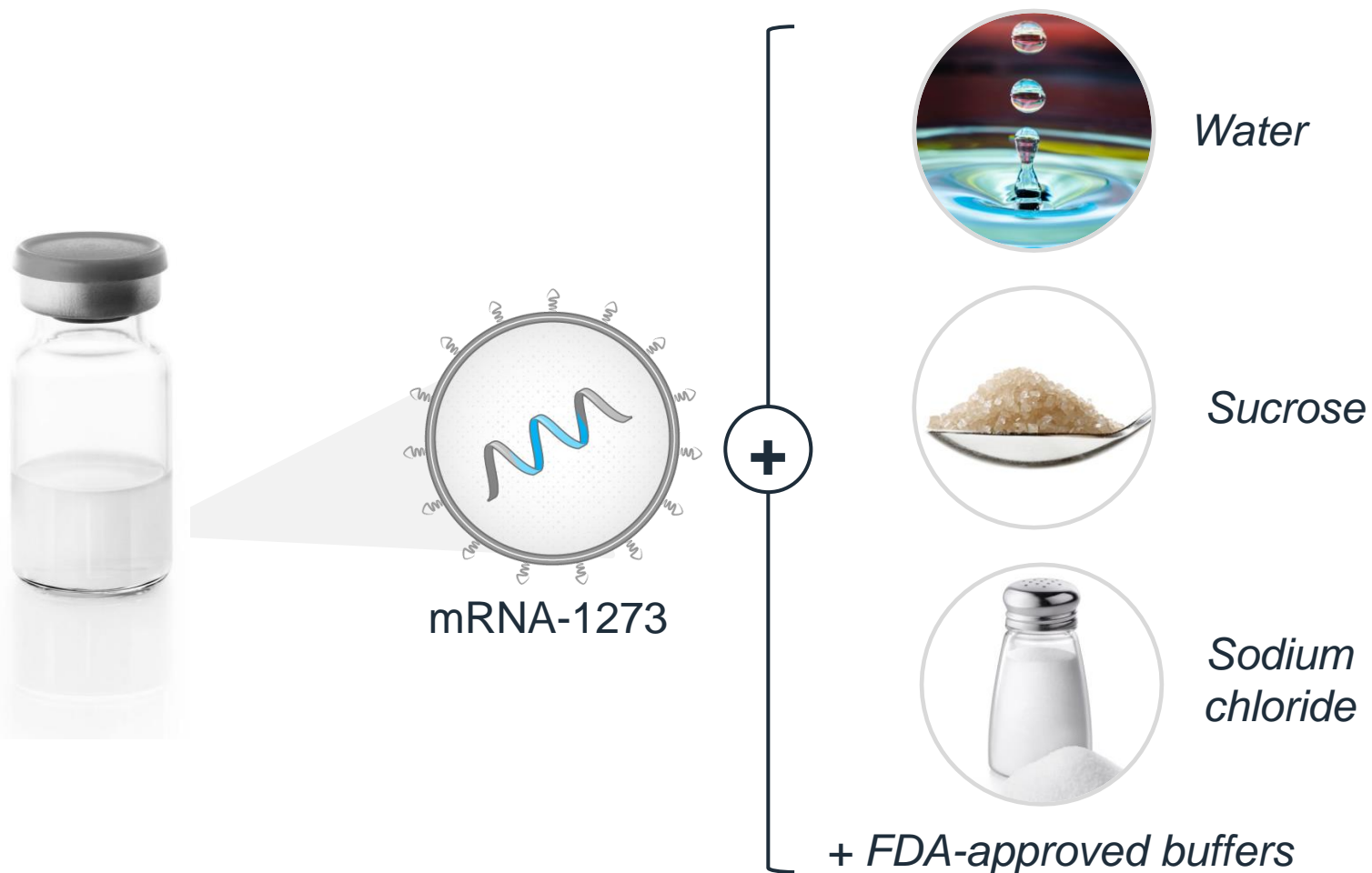
**mRNA in Lipid nanoparticle (LNP)**

*Electron micrograph of mRNA-1273*



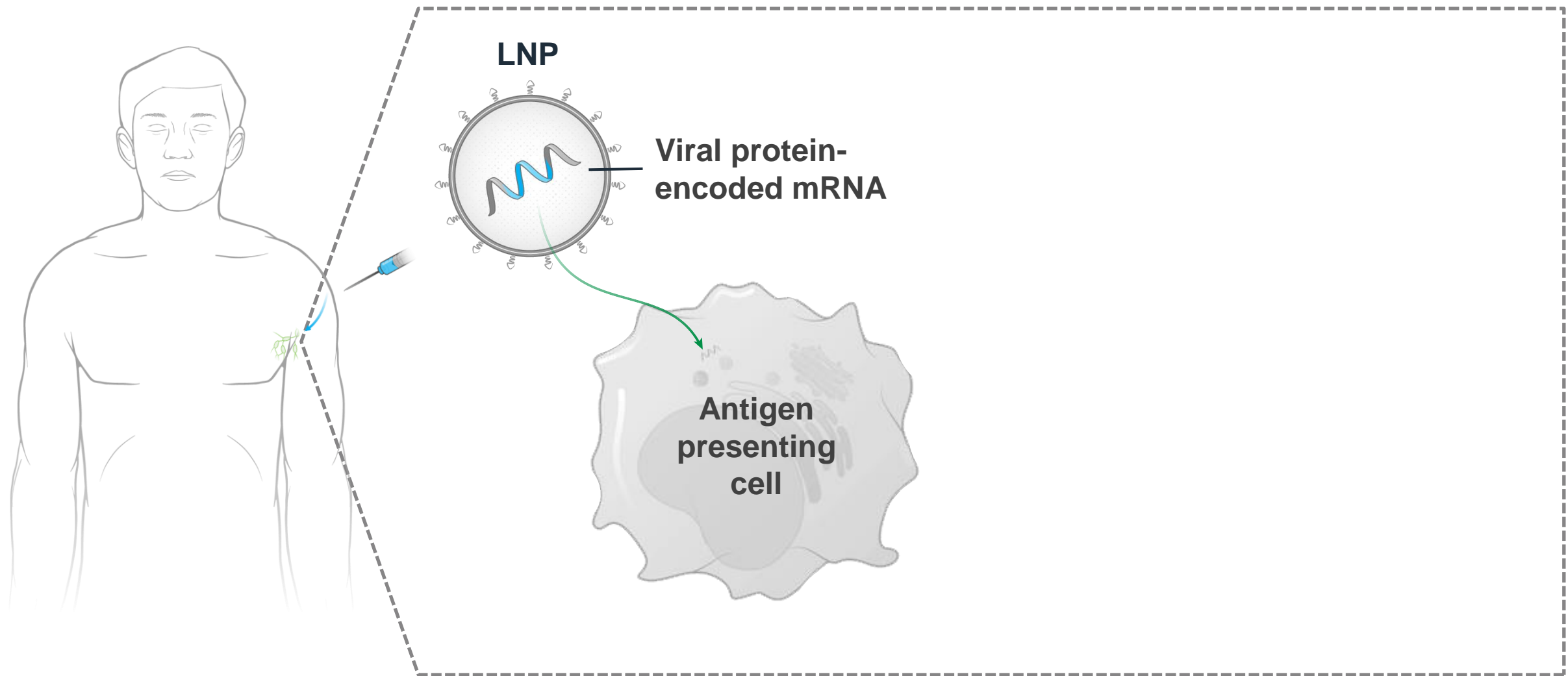


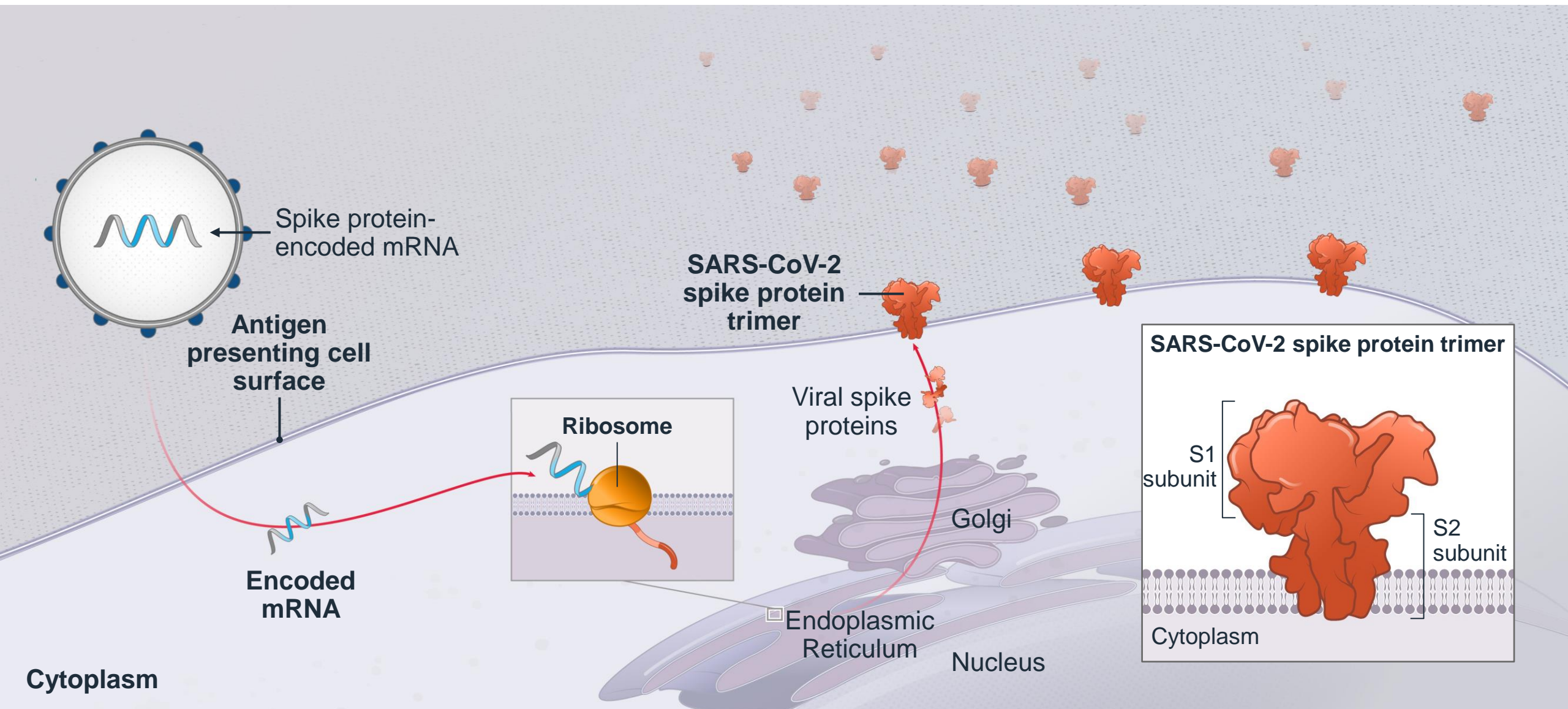
# In the Vial



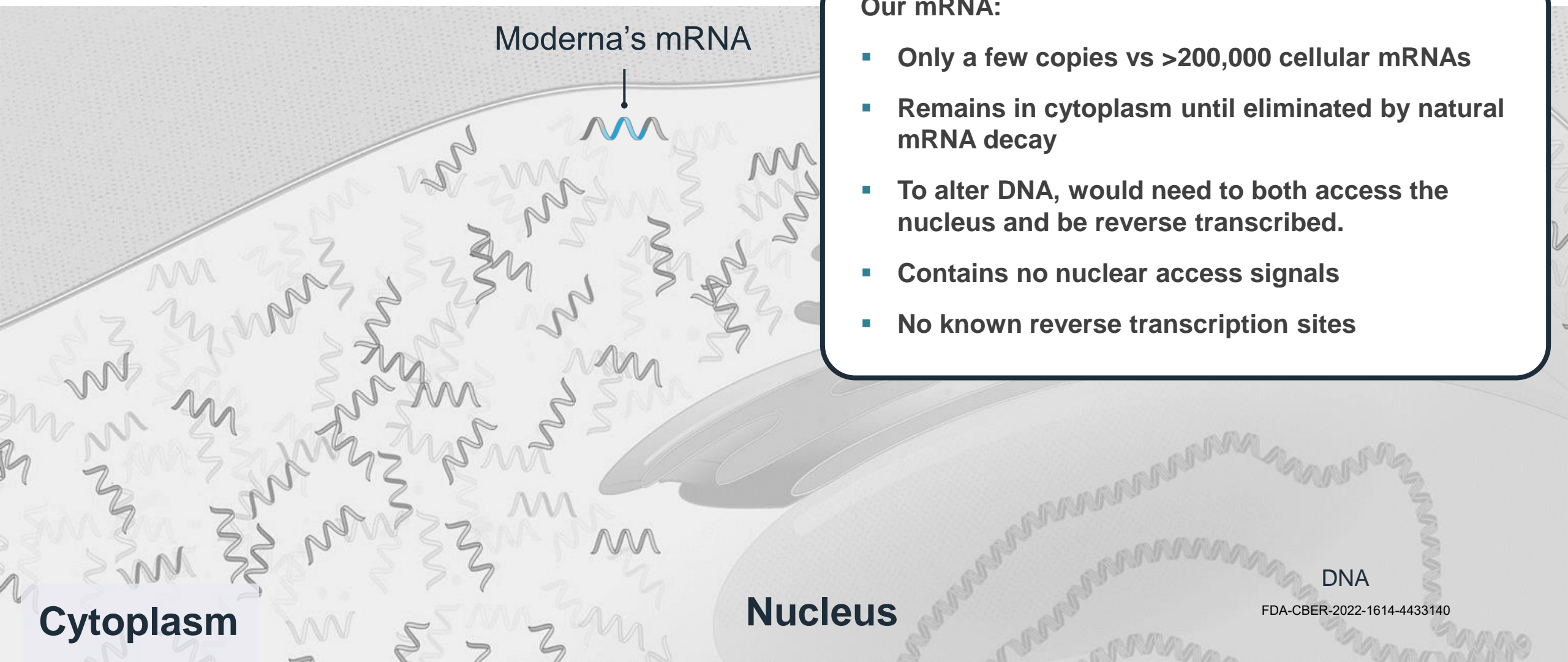
- **No preservatives**
- **No antibiotics**
- **No adjuvants**
- **All active components biodegradable**







# Our mRNA Vaccine Cannot Alter DNA



## Our mRNA:

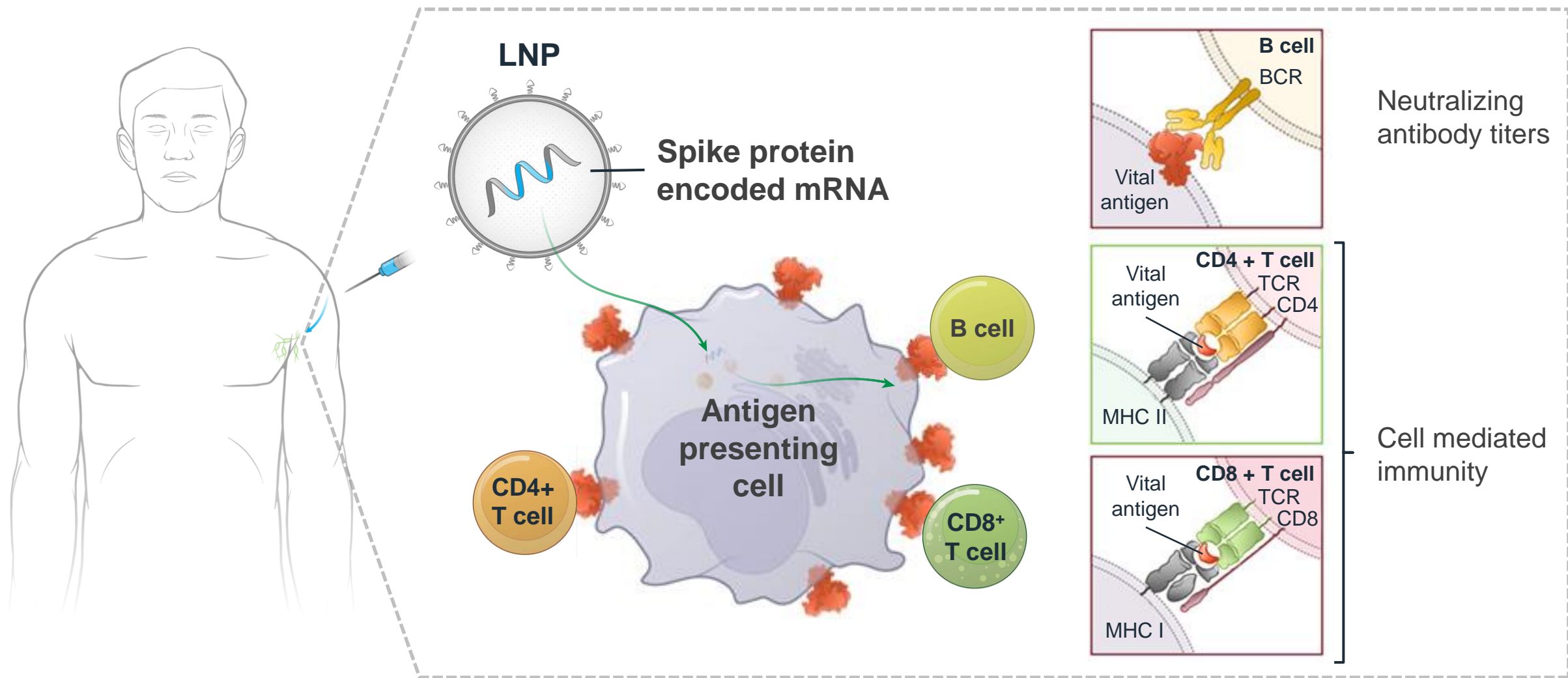
- Only a few copies vs >200,000 cellular mRNAs
- Remains in cytoplasm until eliminated by natural mRNA decay
- To alter DNA, would need to both access the nucleus and be reverse transcribed.
- Contains no nuclear access signals
- No known reverse transcription sites

Cytoplasm

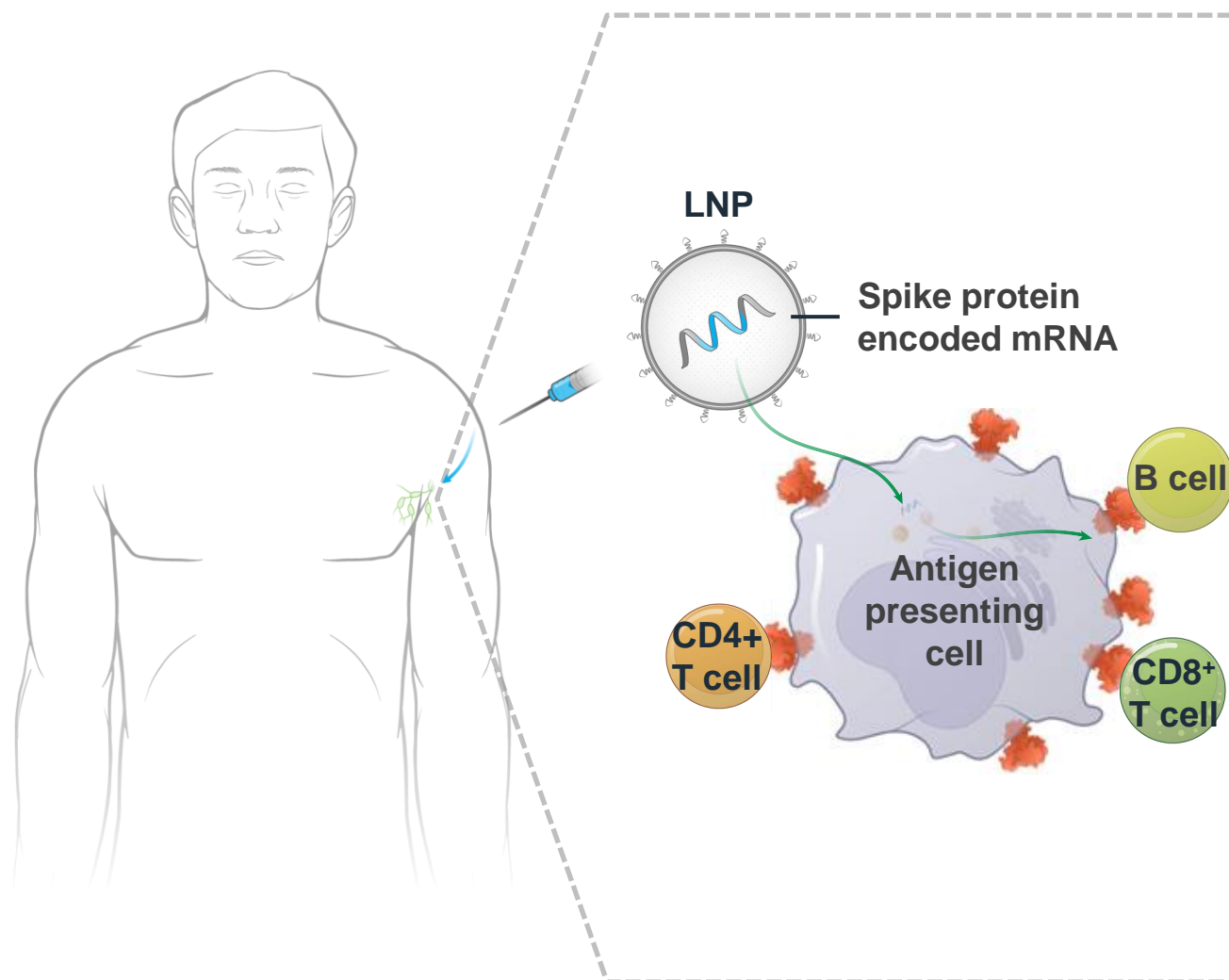
Nucleus

DNA

FDA-CBER-2022-1614-4433140







## 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*)
- LNP allows mRNA to mimic an infection, but with no true infection
- mRNA can neither interact with nor integrate into DNA

# mRNA-1273 Efficacy

*Jacqueline Miller, MD, FAAP*

Senior Vice President, Therapeutic Head,  
Infectious Diseases

Moderna, Inc



# mRNA-1273 Development Plan Evaluated > 15,000 Recipients of 100- $\mu$ g dose in 3 Clinical Trials

## Phase 1 Study 101

N = 120

Open-Label

Doses Studied:  
25, 50, 100, or 250  $\mu$ g

Day 119 safety and  
immunogenicity

## Phase 2 Study 201

N = 600

Randomized,  
Observer-Blind,  
Placebo-Controlled

Doses Studied:  
50 or 100  $\mu$ g

Day 57 safety and  
immunogenicity

## Phase 3 Study 301

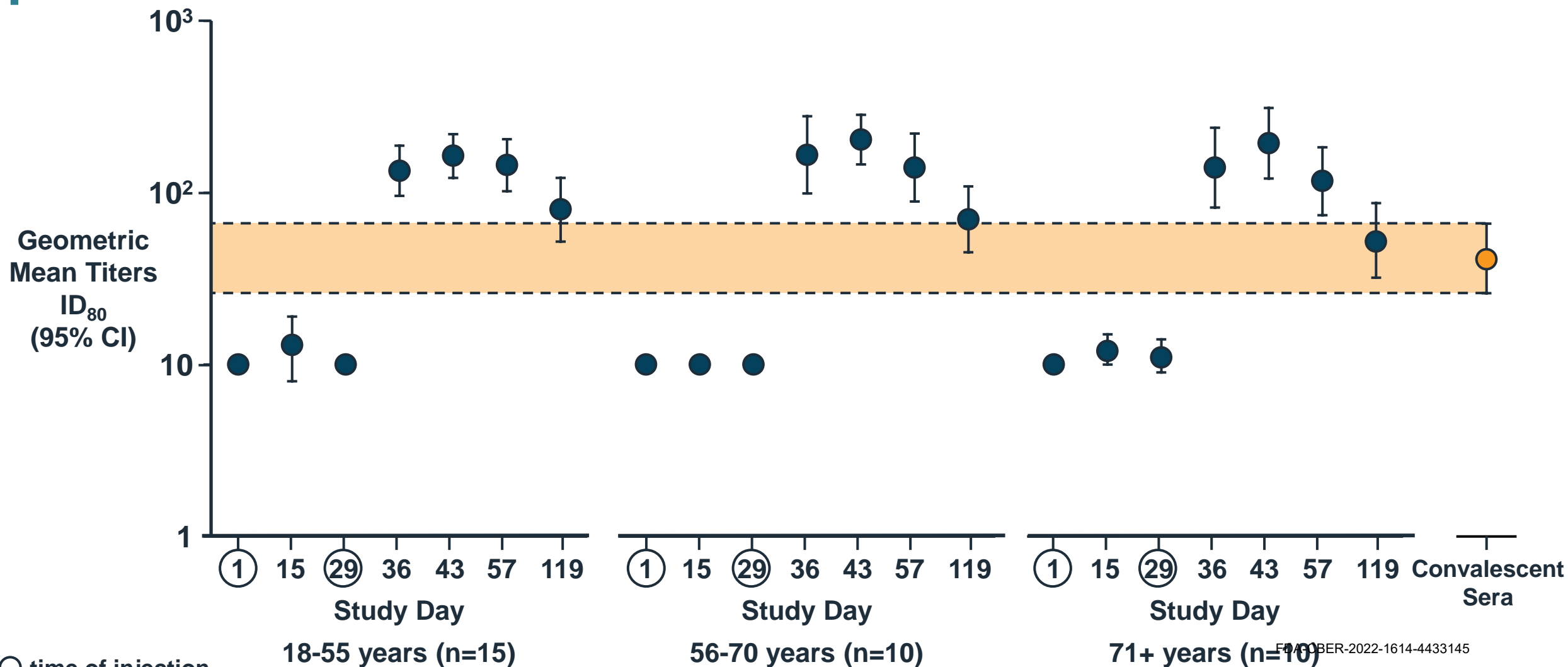
N = 30,420

Randomized,  
Observer-Blind,  
Placebo-Controlled

Dose Studied:  
100  $\mu$ g

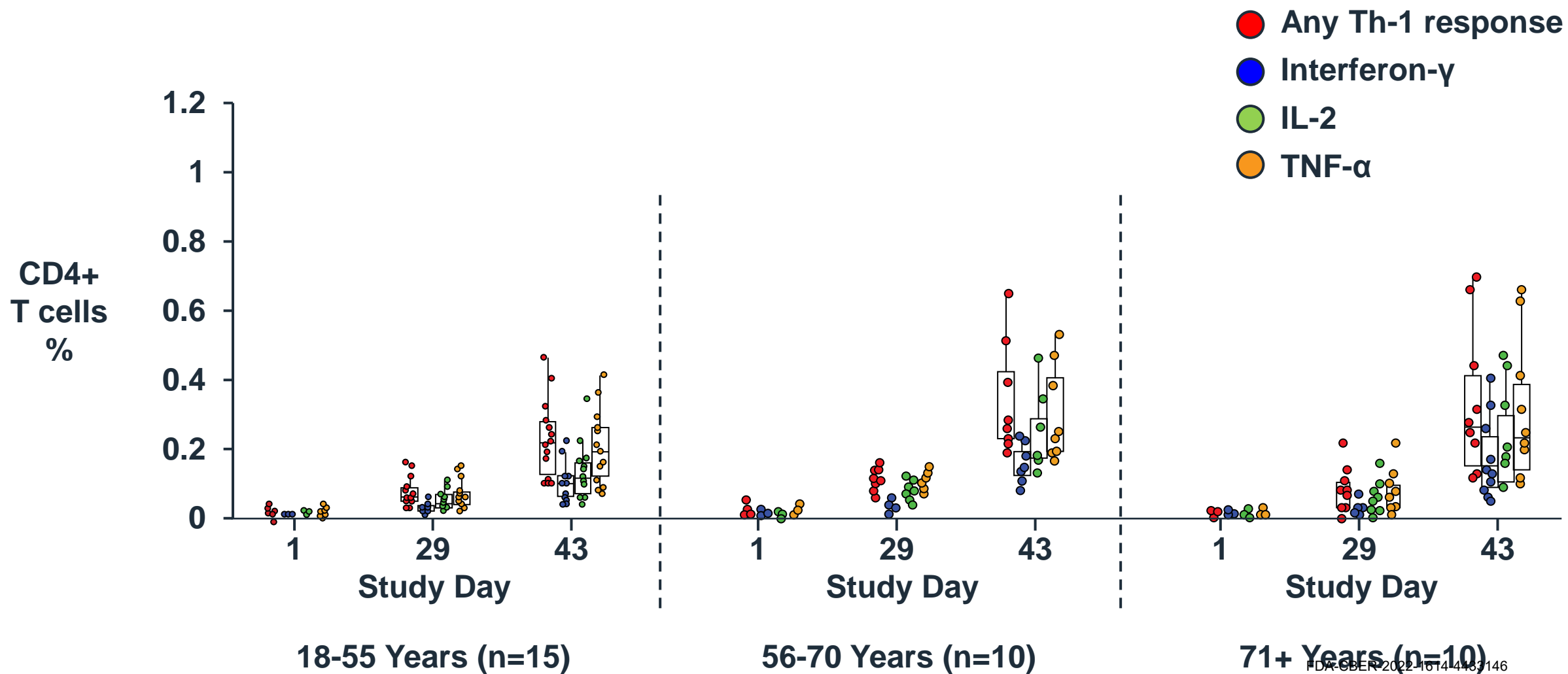
Pivotal EUA efficacy  
and safety data

# Study 101: mRNA-1273 100 µg Neutralizes SARS-CoV-2 Across All Age Groups (Pseudovirus Neutralization Assay)



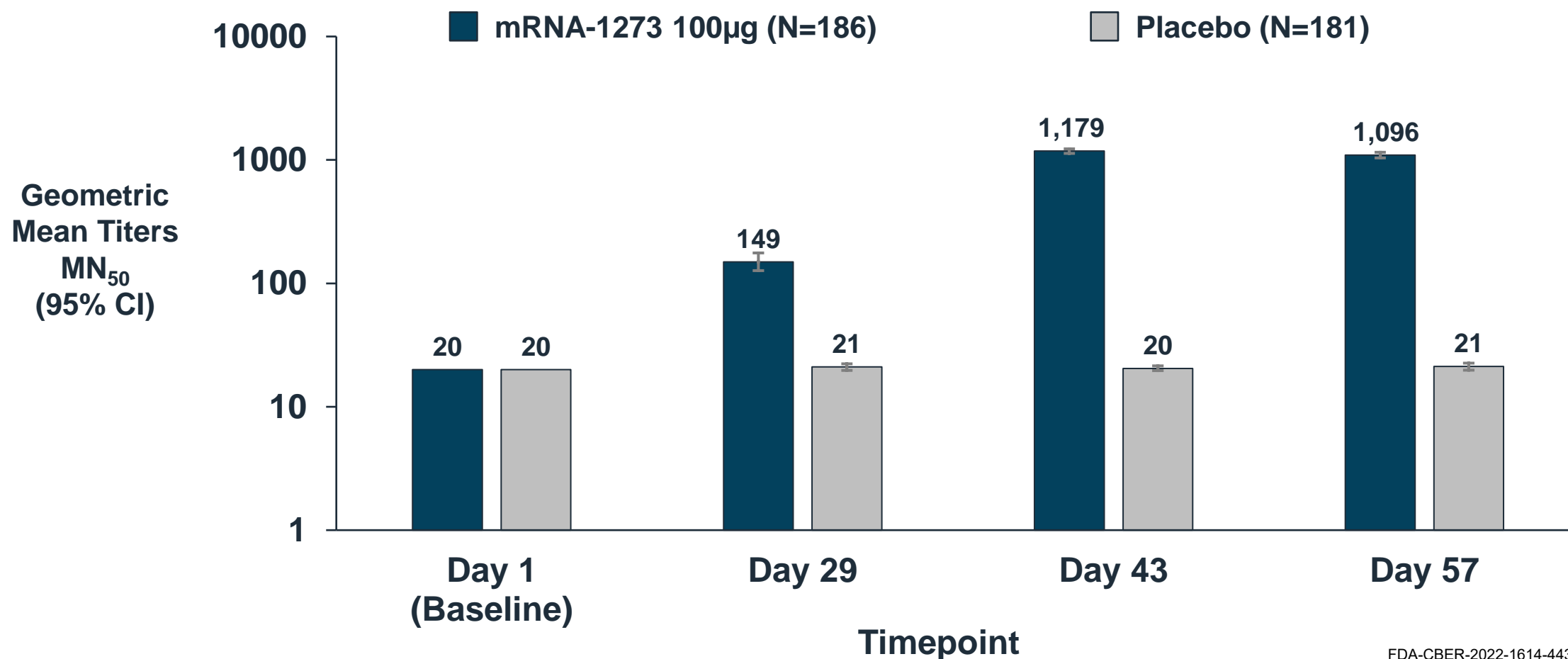


# Study 101: mRNA-1273 Induces CD4+ T-Cell Response at 14 Days Post 2<sup>nd</sup> Injection



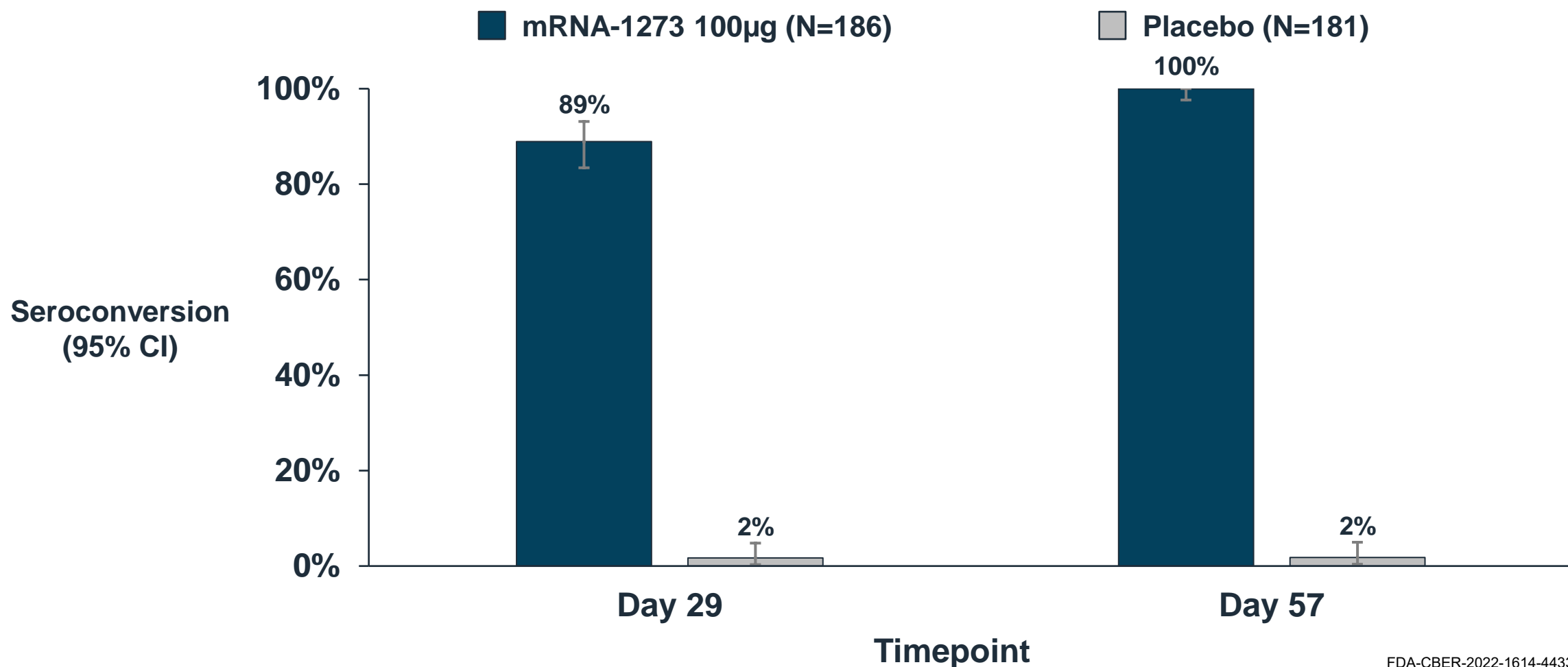
# Study 201: mRNA-1273 Induces Neutralizing Antibodies to SARS-CoV-2

*(Per Protocol Set, WT Virus Microneutralization [MN] Assay)*



# Study 201: All Participants Who Received mRNA-1273 Seroconverted After 2<sup>nd</sup> Injection

*(Per Protocol Set, WT Virus Microneutralization [MN] Assay)*



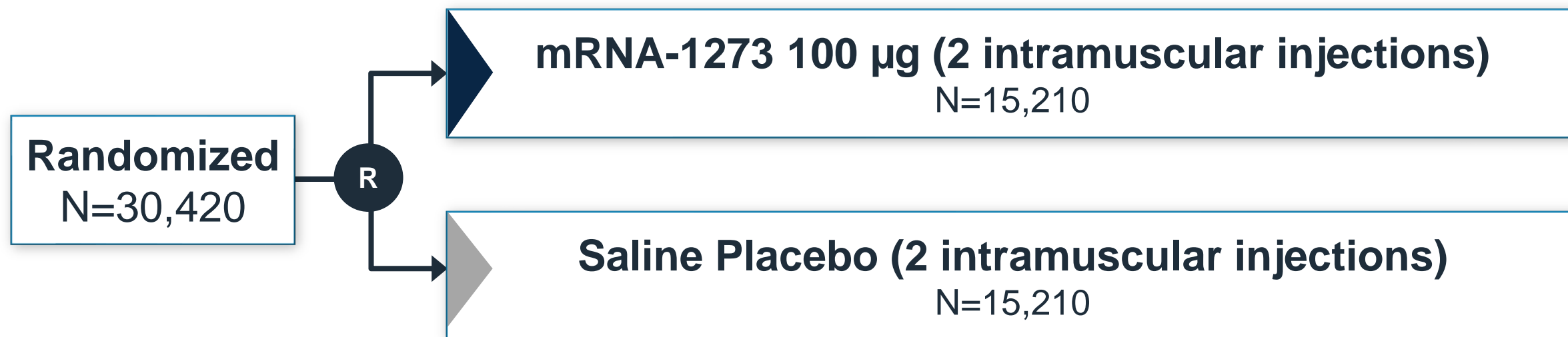
# Summary of Studies 101 & 201 mRNA-1273 Immunogenicity Data

- Neutralizing antibody titers observed in all participants following 2<sup>nd</sup> injection
- GMTs across age strata numerically higher than in pool of convalescent sera
- Neutralizing antibodies persisted for at least 3 months and remained numerically higher than convalescent sera
- Strong Th-1 dominant, CD4+ T-cell response observed
  - Consistent results with preclinical studies
  - No evidence for vaccine-associated enhanced disease



# Study 301

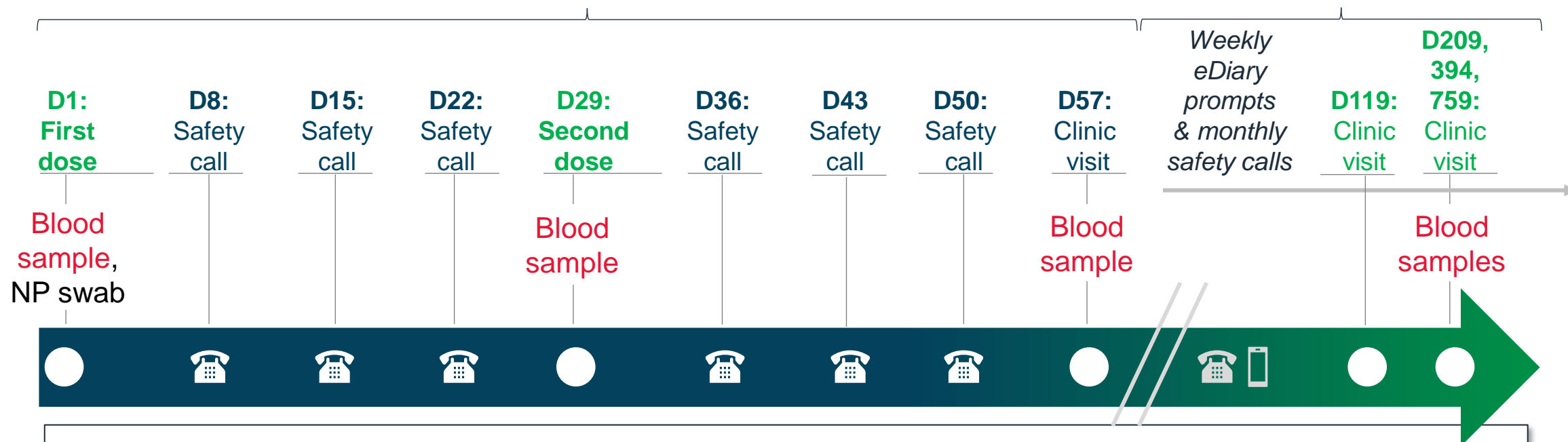
# Study 301: Pivotal, Randomized, Placebo-Controlled Evaluation of Efficacy and Safety



# Study 301: Scheduled Visits and Safety Calls

## Vaccination Phase

## Surveillance Phase



**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: Designed to Include Participants at Risk for Severe COVID-19 Disease

Strata	Target Sample Size
≥ 65 years with and without comorbid conditions	25-50%
≥ 18 to < 65 years with comorbid conditions	
≥ 18 to < 65 years without comorbid conditions	50-75%

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



# Study 301 Primary and Key Secondary Efficacy Objectives

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

a. Baseline SARS-CoV-2 negative participants

b. Asymptomatic infection analysis relies on serologic data not available at the time of EUA submission

# 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,  $SpO_2 \leq 93\%$  on room air at sea level or  $PaO_2/FIO_2 < 300$  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

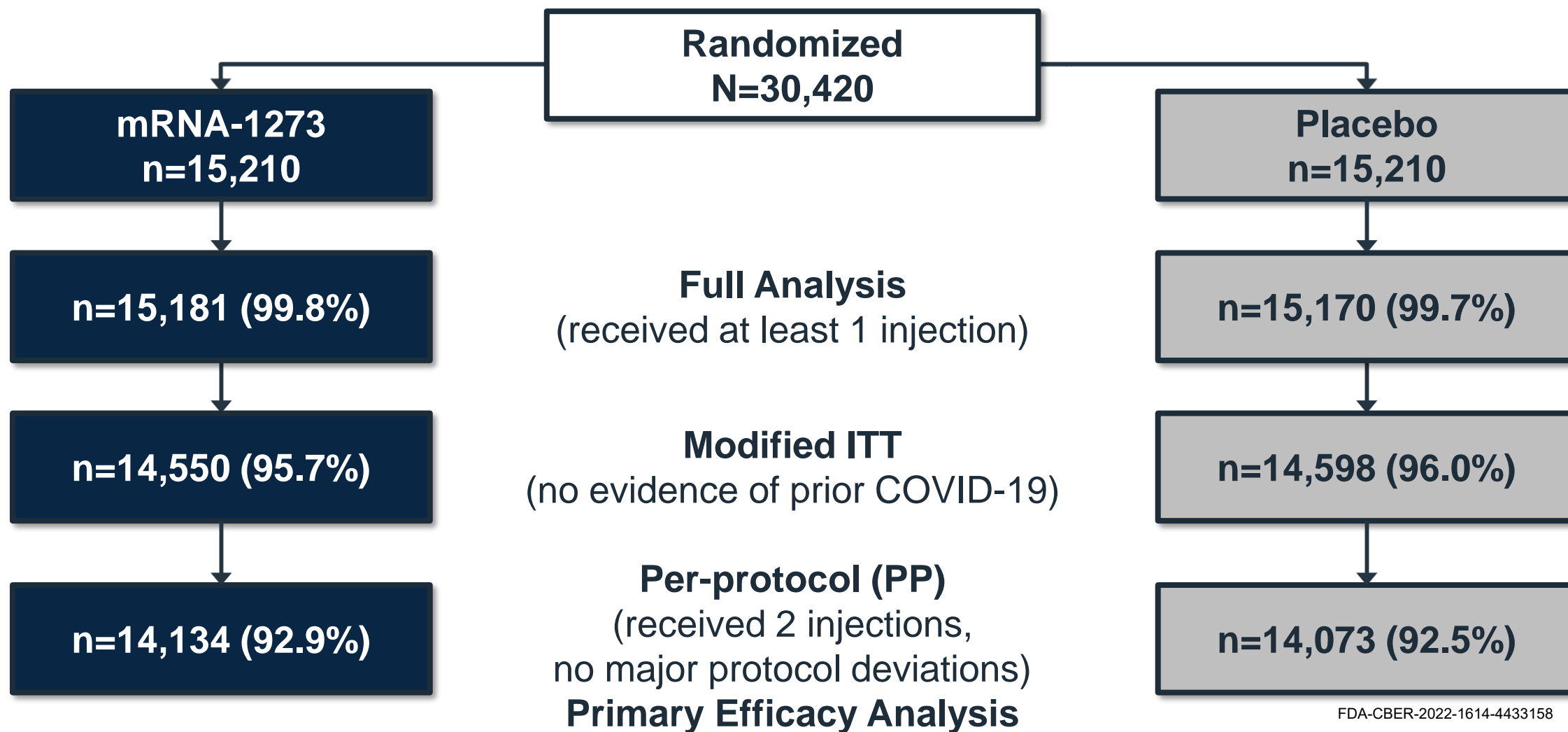
RR: respiratory rate; HR: heart rate; BPM: beats per minute;  $SpO_2$ : oxygen saturation;  $PaO_2/FIO_2$ : arterial oxygen partial pressure over fractional inspired oxygen; mm Hg: pressure measured by millimeters of mercury; ARDS: acute respiratory distress syndrome; SBP: systolic blood pressure; DBP: 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)
  - Continuous monitoring for:
    - Vaccine-associated enhanced respiratory disease
    - Any other safety signal
  - Evaluated interim efficacy analysis and alerted Moderna when criteria met
- 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> injection

# 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	%
Age and health risk for severe COVID-19				
≥ 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%

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

# Study 301: Representative of US Demography

## Full Analysis Set

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

# Study 301: Representative of US Demography

## *Full Analysis Set*

	mRNA-1273 N=15,181		Placebo N=15,170	
	n	%	n	%
Race				
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%
Ethnicity				
Hispanic or Latino	3,121	21%	3,114	21%



# Study 301: Representation of Participants with Medical Risk Factors

## *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: Representation of 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

Subgroup	N	# of Confirmed COVID-19 Cases	
		Confirmed Symptomatic	Severe
Overall	28,207	196	30
Age (years)			
≥ 18 to < 65	21,072	163	20
≥ 65	7,135	33	10
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			
White	17,939	154	26
Communities of Color	10,220	42	4

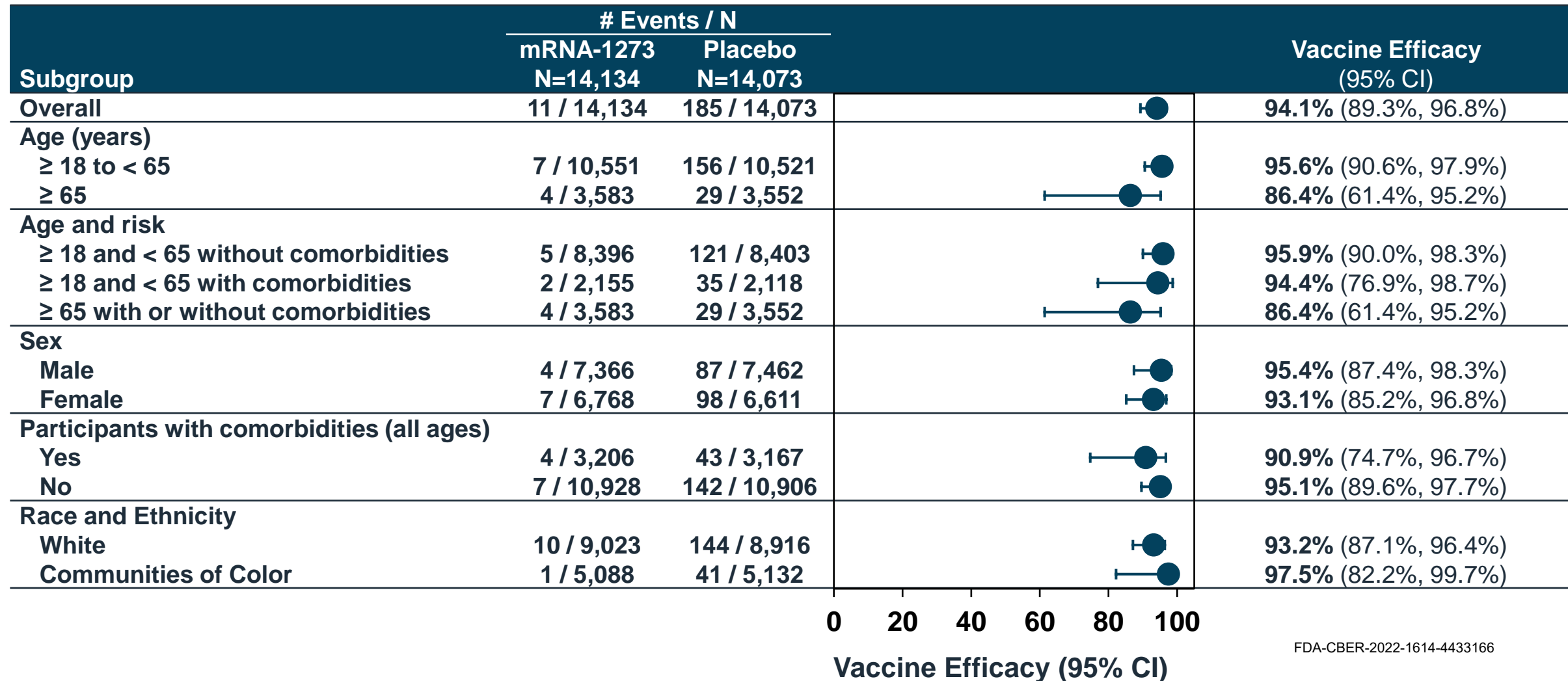
# Study 301: Primary Efficacy Objective Met: VE Against Confirmed, Symptomatic COVID-19 Cases is 94.1%

*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

# 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 FDA-CBER-2022-1614-4433168

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

*Per Protocol*

Symptomatic COVID-19 Cases 14 Days After 1 <sup>st</sup> Injection	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 injection have been adjudicated
- > 96% compliance with 2nd injection



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

## *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> injection	5	11
From 14 days post 1 <sup>st</sup> injection to 2 <sup>nd</sup> injection	3	34
From 2 <sup>nd</sup> injection to 14 days post 2 <sup>nd</sup> injection	0	17
Total	8	62

<sup>1</sup> One clinical symptom from an expanded list and a nasopharyngeal swab positive for SARS-CoV-2 virus FDA-CBER-2022-1614-4433170

# Study 301: Post-Hoc Analysis of NP Swabs for SARS-CoV-2 Testing Prior to Injection 2

## *Per Protocol Population*

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

\* 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

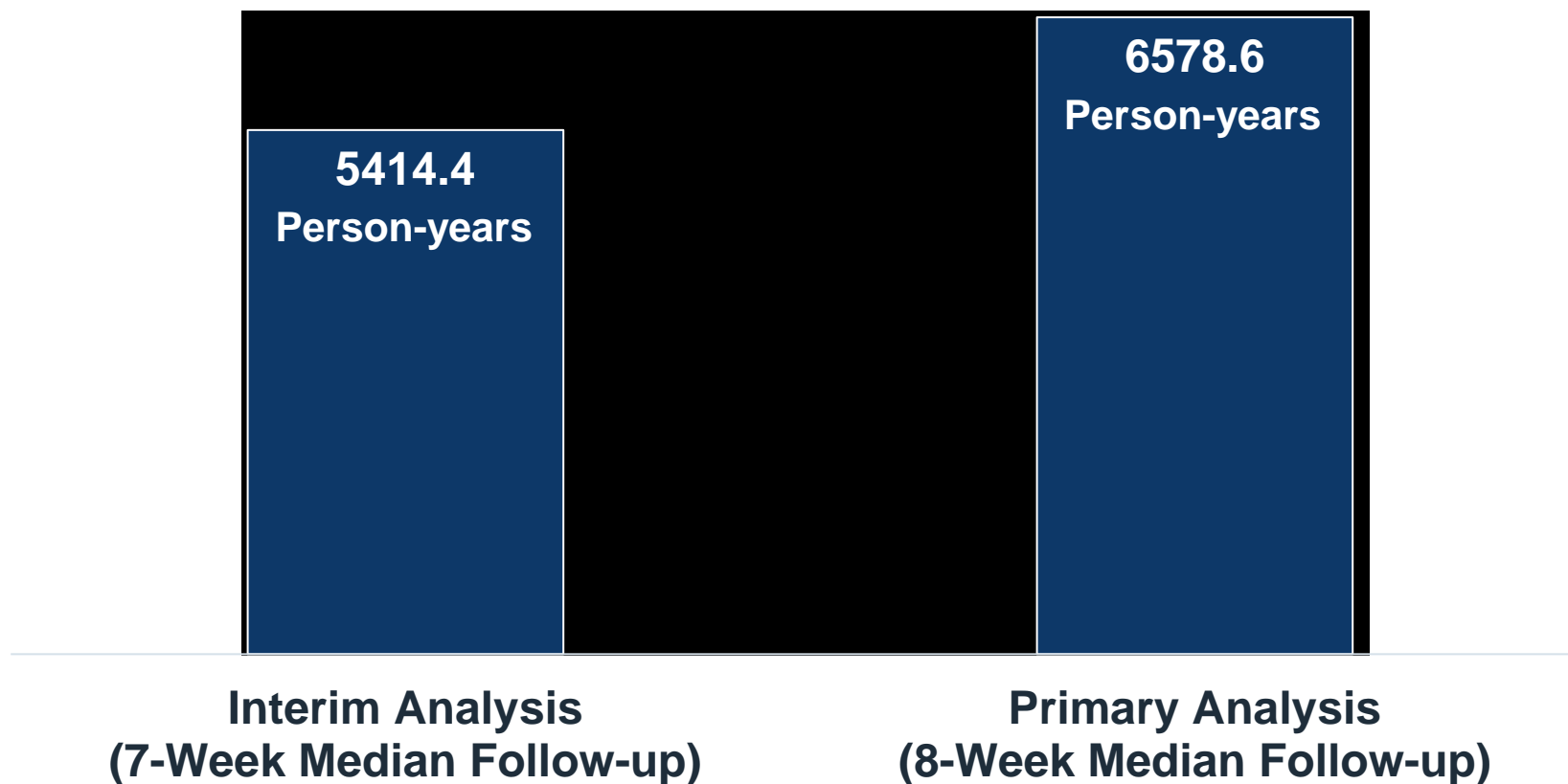
# Study 301: mRNA-1273 100 µg Safety 8-Week Median Follow-up

*David Martin, MD, MPH*

Vice President, Pharmacovigilance  
Moderna, Inc



# Study 301: Primary Analysis Timepoint With 8-Week Median Follow-up



# Study 301: 8-Week Median Exposure Following 2<sup>nd</sup> Injection

*Safety Set, 8-Week Median Follow-up*

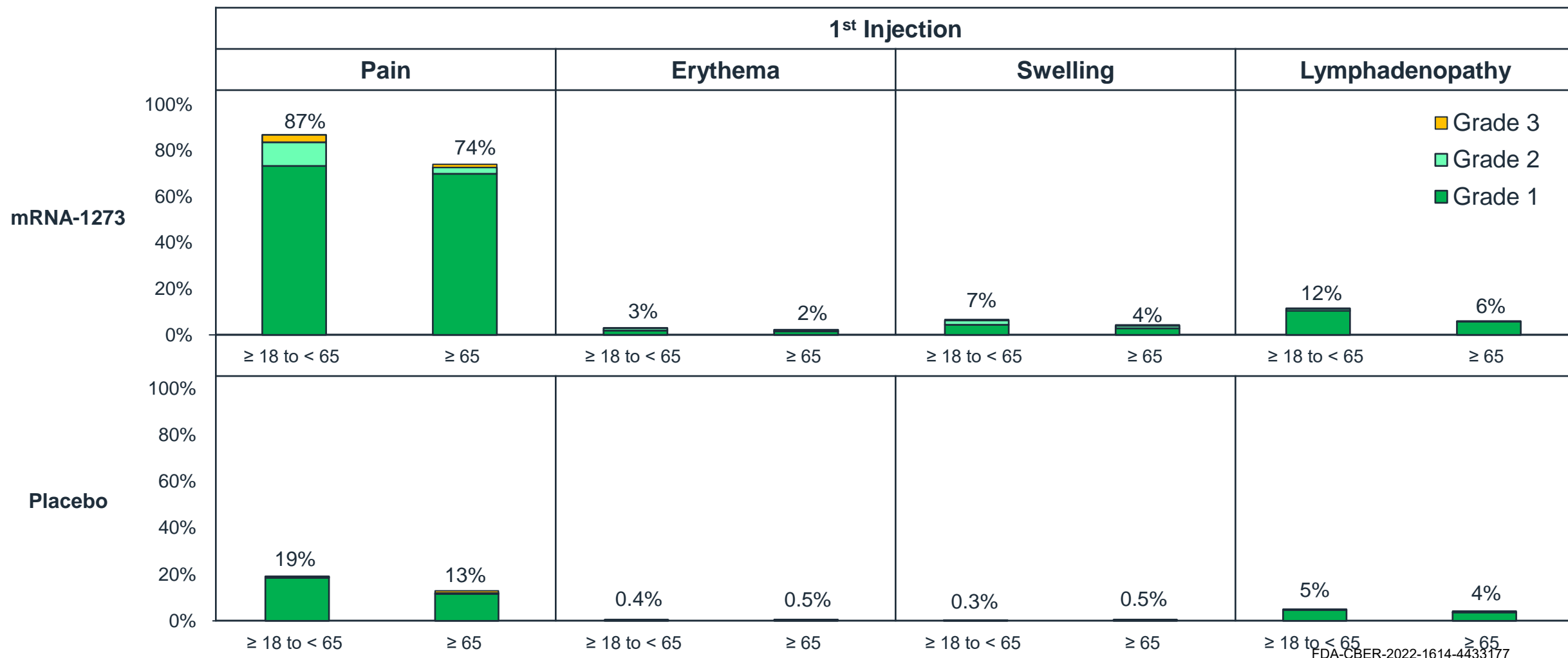
Number of Participants	mRNA-1273 N=15,185		Placebo N=15,166	
	n	%	n	%
Received 1 <sup>st</sup> injection	15,185	100%	15,166	100%
Received 2 <sup>nd</sup> injection	14,715	97%	14,613	96%
Completed ≥ 28 days since 2 <sup>nd</sup> injection	13,386	88%	13,297	88%
Completed ≥ 56 days since 2 <sup>nd</sup>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

# **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, 8-Week Median Follow-up*

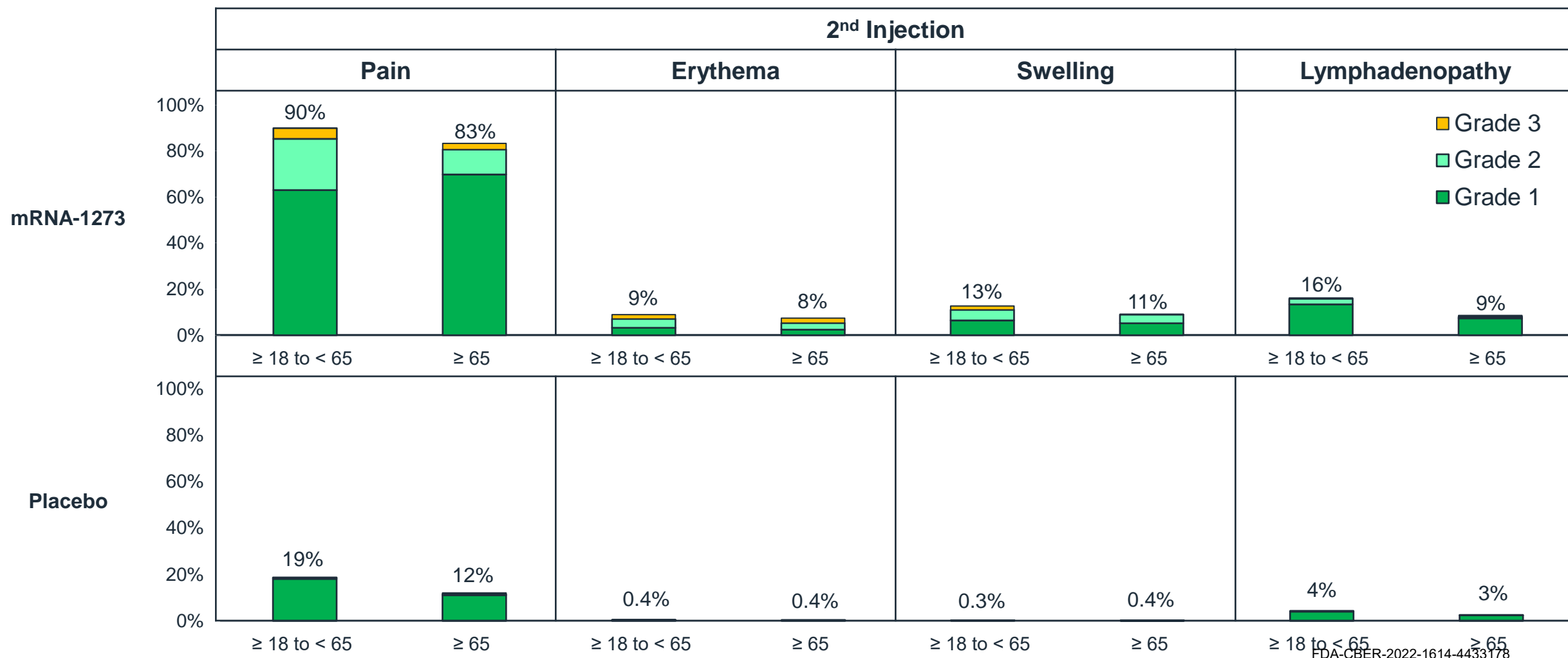


Note: Includes reports within 7 days of either injection



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

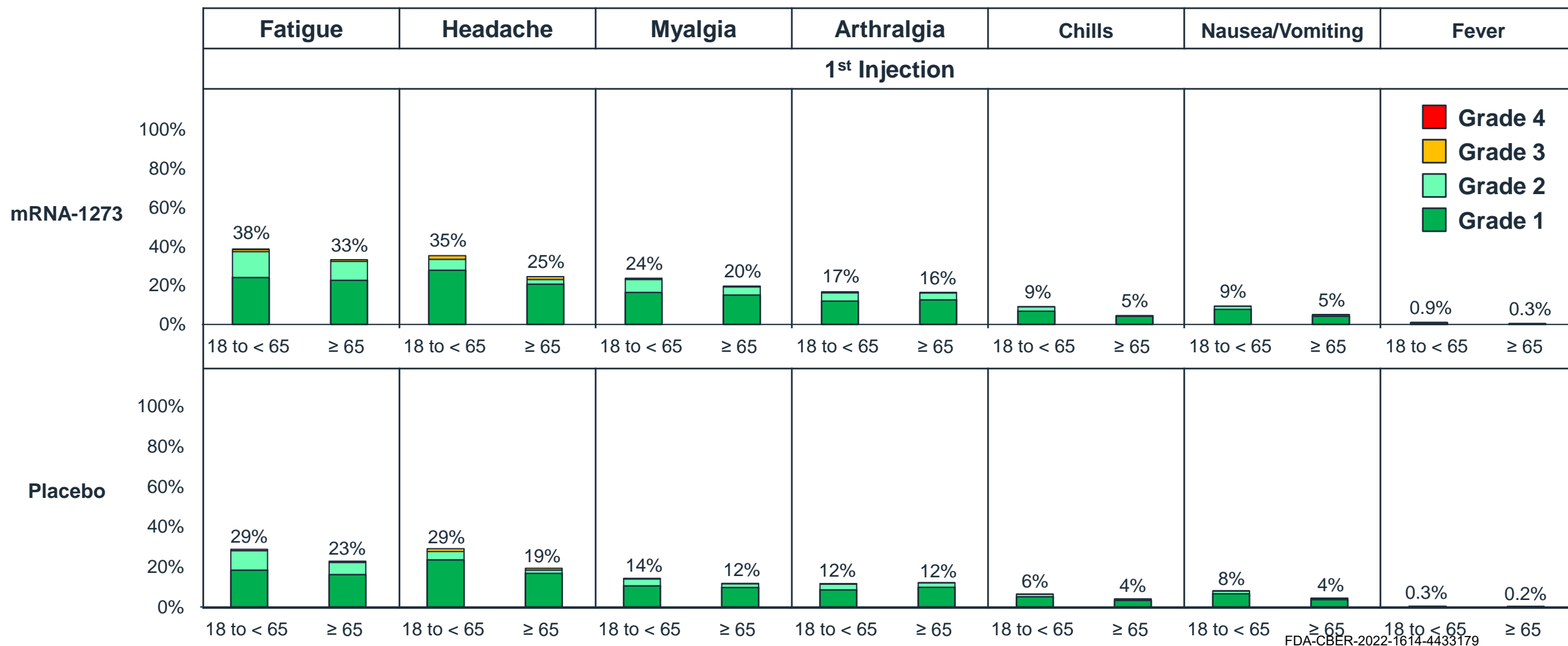
*Safety Set, 8-Week Median Follow-up*



Note: Includes reports within 7 days of either injection

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

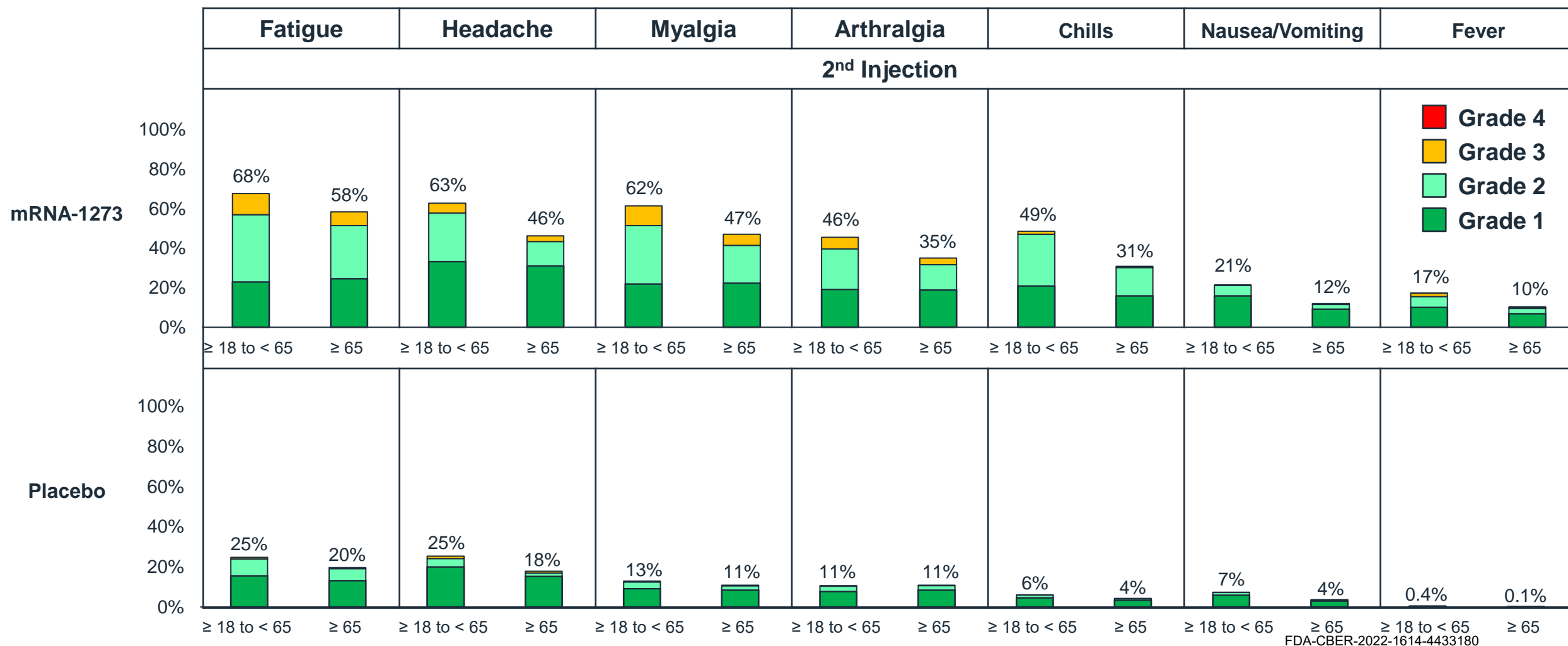
*Safety Set, 8-Week Median Follow-up*



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, 8-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)**

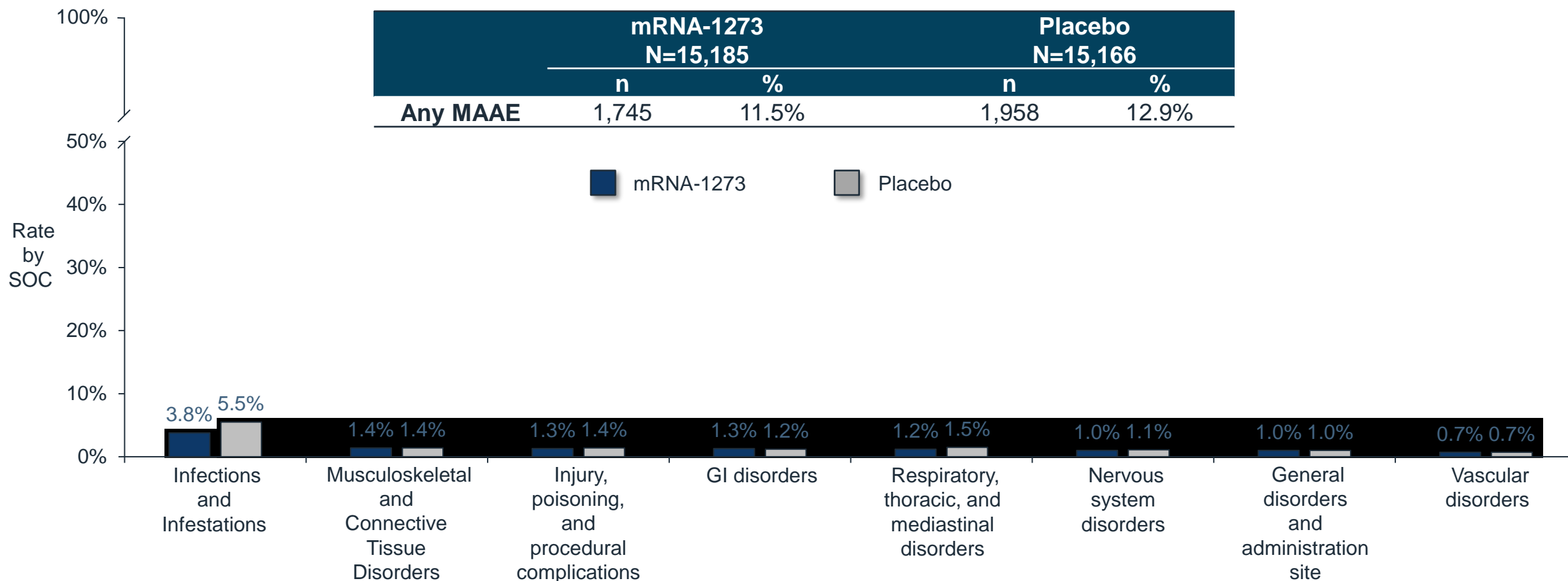
# Study 301: Summary of Unsolicited AEs

## *Safety Set, 8-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, 8-Week Median Follow-up*

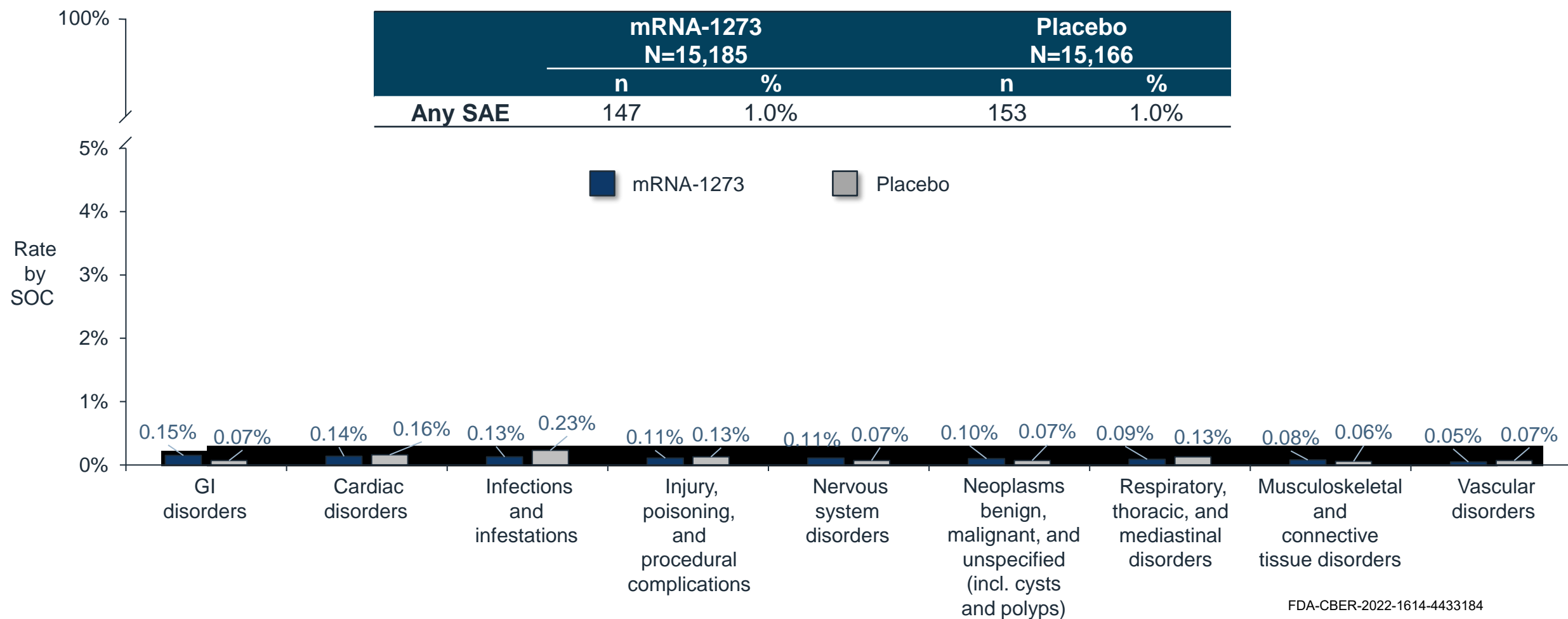


FDA-CBER-2022-1614-4433183

System Organ Class occurring at rate &gt;0.6%

# Study 301: Rates of SAEs Were Comparable Between Groups

*Safety Set, 8-Week Median Follow-up*



FDA-CBER-2022-1614-4433184

System Organ Class occurring at rate &gt;0.05%

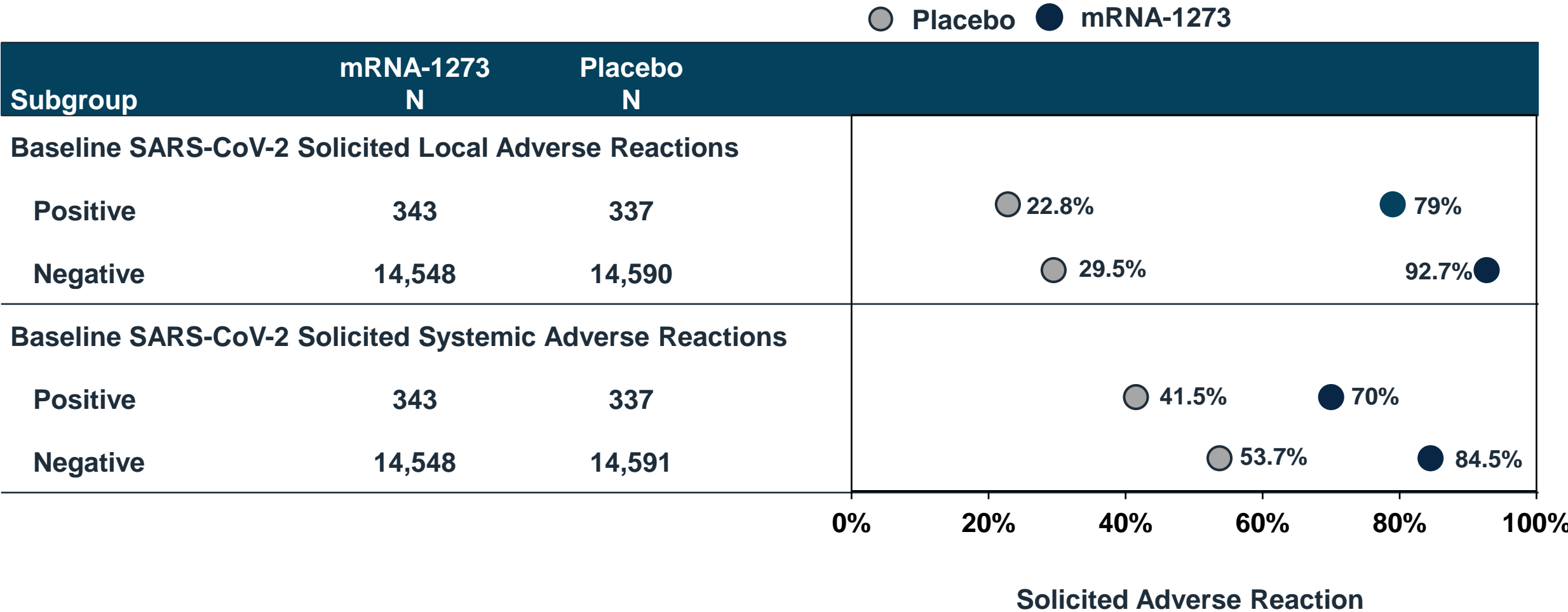
# Study 301: Deaths Through December 3, 2020

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



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

*Safety Set, 8-Week Median Follow-up*



# **Vaccine Safety Monitoring during the EUA**

# Integrated US and Global Safety Monitoring

- US pharmacovigilance plan and Risk Management Plans
  - Safety signal detection in global safety database including adverse event reports from global sources
- Interface with vaccine safety stakeholders
  - US FDA and CDC and associated advisory committees
  - International regulatory and public health agencies

# Monitoring Goals and Methods

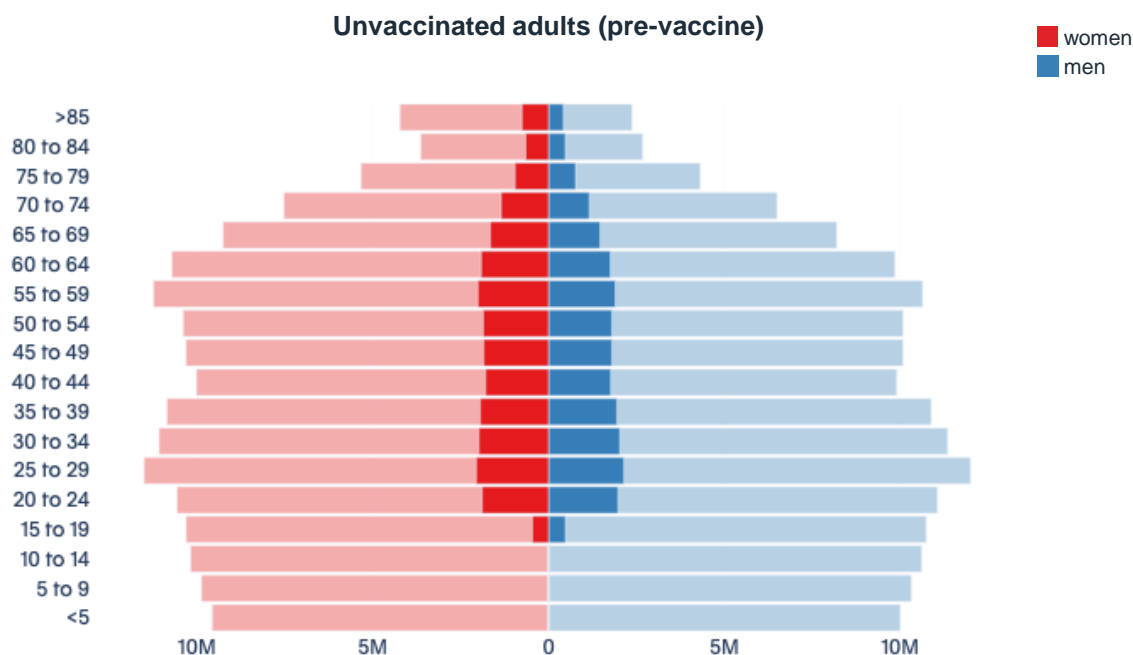
- Identify new safety signals
  - Safety signal detection through open ended surveillance
  - Rapid validation and assessment based on AE reports as well as real world healthcare data
- Address known concerns associated with vaccines in general
  - Monitor AESI in real world healthcare data
  - Enroll pregnant women who receive vaccine in a cohort study
- Monitor long term effectiveness
  - Assess long term effectiveness in an integrated healthcare system

# Active Surveillance complementing USG systems

## Expected Rates of AESIs Among US adults in two pre-vaccine eras\*

## Observed Rates of AESIs Every 2 weeks among US adults in vaccine era

Initial  
population  
distribution  
compared to  
the US  
Census  
distribution



45 million sample versus the US census population

Newly vaccinated adults are added to the population under observation

Open claims provide early visibility on exposure

Common or Rare Adverse Events can be identified

Capacity to Add New Safety Signals to the monitoring plan

Data used

### 45 million US adults

Sampled to closely match US census adult population  
Closed adjudicated health insurance claims

### 45+ million US adults

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

FDA-CBER-2022-1614-4433190

# 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



## Concluding Remarks

**Tal Zaks, MD PhD**

Chief Medical Officer

Moderna, Inc



# Study 301 Data Support Emergency Use Authorization

- Exceed FDA efficacy criteria for BLA
  - VE = 94.1% (89.3%, 96.8%),  $p < 0.0001$
  - Very high efficacy maintained against severe disease
  - Consistency among subgroups
- No evidence of increased risk for enhanced disease
- Safety profile well characterized by > 15,000
  - Majority of solicited injection and systemic AEs reported as mild-to-moderate and resolve, occur  $\leq 7$  days of injection