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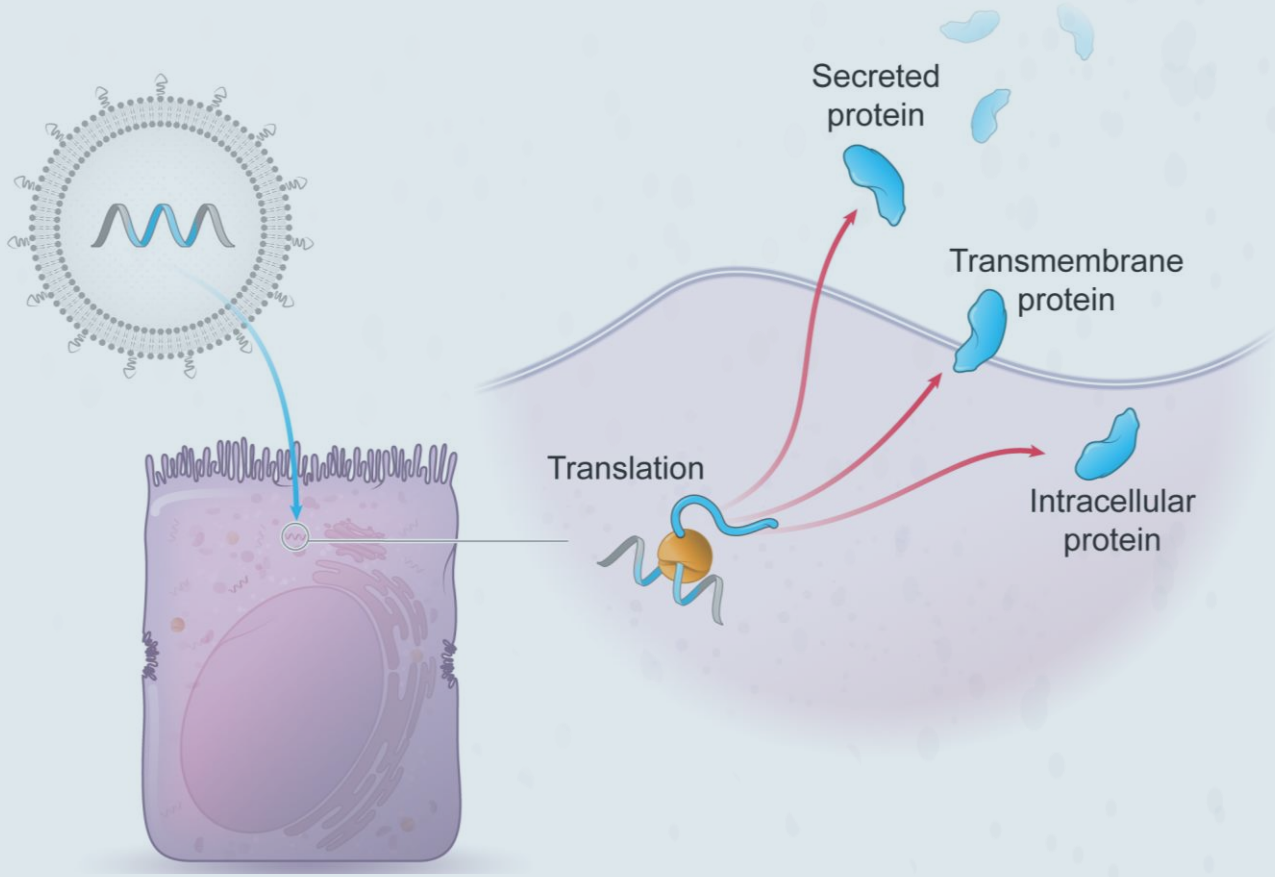

Annual R&D Day

September 17, 2020

Forward-looking statements and disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including regarding: expected timing of enrollment completion for the Phase 3 study of mRNA-1273; the timing and design of the Phase 3 study of mRNA-1647, and the intention to enroll additional participants in the Phase 2 study of mRNA-1647; the Company's intention to create a combination therapy with mRNA-1345 and mRNA-1653 against RSV, hMPV and PIV3; the Company's manufacturing capabilities; the Company's intentions regarding resumption of enrollment and the implementation of changes for paused clinical studies; the probability of success of the Company's vaccines individually and as a portfolio; the Company's timeline to becoming a commercial company; the Company's intention to enter the seasonal flu vaccine business; the Company's development of mRNA-3705 as a next generation MMA candidate; next steps with respect to the Company's clinical and pre-clinical development programs; the potential timing of regulatory applications; and the ability of the Company to accelerate the research and development timeline for any individual product or the platform as a whole. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could", "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, among others: preclinical and clinical development is lengthy and uncertain, especially for a new class of medicines such as mRNA, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance to or in the clinic; no commercial product using mRNA technology has been approved and may never be approved; mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new class of medicines; despite having ongoing interactions with the FDA or other regulatory agencies, the FDA or such other regulatory agencies may not agree with the Company's regulatory approval strategies, components of our filings, such as clinical trial designs, conduct and methodologies, or the sufficiency of data submitted; the fact that the rapid response technology in use by Moderna is still being developed and implemented; the fact that the safety and efficacy of mRNA-1273 has not yet been established; potential adverse impacts due to the global COVID-19 pandemic such as delays in clinical trials, preclinical work, overall operations, regulatory review, manufacturing and supply chain interruptions, adverse effects on healthcare systems and disruption of the global economy; and those other risks and uncertainties described under the heading "Risk Factors" in Moderna's most recent Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission (SEC) and in subsequent filings made by Moderna with the 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 contained 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 hereof.

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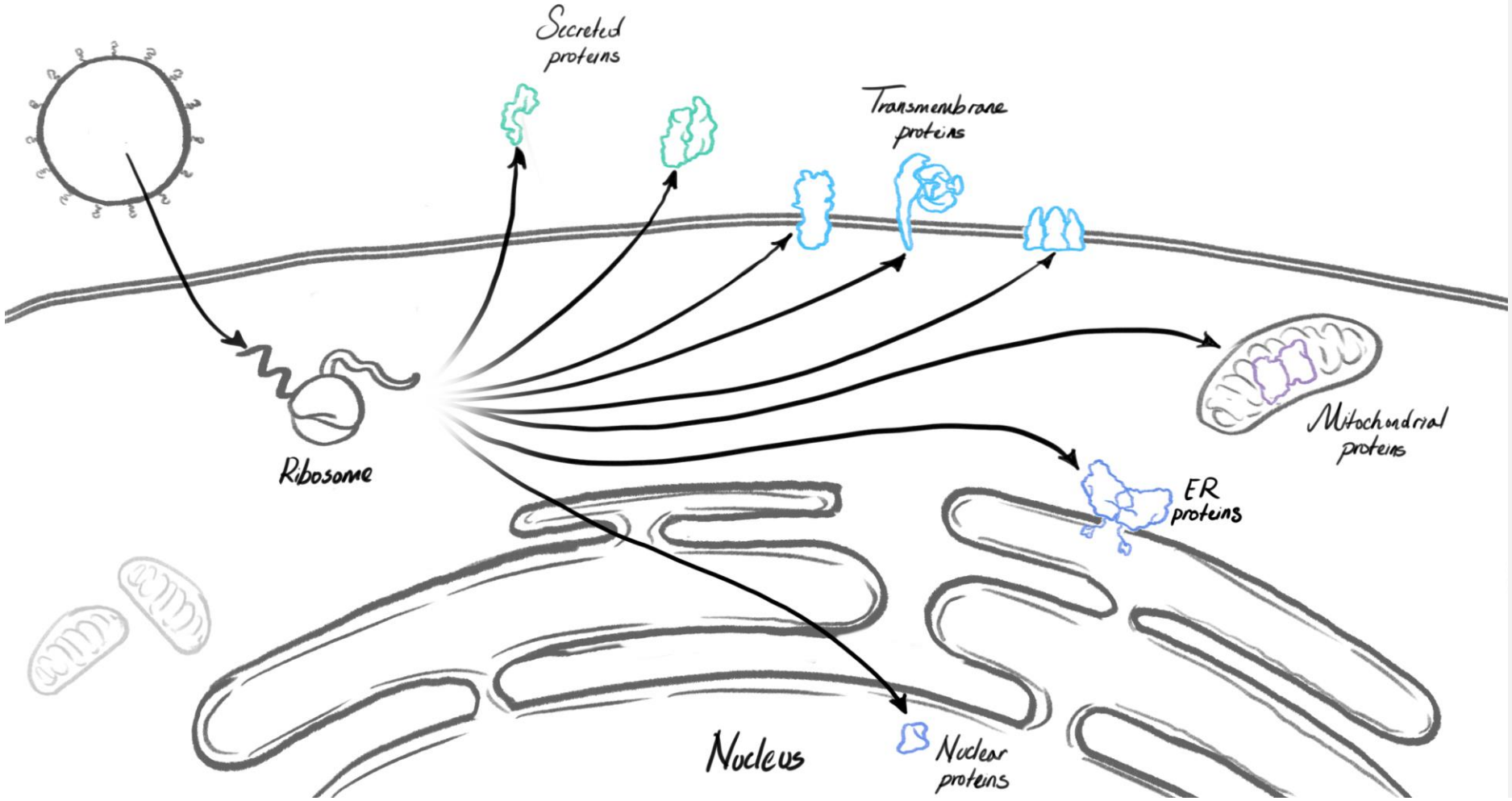
mRNA as a potential new class of medicines



1. Large product opportunity
2. Higher probability of technical success
3. Accelerated research and development timelines
4. Greater capital efficiency over time vs. recombinant technology

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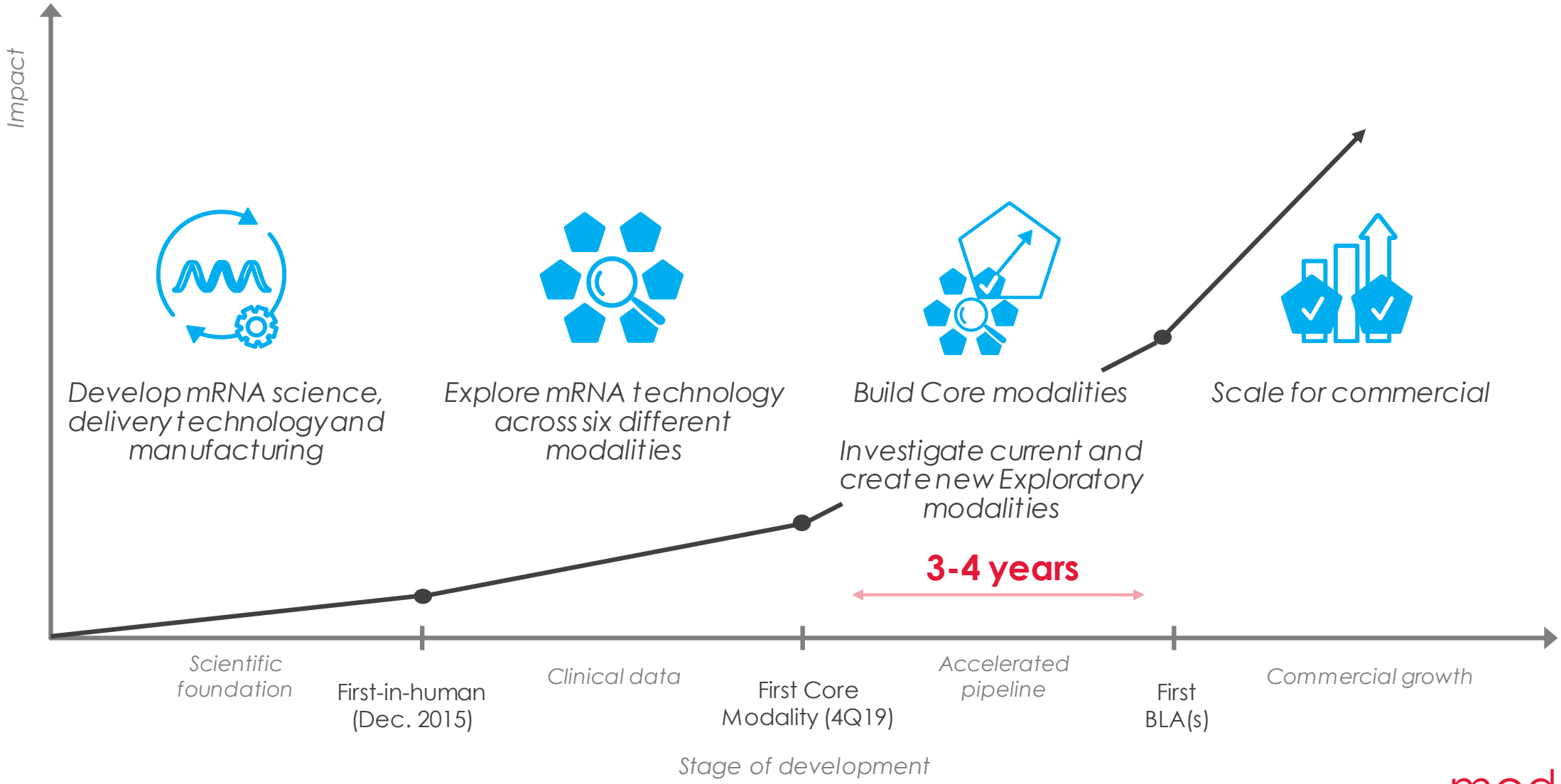
Progression towards a new class of medicines

Strategic plan presented in February 2020



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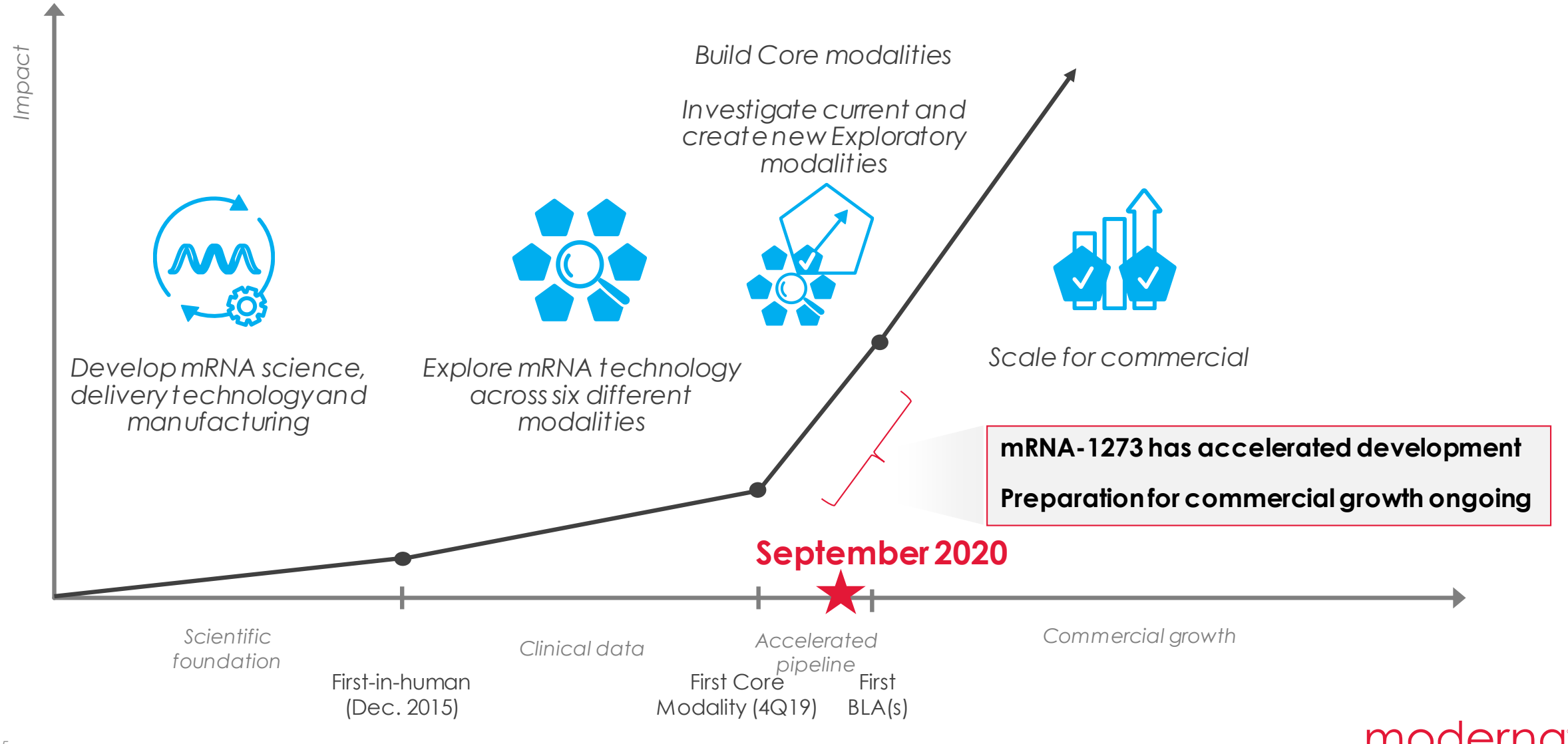
COVID-19 vaccine (mRNA-1273) has been a 3-4 year accelerator to Moderna becoming a commercial company



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A lot has changed in 12 months since R&D Day 2019…

	Sept. 2019	Sept. 2020
Phase 3 candidates	0	1
Phase 2 candidates	2	4
Early stage development candidates (Preclinical and Phase 1)	18	18
Therapeutic area	Infectious diseases Immuno-oncology Cardiovascular Rare diseases	Infectious diseases Immuno-oncology Cardiovascular Rare diseases Auto-immune diseases
Patients & healthy participants enrolled	>1,300	>27,000
Cash and investments	$1.44 billion (as of June 30, 2019)	$3.1 billion (as of June 30, 2020)
Employees	>800	>1,100

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Moderna overview

Moderna has the most advanced mRNA platform

Moderna has one of the most advanced COVID-19 vaccine development programs

Moderna is not only a COVID-19 vaccine company

Moderna has 23 development candidates across a range of infectious diseases and therapeutic areas

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Development pipeline

September 2020

		Preclinical *(incl. Open IND)*	Phase 1	Phase 2	Phase 3	Commercial
Core modalities	Prophylactic vaccines 	EBV; *Pediatric RSV (Open IND)*	Flu (Pandemic); Adult RSV *(mRNA1172)*; Zika; Adult RSV *(mRNA1777)*; hMPV/PIV3	*Phase 2 preparations Zika*; CMV	COVID-19; *Phase 3 preparations CMV*	*Launch preparation COVID-19*
	Systemic secreted & cell surface therapeutics 	Relaxin; PD-L1; IL-2	Chikungunya antibody			
	Cancer vaccines 		KRAS	Personalized Cancer Vax		
Exploratory modalities	Intratumoral immuno-oncology 		IL-12; OX40L/IL-23/IL-36γ	OX40L		
	Localized regenerative therapeutics 			VEGF		
	Systemic intracellular therapeutics 	MMA; PA *(open IND)*; PKU; GSD1a				

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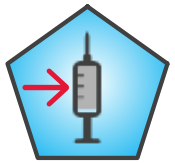
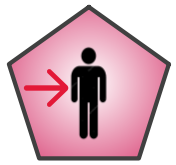
New clinical data presented today



CMV vaccine (mRNA-1647)

- Positive interim analysis from Phase 2 study
- Phase 3 study to begin in 2021 at the selected 100 µg dose



Antibody against Chikungunya virus (mRNA-1944)

- Positive data from additional cohorts of Phase 1 study
- Two-dose regimen of Chikungunya antibody demonstrates the platform's ability for safe repeat dosing

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Business and pipeline updates announced today

Moderna is going to enter the seasonal Flu vaccine business

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Seasonal influenza (flu) overview

- Seasonal flu (type A and type B) epidemics occur seasonally and vary in severity each year, causing respiratory illnesses and placing substantial burden on healthcare systems
- **Disease burden:**
  - Global: The WHO estimates globally about 3,000,000-5,000,000 severe cases of flu each year, and 290,000-650,000 flu-related respiratory deaths[1]
  - US: About 8% of the US population experiences symptoms from flu each year in the US, with 140,000-810,000 hospitalizations and 12,000-61,000 deaths per year[2]
  - Peak flu activity is seen in temperate climates during fall to winter and is reflected in increases in outpatient visits, urgent care visits, and hospitalizations
  - **In the US, the estimated average economic burden of flu is ~$11 billion per year[3]**
  - Strain mismatch in egg-based vaccine platforms can result in significant loss of vaccine efficacy
- **Unmet need: Currently approved vaccines are ~40-60% effective and face significant challenges from strain mismatch**[4]; high-risk groups would benefit from higher efficacy

Flu 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). Accessed 09 Sep 2020.
2. Centers for Disease Control and Prevention. Disease burden of influenza. Available at: https://www.cdc.gov/flu/about/burden/index.html. Accessed 09 Sep 2020.
3. Putri W et al. Economic burden of seasonal influenza in the United States. *Vaccine* 2018;36(27):3960-3966.
4. Centers for Disease Control and Prevention. Vaccine Effectiveness: How Well Do the Flu Vaccines Work? Available at: https://www.cdc.gov/flu/vaccines-work/vaccineeffect.htm. Accessed 09 Sep 2020.

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Potential combination vaccine for older adults

Prophylactic vaccines

- hMPV/PIV3 (mRNA-1653)
- Six mRNA's per vial in CMV vaccine (mRNA-1647)
- **Phase 1 safety and immunogenicity data demonstrated in each of these viruses**

COVID-19

Flu

RSV

hMPV

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Two new R&D collaborations announced today

Vertex collaboration

Moderna and Vertex establish a new collaboration to treat cystic fibrosis using gene editing ($75m upfront)

Chiesi Group collaboration

Moderna and Chiesi Group establish a new collaboration to develop an mRNA candidate for Pulmonary Arterial Hypertension (PAH) ($25m upfront)

Agenda

Introduction	*Stéphane Bancel, CEO*	*8:00-8:15 AM*
Systemic Secreted and Cell Surface Therapeutics • **Chikungunya Antibody**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer*	*8:15-8:30 AM*
Intracellular Therapeutics • **PA** • **MMA**	*Stephen Hoge, M.D., President*	*8:30-8:45 AM*
Intratumoral Immuno-Oncology • **Overview of Intratumoral Approach** • **OX40L Phase 1** • **Triplet Phase 1**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer* *Antonio Jimeno, M.D., Ph.D., University of Colorado School of Medicine*	*8:45-9:30 AM*
Coffee Break		*9:30-9:40 AM*
Prophylactic Vaccines • **CMV Vaccine** • **RSV, hMPV/PIV3 Vaccine** • **Regulatory Guidance and Development of Pediatric Vaccines** • **COVID-19 Vaccine**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer* *Lori Panther, M.D., MPH, Senior Director of Clinical Development, Infectious Diseases* *Allison August, M.D., Senior Director of Clinical Development, Infectious Diseases* *Terry Nolan, M.D., Ph.D., The University of Melbourne* *Jacqueline Miller, M.D., FAAP, SVP, Infectious Disease Development* *Juan Andres, Chief Technical Operations and Quality Officer*	*9:40-11:00 AM*
New Research & Development	*Stephen Hoge, M.D., President*	*11:00-11:10 AM*
Conclusion	*Stéphane Bancel, CEO*	*11:10-11:20 AM*
Q&A		*11:20-12:00 PM*

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Tal Zaks, M.D., Ph.D.
Chief Medical Officer

Antibody against Chikungunya Virus (mRNA-1944)

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Antibody against Chikungunya virus (mRNA-1944)

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Systemic secreted & cell surface therapeutics	**mRNA-1944**	Antibody against Chikungunya virus					Worldwide *DARPA funded*
	AZD7970	Relaxin *Heart failure*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales
	mRNA-6981	PD-L1 *Autoimmune hepatitis*					Worldwide
	mRNA-6231	IL-2 *Autoimmune disorders*					Worldwide

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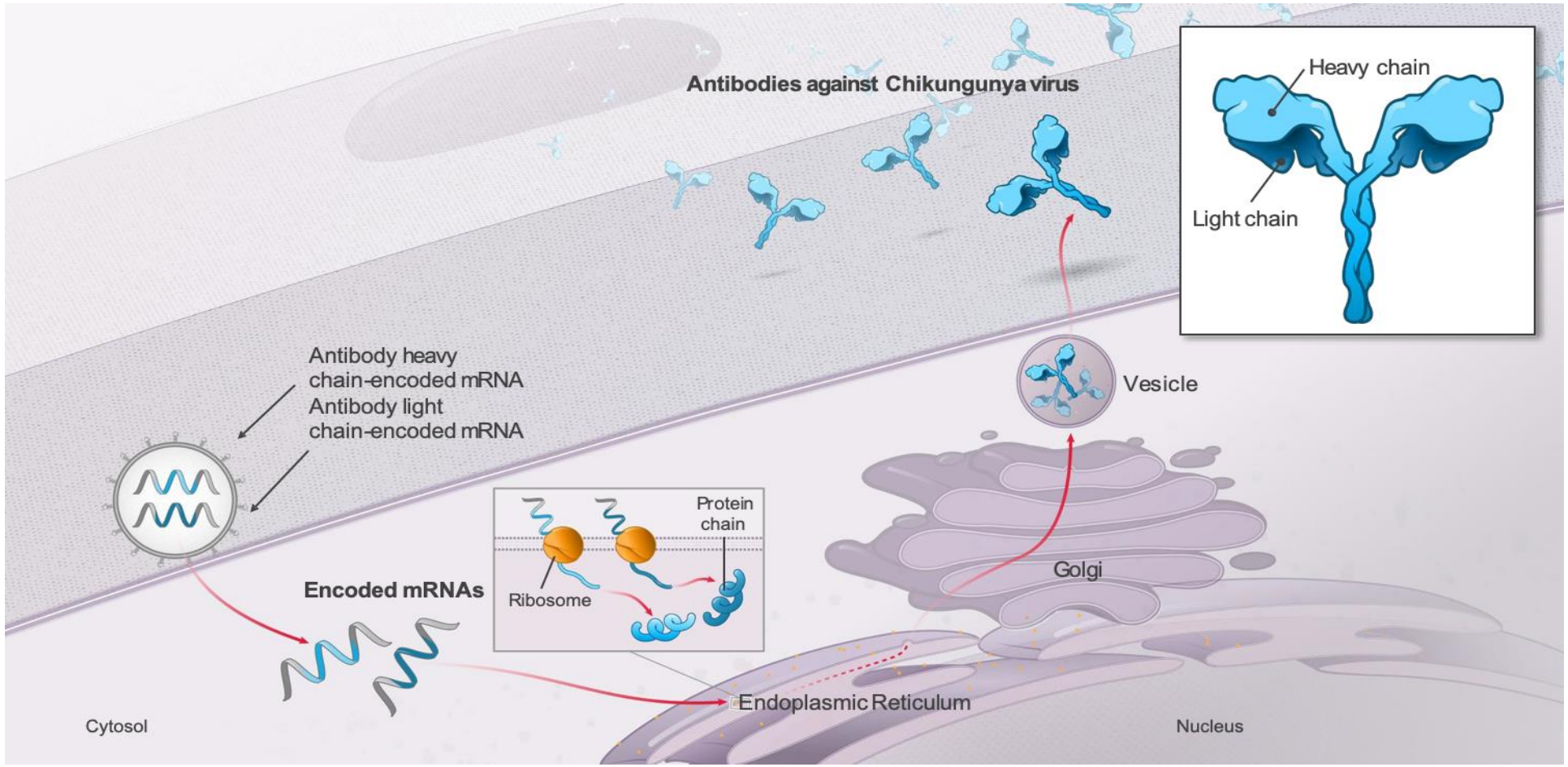
mRNA-1944 contains two mRNAs that encode for the heavy and light chains of CHKV-24 antibody, which may confer passive immunity



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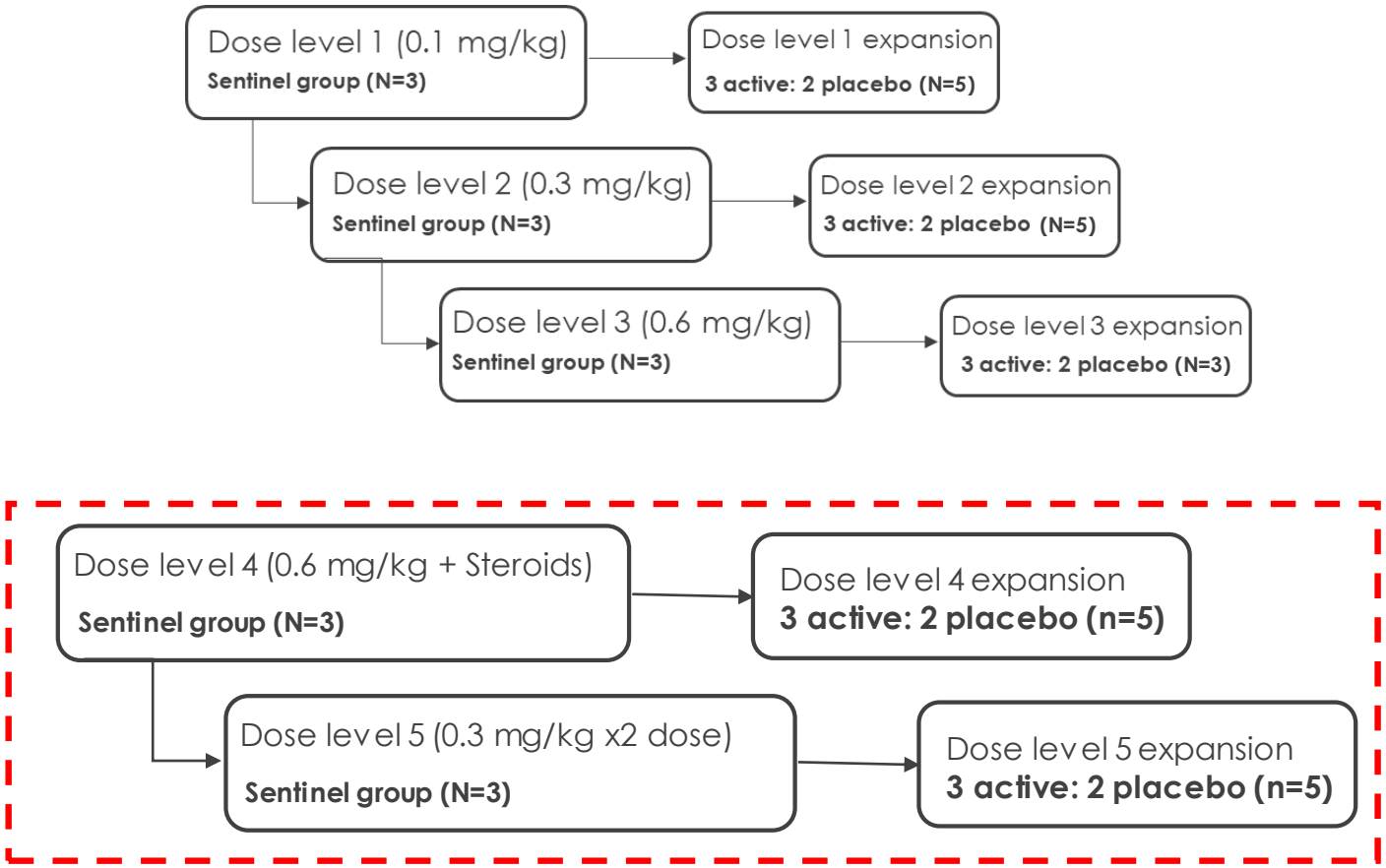
Phase 1 trial design (mRNA-1944) amended to repeat dose

- Randomized, placebo-controlled, single ascending dose study in healthy adults
- All subjects received premedication with antihistamines

Key Objectives

- **Safety**: Evaluate safety and tolerability of escalating doses of mRNA-1944 administered via intravenous infusion
- **Translation of protein**: Evaluate pharmacology of mRNA-1944
- **Activity**: Determine ability of antibody to neutralize viral infection



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Overall treatment-related adverse events, by toxicity grade

	mRNA-1944						Placebo
Treatment-related Adverse Events n (%)	**0.1 mg/kg N=6**	**0.3 mg/kg N=6**	**0.6 mg/kg N=4**	**0.6 mg/kg + steroid[1] N=6**	**0.3 mg/kg 2 dose[2] N=6**	**All N=28**	**All N=10**
Any	1 (16.7)	1 (16.7)	4 (100.0)	6 (100.0)	5 (83.3)	17 (60.7)	2 (20.0)
Grade 1	1 (16.7)	1 (16.7)	2 (50.0)	4 (66.7)	2 (33.3)	10 (35.7)	2 (20.0)
Grade 2			1 (25.0)	2 (33.3)	3 (50.0)	6 (21.4)	
Grade 3			1 (25.0)[3]			1 (3.6)	
Grade 4							

In each group, a participant was counted once if the participant reported one or more events
Participants received antihistamine 90 minutes prior to infusion

1. 0.6 mg/kg group received dexamethasone in addition to antihistamine as premedication regimen
2. Participants were administered two 0.3 mg/kg doses on Days 1 and 8
3. Sinus tachycardia; participant experienced a Grade 3 laboratory abnormality of increased white blood cell count

- Overall 19 participants (50%) reported treatment-related AEs with the highest frequencies in the 0.6 mg/kg groups
- The most common AEs were headache (32%), nausea (25%), myalgia (18%), dizziness (14%) and chills (14%)
- All adverse events were transient and resolved spontaneously without treatment
- No serious adverse events (SAEs) were reported nor discontinuations
- No meaningful changes in liver or kidney laboratory results

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Safety and tolerability of second dose appears similar to the first dose

	0.3 mg/kg 2 dose mRNA-1944	
Adverse Events n (%)	**Dose 1 N=6**	**Dose 2 N=6**
Any	5 (83.3%)	3 (50%)
Grade 1	3 (50%)	2 (33.3%)
Grade 2	2 (33.3%)	1 (16.7%)

A participant may be counted in both dose 1 and dose 2

- The most common AEs reported in the 0.3 mg/kg 2-dose regimen were nausea (50%), vomiting (33%), flushing (33%) and decreased appetite (33%)
- No Grade 3 events occurred
- Percentage of participants reporting any AE did not increase with the second dose as compared with the first dose
- No exacerbation or worsening of symptoms reported in any participant after dose 2 compared with dose 1
- The rate and severity distribution of AEs was lower than those reported in the 0.6 mg/kg cohorts
- AE profile was similar to that of previous cohorts
- No clinically significant lab abnormalities

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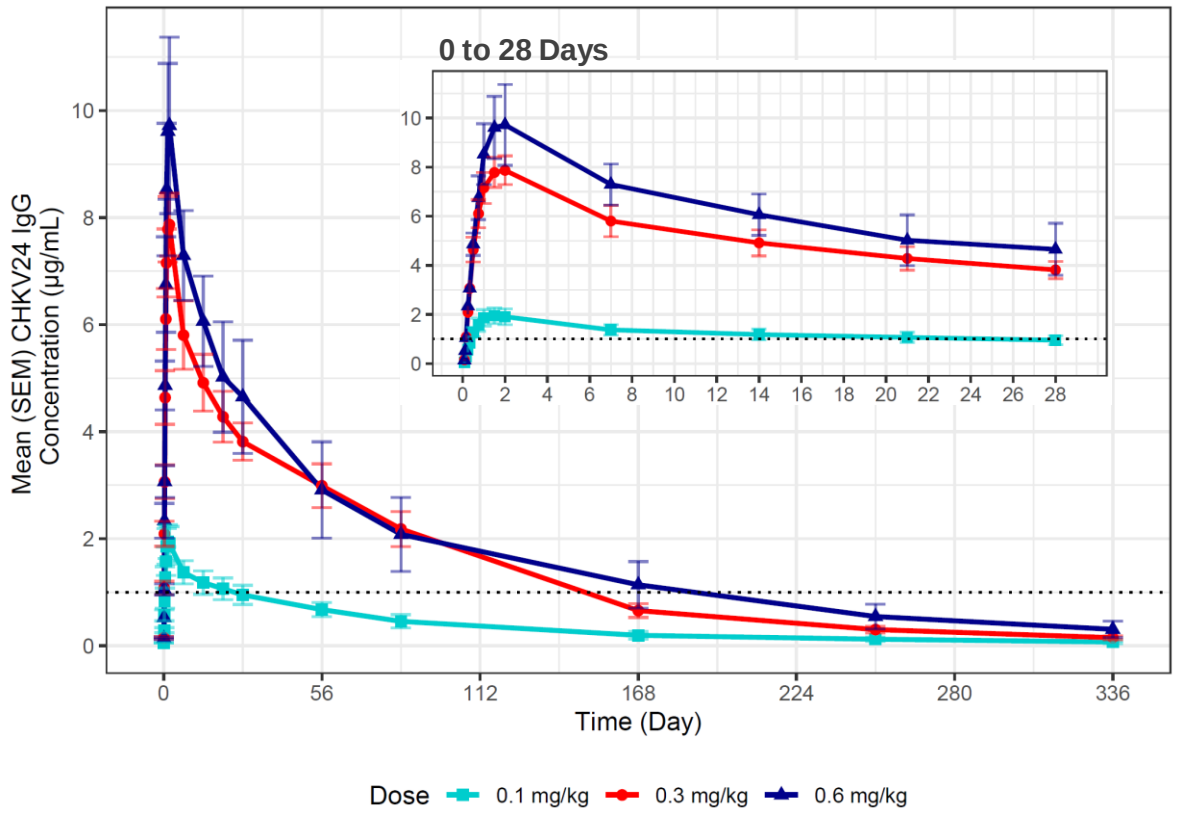
Dose dependent pharmacology to potentially therapeutic levels seen in first three cohorts

Cohort	0.1 mg/kg N=6	0.3 mg/kg N=6	0.6 mg/kg N=4
E_{max} (µg/mL)	2.0	7.9	10.2
E_{max} range (µg/mL)	1.1-3.1	6.3-10.0	7.0-14.2
E_{max} % CV	40.4%	18.2%	29.6%



Pharmacology

- Administration of mRNA-1944 resulted in dose-related increase in levels of CHKV-24
- Half life (t1/2) of antibody was ~69 days
- A single 0.3 mg/kg dose led to CHKV-IgG expression that exceeded the 1 µg/mL target concentration for at least 16-weeks post single dose

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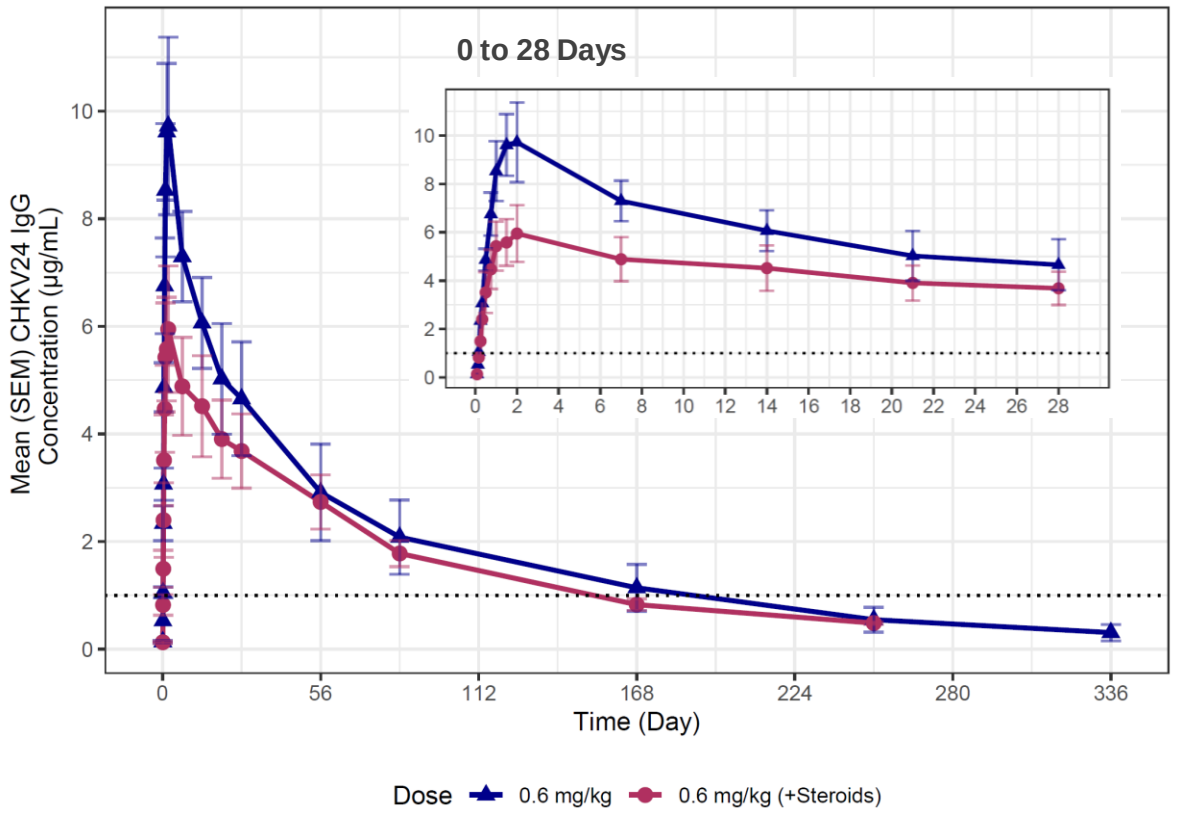
Phase 1 interim analysis with steroid premedication

Cohort	0.6 mg/kg N=4	0.6 mg/kg w/ steroids N=6
E_{max} (µg/mL)	10.2	6.1
E_{max} range (µg/mL)	7.0-14.2	2.3-10.5
E_{max} % CV	29.6%	47%



Pharmacology

- Steroid premedication at 0.6 mg/kg led to ~1.7-fold reduction in CHKV-IgG exposure (Emax)
- Time-course of IgG production and clearance was similar between cohorts with or without steroid premedication

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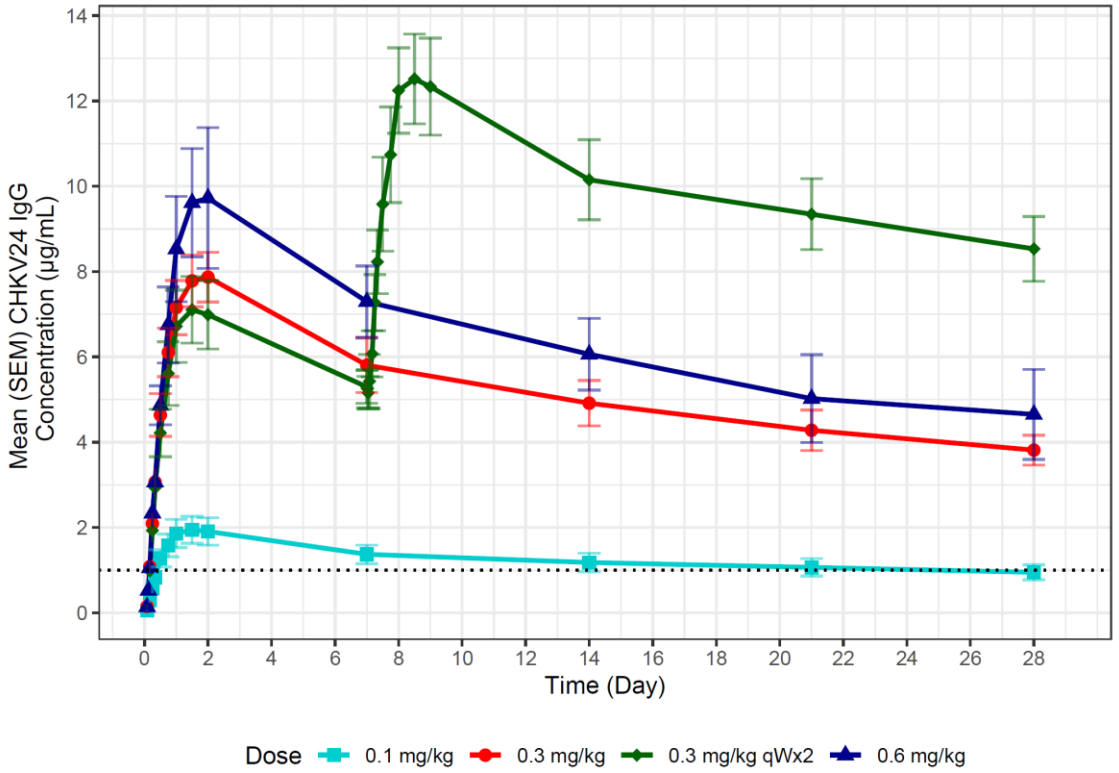
Phase 1 interim analysis with two-dose regimen

Cohort	0.1 mg/kg N=6	0.3 mg/kg N=6	0.6 mg/kg N=4	0.3 mg/kg Wx2 Dose 1 N=6	0.3 mg/kg Wx2 Dose 2 N=6
E_{max} (µg/mL)	2.0	7.9	10.2	7.2	12.9
E_{max} range (µg/mL)	1.1-3.1	6.3-10.0	7.0-14.2	4.0-9.7	8.2-16.7
E_{max} % CV	40.4%	18.2%	29.6%	26.9%	21.4%



Pharmacology

- Consistent CHKV-IgG exposure (Emax) was seen after the first dose between Cohort 3 (0.3 mg/kg single dose) and Cohort 7 (0.3 mg/kg qWx2)
- Administration of the second 0.3 mg/kg dose in the 0.3 mg/kg qWx2 cohort led to an approximately 1.8-fold accumulation of CHKV-IgG exposure (Emax)

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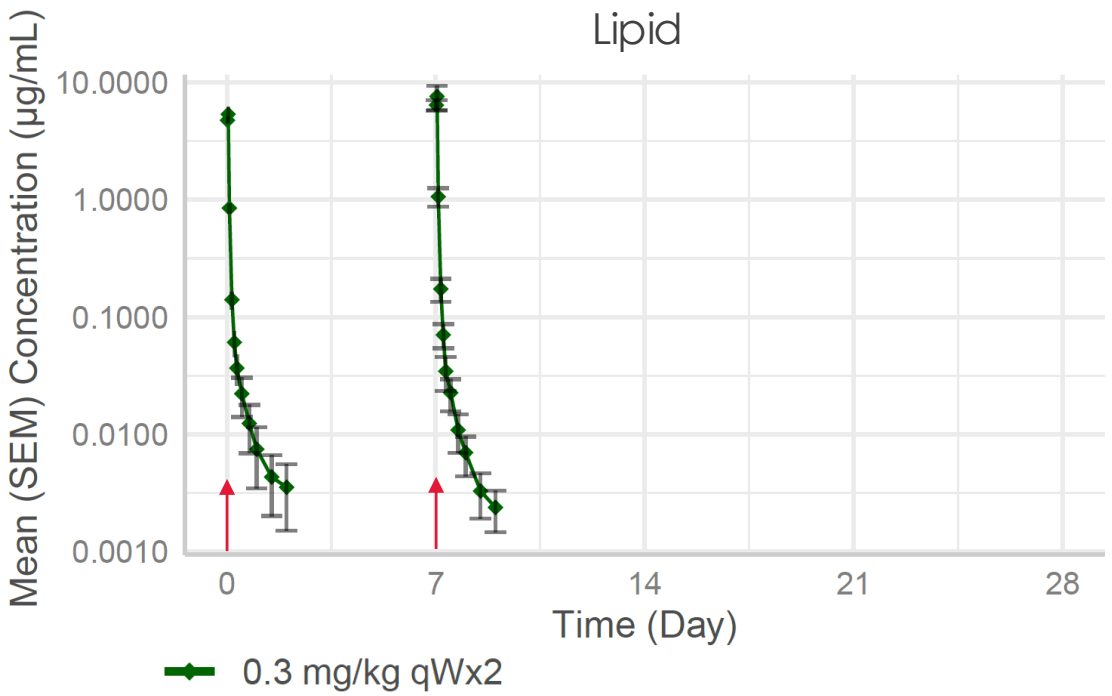
Lipid components have a short half life with no significant accumulation between doses



Pharmacokinetics

- No significant accumulation of lipid components of mRNA-1944 was seen after administration of the second weekly dose due to the rapid elimination from systemic circulation

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Antibody against Chikungunya virus (mRNA-1944)

Summary of Phase 1 interim analysis

- No serious adverse events (SAEs) were reported; The most common AEs were headache (32%), nausea (25%), myalgia (18%), dizziness (14%) and chills (14%)
- Administration of mRNA-1944 resulted in dose-dependent increases in levels of antibody against Chikungunya (CHKV-24)
- Neutralizing antibodies were observed at all dose levels, indicating functional antibody production by mRNA-1944
- CHKV-IgG half-life was estimated to be ~69 days
- A single 0.3 mg/kg dose led to CHKV-IgG expression that exceeded the 1 µg/mL target concentration for at least 16-weeks post single dose
- Administration of the second 0.3 mg/kg dose in the 0.3 mg/kg qWx2 cohort led to an approximately 1.8-fold accumulation of CHKV-IgG exposure (Emax) while maintaining a favorable tolerability profile
- As a result of rapid systemic clearance, no significant accumulation of lipid was seen after administration of the second weekly dose
- Safety and increased CHKV-IgG production in the two-dose regimen shows the platform's ability for repeat dosing

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Stephen Hoge, M.D.
President

Systemic Intracellular Therapeutics

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Systemic Intracellular Therapeutics

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Systemic intracellular therapeutics	**mRNA-3927**	PCCA/PCCB *Propionic acidemia, PA*					Worldwide
	mRNA-3705	MUT *Methylmalonic acidemia, MMA*					Worldwide
	mRNA-3283	PAH *Phenylketonuria, PKU*					Worldwide
	mRNA-3745	G6Pase *Glycogen storage disease type 1a, GSD1a*					Worldwide

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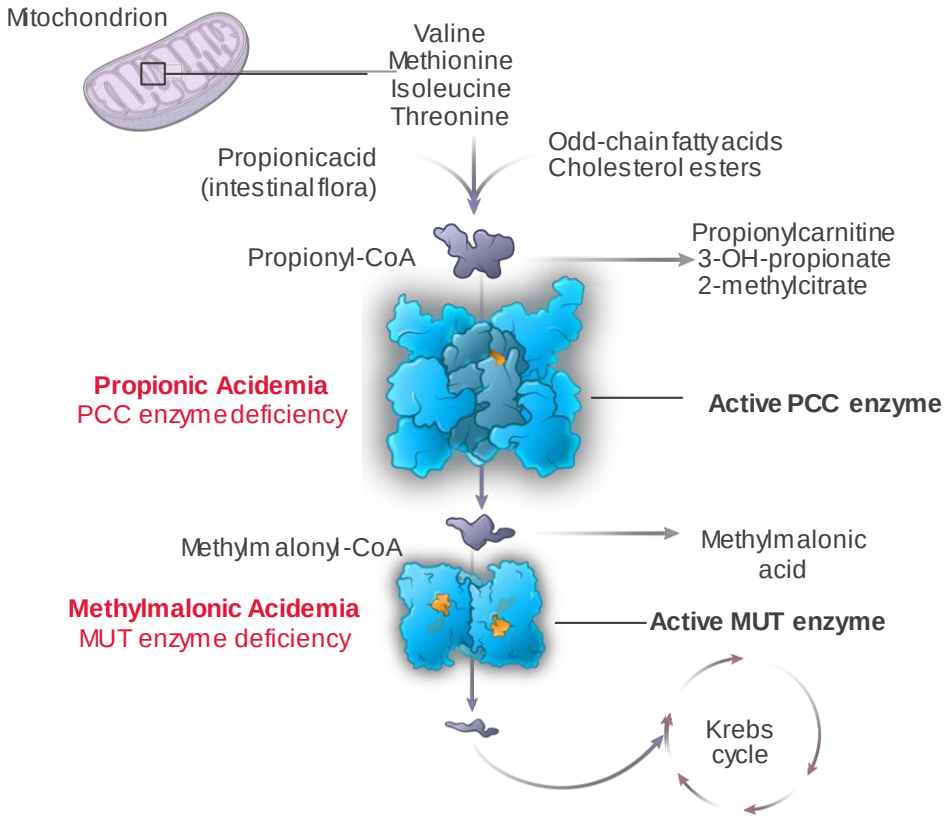
Organic acidemias

Multiple candidates targeting same metabolic pathway



MMA and PA

- Similar biology and disease pathology
- Shared treating clinicians and centers of excellence
- Relative prevalence in any given locale is a function of local founder effects/consanguinity
  - MMA: ~500-2,000 patients in the US*
  - PA: ~325-2,000 patients in the US*

*Based on estimated birth prevalence (MMA: 0.3-1.2:100,000 newborns; PA: 0.2-1.2:100,000 newborns) and mortality rates

mRNA advantages

*Ability to encode for **intracellular** proteins, **localized** to mitochondria*

*Ability to **titrate dose to response***

*Potential to treat during **acute** metabolic decompensations*

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Propionic acidemia (PA) overview

- **Disease overview**: Rare, autosomal recessive organic acidemia/aciduria, caused by PCC mitochondrial enzyme deficiency
  - The PCC enzyme is a dodecamer made up of alpha (PCCA) and beta (PCCB) subunits
  - PCC deficiency arises out of a mutation in PCCA (PA Type I) or PCB (PA Type II)

- **Prevalence**: ~1:100-250K births
  - ~325-2,000 patients in the US

- Primarily **a pediatric disease** with majority of cases presenting within 3 days of life
  - **Significant mortality & morbidity**

- **Treatment**: There is **no approved therapy for PA**
  - Standard of care included dietary and palliative measures
  - Liver transplant shown to improve biochemical and clinical outcomes

Clinical manifestations	
Neonatal period	Neurological complications Optic atrophy Growth retardation Arrhythmias & cardiomyopathy Life-threatening metabolic crises Pancreatitis

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Propionic acidemia program update

Propionic Acidemia (PA)

(mRNA-3927)

- Chronic treatment for patients with propionic acidemia which replaces the missing or dysfunctional mitochondrial enzyme propionyl-CoA carboxylase (PCC)
- mRNA-3927 has received FDA Fast Track Designation, FDA orphan drug designation, FDA rare pediatric disease designation and EMA orphan drug designations
  - Open IND
- Protocol amendment during COVID-19 pause:
  - Amended our protocol to a novel dose-optimization clinical trial design
  - Less burdensome on patients, their families and our clinical partners
  - Plan to launch an extension study for continued dosing of patients upon positive risk/benefit profile from Phase 1/2 trial

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Propionic acidemia (mRNA-3927) Phase 1/2 trial protocol amended to a novel dose optimization trial

Key objective

- To evaluate the safety and pharmacology of mRNA-3927 in patients 1 year of age and older with propionic acidemia (PA)

Primary endpoint

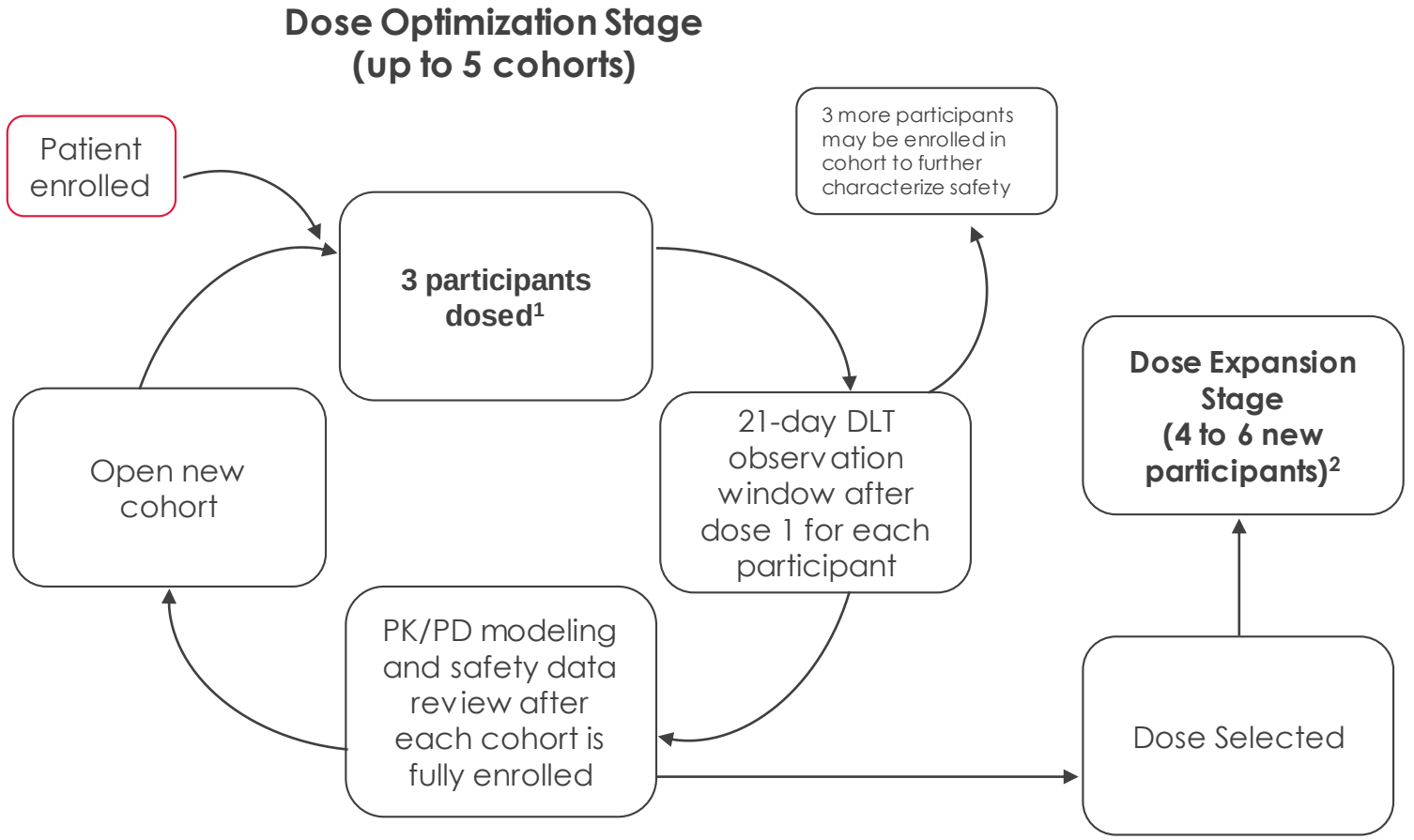
- Safety
- Pharmacokinetics
- Pharmacodynamics

Secondary endpoint

- Incidence and severity of adverse events (AEs)
- Change in plasma biomarkers: methylcitric acid (2-MC) and Hydroxypropionic acid (3-HP)

Trial progress

- Site initiation was paused due to COVID-19 disruptions
- Study start-up has resumed



DLT = dose-limiting toxicity; PD = pharmacodynamic(s); PK – pharmacokinetic(s)
1. The first 2 participants will be ≥ 8 years of age
2. In the dose expansion stage, a minimum of 2 participants with each subtype (PCCA and PCCB) will be enrolled

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Systemic Intracellular Therapeutics

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Systemic intracellular therapeutics	mRNA-3927	PCCA/PCCB *Propionic acidemia, PA*					Worldwide
	mRNA-3705	MUT *Methylmalonic acidemia, MMA*					Worldwide
	mRNA-3283	PAH *Phenylketonuria, PKU*					Worldwide
	mRNA-3745	G6Pase *Glycogen storage disease type 1a, GSD1a*					Worldwide

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Methylmalonic acidemia (MMA) overview

- **Disease overview**: Rare, autosomal recessive organic acidemia/aciduria
  - Defective or deficient MUT enzyme (methylmalonic CoA mutase)
- Disease is progressive, involves multiple organ systems and is highly lethal; includes risk of life-threatening metabolic decompensation episodes
- Primarily a pediatric disease with onset in early infancy; significant mortality and morbidity
- **Prevalence**: ~1:100K (except in the Middle East where it is higher, 6:100K)
- **Treatment**: There is no approved therapy for MMA
  - Current interventions include: dietary restriction, cofactor therapy and carnitine
  - Liver and/or kidney transplant is the only effective treatment, even in infants (but transplant is not curative)

Clinical manifestations	
Neonatal period	Neurological complications Growth retardation High mortality Life-threatening metabolic crises Pancreatitis Renal complications

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MMA program update

Methylmalonic Acidemia (MMA)

(mRNA-3705)

- Chronic treatment for patients with methylmalonic acidemia which replaces faulty enzyme methylmalonic-CoA mutase (MUT)
- Due to COVID-19, enrollment and new site initiation was paused for methylmalonic acidemia (MMA; mRNA-3704)
- *Update today*: We have leveraged the pause due to COVID-19 to improve clinical trial design and bring forward a next generation product (mRNA-3705)

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Moving forward with next generation MMA candidate (mRNA-3705)

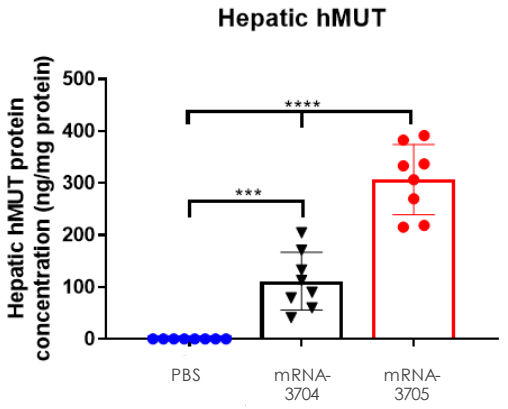
MMA (mRNA-3705)

- Introduction of a drug product with better pharmacology (new mRNA)
- Same LNP, also used in mRNA-1944
- Taken opportunity to revise clinical protocol to improve patient experience and operational feasibility

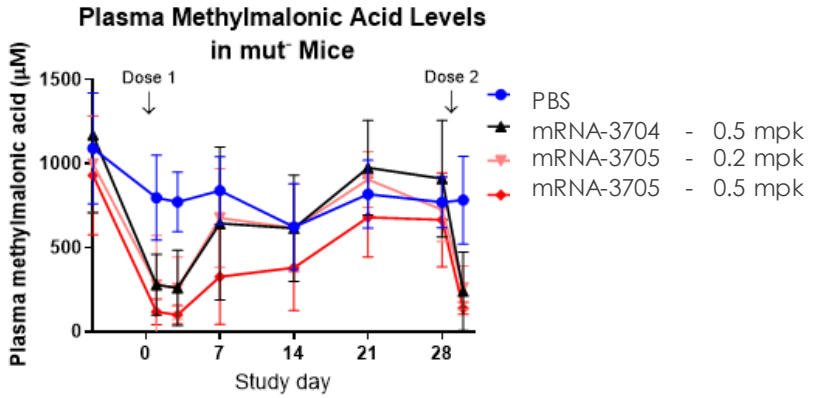
Next steps

- File new IND and CTA applications for mRNA-3705

mRNA-3705 produces **higher levels of hMUT** enzyme in the liver of rats



mRNA-3705 showed **greater potency** and **prolonged lowering of MMA** in mut- mice



*P<0.05, ***P<0.001, ****P<0.0001 by one-way ANOVA followed by Tukey's multiple comparisons test

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Rare diseases summary

mRNA advantages in rare diseases

- Target **intracellular** proteins
- Protein complexes with **multiple subunits**
- Able to **tailor dosing** to clinical response
- Does not require entry to cell nucleus

Next steps in rare diseases

- **PA** – First patient dosed
  MMA – IND/CTA submission for mRNA-3705
  GSD1a – IND filing
  PKU – IND filing
- Aim to **clinically de-risk the systemic intracellular** modality
- Develop new development candidates and modalities in rare diseases

Moderna's commitment to rare diseases

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Tal Zaks, M.D., Ph.D.
Chief Medical Officer

Intratumoral Immunotherapy

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Oncology development candidates

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Cancer vaccines	**mRNA-4157**	Personalized cancer Vaccine (PCV)					50-50 global profit sharing with Merck
	mRNA-5671/ Merck V941	KRAS vaccine, CRC, NSCLC, pancreatic cancer					50-50 global profit sharing with Merck
Intratumoral immuno-oncology	**mRNA-2416**	OX40L *Solid tumors/lymphoma Advanced ovarian cancer*		Solid tumors/lymphoma	Ovarian		Worldwide
	mRNA-2752	OX40L/IL-23/IL-36γ (triplet) *Solid tumors/lymphoma*					Worldwide
	MEDI1191	IL-12 *Solid tumors*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales

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Intratumoral immuno-oncology

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Intratumoral immuno-oncology	**mRNA-2416**	OX40L *Solid tumors/lymphoma* *Advanced ovarian cancer*		Solid tumors/lymphoma	Ovarian		Worldwide
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	MEDI1191	IL-12 *Solid tumors*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales

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Antonio Jimeno, M.D., Ph.D.

Professor of Medicine/Oncology and Otolaryngology at University of Colorado School of Medicine

Dr. Jimeno is a tenured Professor at the University of Colorado Cancer Center (UCCC). His laboratory and clinical research efforts are aimed at discovering new therapies, and improving the treatment outcomes and quality of life of patients with cancer with a focus on head and neck squamous cell cancer (HNSCC). He has developed PDX and humanized models to study cancer, and their application in new drug testing.

He serves as the co-Director of the Phase One, Expanded and Molecular Studies program, Director of the Head and Neck Cancer Clinical Research program, and as co-Leader of the Developmental Therapeutics (DT) program.

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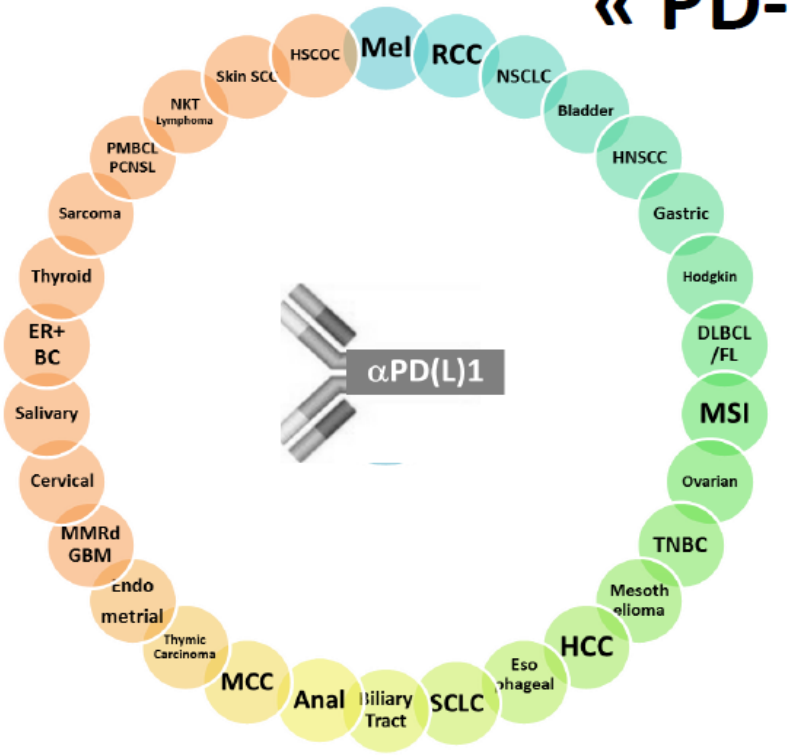
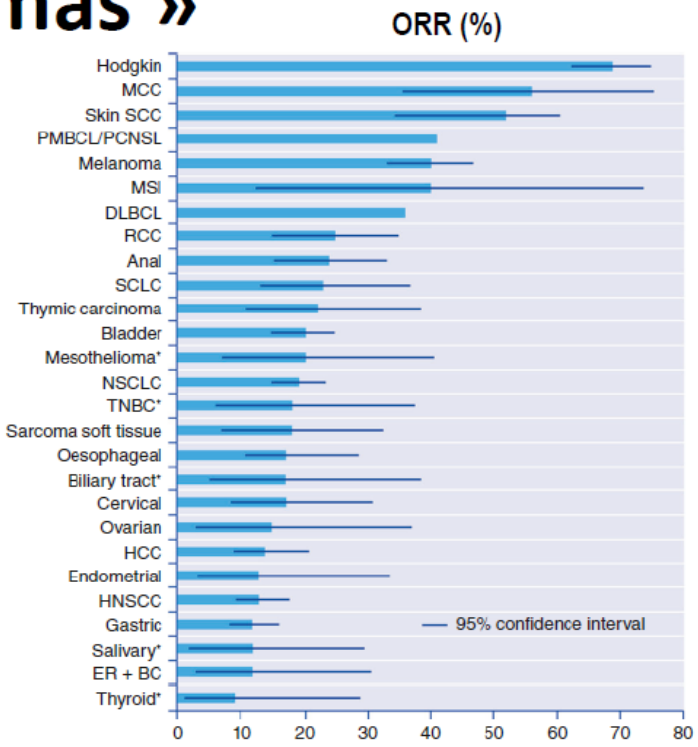
Anti-PD(L)1 therapy 2020

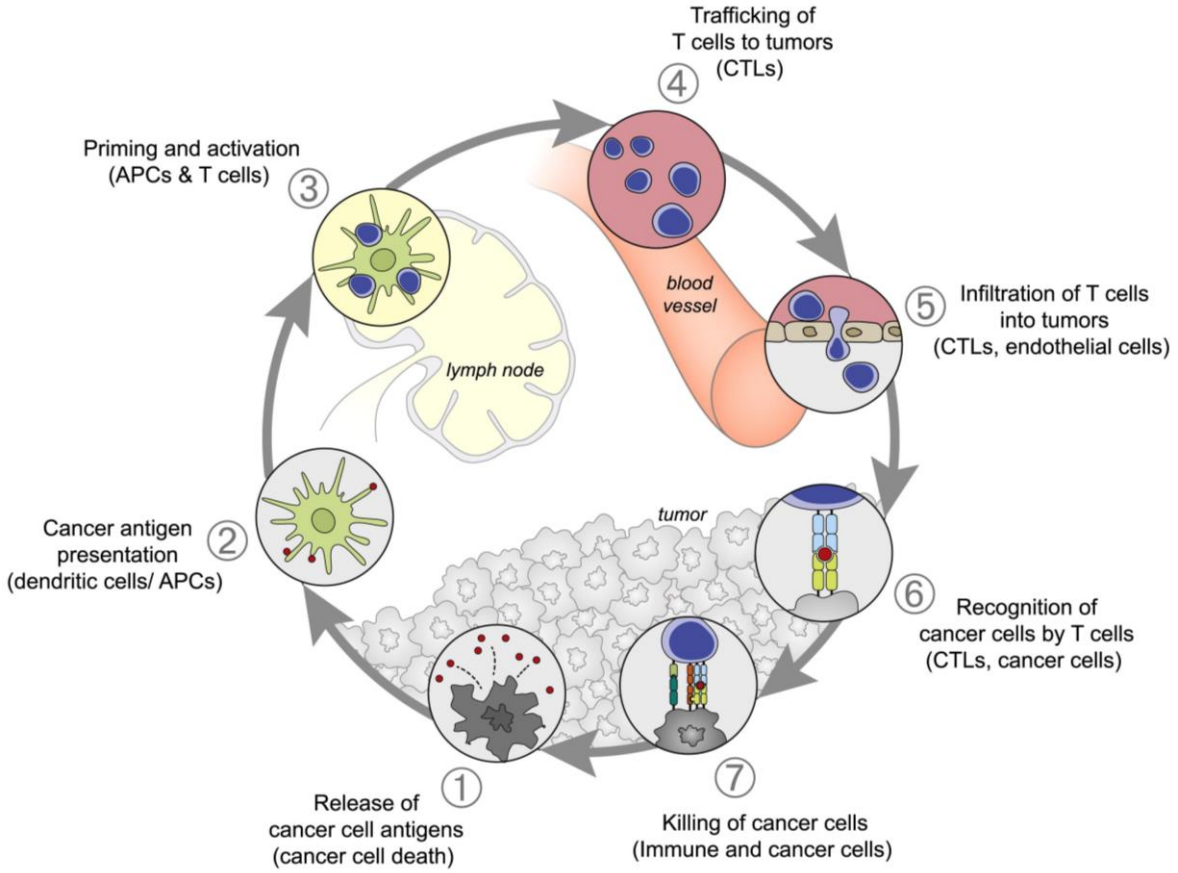
How do we increase patient benefit?

Cancers with Sensitivity to PD(L)1 Blockade: « PD-lomas »



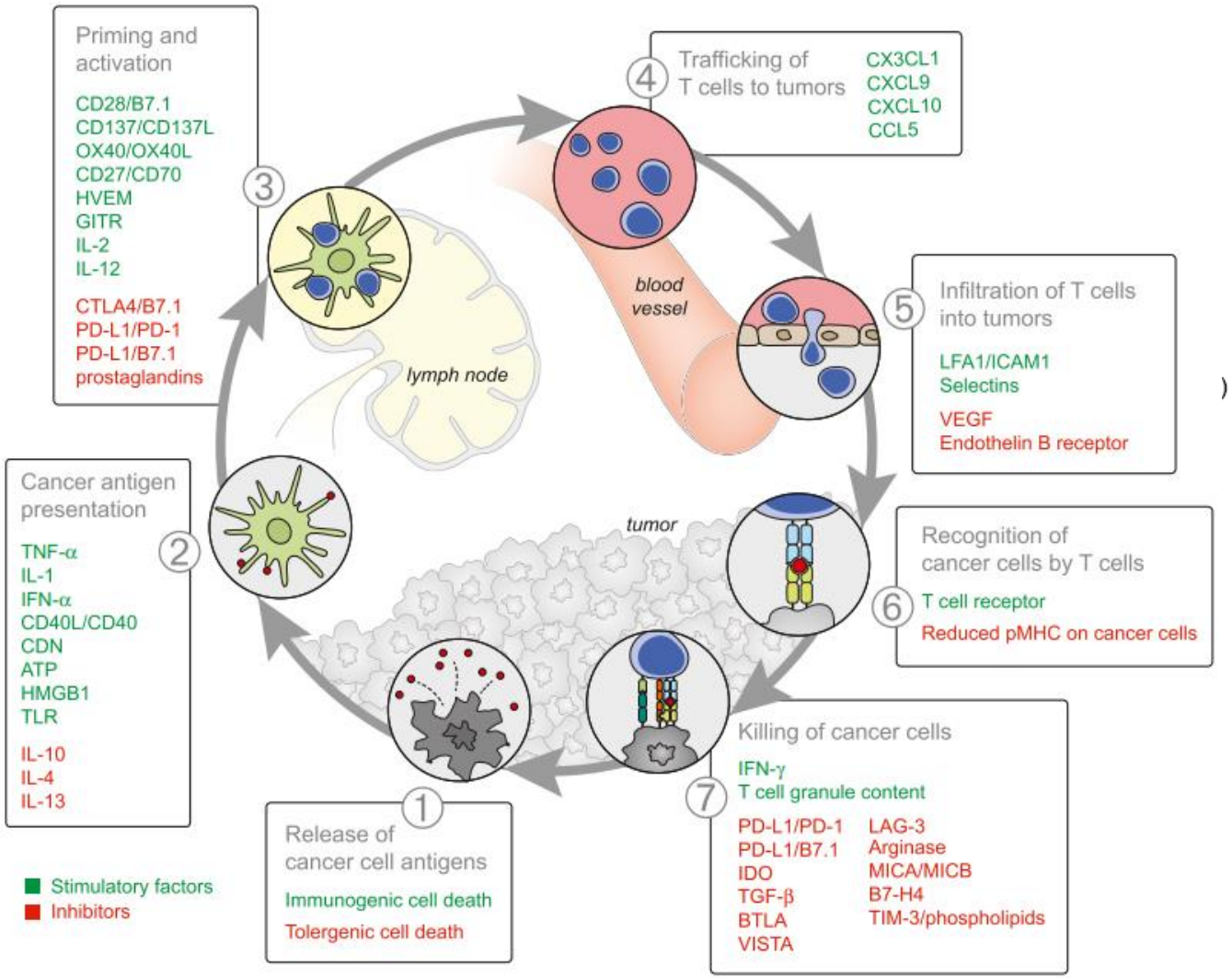


The Cancer-Immunity Cycle



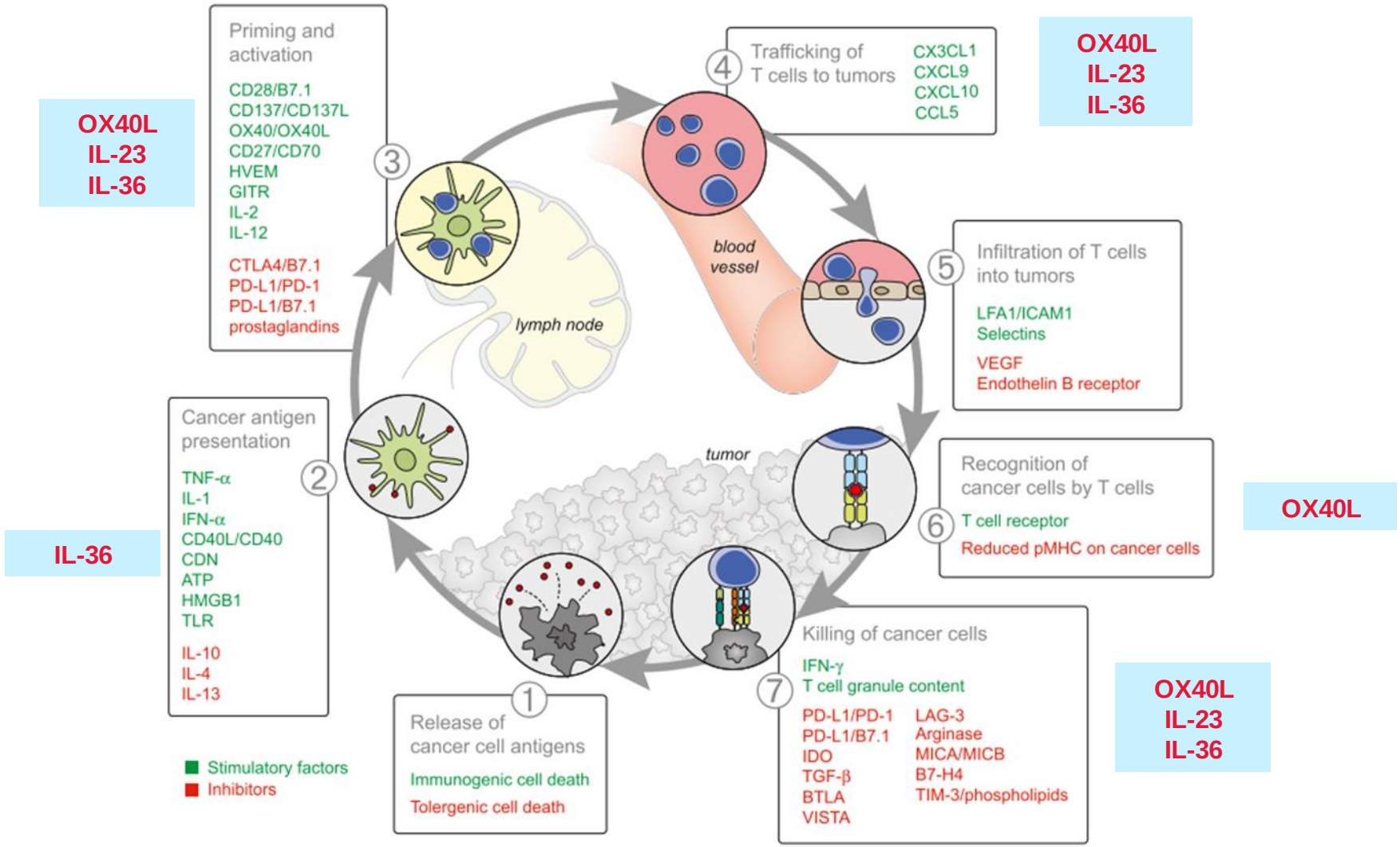
Chen and Mellman, Immuity 2013

Stimulatory and Inhibitory factors of the Cancer-Immunity Cycle



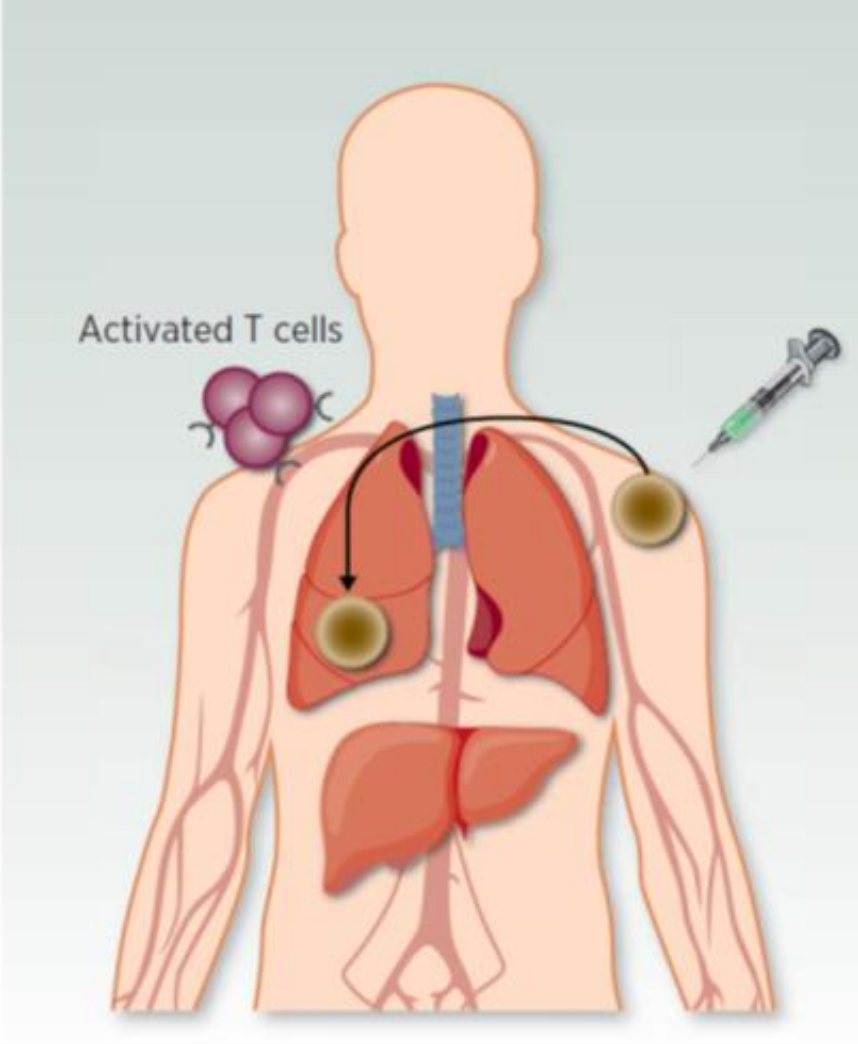
Chen and Mellman, Immunity 2013

Stimulatory and Inhibitory factors of the Cancer-Immunity Cycle



Chen and Mellman, Immunity 2013

What is intratumoral (iTu) therapy?
What are the advantages of iTu over systemic Rx?



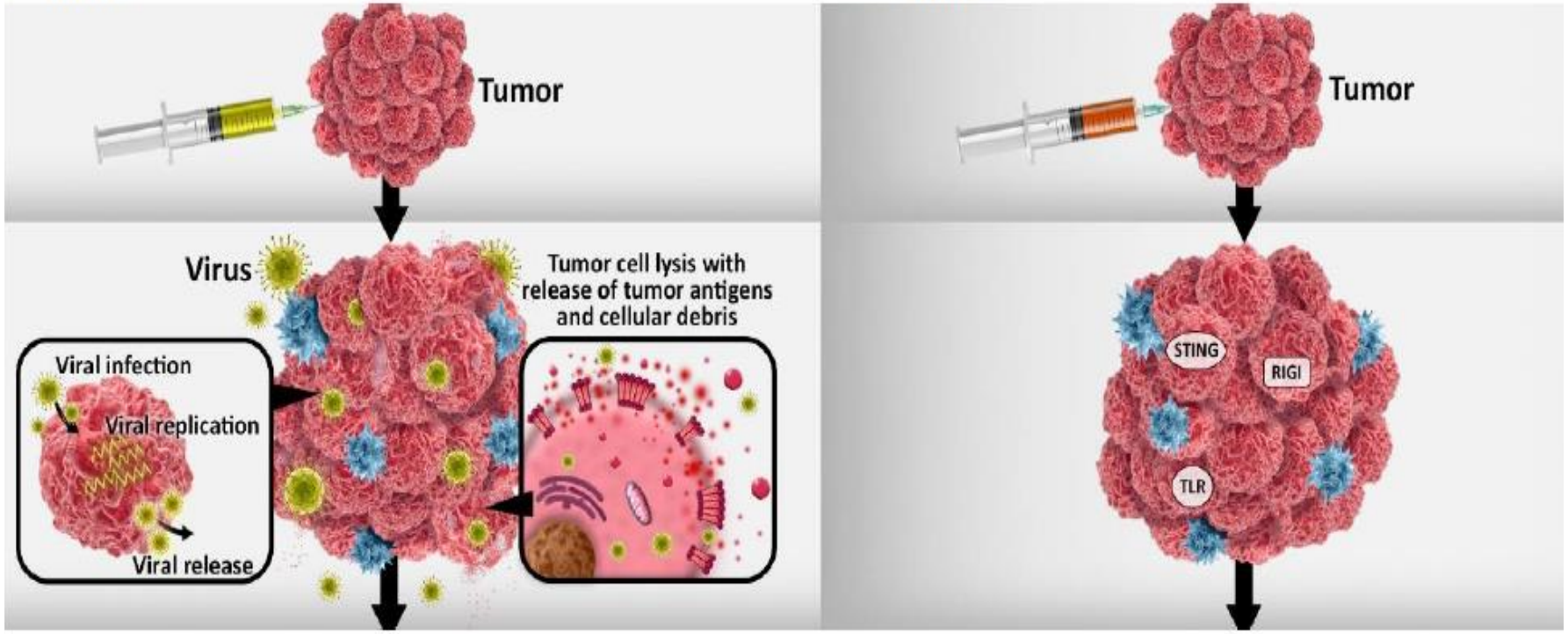
Hong, WX et. al; 2020, CCR

	Systemic Rx	Intratumoral mRNA Rx
Therapeutic principle	• Systemic effect	• Systemic effect; drains into tumor lymph nodes (extends to non-injected lesions) • Superior T-cell priming; multiclonal response
Toxicity	• Can be substantial	• Local administration should minimize toxicity of agents otherwise not tolerable • Minimal toxicity may allow for combination of multiple targets in one agent
Patient eligibility and feasibility	• Injectable lesion not necessary	• Injectable lesion must be available • Need coordination of investigational radiologist
Drug Production	• Off the shelf • Usually one target/product	• Off-the-shelf • Multiple targets can be added in one therapeutic

Examples of iTu agents

Oncolytic Viruses:
- T_V EC (HSV-1/GM-CSF)
- Coxsackievirus A21
- Others

Immune Agonists:
- Checkpoint agonists e.g. OX40L
- Cytokines (IFN-γ, interleukins e.g. IL-1, 12, 23, 36)
- Growth factors e.g. GM-CSF
- STING and RIG-1 agonists
- Others



Yuan J, SITC 2019

OX40L (mRNA-2416)

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Intratumoral immuno-oncology	**mRNA-2416**	OX40L *Solid tumors/lymphoma* *Advanced ovarian cancer*		Solid tumors/lymphoma	Ovarian		Worldwide
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	MEDI1191	IL-12 *Solid tumors*					50-50 U.S. profit sharing; AZ to pay royalties on ex-U.S. sales

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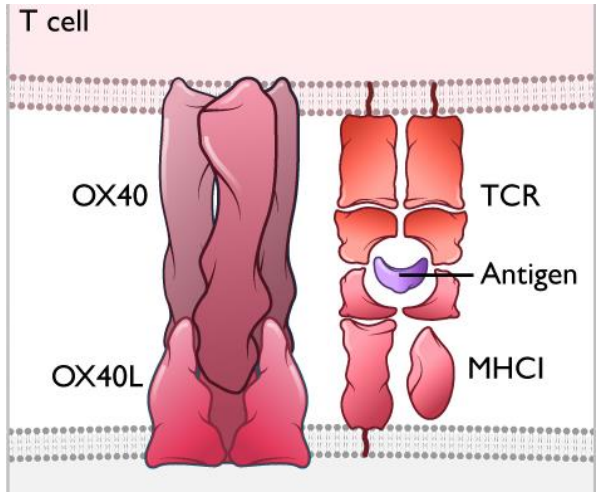
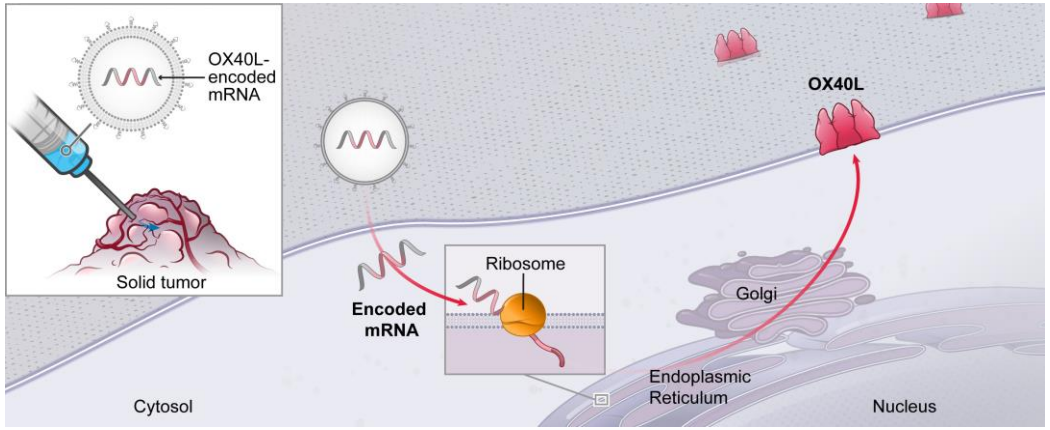
mRNA-2416 Encodes OX40L and is Injected Directly into a Tumor





OX40L:

- Homotrimeric protein normally expressed on professional antigen presenting cells (APCs)
- T cell co-stimulator which promotes effector T cell proliferation and enhanced survival in the presence of a recognized antigen
- Can inhibit suppressive activity of T-regs

- When mRNA-2416 is delivered into a tumor, cells in the tumor are directed to express OX40L protein in its native membrane-bound form, which in turn, may lead to a stronger T cell attack against the tumor and promote abscopal effects

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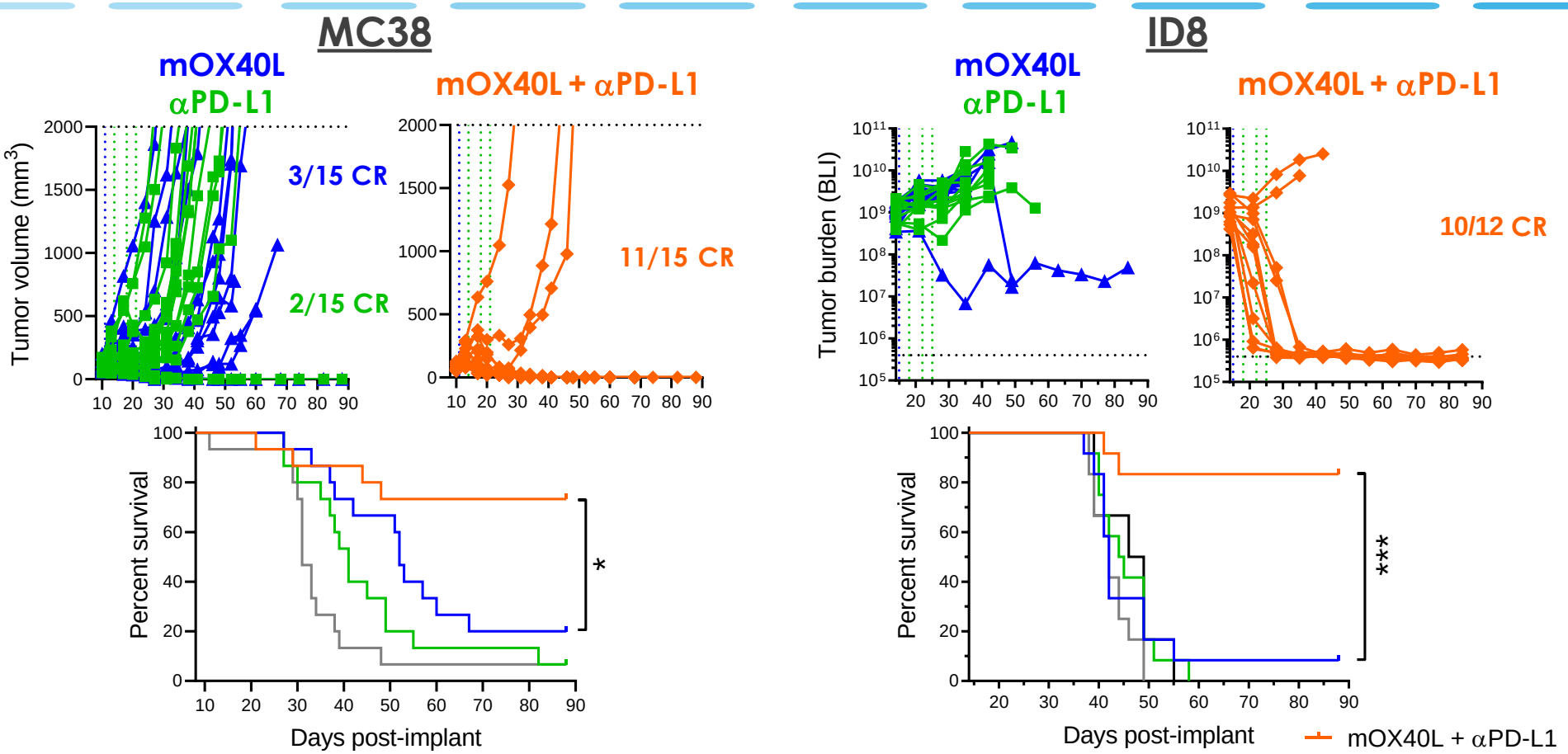
Preclinical models demonstrate synergistic effect of combination OX40L and aPD-L1



Anti-tumor efficacy in MC38-S and ID8 mouse syngeneic colon and ovarian carcinoma tumor models

- mOX40L single dose at 6.25 µg intratumorally (MC38-S) or 0.5 mg/kg intraperitoneally (ID8), on day 11 or 15 post tumor implantation, respectively
- aPD-L1 at 10 mg/kg, twice per week
- Control: non-translating mRNA. Log-rank test (Mantel-Cox), all animals included

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OX40L (mRNA-2416)

Phase 1/2 combination with durvalumab fully enrolled; Phase 2 dose expansion ongoing

Key Objectives

- Evaluate safety and tolerability of mRNA-2416 administered intratumorally
- Define the maximum tolerated dose and recommended dose for expansion
- Other endpoints include pharmacokinetic analyses as well as assessment of biomarkers of immunological response in tumor

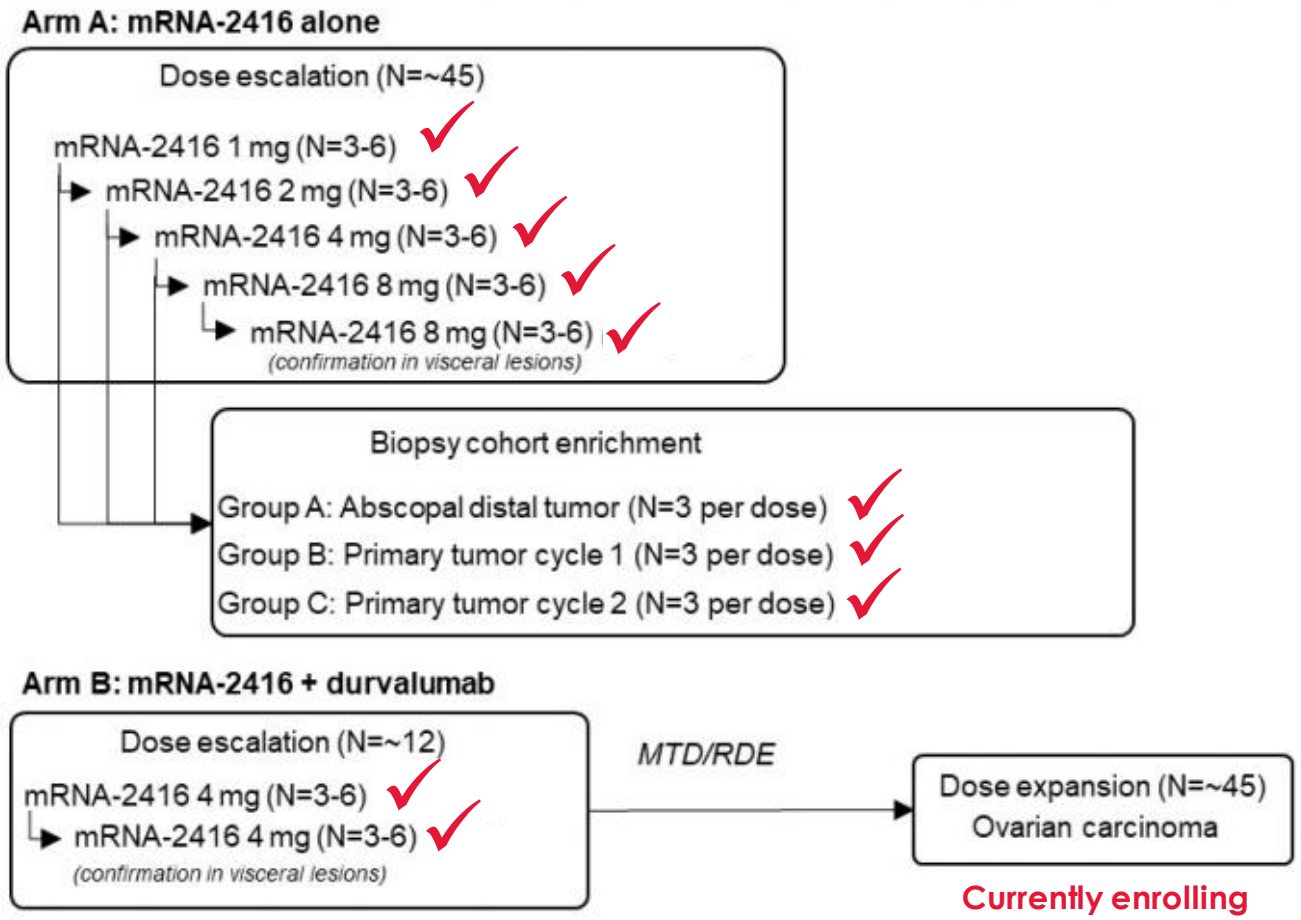
Dosing

Arm A:

- mRNA-2416 up to 8 mg iTu q2W x 2, then up to qmonthly x 5

Arm B and Dose expansion arm:

- mRNA-2416 up to 8 mg iTu q2W x 2, then up to qmonthly x 5
- Durvalumab 1500 mg IV qmonthly x 6



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OX40L (mRNA-2416)

Data presented at AACR 2020

- 39 patients evaluated for safety and efficacy as mRNA-2416 monotherapy
- Overall mRNA-2416 monotherapy has been tolerable at all dose levels with no dose-limiting toxicities (DLTs) reported and majority of related AE's being grade 1 or grade 2

Related Adverse Events*		
	Arm A (monotherapy)	
	Grade 2	Grade 3
Back Pain	-	1
Chills	2	-
Decreased Appetite	2	-
Fatigue	7	1
Flushing	3	-
Hypersensitivity	2	-
Influenza Like Illness	-	1
Injection Related Reaction	5	1
Injection Site Pain	3	-
Injection Site Reaction	2	-
Myalgia	-	1
Nausea	1	1
Skin Ulcer	-	1

Responses in patients (n=39)	
	Arm A (monotherapy)
Best Overall Response	
Complete Response (CR)	-
Partial Response (PR)	-
Stable Disease (SD)	14
Progressive Disease (PD)	15

AEs: ≥ 2 patients reporting treatment-related grade 2 events
AEs: ≥ 1 patient reporting treatment-related grade 3 events
No mRNA-2416 related grade 4/5 AEs were reported
* Related AEs of at least grade 2 highest grade reported once per patient

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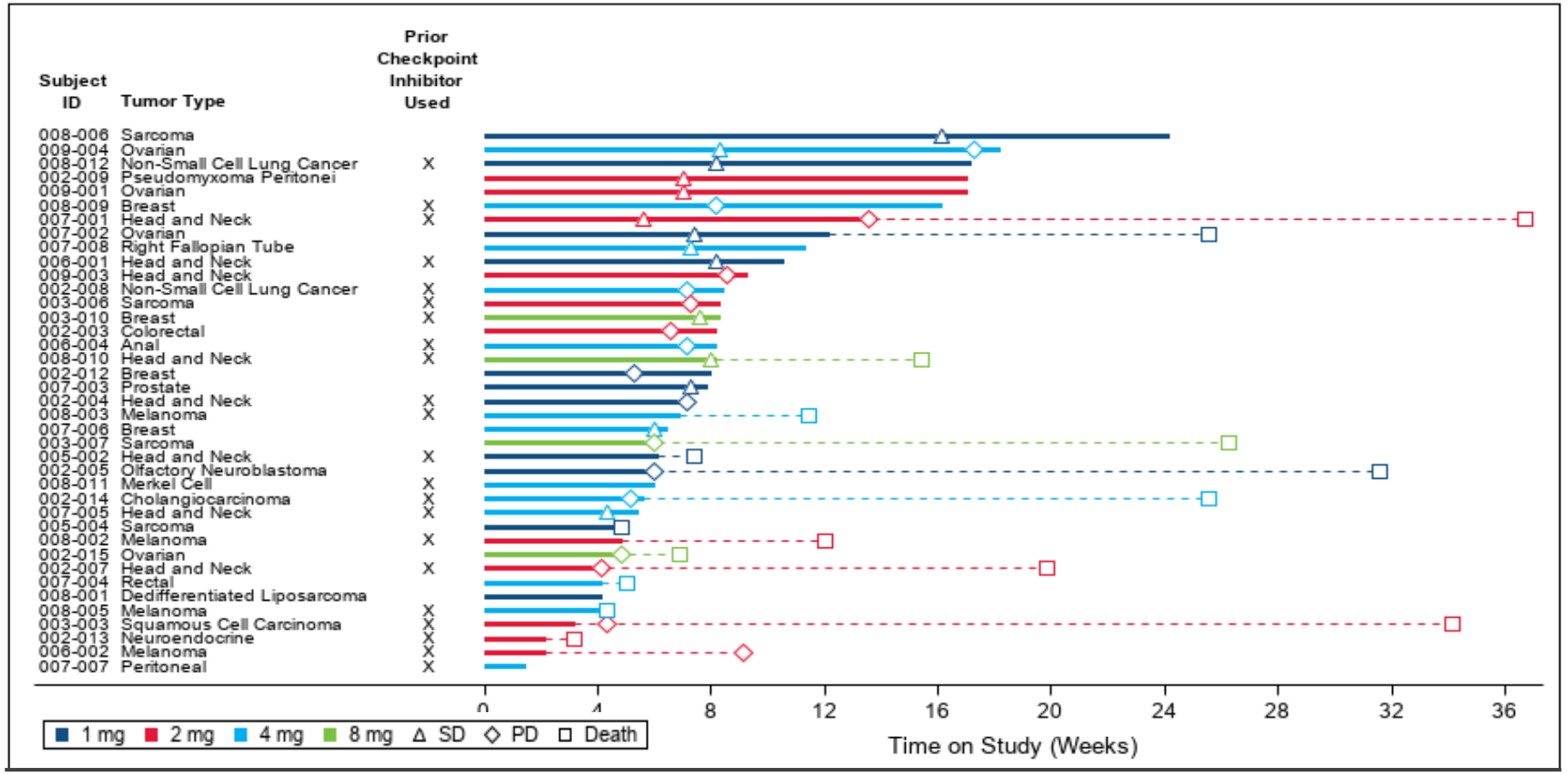
OX40L (mRNA-2416)

Data presented at AACR 2020

mRNA-2416-P101 Swimmer plot: ARM A monotherapy per RECIST 1.1



- 14/39 had stable disease (SD), of these patients 6 had SD for ≥14 weeks
- 4/6 ovarian patients on study had SD; 1 patient with sarcoma on drug for entire study (24 weeks)

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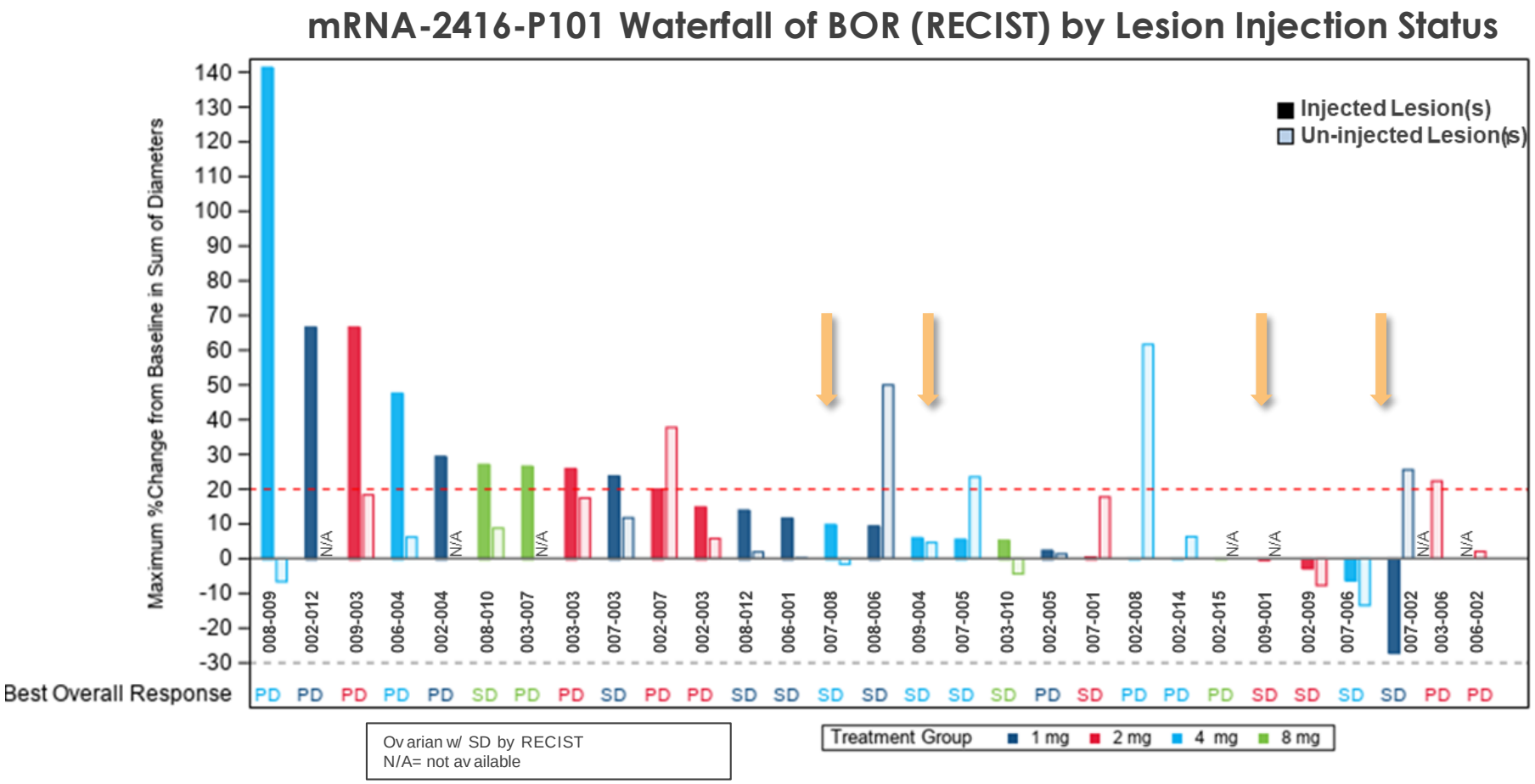
OX40L (mRNA-2416)

Data presented at AACR 2020



- 14 patients with best overall response of stable disease by RECIST
- 4 patients with tumor shrinkage in injected lesions
- 5 patients overall had reduction in un-injected lesions
- Overall 2 patients had tumor shrinkage in both injected and un-injected lesions, 2 patients had tumor shrinkage in their injected lesions only (Ovarian), while 3 patients had tumor shrinkage in their un-injected lesions only

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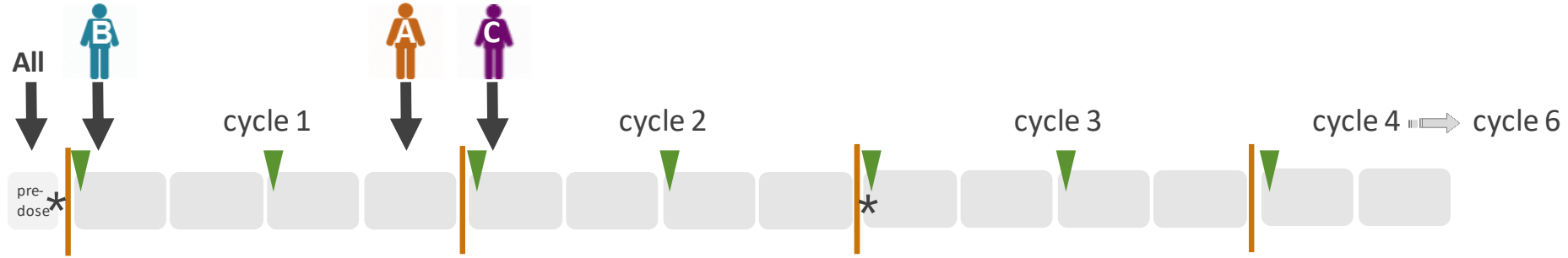
Phase 1 dosing & biopsy collection schedule and biomarker readouts from arm A (monotherapy mRNA-2416)



= OX40L on days 1 & 15 per cycle

= 1 week

= Tumor biopsy

* = Tumor assessment (imaging)

Biopsy assignment groups

- Abscopal tu: C1, D22-28
- Injected tu: C1, D2-3
- Injected tu: C2, D2-3

- n=3 pts per group, per dose
- Baseline biopsy for all

Biomarker Readouts from FFPE Biopsies

- Multiplexed Quantitative Immunofluorescence (QIF)
  - OX40L protein expression
  - T cell abundance, activation
- Whole transcriptome (RNAseq) for assessing baseline and post-treatment inflammatory states
  - PD-L1/ PD-1 axis
  - T cell-inflamed/ activation signatures

FFPE= formalin-fixed, paraffin embedded

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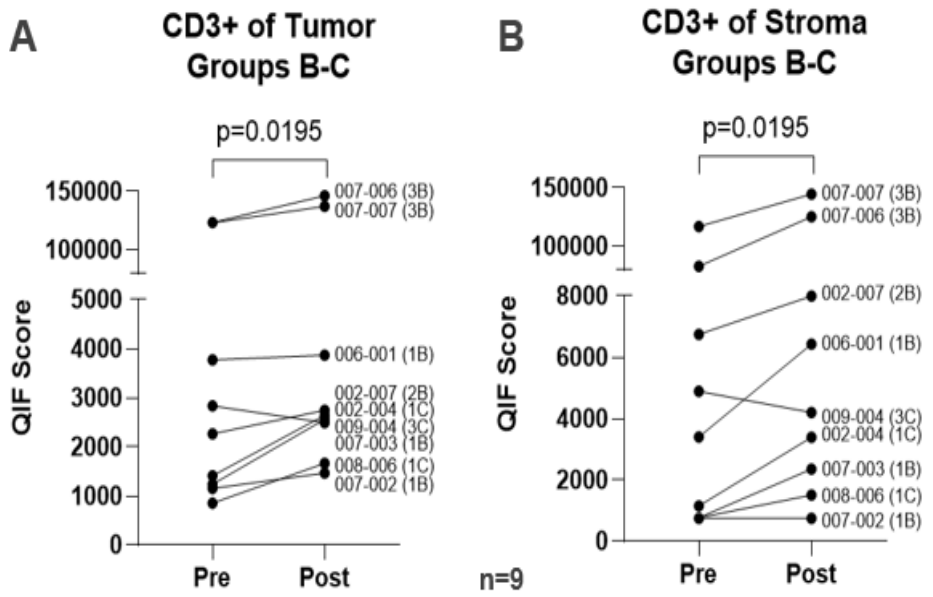
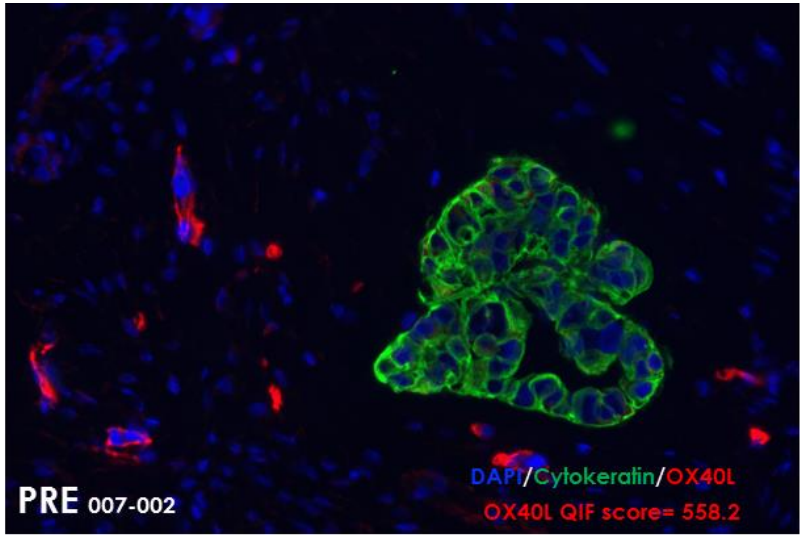
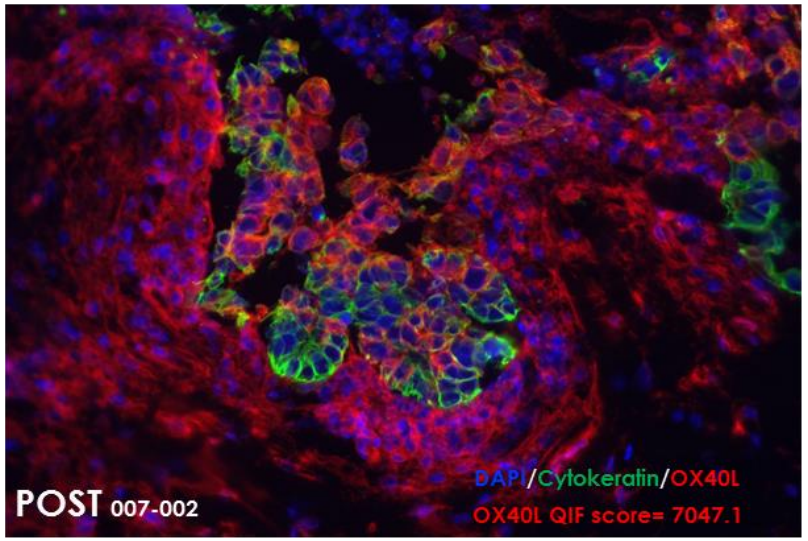
Protein expression by QIF of OX40L & T cell scores post-mRNA-2416 in injected lesions

- Increased OX40L protein expression observed in the tumor microenvironment (TME) in several cases, including in an ovarian patient, 007-002 with the most marked increase, as shown here
- Increased CD3+ T cells in the TME, in both tumor and stromal compartments



Data points labeled with patient ID (dose level+ cohort; dose levels: 1= 1mg; 2= 2mg; 3= 4mg; cohorts: B= bx at C1D2-3; C=bx at C2D2-3)





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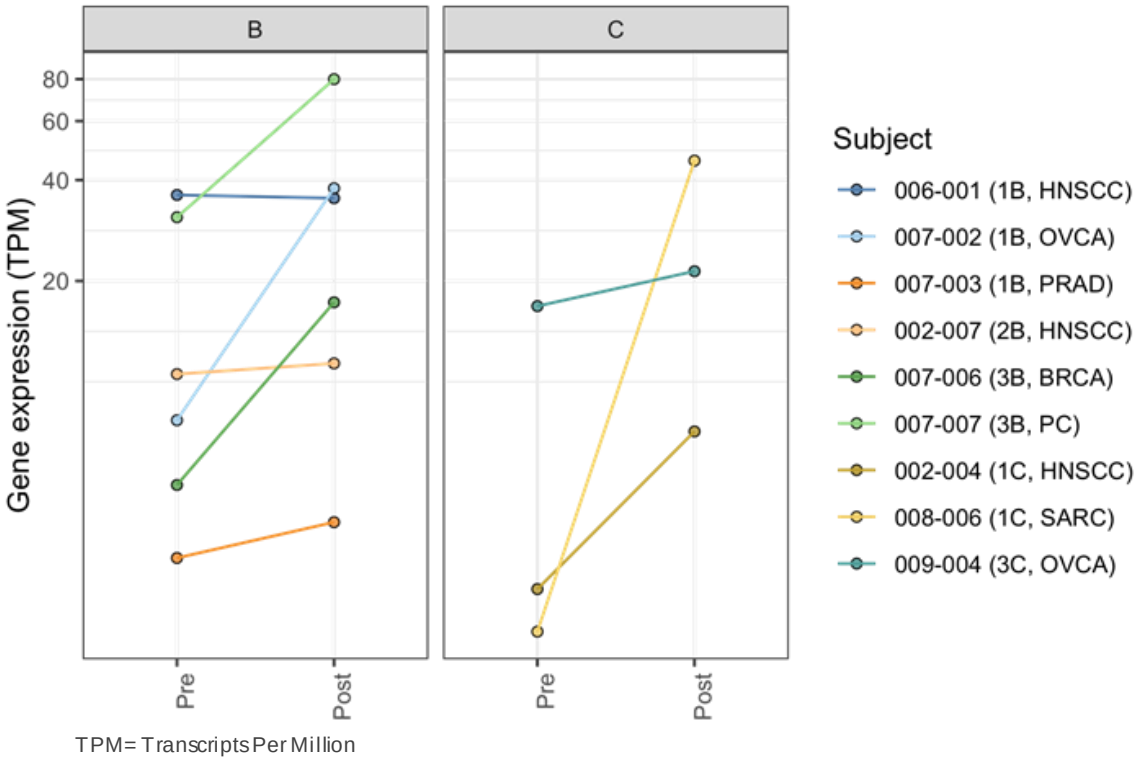
Increased PD-L1 ranked score in 5/9 patients post-treatment

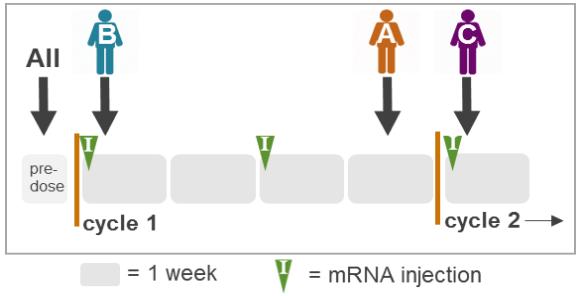


TPM= Transcripts Per Million

Patient ID (dose level, cohort, tumor type)	PD-L1 (TPM)		Fold change	Quartile (TCGA)	
	Pre	Post		Pre	Post
008-006 (1C, SARC)	1.80	45.70	25.42	0-25	75-100
007-002 (1B, OVCA)	7.68	37.81	4.92	25-50	75-100
007-006 (3B, BRCA)	4.92	17.26	3.51	25-50	50-75
002-004 (1C, HNSCC)	2.41	7.11	2.95	0-25	50-75
007-007 (3B, PC)	30.99	79.98	2.58	75-100	75-100
007-003 (1B, PRAD)	2.98	3.81	1.28	0-25	25-50
009-004 (3C, OVCA)	16.82	21.38	1.27	50-75	50-75
002-007 (2B, HNSCC)	10.54	11.35	1.08	50-75	50-75
006-001 (1B, HNSCC)	36.10	35.32	0.98	75-100	75-100
Median	5.68				

Quartile rankings defined using PD-L1 transcript levels across TCGA dataset (RNAseq data, 9654 samples across 33 tumor types)

- **5 of 9 Group B/C cases (injected lesions) with increased quartile ranking of PD-L1**
  - PD-L1 at transcript level reported to have high positive predictive value for response to anti-PD-1/PD-L1 Abs (Conroy et al., 2019)



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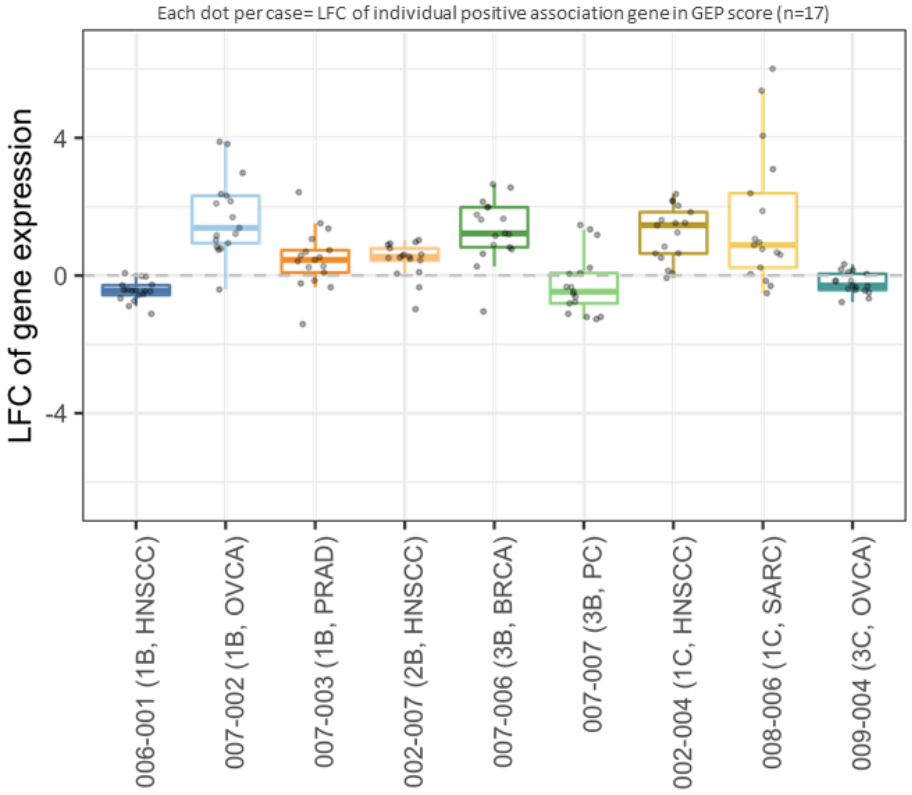
Increased T cell-inflamed GEP ranked score in 6/9 patients after mRNA-2416 treatment

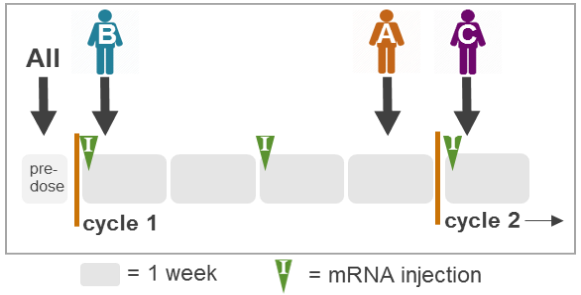


LFC= Log Fold Change

Patient ID (dose level, cohort, tumor type)	GEP score		Fold change	Quartile (TCGA)	
	Pre	Post		Pre	Post
007-006 (3B, BRCA)	1.27	1.77	1.39	0-25	50-75
008-006 (1C, SARC)	1.50	2.05	1.37	0-25	75-100
007-002 (1B, OVCA)	1.53	2.00	1.31	25-50	50-75
002-004 (1C, HNSCC)	1.25	1.52	1.22	0-25	25-50
007-003 (1B, PRAD)	1.32	1.52	1.15	0-25	25-50
002-007 (2B, HNSCC)	1.60	1.79	1.12	25-50	50-75
009-004 (3C, OVCA)	1.95	1.88	0.96	50-75	50-75
007-007 (3B, PC)	2.26	2.16	0.95	75-100	75-100
006-001 (1B, HNSCC)	2.48	2.32	0.93	75-100	75-100
Median	1.50				

GEP score:

- GEP = Gene Expression Profile; 18-gene signature; predictive of pembro response (Ayers et al., 2017; Cristescu et al., 2018)
- GEP Quartile rankings determined across TCGA



- **6 of 9 Group B/C cases (injected lesions) with increased quartile ranking of T-cell inflamed GEP scores**
  - Cases without increased GEP ranking post-treatment had elevated GEP scores at baseline (eg, 007-007 and 006-001)

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OX40L (mRNA-2416)

Conclusions from AACR 2020 presentation

- mRNA-2416 is well tolerated when given as monotherapy at all dose levels studied with no DLTs reported
  - The majority of TEAEs reported were grade 1/2, and no grade 3 TEAEs > 3%
- 14/39 patients achieved a best overall response (BOR) of stable disease (SD), of these patients 6 had SD for ≥14 weeks.
- 4/6 Ovarian Patients achieved a best overall response (BOR) of stable disease (SD) along with noted clinical observation of tumor regression in injected as well as un-injected lesions supporting further investigation of this histology
- Patients treated with mRNA-2416 displayed increased OX40L protein and T-cell infiltration in the TME, upregulation of PD-L1 transcript, and activation of a pro-inflammatory gene expression response, while murine studies combining mRNA-2416 with PD-L1 blockade resulted in synergistic anti-tumoral efficacy
- The observations of broad pro-inflammatory activity and beneficial changes in the TME with upregulation of PD-L1 support the evaluation of combination intratumoral mRNA-2416 with the anti-PD-L1 inhibitor durvalumab in solid tumors, which is ongoing in Part B of this study with a focus on advanced Ovarian carcinoma

OX40L/IL-23/IL-36γ (triplet)

Modality	ID #	Program *Indication*	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
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Immune modulation with OX40L, IL-23, IL-36γ

	OX40L	IL-23	IL-36γ
	Transmembrane T cell co-stimulatory protein	**Proinflammatory cytokine of the IL-12 family** • Reported to prime DC • Activates other cells that bridge innate to adaptive immunity (NKT, ILCs, γδ T cells)	**Proinflammatory cytokine of the IL-1 family** • Acts on DCs to promote maturation and ↑ cytokine/chemokines
	• Promotes Th1, Th2, Th9; suppresses Treg • Enhances expansion and survival of CD4 and CD8 T cells → promotes memory	• Expands and maintains Th17 • Acts on antigen experienced T cells	• Enhances T cell proliferation, Th1, Th9 differentiation
	• Preclinical monotherapy efficacy established and reported	• Preclinical monotherapy efficacy established and reported • Clear role in human barrier immunity and inflammatory disease	• Reported to preclinically enhance anti-cancer immunity • Clear role in human barrier immunity and inflammatory disease

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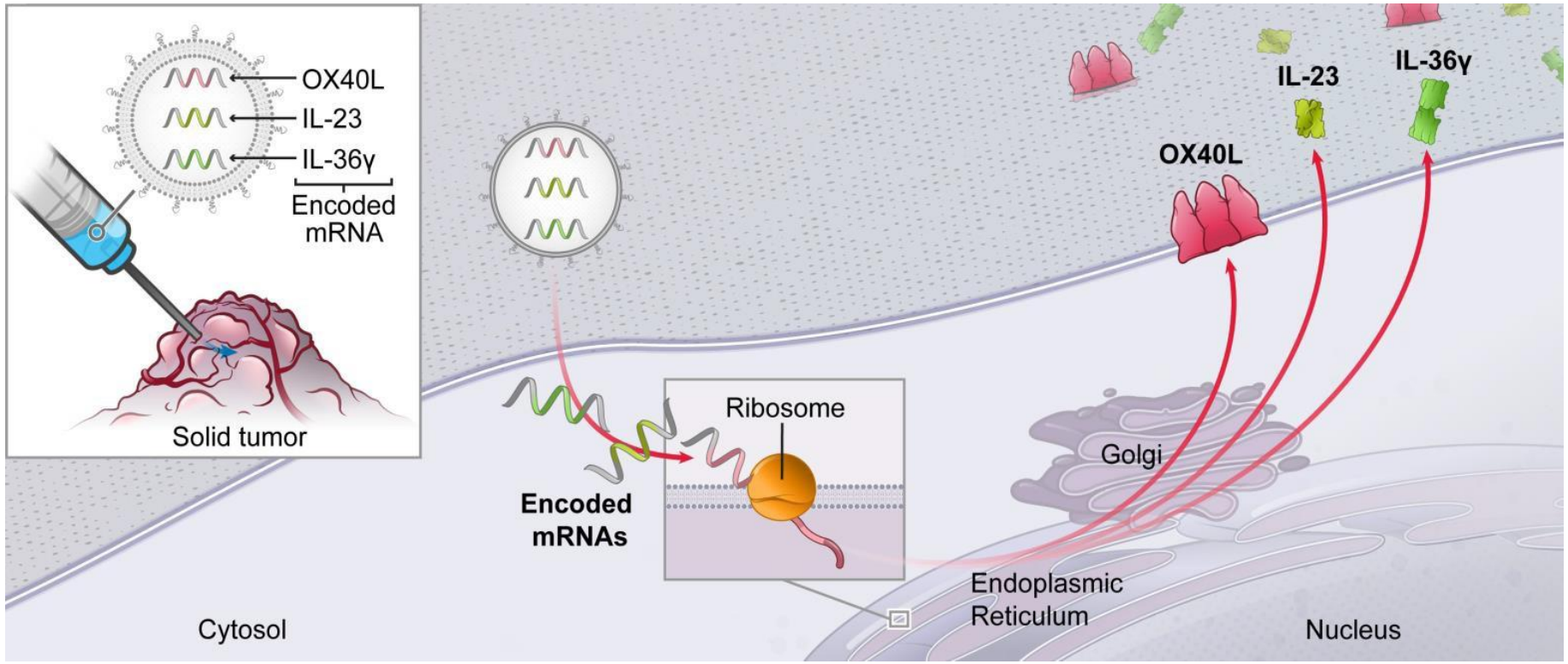
OX40L/IL-23/IL-36γ (mRNA-2752) overview

- Moderna's technology enables novel combinations of targets
- Intratumoral delivery may enable delivery of targets locally that are too toxic systemically



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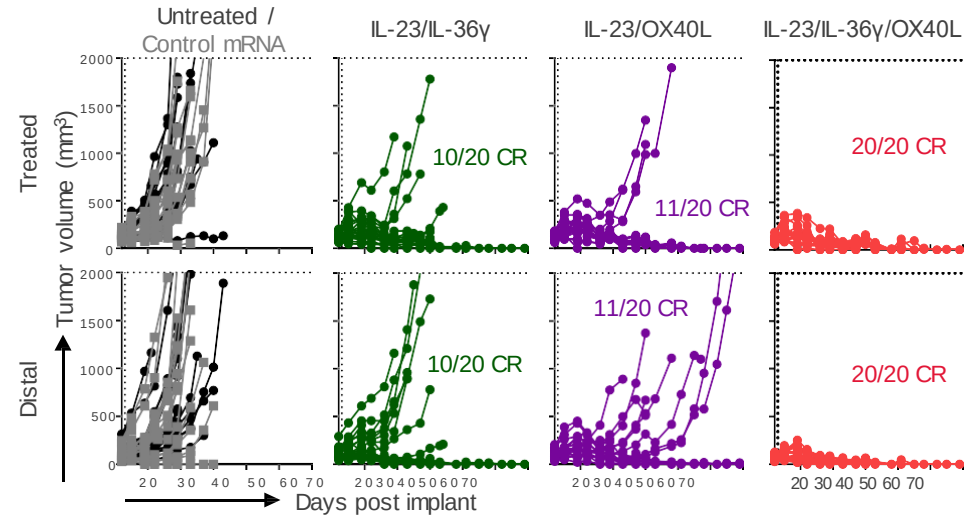
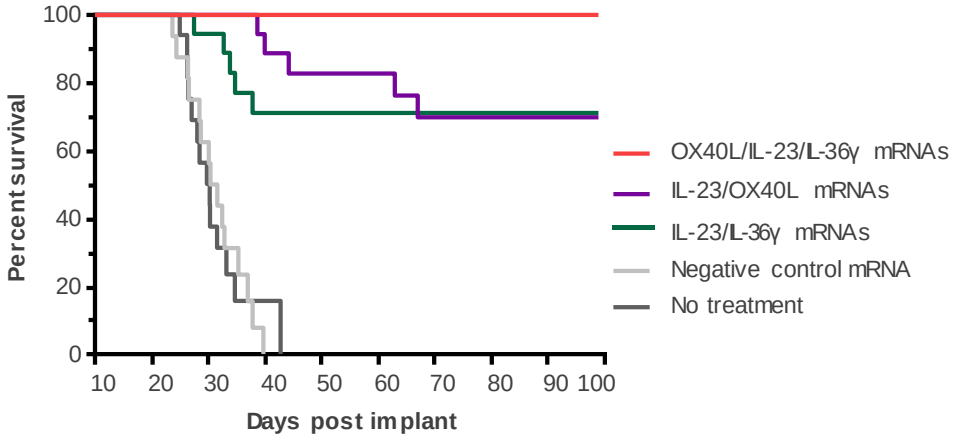
OX40L/IL-23/IL-36γ

Preclinical data – combination of 3 targets demonstrates synergistic effects

Species: Mouse



Species: Mouse



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Durable anticancer immunity from intratumoral administration of IL-23, IL-36γ, and OX40L mRNAs

- Tumor volumes of both the treated and untreated tumors. Mice carrying bilateral MC38-S tumors received mRNA injected into the right flank tumor only
- Local triplet mRNA treatment has global effects including on distal untreated tumors
- 100% (n=20) complete responders with mouse OX40L/IL-23/IL-36γ in MC38 dual flank syngeneic mouse model study

[1]Durable anticancer immunity from intratumoral administration of IL-12, IL-36γ and OX40L mRNA's; Science Translation Medicine; Hewitt et al., 2019

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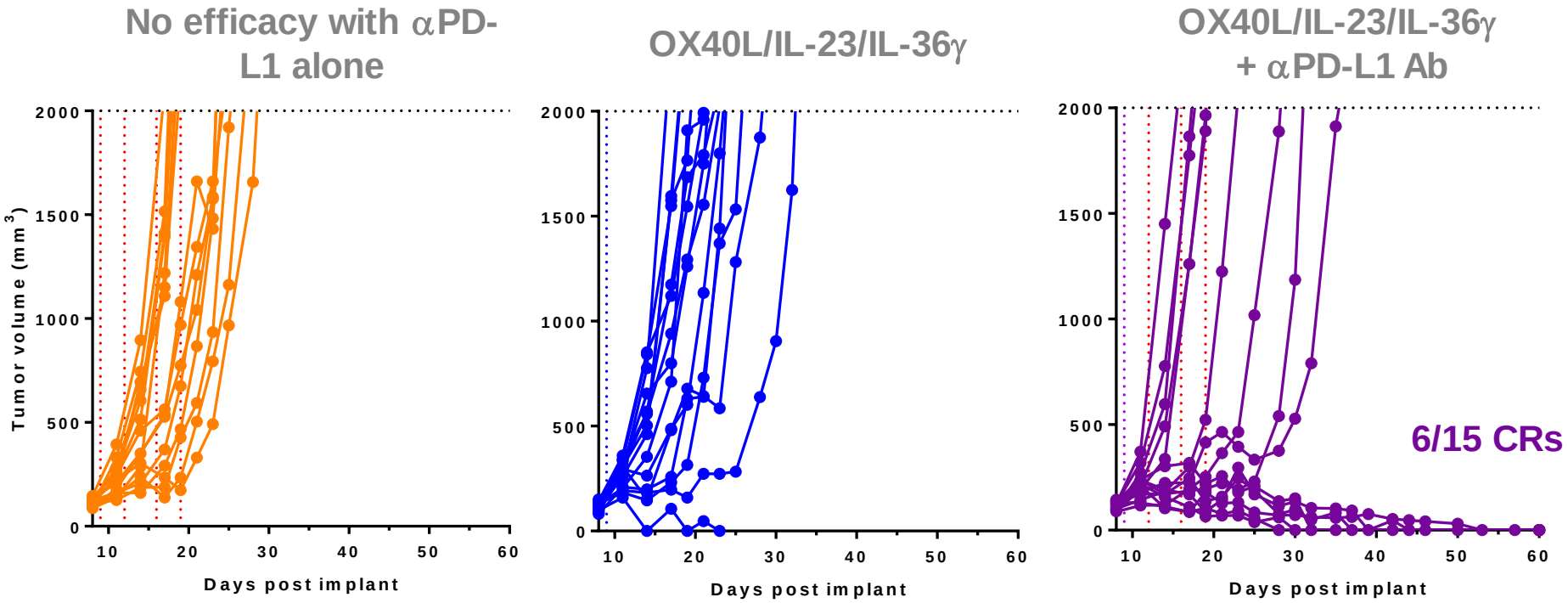
Combination treatment of aPD-L1 Ab + OX40L/IL-23/IL-36γ mRNA iTu is synergistic in immunologically barren B16F10 model



- OX40L/IL-23/IL-36γ mRNA given iTu day 1 + mouse aPD-L1 Ab IP 10 mg/kg twice weekly x 2
- ITu OX40L/IL-23/IL-36γ mRNA-monotherapy can achieve CRs even in models that are completely refractory to systemic checkpoint inhibitor treatment

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OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752)

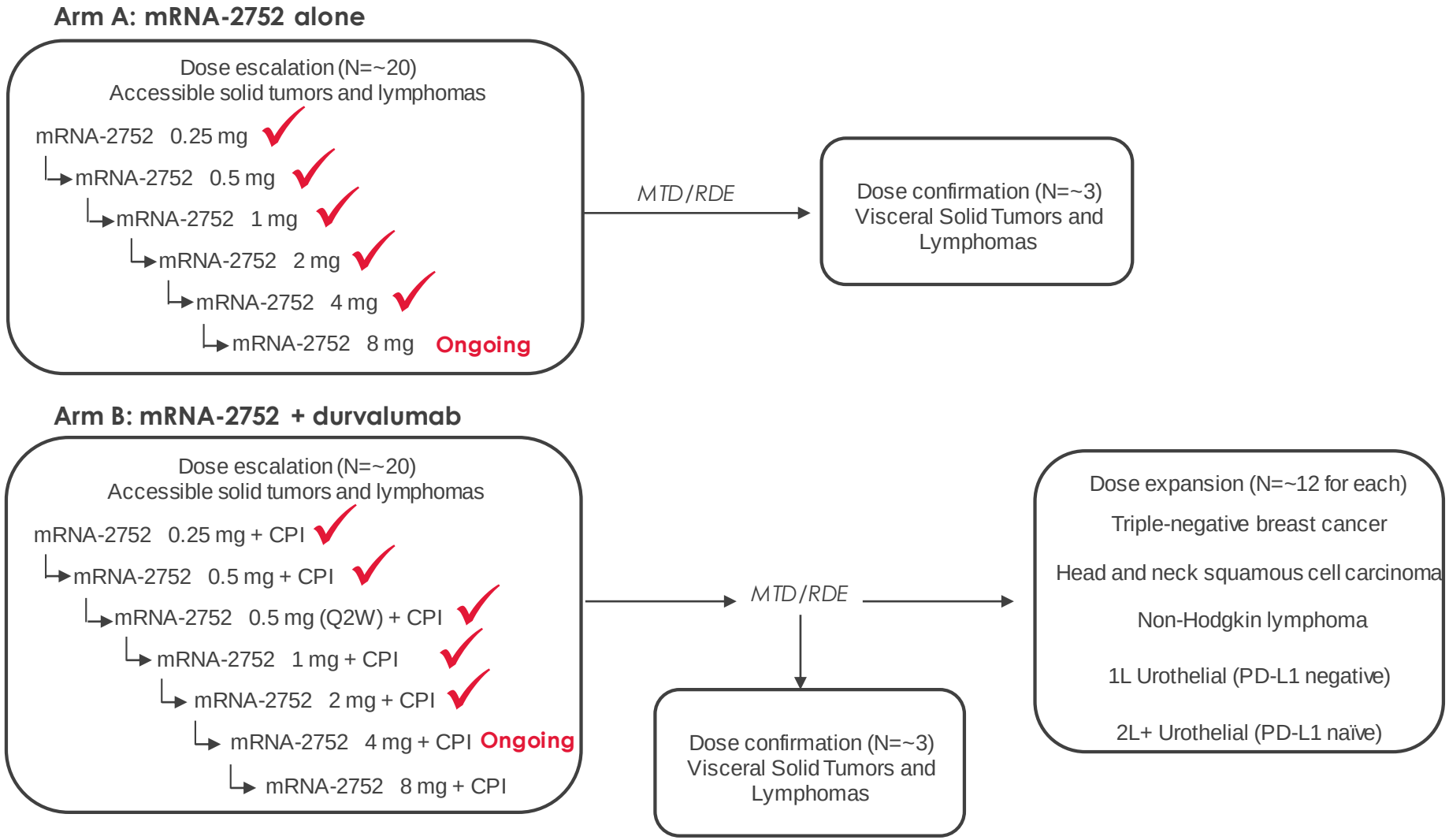
Phase 1 ongoing; patients dosed in combination with durvalumab

Key Objectives

- Evaluate safety and tolerability of mRNA-2752 administered alone and in combination with PD-L1 inhibitor
- Define maximum tolerated dose (MTD) and recommended dose for expansion for mRNA-2752 alone and in combination with durvalumab
- Intended to assess: (1) Anti-tumor activity, (2) Protein expression in tumors and (3) Pharmacokinetics

Dosing

- mRNA-2752 Q2W for Cycle 1 and Q4W for Cycles 2-6 and durvalumab 1500 mg Q4W



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OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752)

Data presented at ASCO 2020

- At ASCO 2020, we present findings from a first-in-human study of iTu mRNA-2752 in solid tumor patients as monotherapy or in combination with durvalumab. As of April 8, 2020, 29 patients were evaluable for safety and 23 patients evaluable for efficacy.

Related Adverse Events*				
	Arm A		Arm B	
	Grade 1-2	Grade 3	Grade 1-2	Grade 3
Injection site erythema	6	-	3	-
Injection site pain	6	-	2	-
Pyrexia	5	1**		
Chills	3	1**		
Fatigue	3	1**		
Alanine aminotransferase increased	2	-		
Aspartate aminotransferase increased	2	-		
Back pain	2	-		
Rash maculo-popular	2	-		
Injection site reaction	-	1**		
Malaise	-	1**		

Responses in evaluable patients per RECIST 1.1		
Best Overall Response	Arm A (n=15)	Arm B (N=8)
Partial Response	-	1
Stable Disease (SD)	5	4
Progressive Disease (PD)	10	3

*Treatment-related AEs reported once per patient. **All Gr 3 events observed in 1 patient @ 4mg dose
AEs: ≥ 2 patients (grade 1-2), ≥ 1 patient (grade 3), No Gr 4 or 5 AEs were reported

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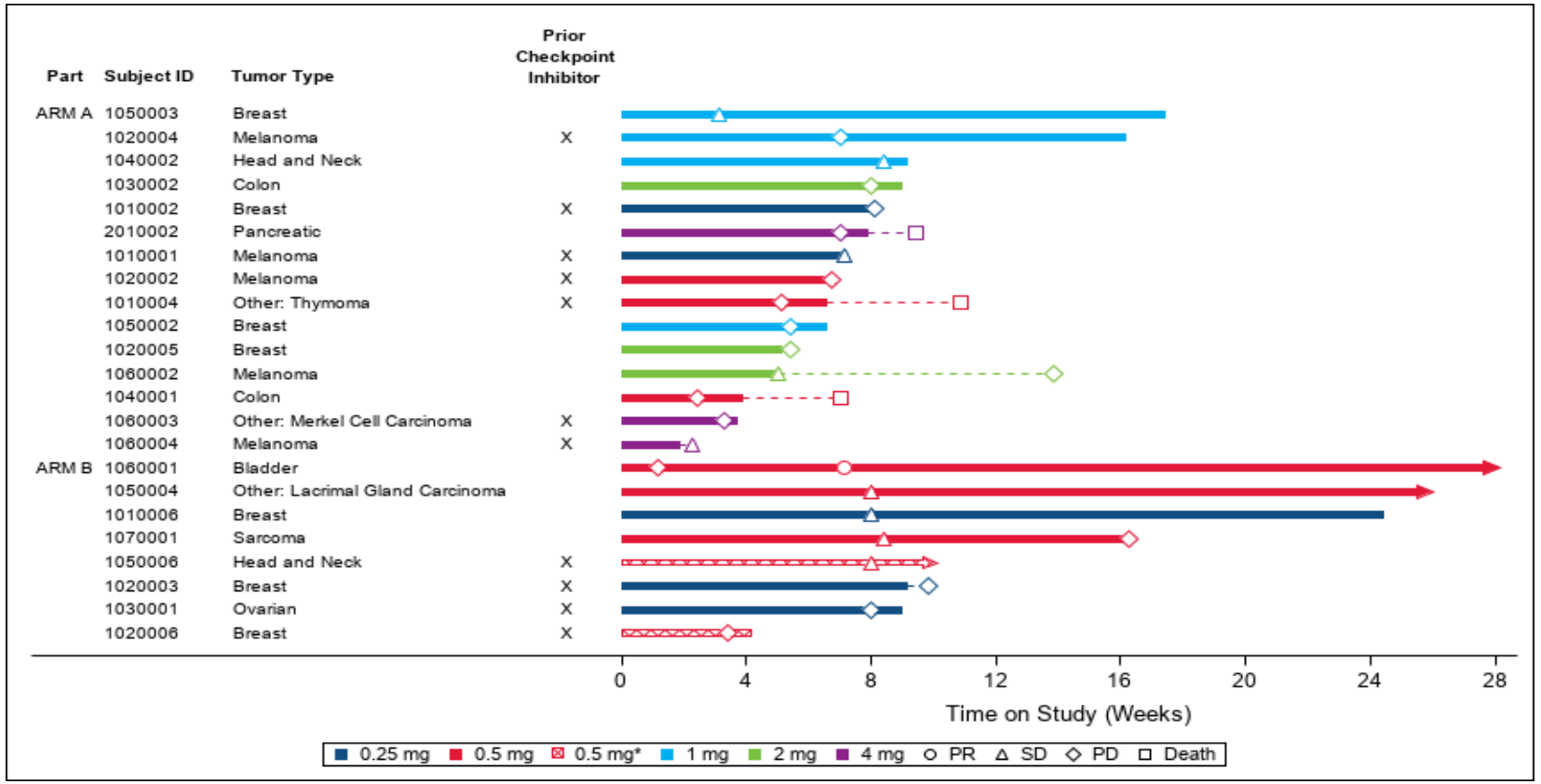
OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752)

Data presented at ASCO 2020

mRNA-2752-P101 swimmer plot: per RECIST 1.1



17 patients on Arm A with duration on study up to 16 weeks. 12 patients on Arm B up to 28 weeks on study and continuing at time of data cutoff.

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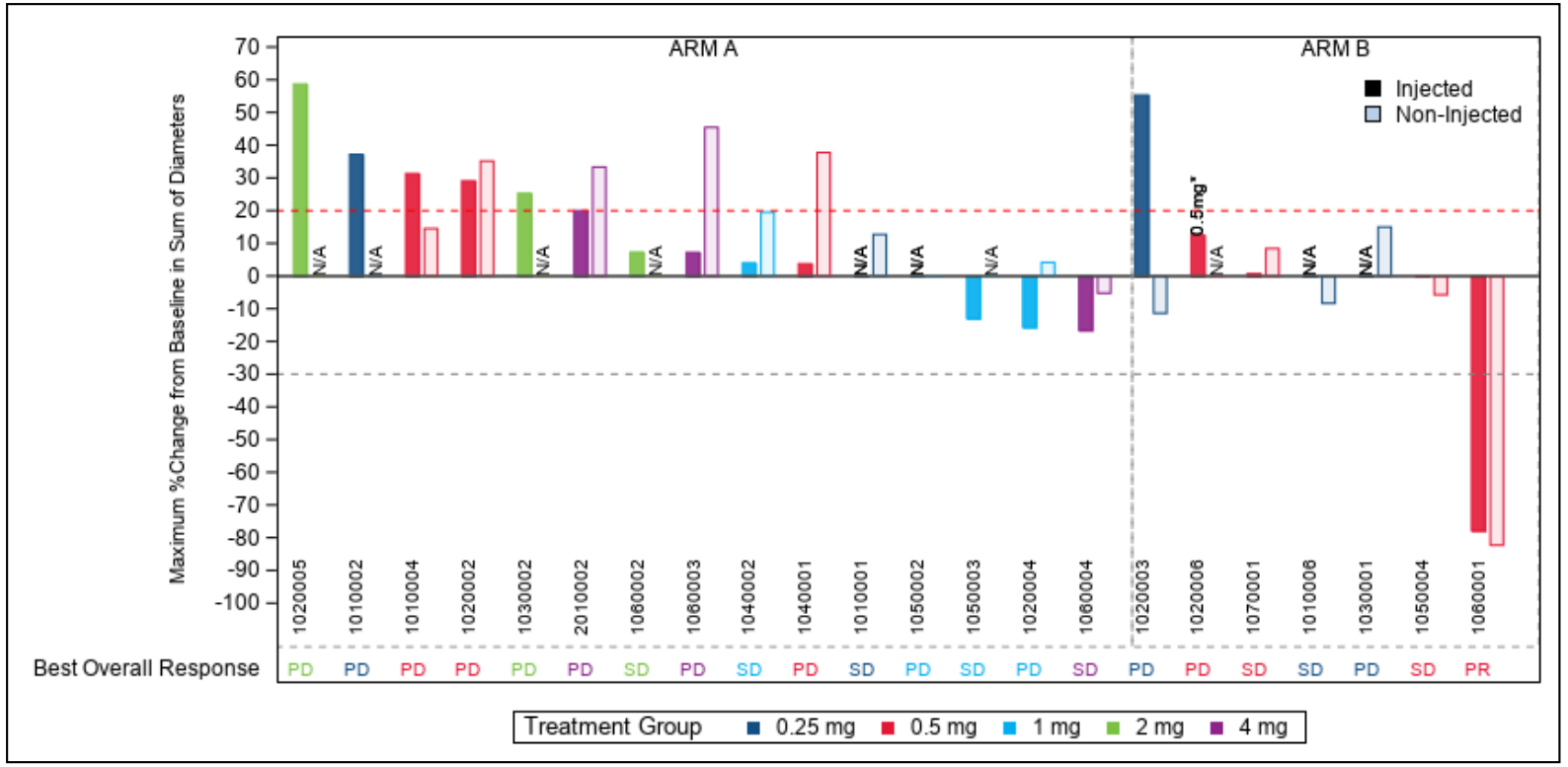
OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752)

Data presented at ASCO 2020

mRNA-2752-P101 Waterfall Plot of Maximum %Change from Baseline in Sum of Diameters of Target Lesions Based on Investigator Assessment per RECIST 1.1



Tumor shrinkage in both injected and un-injected target lesions in both monotherapy and in combination

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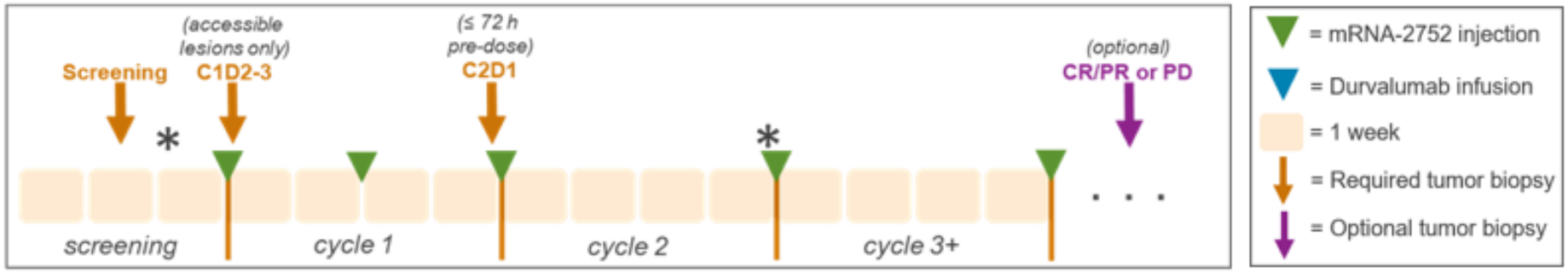
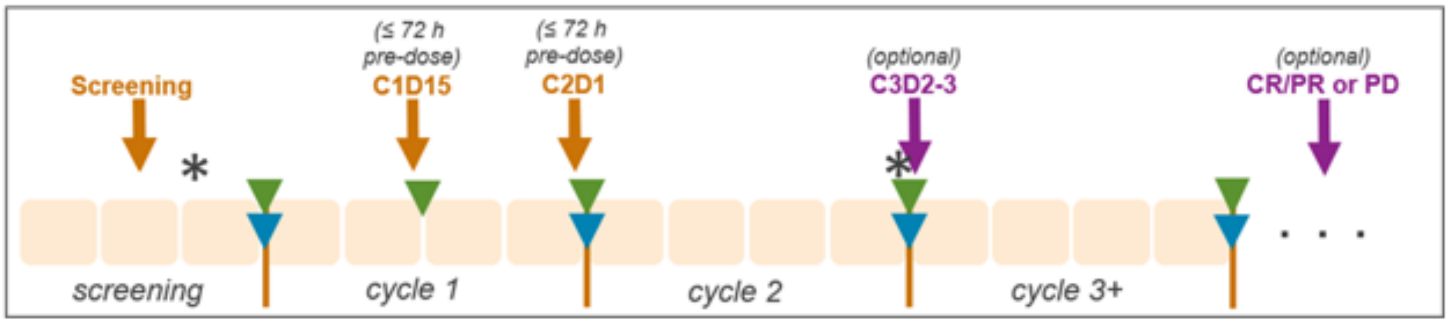
Phase 1 dosing & biopsy collection schedule from arms A and B (mRNA-2752 +/- durvalumab)

Dose Escalation/Confirmation

Arm A: mRNA-2752 monotherapy



Arm B: mRNA-2752 + Durvalumab Combo



- Collection of newly obtained tumor samples during screening and at 1 other time point

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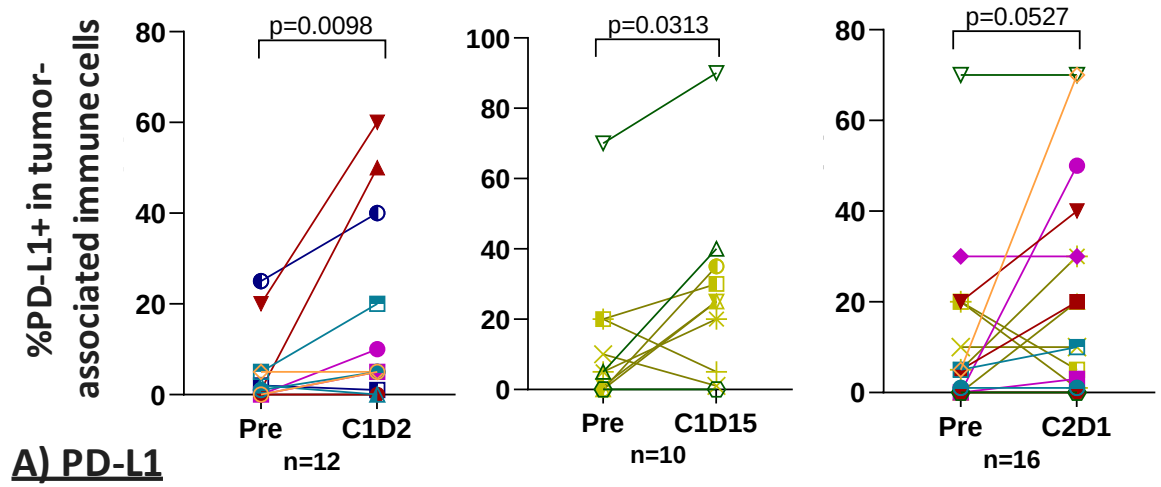
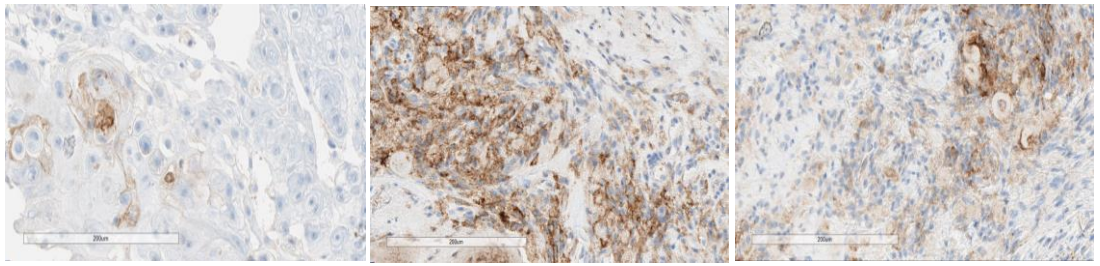
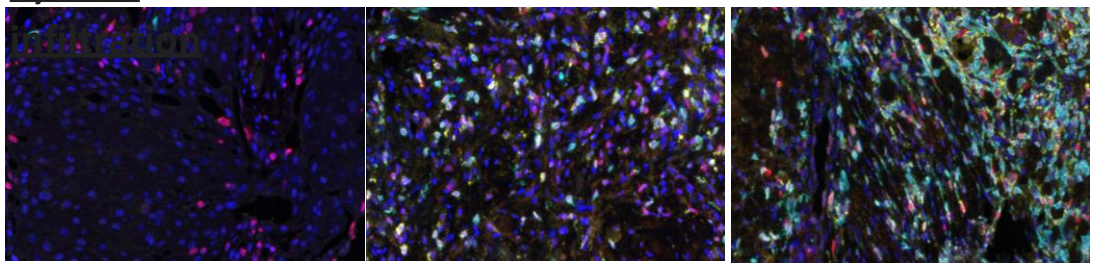
PD-L1 expression is increased after mRNA-2752 treatment





B)T-cell



Pre-treatment C1D15 C2D1

- **%PD-L1+ in tumor-associated immune cells is shown at baseline *versus* C1D2 (Arm A monotherapy) , C1D15 (Arm B combination), and C2D1 (Arms A and B)**
- **Elevated PD-L1 and T cell populations post-treatment in patient with PR.** Representative pre- and post- treatment biopsies from squamous-cell bladder cancer patient with partial response by RECIST 1.1.

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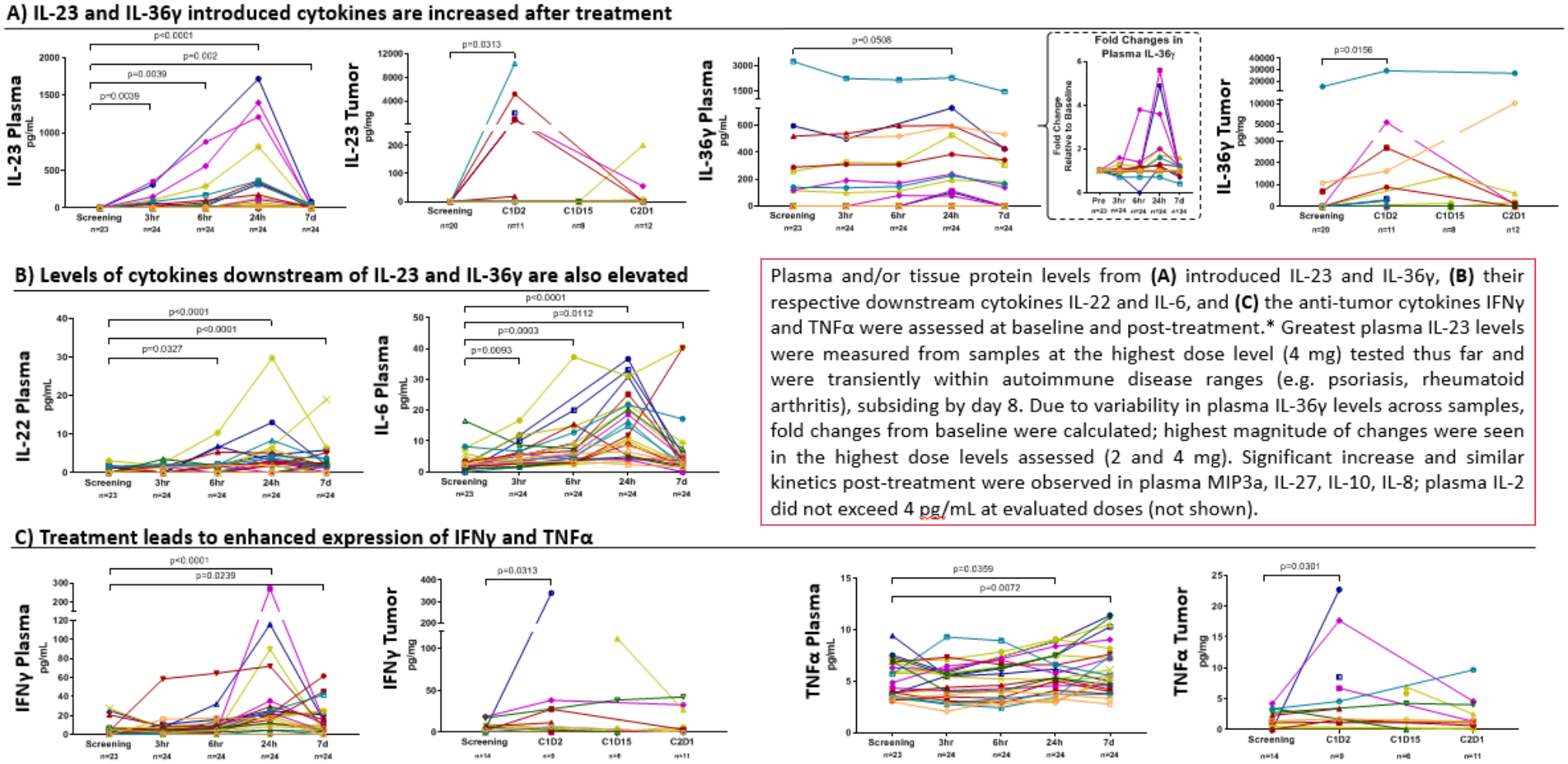
Elevated IL-23, IL-36γ, IFN-γ and TNF-α after treatment with mRNA-2572 +/- durvalumab



Plasma and/or tissue protein levels from **(A)** introduced IL-23 and IL-36γ, **(B)** their respective downstream cytokines IL-22 and IL-6, and **(C)** the anti-tumor cytokines IFNγ and TNFα were assessed at baseline and post-treatment.* Greatest plasma IL-23 levels were measured from samples at the highest dose level (4 mg) tested thus far and were transiently within autoimmune disease ranges (e.g. psoriasis, rheumatoid arthritis), subsiding by day 8. Due to variability in plasma IL-36γ levels across samples, fold changes from baseline were calculated; highest magnitude of changes were seen in the highest dose levels assessed (2 and 4 mg). Significant increase and similar kinetics post-treatment were observed in plasma MIP3a, IL-27, IL-10, IL-8; plasma IL-2 did not exceed 4 pg/mL at evaluated doses (not shown).

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OX40L/IL-23/IL-36γ (Triplet) (mRNA-2752)

Conclusions from ASCO 2020 presentation

- iTu mRNA-2752 given as monotherapy and in combination with durvalumab is tolerable at all dose levels studied with no DLTs reported and the majority of related AE's being grade 1 or 2
- Administration of iTu mRNA-2752 is associated with tumor shrinkage in both injected and non-injected lesions in both monotherapy and in combination, with 1 PR in a PD-L1 low squamous-cell bladder patient
- Increased IL-23 and IL-36γ protein expression after 6-24 hours in tumor and/or plasma
- Analyses of tumor and plasma biomarkers suggest a sustained immunomodulatory effect of treatment that includes elevated PD-L1, IFN-γ, TNF-α and levels
- Plasma IFN-γ and TNF-α levels were well below what has been suggested as clinically toxic levels
- These data support the ongoing testing of the mRNA-2752/durvalumab combination in Arm B of the Phase I study

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Agenda

Introduction	*Stéphane Bancel, CEO*	*8:00-8:15 AM*
Systemic Secreted and Cell Surface Therapeutics • **Chikungunya Antibody**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer*	*8:15-8:30 AM*
Intracellular Therapeutics • **PA** • **MMA**	*Stephen Hoge, M.D., President*	*8:30-8:45 AM*
Intratumoral Immuno-Oncology • **Overview of Intratumoral Approach** • **OX40L Phase 1** • **Triplet Phase 1**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer* *Antonio Jimeno, M.D., Ph.D., University of Colorado School of Medicine*	*8:45-9:30 AM*
Coffee Break		*9:30-9:40 AM*
Prophylactic Vaccines • **CMV Vaccine** • **RSV, hMPV/PIV3 Vaccine** • **Regulatory Guidance and Development of Pediatric Vaccines** • **COVID-19 Vaccine**	*Tal Zaks, M.D., Ph.D., Chief Medical Officer* *Lori Panther, M.D., MPH, Senior Director of Clinical Development, Infectious Diseases* *Allison August, M.D., Senior Director of Clinical Development, Infectious Diseases* *Terry Nolan, M.D., Ph.D., The University of Melbourne* *Jacqueline Miller, M.D., FAAP, SVP, Infectious Disease Development* *Juan Andres, Chief Technical Operations and Quality Officer*	*9:40-11:00 AM*
New Research & Development	*Stephen Hoge, M.D., President*	*11:00-11:10 AM*
Conclusion	*Stéphane Bancel, CEO*	*11:10-11:20 AM*
Q&A		*11:20-12:00 PM*

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Lori Panther, M.D., M.P.H
Senior Director of Clinical Development, Infectious Diseases

CMV Vaccine (mRNA-1647)

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Cytomegalovirus (CMV) vaccine (mRNA-1647)

Modality	ID #	Program	Preclinical development / Phase 1 / Phase 2 / Phase 3 and commercial	Moderna rights
Prophylactic vaccines	mRNA-1273	COVID-19 vaccine		Worldwide *BARDA funded*
	mRNA-1647	Cytomegalovirus (CMV) vaccine		Worldwide
	mRNA-1653	hMPV/PIV3 vaccine	Phase 1 (healthy volunteers) → Phase 1b (Age de-escalation) Seropositives	Worldwide
	mRNA-1172/ Merck V172	Respiratory syncytial virus (RSV) vaccine		Merck to pay milestones and royalties
	mRNA-1777	Respiratory syncytial virus (RSV) vaccine		
	mRNA-1893	Zika vaccine		Worldwide *BARDA funded*
	mRNA-1345	Pediatric respiratory syncytial virus (RSV) vaccine *Future respiratory combo*		Worldwide
	mRNA-1189	Epstein-Barr virus (EBV) vaccine		Worldwide
	mRNA-1851	Influenza H7N9 vaccine		Worldwide *Advancing subject to funding*

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Congenital cytomegalovirus overview

- Cytomegalovirus: **CMV is a common infection and is the leading cause of birth defects in the US**
  - 0.65% of US newborns infected annually (~25,000 US newborns)[1]

- **Disease burden**: Significant impact on survivors, families, caregivers and health systems[2]
  - An estimated 10% - 15% of newborns with congenital CMV infection are severely ill at birth
  - Approximately 4% - 12% of children with symptomatic CMV will die in their first year of life, and 70% - 80% will survive to suffer lifelong disabilities

- **Unmet need**: No approved CMV vaccine

CMV infection sequelae[3,4]	
Neonatal period	Jaundice Microcephaly Hearing loss Vision loss Seizures Low birth weight
Infancy, childhood, adulthood	Deafness/Hearing loss Neurodevelopmental delay Seizures

1. Dollard et al, New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection, Rev Med Virol, 2007
2. Boppana et al. Symptomatic congenital cytomegalovirus infection: Neonatal morbidity and mortality, Pediatric Infectious Disease Journal, 1992
3. Manicklal et al, The silent global burden of congenital cytomegalovirus, Clinical Microbiology Reviews, 2013
4. Lopez et al, The impact of cytomegalovirus reactivation and its treatment on the course of inflammatory bowel disease, AP&T, 2014

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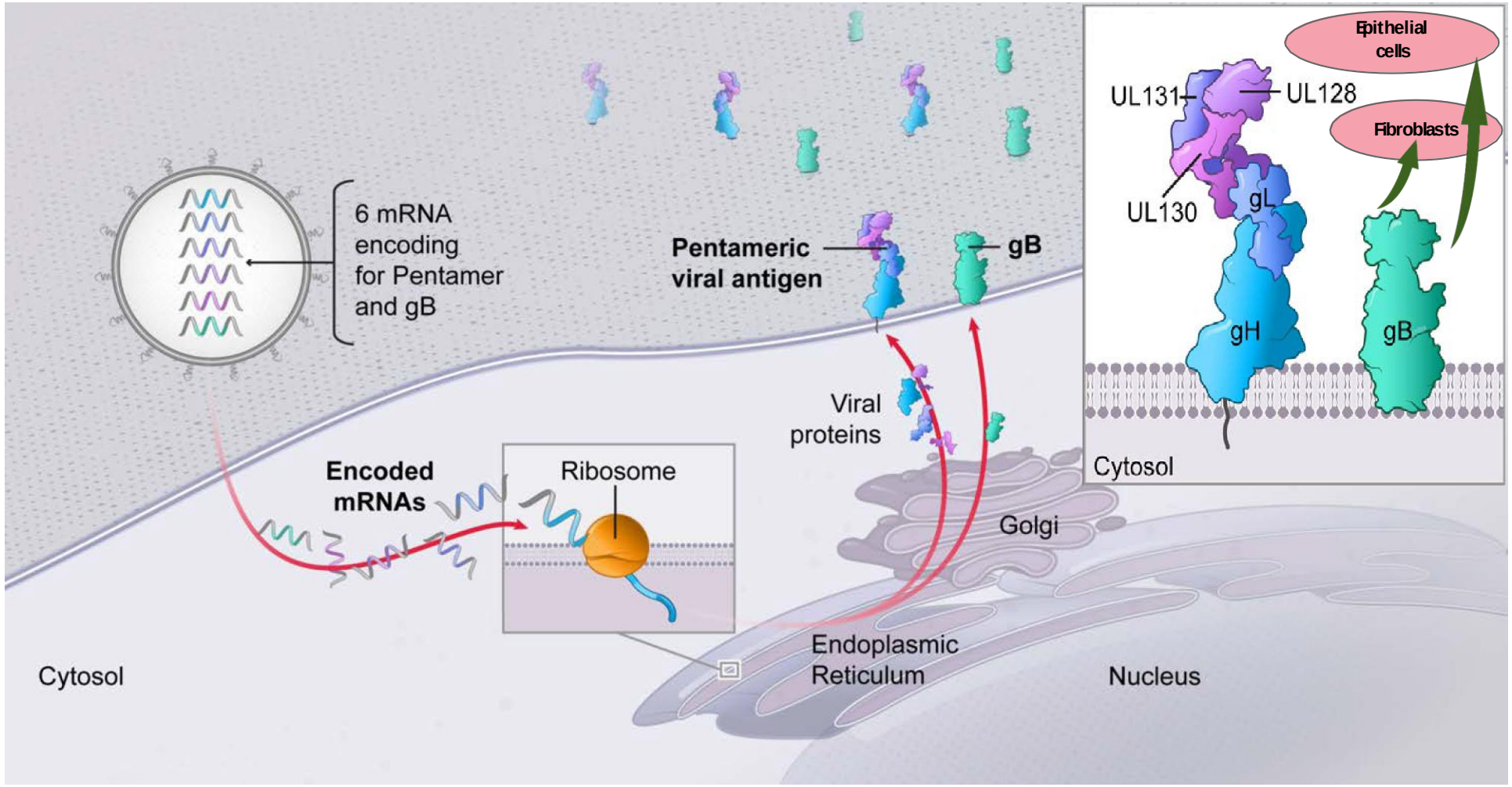
CMV vaccine (mRNA-1647) includes 6 mRNAs

5 encode the pentamer, 6th encodes gB antigen



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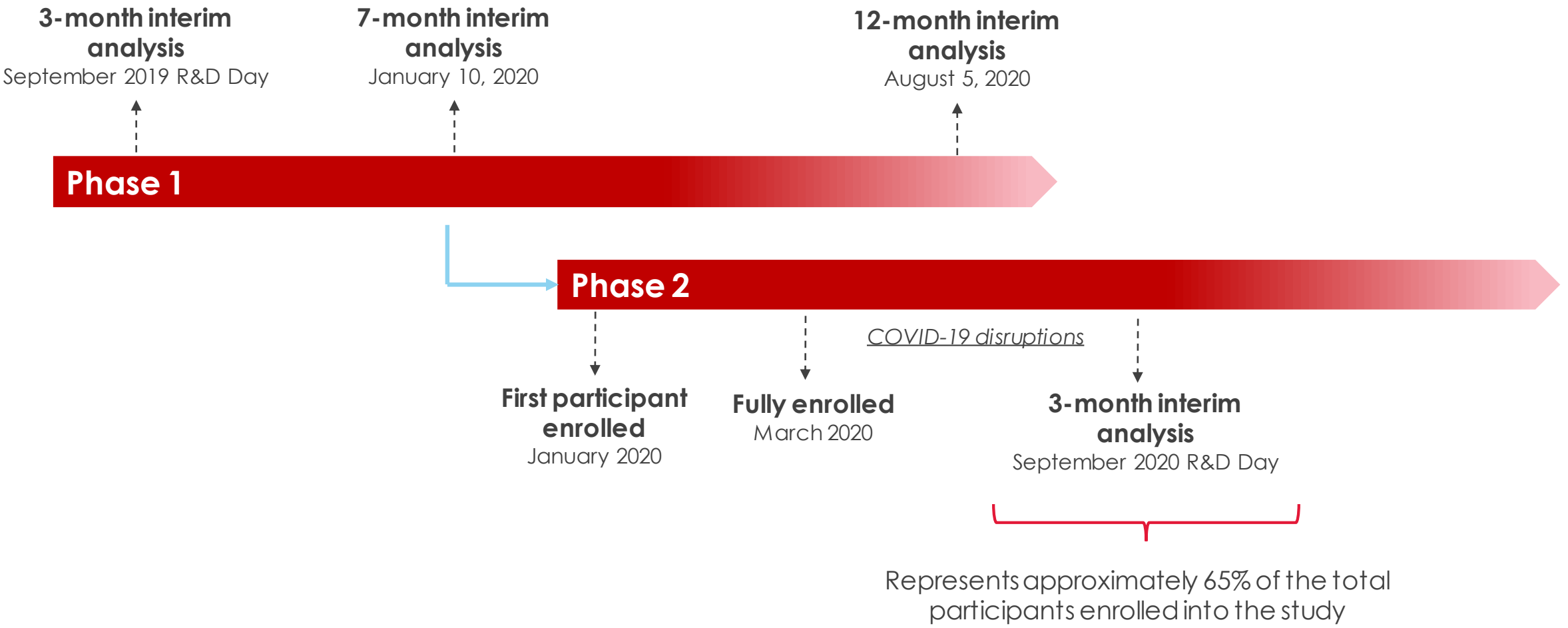
CMV vaccine (mRNA-1647) clinical development



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Key changes to mRNA-1647 in Phase 2 clinical trial

- **Improved potency**
  - Improved ratio of mRNA components to increase potency
- **Improved tolerability**
  - Optimized the manufacturing process to improve tolerability
- **Lyophilization**
  - Phase 2 utilizes the intended Phase 3 and commercial formulation

Liquid, Single-Dose Vial,
-20°C storage ≥6 months shelf-life

Lyophilized, Single-Dose (0.5mL),
5°C storage ≥ 18months shelf-life

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CMV vaccine (mRNA-1647) Phase 1 12-month interim analysis

- **Safety:** The vaccine was generally well-tolerated and there were no vaccine-related serious adverse events (SAEs). Safety and tolerability at the 300µg dose level was comparable to that observed at the 180µg dose level

- **In the CMV-seronegative 30, 90, and 180 µg groups at Month 12 (6 months after the 3rd vaccination), neutralizing antibody titers:**
  - Against epithelial cell infection (a measure of immune response to intact CMV pentamer antigen) were 3.6-fold and 3.9-fold higher than the natural infection benchmark in the 90µg and 180µg treatment groups
  - Against fibroblast infection (a measure of immune response to CMV gB antigen) approximated the natural infection benchmark in the 90µg and 180µg treatment groups

- **In the CMV-seropositive 30, 90, and 180 µg groups, neutralizing antibody titers:**
  - Continued to show boosting response with geometric mean ratios (GMRs) of neutralizing antibodies against epithelial cell infection ranged 14-fold to 31-fold across the 30µg, 90µg and 180µg treatment groups
  - GMRs of neutralizing antibodies against fibroblast infection ranged 6-fold to 8-fold

- **Early evidence of immune persistence out to 12 months (6 months after the 3rd vaccination)**

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CMV vaccine (mRNA-1647) Phase 2 trial overview

Key objective

- To assess the safety and immunogenicity of the Phase 3 and commercial mRNA-1647 in a narrow range of doses

Primary endpoints

- Defined safety parameters
- Neutralizing antibodies against CMV infection of epithelial cells and fibroblasts

Secondary endpoint

- GMT of anti-gB specific IgG and anti-Pentamer specific IgG as measured by ELISA

Trial progress

- First participant dosed on January 9, 2020
- Trial fully enrolled (i.e. all participants completed 1st vaccination) March 3, 2020
- **COVID-19 presented a unique challenge due to the disruption of clinical site activities and ability for participants to safely receive the 2nd vaccination**
- The mRNA-1647 protocol was amended to broaden the visit window for the 2nd vaccination to safeguard study participants and study site personnel

CMV-seronegative Group
n = 180
Participants enrolled in a 3:1 ratio of mRNA-1647:placebo

50 µg mRNA-1647 or placebo (n = 60)
→ 100 µg mRNA-1647 or placebo (n = 60)
→ 150 µg mRNA-1647 or placebo (n = 60)

CMV-seropositive Group
n = 72
Participants enrolled in a 3:1 ratio of mRNA-1647:placebo

50 µg mRNA-1647 or placebo (n = 24)
→ 100 µg mRNA-1647 or placebo (n = 24)
→ 150 µg mRNA-1647 or placebo (n = 24)

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CMV vaccine (mRNA-1647) Phase 2 interim analysis

Solicited adverse reactions (ARs) post 1st vaccination, solicited safety set

		CMV Serostatus at Baseline							
		CMV-seronegative				CMV-seropositive			
		Placebo N=30	50 µg N=31	100 µg N=24	150 µg N=32	Placebo N=12	50 µg N=15	100 µg N=10	150 µg N=11
Local ARs	**Pain**	4/30 (13) -	26/31 (84) -	23/24 (96) 2 (8)	29/32 (91) 2 (6)	3/12 (25) -	12/15 (80) 2 (13)	8/10 (80) -	7/11 (64) -
	Redness	-	1/31 (3) -	-	3/32 (9) -	-	-	-	1/11 (9) -
	Swelling	-	1/31 (3) -	-	2/32 (6) -	-	-	-	1/11 (9) -
	Axillary swelling/tenderness (same side as vaccination)	-	1/31 (3) -	8/24 (33) -	4/32 (13) -	2/12 (17) -	1/15 (7) -	-	3/11 (27) -
Most common systemic ARs	**Fever**	-	-	-	1/32 (3) -	-	-	-	3/11 (27) 1 (9)
	Headache	10/30 (33) 2 (7)	7/31 (23) -	10/24 (42) -	10/32 (31) -	4/12 (33) -	7/15 (47) -	4/10 (40) -	6/11 (55) -
	Fatigue	9/30 (30) 1 (3)	9/31 (29) -	8/24 (33) -	14/32 (44) -	3/12 (25) -	11/15 (73) 2 (13)	4/10 (40) -	4/11 (36) -
	Myalgia	4/30 (13) 2 (7)	2/31 (7) -	6/24 (25) -	11/32 (34) -	1/12 (8) -	8/15 (53) 3 (20)	5/10 (50) -	6/11 (55) -
	Arthralgia	2/30 (7) 2 (7)	-	3/24 (13) -	5/32 (16) -	1/12 (8) -	7/15 (47) -	4/10 (40) -	2/11 (18) -
	Nausea	3/30 (10) 2 (7)	2/31 (7) -	1/24 (4) -	2/32 (6) -	-	4/15 (27) -	1/10 (10) -	1/11 (9) -
	Chills	3/30 (10) 1 (3)	3/31 (10) -	4/24 (17) -	5/32 (16) -	-	6/15 (40) -	2/10 (20) -	4/11 (36) -
	Rash	2/30 (7)	2/31 (7)	3/24 (13)	1/32 (3)	3/12 (25)	2/15 (13)	-	1/11 (9)

Values represent n/N1 (%) participants reporting each AR, N1 = number of subjects reporting the symptom, red text=grade 3 ARs

- Injection site pain was the most commonly reported solicited local AR
- The most common solicited systemic ARs were headache, fatigue, and myalgia in both CMV-seronegative and CMV-seropositive mRNA-1647 treatment groups.
- No serious adverse events (SAEs) were reported
- No unsolicited events leading to study discontinuation

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CMV vaccine (mRNA-1647) Phase 2 interim analysis

Solicited adverse reactions (ARs) post 2nd vaccination, solicited safety set

		CMV Serostatus at Baseline							
		CMV-seronegative				CMV-seropositive			
		Placebo N=30	50 µg N=31	100 µg N=24	150 µg N=32	Placebo N=12	50 µg N=15	100 µg N=10	150 µg N=11
Local ARs	**Pain**	5/30 (17) -	28/31 (90) 2 (7)	23/24 (96) -	30/32 (94) -	-	13/15 (87) 1 (7)	7/10 (70) -	8/11 (73) 1 (9)
	Redness	-	-	2/24 (8) -	5/32 (16) 1 (3)	-	-	-	2/11 (18) 1 (9)
	Swelling	-	-	1/24 (4) -	5/32 (16) 2 (6)	-	2/15 (13) -	-	1/11 (9) -
	Axillary swelling/tenderness (same side as vaccination)	1/30 (3) -	4/31 (13) -	7/24 (29) -	6/32 (19) -	-	3/15 (20) -	2/10 (20) -	2/11 (18) -
Most common systemic ARs	**Fever**	-	1 (3) -	-	3/32 (9) 1 (3)	-	-	-	2/11 (18) 1 (9)
	Headache	11/30 (37) -	14/31 (45) 2 (7)	13/24 (54) 3 (13)	17/32 (53) -	6/12 (50) 2 (17)	9/15 (60) -	5/10 (50) -	4/11 (36) 1 (9)
	Fatigue	7/30 (23) -	14/31 (45) 1 (3)	9/24 (38) 1 (4)	17/32 (53) 2 (6)	2/12 (17) -	11/15 (73) 1 (7)	3/10 (30) -	7/11 (63) 1 (9)
	Myalgia	1/30 (3) -	16/31 (52) 2 (7)	12/24 (50) 2 (8)	15/32 (47) 3 (9)	1/12 (8) -	11/15 (73) 1 (7)	6/10 (60) -	6/11 (55) 1 (9)
	Arthralgia	2/30 (7) -	12/31 (39) 1 (3)	10/24 (42) 1 (4)	11/32 (34) -	1/12 (8) -	6/15 (40) 1 (7)	5/10 (50) -	4/11 (36) -
	Nausea	-	6/31 (19) -	3/24 (13) -	7/32 (22) -	1/12 (8) -	4/15 (27) -	2/10 (20) -	2/11 (18) -
	Chills	1/30 (3) -	8/31 (26) 1 (3)	9/24 (38) 1 (4)	16/32 (50) -	-	6/15 (40) -	3/10 (30) -	6/11 (55) 1 (9)
	Rash	-	-	2/24 (8)	6/32 (19)	1/12 (8)	1/15 (7)	1/10 (10)	-

- After the 2nd vaccination, the rate and severity distribution of solicited ARs in the CMV-seronegative and CMV-seropositive mRNA-1647 treatment groups were generally similar

Values represent n/N1 (%) participants reporting each AR, N1 = number of subjects reporting the symptom, red text=grade 3 ARs

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CMV vaccine (mRNA-1647) Phase 2 interim analysis

Immunogenicity in CMV-seronegative participants, per-protocol set

Neutralizing Antibodies Against Epithelial Cell Infection Phase 2 CMV-seropositive cohort GMT benchmark = 3,924				
	Placebo	**50 µg**	**100 µg**	**150 µg**
GMT baseline	8	8	8	8
GMT Month 1 (post 1st vaccination)	9.7	955	2,100	3,109
GMT Month 2	8	1,115	1,076	1,773
GMT Month 3 (post 2nd vaccination)	8	57,028	49,302	49,706
GMT/benchmark Month 3	--	14.5	12.6	12.7

Neutralizing Antibodies Against Fibroblast Infection Phase 2 CMV-seropositive cohort GMT benchmark = 3,955				
	Placebo	**50 µg**	**100 µg**	**150 µg**
GMT baseline	8	8	8	8
GMT Month 1 (post 1st vaccination)	8	73	175	136
GMT Month 2	8	37	71	83
GMT Month 3 (post 2nd vaccination)	8	3,856	3,242	4,638
GMT/benchmark Month 3	--	1.0	0.8	1.2

GMT = geometric mean titer; CMV-seropositive benchmark values derived from baseline values of all CMV seropositive participants

Subject n at each timepoint, epithelial cell and fibroblast infection

	Placebo	50 µg	100 µg	150 µg
Baseline	29	30	23	32
Month 1	28	30	23	30
Month 2	29	29	22	32
Month 3	29	30	22	32

- Neutralizing antibody titers against epithelial cell infection were boosted to at least 12-fold over the baseline GMT of CMV-seropositive participants
  - The 3 month neutralizing antibody titers GMTs in the 50, 100, and 150 µg treatment groups were generally numerically similar
- Neutralizing antibody titers against fibroblast infection were generally equivalent to the baseline GMT in CMV-seropositive participants
  - The 3 month neutralizing antibody titers GMTs in the 50, 100, and 150 µg treatment groups were generally numerically similar

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CMV vaccine (mRNA-1647) Phase 2 interim analysis

Immunogenicity in CMV-seropositive participants, per-protocol set

Neutralizing Antibodies Against Epithelial Cell Infection Phase 2 CMV-seropositive cohort GMT benchmark = 3,924				
	Placebo	**50 µg**	**100 µg**	**150 µg**
GMT baseline	2,938	2,250	5,935	7,480
GMT Month 1 (post 1st vaccination)	9,157	27,062	52,989	116,899
GMT Month 2	7,677	30,228	51,008	88,939
GMT Month 3 (post 2nd vaccination)	7,245	102,850	81,111	126,075
GMR Month 3	1.8	26.2	20.7	32.1

Neutralizing Antibodies Against Fibroblast Infection Phase 2 CMV-seropositive cohort GMT benchmark = 3,955				
	Placebo	**50 µg**	**100 µg**	**150 µg**
GMT baseline	2,545	2,507	6,377	7,117
GMT Month 1 (post 1st vaccination)	6,452	5,686	14,251	21,341
GMT Month 2	5,710	5,449	14,735	11,983
GMT Month 3 (post 2nd vaccination)	8,138	9,970	11,652	13,208
GMR Month 3	2.1	2.5	2.9	3.3

GMT = geometric mean titer; GMR = geometric mean ratio (post-baseline/baseline titers); CMV-seropositive benchmark values derived from baseline values of all CMV seropositive participants

- Neutralizing antibody titers in the epithelial cell infection were boosted to GMTs at least 20-fold to greater than 32-fold over the respective baseline GMT after the 2nd vaccination
- Neutralizing antibody titers against fibroblast infection boosted to levels at least 2-fold over the respective baseline GMT

Subject n at each timepoint, epithelial cell and fibroblast infection

	Placebo	50 µg	100 µg	150 µg
Baseline	10	15	10	11
Month 1	9	15	10	11
Month 2	10	15	9	11
Month 3	10	14	10	11

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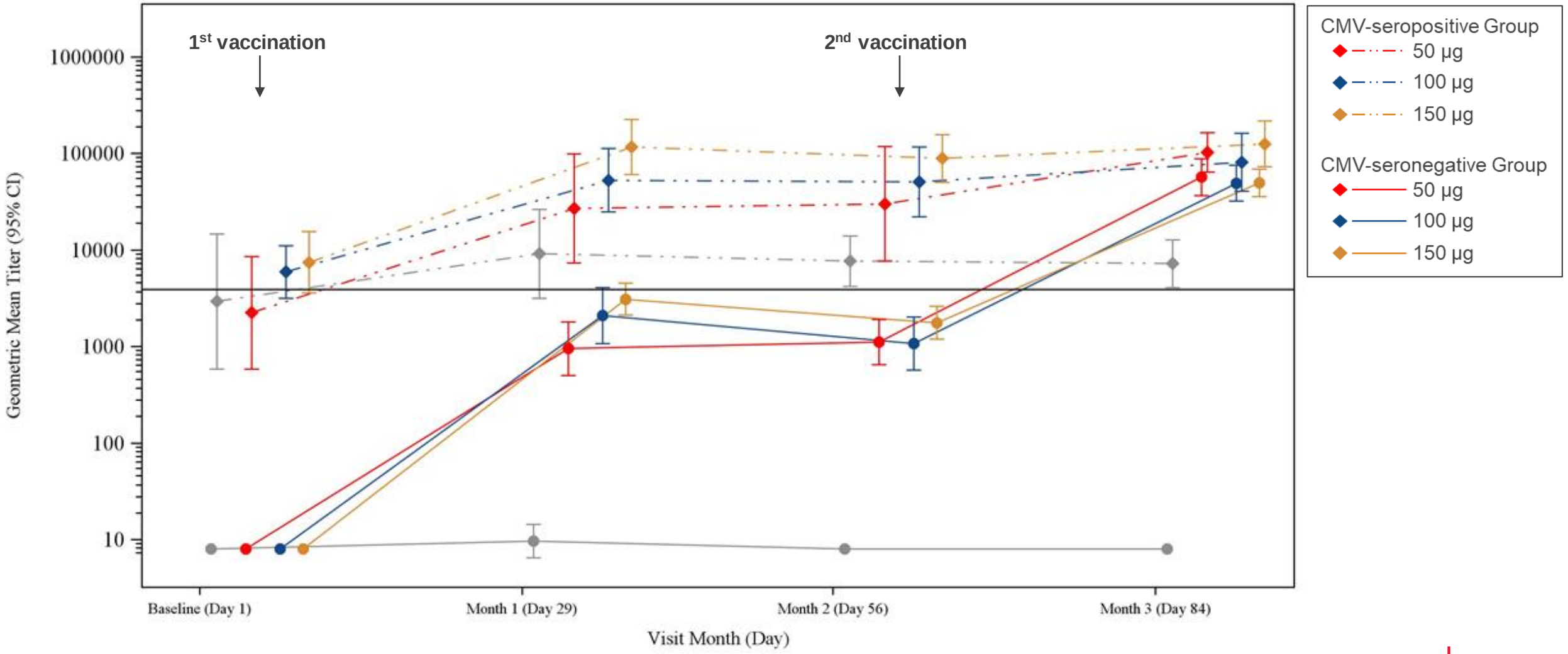
Neutralizing antibodies against epithelial cell infection through month 3

CMV serostatus and vaccination group, per-protocol set



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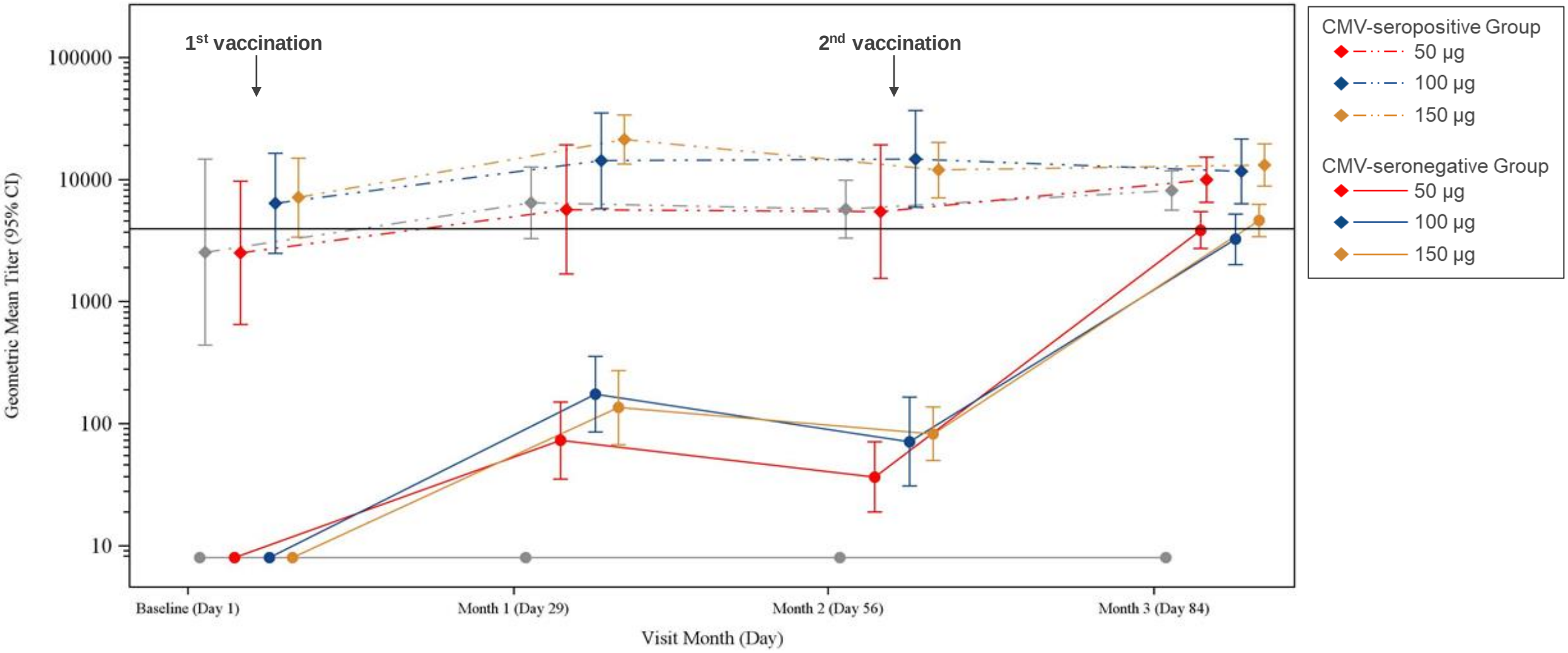
Neutralizing antibodies against fibroblast infection through month 3

CMV serostatus and vaccination group, per-protocol set



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Late stage development for CMV vaccine (mRNA-1647)

Phase 2 study

- Utilizes intended Phase 3 formulation; same lipid nanoparticle (LNP) used in Phase 1
- 3-month interim analysis informed dose level choice for further development
- Intend to file a protocol amendment to enroll more participants at the 100 µg dose level

Planned pivotal Phase 3 trial

- **Based on the Phase 2 interim analysis, the Phase 3 pivotal trial will test the 100 µg dose level**
- **Primary endpoint**: prevention of primary CMV infection in seronegative women aged 16-40 years
- Intended to begin in 2021 in North America and Europe
- Expect enrollment of <8,000 participants
- Joint National Scientific Advice (Belgium, Germany) meeting in 1Q20; received constructive feedback
- Preparation and product manufacturing underway
- Phase 3 trial additional details to be announced at later date

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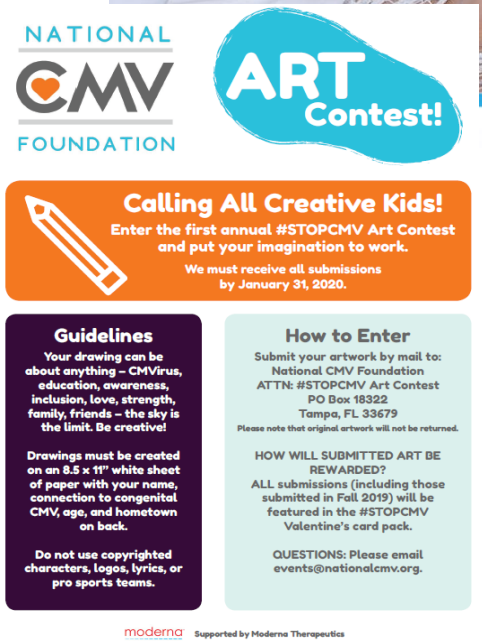
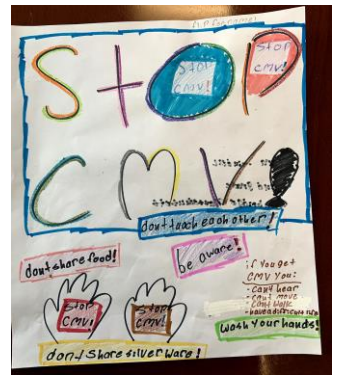
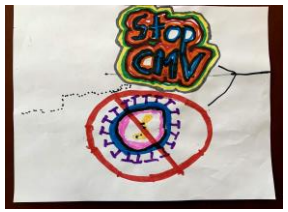
CMV awareness activities 2020

- In January 2020 – #STOPCMV Kids Art Contest
- In February 2020 – Sponsored 3 to run NYC Half Marathon
- In June 2020 – Sponsored CMV Podcast Series with National CMV foundation
- In honor of National CMV Awareness Month supported a series of CMV Voices to raise awareness of CMV







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Allison August, M.D.
Senior Director of Clinical Development, Infectious Diseases

RSV (mRNA-1345) and hMPV/PIV3 (mRNA-1653) Vaccines

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Pediatric respiratory vaccines

Modality	ID #	Program	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
Prophylactic vaccines	mRNA-1273	COVID-19 vaccine					Worldwide *BARDA funded*
	mRNA-1647	Cytomegalovirus (CMV) vaccine					Worldwide
	mRNA-1653	hMPV/PIV3 vaccine	Phase 1 (healthy volunteers)	Phase 1b (Age de-escalation) Seropositives			Worldwide
	mRNA-1172/ Merck V172	Respiratory syncytial virus (RSV) vaccine					Merck to pay milestones and royalties
	mRNA-1777	Respiratory syncytial virus (RSV) vaccine					
	mRNA-1893	Zika vaccine					Worldwide *BARDA funded*
	mRNA-1345	Pediatric respiratory syncytial virus (RSV) vaccine *Future respiratory combo*					Worldwide
	mRNA-1189	Epstein-Barr virus (EBV) vaccine					Worldwide
	mRNA-1851	Influenza H7N9 vaccine					Worldwide *Advancing subject to funding*

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Pediatric respiratory syncytial virus (RSV) overview

- RSV is the leading cause of unaddressed severe lower respiratory tract disease and hospitalization in infants and young children worldwide
- **Disease burden**: Major cause of hospitalization due to respiratory infection
  - Hospitalization rate in children <5 years old in the U.S.: ~3:1000[1]
  - Annually over 2 million medically attended RSV infections in children <5 years old in the U.S., more than 86,000 are hospitalized
  - Globally it is estimated over ~33 million episodes of acute lower-respiratory tract infection, 3.2 million hospitalizations and as many as 118,000 deaths per year
  - We estimate pediatric RSV results in ~$2 billion in annual medical costs in the U.S.
- **Target population**: Young children
- **Unmet need**: No approved RSV vaccine

RSV infection	
Infancy, childhood, adulthood	Fevers Nasal congestion Breathing difficulties Wheezing Chest congestion Bronchiolitis Pneumonia

1. Williams JV, Edwards KM, Weinberg GA, et al. Population-based incidence of human metapneumovirus infection among hospitalized children. *J Infect Dis*. 2010;201(12):1890-8.s

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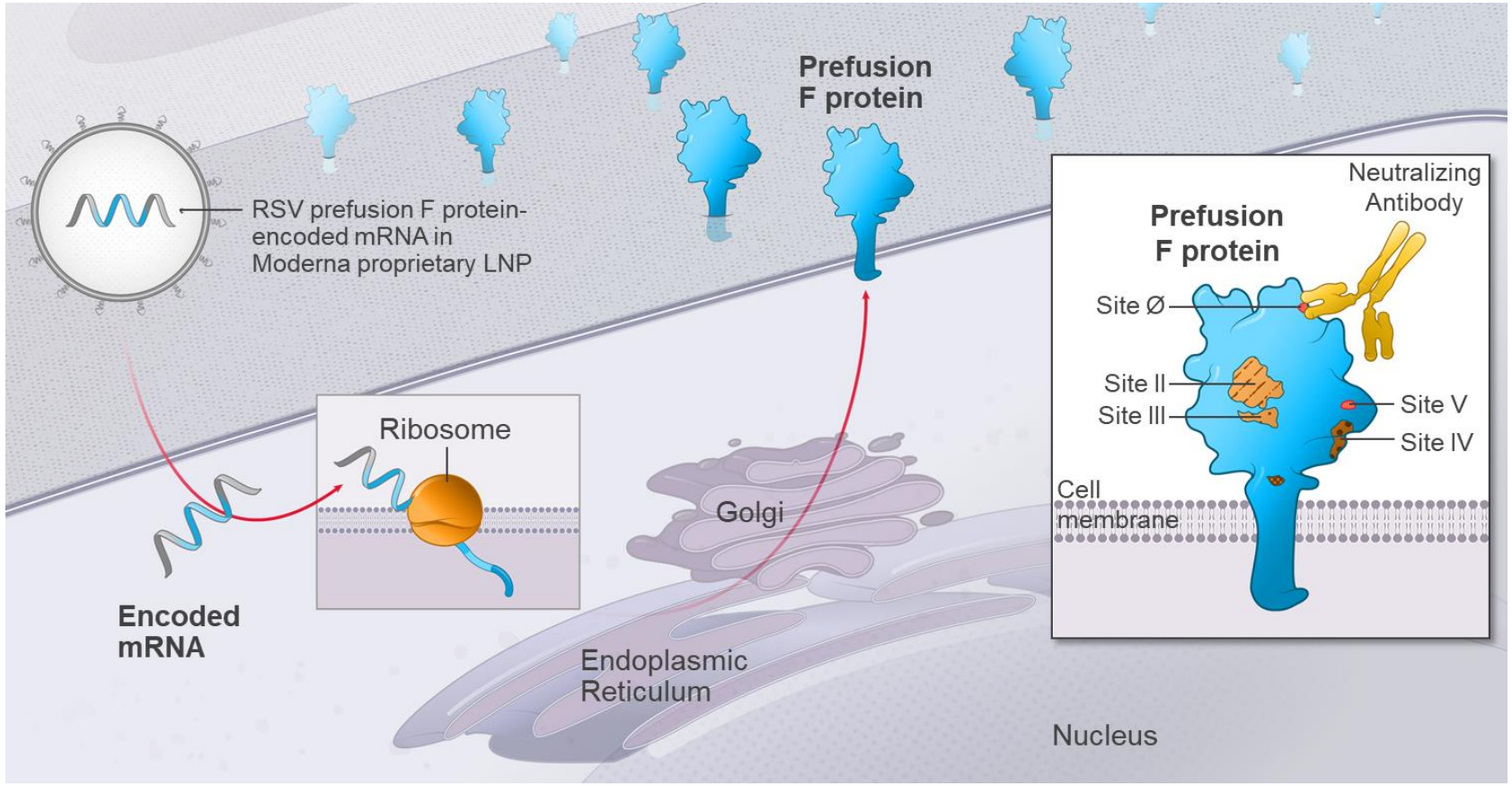
Pediatric RSV vaccine (mRNA-1345)

Encodes for a stabilized prefusion F glycoprotein



- Prefusion F elicits a superior neutralizing antibody response compared to the post-fusion protein
- mRNA-1345 will use the same LNP as our hMPV/PIV3 (mRNA-1653), CMV (mRNA-1647) and COVID-19 (mRNA-1273) vaccines

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Pediatric RSV vaccine (mRNA-1345)

IND opened and actively screening participants

Key objective

- To evaluate the safety and immunogenicity of mRNA-1345 when administered to adults and to children 12-36 months of age with serologic evidence of prior exposure

Primary endpoints

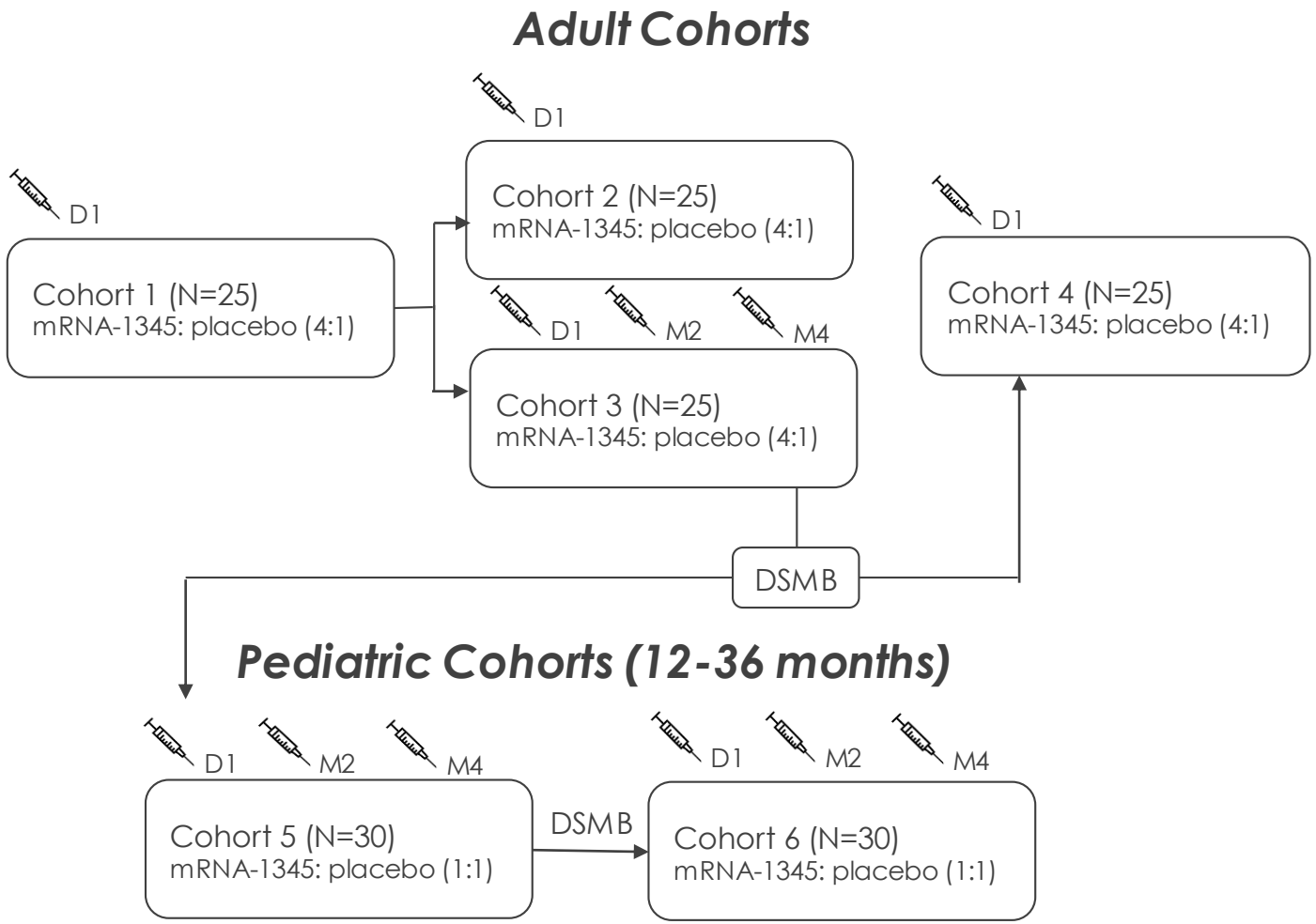
- Safety

Secondary endpoint

- Neutralizing antibodies against RSV

Trial progress

- IND opened in August 2020
- Sites are open and actively screening participants



Abbreviations
D = Day, M = Month, DSMB = Data Safety Monitoring Board

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

- hMPV and PIV3 are RNA viruses that are important causes of respiratory tract infections, particularly in children
- Increasing rates of diagnosis and association with hospitalization for respiratory illness
- **Disease burden**: Major cause of hospitalization due to respiratory infection
  - Symptoms range from mild upper respiratory tract infection to life threatening severe bronchiolitis and pneumonia
  - Both viruses cause clinically indistinguishable disease
- **Target population**: Infants
  - 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
- **Unmet need**: No approved hMPV or PIV3 vaccine
  - Other companies' previous attempts focused only on hMPV or PIV alone (no known attempts at a combination vaccine)

hMPV and PIV3 infection sequelae

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

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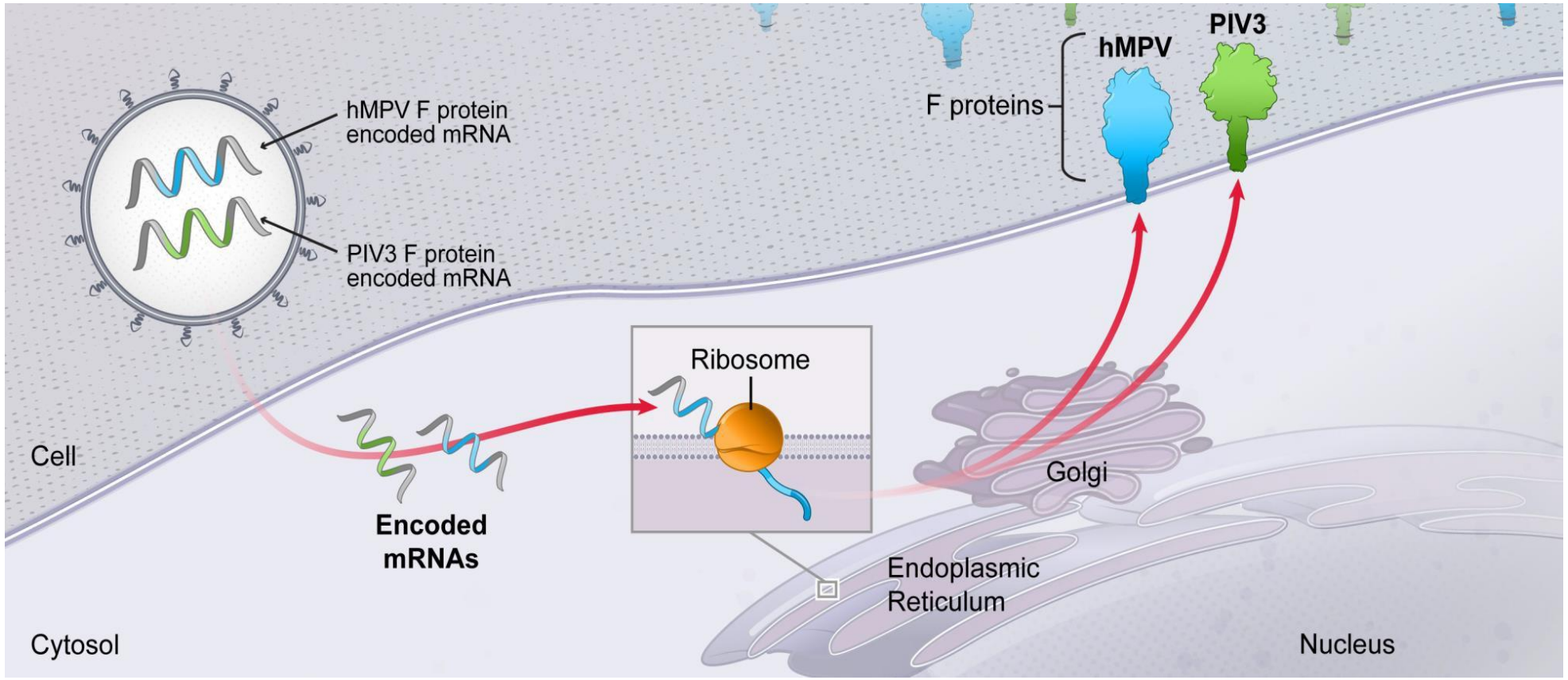
hMPV/PIV3 vaccine (mRNA-1653)

Combines mRNAs encoding antigens from two different viruses



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hMPV/PIV3 (mRNA-1653) Phase 1b trial

First mRNA vaccine to be evaluated in children

Key objective

- To evaluate the safety and immunogenicity of mRNA-1652 when administered to adults and to children 12-36 months of age with serologic evidence of prior exposure

Primary endpoint

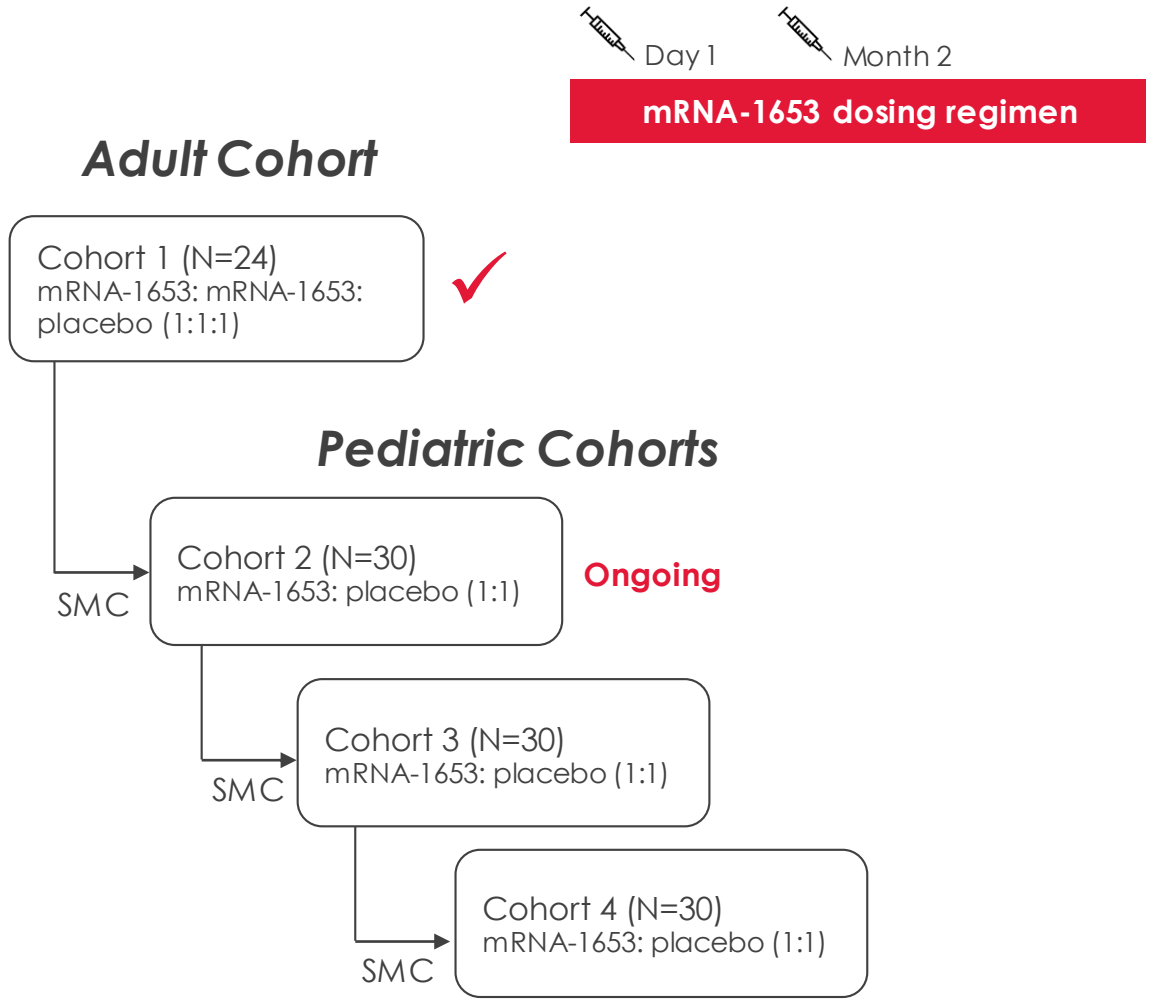
- Safety

Secondary endpoint

- Neutralizing antibodies against hMPV and PIV3

Trial progress

- Adult cohort is completed; First 10 pediatric participants dosed in trial before COVID-19 related disruptions
- Sites are open and actively recruiting participants



Abbreviations
SMC = Safety Monitoring Committee

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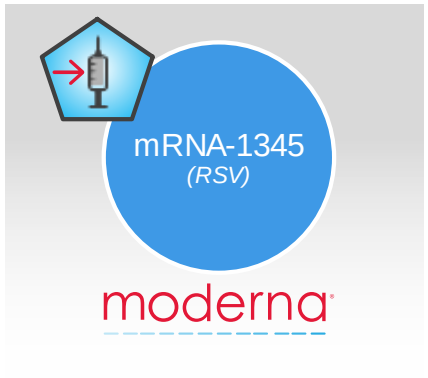
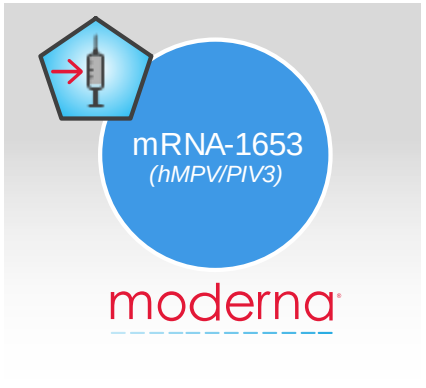
Pediatric respiratory diseases

RSV, hMPV and PIV3 are leading causes of respiratory illness in young children

	RSV *Respiratory syncytial virus*	**hMPV** *Human metapneumovirus*	**PIV3** *Parainfluenza virus type 3*
Epidemiology	• **Hospitalization rate in children** < 5 years old in the U.S.:~**3:1000**[1] • Associated with estimated 2 million medically attended infections	• **Hospitalization rate in children** < 5 years old in the U.S.:**~1.2:1000**[1] • Associated with estimated 1 million outpatient clinic visits and > 250k ED visits annually among U.S. children < 5 years old[2]	• **Hospitalization rate in children** < 5 years old in the U.S.:**~0.5:1000**[1]
Clinical disease	Upper and lower respiratory tract infection		





1. Williams JV, Edwards KM, Weinberg GA, et al. Population-based incidence of human metapneumovirus infection among hospitalized children. *J Infect Dis*. 2010;201(12):1890-8.
2. Edwards KM, Y. Zhu, M.R. Griffin, G.A. Weinberg, C.B. Hall, P.G. Szilagyi, *et al.* Burden of human metapneumovirus infection in young children. *N. Engl. J. Med.*, 2013;368(7):633-643.

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Pediatric respiratory diseases

RSV, hMPV and PIV3 are leading causes of respiratory illness in young children

	RSV *Respiratory syncytial virus*	**hMPV** *Human metapneumovirus*	**PIV3** *Parainfluenza virus type 3*
Epidemiology	• **Hospitalization rate in children** < 5 years old in the U.S.:~**3:1000**[1] • Associated with estimated 2 million medically attended infections	• **Hospitalization rate in children** < 5 years old in the U.S.:**~1.2:1000**[1] • Associated with estimated 1 million outpatient clinic visits and > 250k ED visits annually among U.S. children < 5 years old[2]	• **Hospitalization rate in children** < 5 years old in the U.S.:**~0.5:1000**[1]
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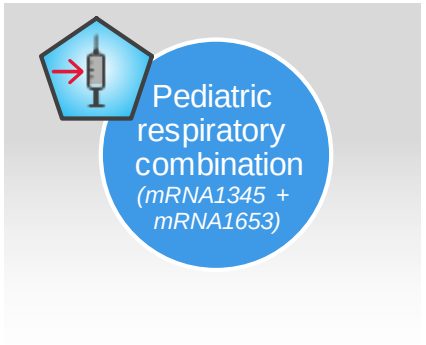

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Terry Nolan, M.D., Ph.D.

Peter Doherty Institute for Infection and Immunity, The University of Melbourne

Prof. Nolan is a pediatrician and clinical epidemiologist, graduated from the University of Western Australia, trained in paediatrics at the Royal Children's Hospital in Melbourne and at the Montréal Children's Hospital, and was awarded a PhD in in epidemiology and biostatistics from McGill University in Montréal. His expertise relates to immunisation, pandemic planning and response, and clinical trials of new vaccines. He is a past Chair of the Australian Technical Advisory Group on Immunisation (ATAGI), was a member and then Deputy Chair of the National Health and Medical Research Council's (NHMRC) Research Committee over nine years. He has more than 240 publications in refereed journals. He is a Fellow of the Australian Academy of Health and Medical Sciences, and a past member of SAGE, the World Health Organization's main advisory group on vaccines and Immunisation. Prof. Nolan is a recipient of several Awards, including the prestigious Officer of Order of Australia.

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Terry Nolan MD PhD
Peter Doherty Institute
for Infection and Immunity
The University of Melbourne

Vaccines and Prevention of Children's Diseases

Epochs and Opportunities

Advances

+Polio

+Diphtheria, tetanus, pertussis

+Meningitis

+Diarrheal disease

+Pneumonia

+Measles, mumps, rubella, and varicella

Epochs and Quantum Shifts

- Basic vaccinology
  - Conjugate bacterial vaccines (simple, then complex multiple serotypes)
  - Reverse vaccinology (men B)
  - Nucleic acid vaccines
- Combination vaccines
  - Infant combos, MMR-V, mening (HibMenC, HibMenCY, menACWY, menABCWY)
- Mandatory vaccination policies
  - Shifting tolerance of freedom not to vaccinate
  - Herd immunity is everyone's responsibility

Combination Vaccines

+Have made the infant schedule feasible as new vaccines have emerged

+Potential for further efficiency probably not fully realized

Hexavalent vaccine for infants

HUMAN VACCINES & IMMUNOTHERAPEUTICS
https://doi.org/10.1080/21645515.2020.1764826

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REVIEW

OPEN ACCESS Check for updates

Control of vaccine preventable diseases in Australian infants: reviewing a decade of experience with DTPa-HBV-IPV/Hib vaccine

Julianne Bayliss [a], Michael Nissen [b], Damita Prakash [a], Peter Richmond [c], Kyu-Bin Oh [d], and Terry Nolan [e]

[a]Medical Affairs, GSK, Melbourne, Australia; [b]Scientific Affairs & Public Health, GSK, Singapore, Singapore; [c]Division of Paediatrics and Centre for Child Health Research, University of Western Australia, Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, Perth Children's Hospital, Perth, Australia; [d]Medical Affairs, GSK, Singapore, Singapore; [e]Vaccine and Immunisation Research Group (Virgo), University of Melbourne, School of Population and Global Health and Murdoch Children's Research Institute, Melbourne, Australia

ABSTRACT

The combined vaccine against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis, and *Haemophilus influenzae* b (DTPa-HBV-IPV/Hib, Infanrix Hexa, GSK) has been used for childhood immunization in Australia according to a two-, four-, six-month schedule since 2009. We reviewed data available in the Australian National Notifiable Diseases Surveillance System, annual vaccination coverage reports, the Database of Adverse Event Notifications, and peer-reviewed literature to assess vaccine coverage rates, incidence of all six vaccine preventable diseases, and the safety profile of DTPa-HBV-IPV/Hib vaccine in Australian infants over a period of ten years of exclusive use. Between 2009 and 2018 vaccine coverage for infants aged 12 months increased from 91.7% to 94.0% and from 84.9% to 92.6% for all and for Indigenous infants, respectively. Over the same time period, there were no reports of poliomyelitis, diphtheria or tetanus in infants <12 months of age. The incidence of hepatitis B among Australian infants <12 months of age remains 10 to 20-fold lower than the national average. Control of *Haemophilus influenzae* b (Hib) and pertussis disease has continued to be challenging. Timely administration of the primary series, as well as increasing coverage rates, particularly among Indigenous children, has contributed to improvements in Hib and pertussis disease control. The incorporation of additional strategies such as adjustment of the first vaccination encounter to six weeks of age, parental cocooning, and most recently maternal vaccination has further reduced the burden of pertussis, particularly during the first six months of life. The frequency of the ten most common adverse events related to the DTPa-HBV-IPV/Hib vaccine demonstrates an acceptable safety profile. Data collected over ten years of consistent, exclusive use of the DTPa-HBV-IPV/Hib vaccine in Australia highlights combination vaccination as a cornerstone in maintaining infant health.

ARTICLE HISTORY
Received 21 November 2019
Revised 2 April 2020
Accepted 29 April 2020

KEYWORDS
Australia; combination vaccines; coverage; infant vaccination; safety; DTPa-HBV-IPV/Hib; hepatitis B; *Haemophilus influenzae* type b; pertussis

Julianne Bayliss, Michael Nissen, Damita Prakash, Peter Richmond, Kyu-Bin Oh & Terry Nolan (2020). Control of vaccine preventable diseases in Australian infants: reviewing a decade of experience with DTPa-HBV-IPV/Hib vaccine,Human Vaccines & Immunotherapeutics, DOI: 10.1080/21645515.2020.1764826

Advantages of Combination Vaccines

+Coverage

+Convenience

+Cost of materials reduced

+Storage simpler

+Marketing (lesser known components get a free ride)

+Parent acceptability (no ‘pin cushion’)

  + Paradoxically may alleviate some of ‘antigen overload’ anxiety

Concerns about too many immunizations

PEDIATRICS®
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Do Parents Understand Immunizations? A National Telephone Survey

Bruce G. Gellin, Edward W. Maibach, Edgar K. Marcuse and for the National Network for Immunization Information Steering Committee?

Pediatrics 2000;106;1097
DOI: 10.1542/peds.106.5.1097

Objective and Methods. To assess parents' understanding of vaccine-preventable diseases, vaccines, immunization practices, and policies, we conducted a telephone survey in the United States with a nationally representative sample (n = 1600) of parents with children ≤6 years of age, and expectant parents in April and May 1999.

	% Agree (% Strongly Agree)	% Disagree (% Strongly Disagree)
Children should only be immunized against serious diseases.	39 (20)	55 (31)
Children get more immunizations than are good for them.	23 (10)	68 (37)
Immunizations are always proven safe before they are approved for use.	71 (33)	19 (7)
I am concerned that my child's immune system could be weakened by too many immunizations.	25 (9)	63 (33)

Respiratory Viruses as High Value Targets

- Influenza
- Respiratory syncytial virus (RSV)
  - 50-year quest
  - VAERD (vaccine-associated enhanced respiratory disease) risk has plagued development
  - Many candidates from several platforms, maternal and infant
- Parainfluenza virus type 3 (PIV3)
- Human Metapneumovirus (hMPV)

Is there a role for mRNA combination vaccines?

+Capacity to ‘package’ N>1 mRNA for multiple target diseases

+Reduced risk of chemical/immunologic interference

+‘Tunable’ potential a major asset for antigenic drift, without altering the entire construct

+Potential for reduced adjuvant exposure

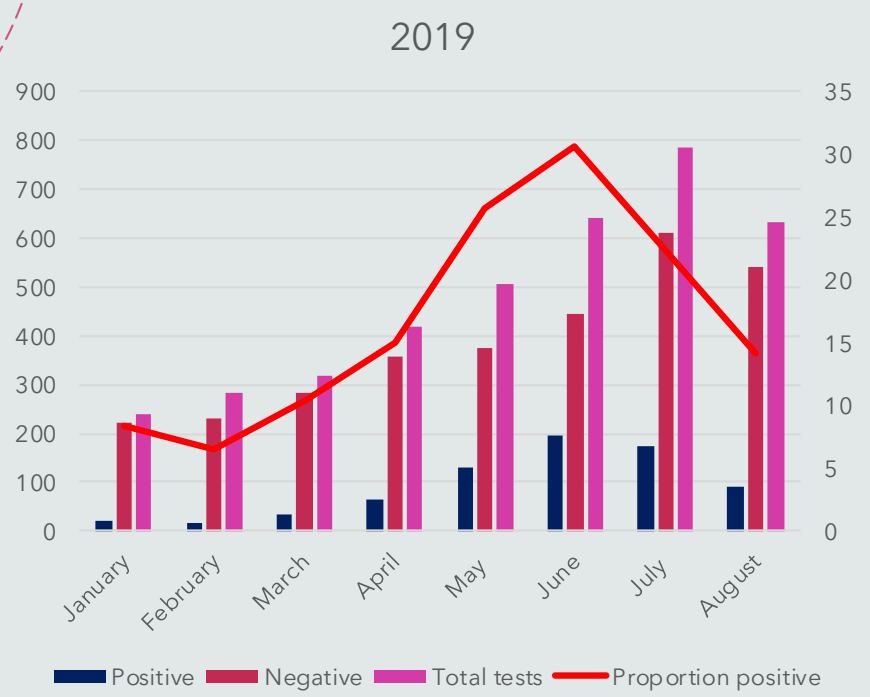
Regulatory touch points

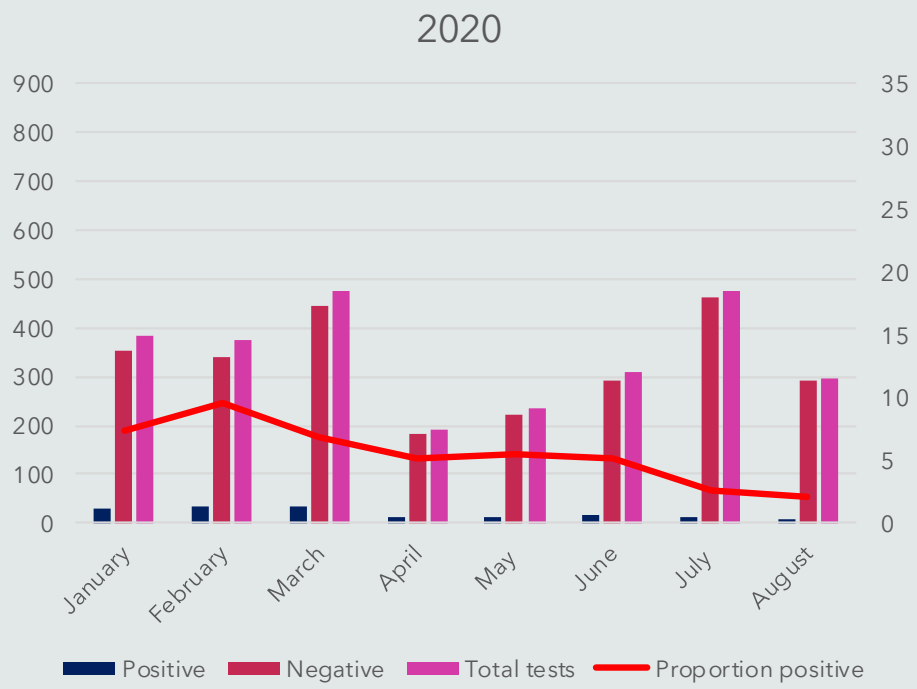
- Adjuvants
  - Regulators ‘don’t like’ adjuvants (quote)
- Safety
  - Shifting baseline on risk management for safety assurance
- Assurance of VE for drifted targets (influenza, SARS-CoV-2)
- Clinical trial complexity
  - Age de-escalation and dose escalation
  - Changes in virus ecology from COVID social impacts

Disrupted virus ecology

- COVID impact mediated through social restriction
- Consequent impact on virus circulation
- Effect on clinical trials programs
  - Reduced seropositives in early childhood
  - Fewer events for a Phase III study

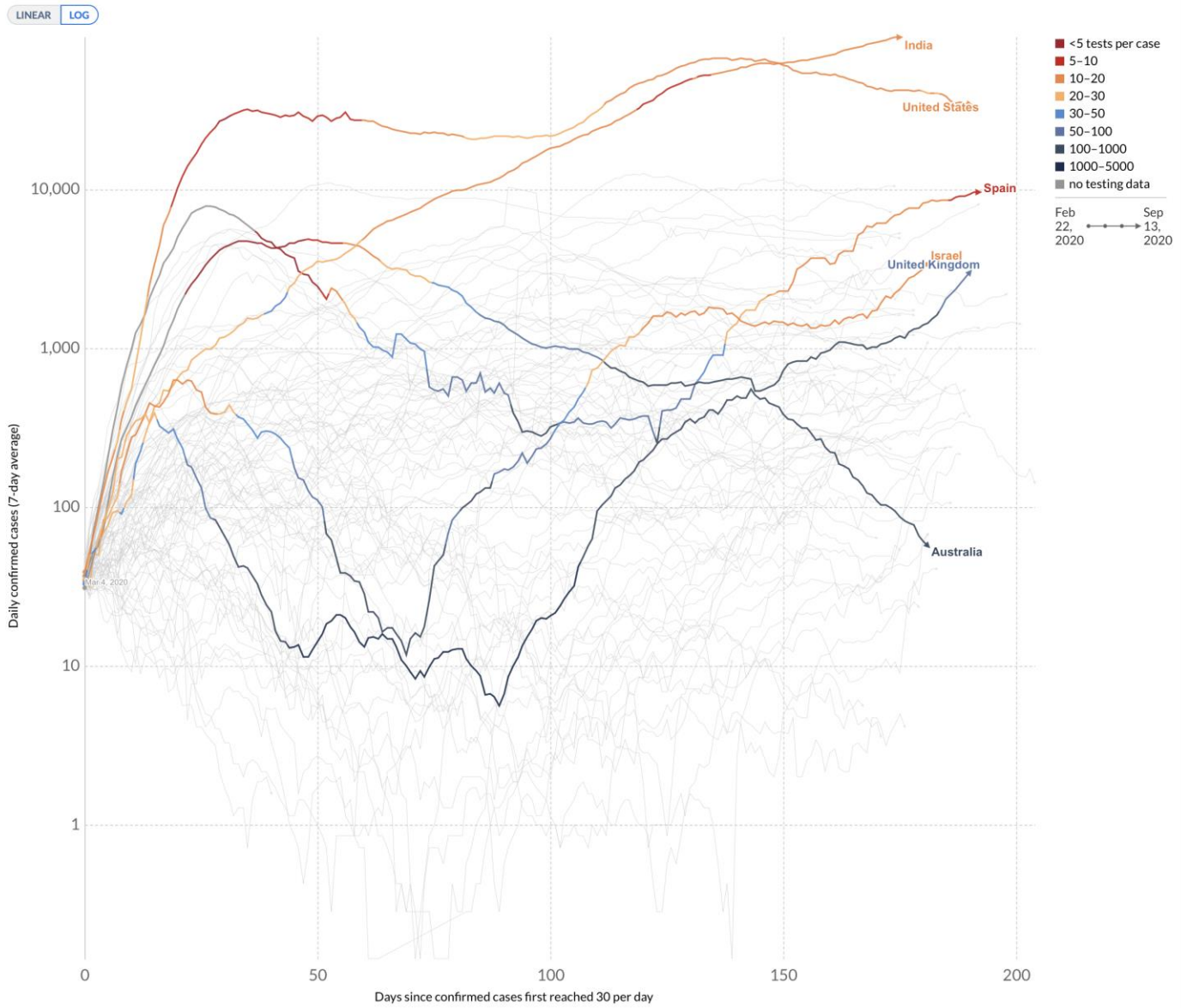
Multiplex RT-PCR for Respiratory Illness and RSV+ at Royal Children's Hospital Melbourne





Daily new confirmed cases of COVID-19

The line is blue when a country performs many tests relative to the size of the outbreak.
Red indicates a low number of tests per case. This suggests that the true number of infections may be far higher than the number of confirmed cases.



Source: European CDC – Situation Update Worldwide – Last updated 13 September, 10:35 (London time), Official data collated by Our World in Data
Note: Only countries for which testing data is available are included. Details about this data can be found at OurWorldInData.org/coronavirus-testing.

OurWorldInData.org/coronavirus • CC BY

What do Governments want? Valuing Vaccines

- Public funding (NIPs) necessary to optimize vaccine uptake
  - Confidence and availability
- Better methods for cost-effectiveness evaluation
- Implementability (simplicity in scheduling and administration)
- In summary, good value for money, and high levels of public and healthcare provider demand

Conclusions

+Advances in vaccine science have provided quantum shifts in value through primary prevention of childhood diseases

+Combination vaccines have a proven track record, and significant future potential

+mRNA vaccines have a lot to offer for the coming epoch

With thanks

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A joint venture between The University of Melbourne and The Royal Melbourne Hospital

Jacqueline Miller, M.D., FAAP
SVP, Infectious Diseases Development

COVID-19 Vaccine (mRNA-1273)

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COVID-19 vaccine (mRNA-1273)

Modality	ID #	Program	Preclinical development / Phase 1 / Phase 2 / Phase 3 and commercial	Moderna rights
Prophylactic vaccines	**mRNA-1273**	COVID-19 vaccine	Phase 3 and commercial	Worldwide *BARDA funded*
	mRNA-1647	Cytomegalovirus (CMV) vaccine	Phase 2	Worldwide
	mRNA-1653	hMPV/PIV3 vaccine	Phase 1 (healthy volunteers) → Phase 1b (Age de-escalation) Seropositives	Worldwide
	mRNA-1172/ Merck V172	Respiratory syncytial virus (RSV) vaccine	Phase 2	Merck to pay milestones and royalties
	mRNA-1777	Respiratory syncytial virus (RSV) vaccine	Phase 2	
	mRNA-1893	Zika vaccine	Phase 2	Worldwide *BARDA funded*
	mRNA-1345	Pediatric respiratory syncytial virus (RSV) vaccine *Future respiratory combo*	Phase 1	Worldwide
	mRNA-1189	Epstein-Barr virus (EBV) vaccine	Phase 1	Worldwide
	mRNA-1851	Influenza H7N9 vaccine	Phase 2	Worldwide *Advancing subject to funding*

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Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) overview

- SARS-CoV-2 virus: novel coronavirus first identified in humans in December 2019 and cause of COVID-19

- **Disease burden (as of September 16, 2020):**
  - Global: 29,621,768 confirmed cases and 936,156 deaths from COVID-19[1]
  - US: 6,609,770 confirmed cases and 196,023 deaths[1]
  - Between 298,589 and 611,783 total deaths are currently projected in the US by January 1, 2021[2]
  - Risk of mortality increases with increasing age (estimated to be ~0.1% for 0-19, ~6% for 60+)[3]
  - Risk of severe disease and mortality increased for persons with pre-existing diseases or comorbid conditions (e.g. cardiovascular disease, diabetes, chronic lung disease, obesity)

- **Unmet need:** There is no approved vaccine for COVID-19

COVID-19 sequelae identified to date[4,5]	
Lungs	Pneumonia Acute Respiratory Distress Syndrome (ARDS) Scarring Pulmonary embolism
Heart	Cardiac injury Inflammation Stroke Blood clots Arrythmia Hypertension
Other	Persistent fatigue Loss of smell or taste Neurologic complications Kidney damage Multisystem Inflammatory Syndrome in Children (MIS-C)

1. Johns Hopkins Coronavirus Resource Center. Available at: https://coronavirus.jhu.edu/. Accessed 16 Sep 2020.
2. COVID-19 Projections. The Institute for Health Metrics and Evaluation, University of Washington. Available at: https://covid19.healthdata.org/united-states-of-america?view=total-deaths&tab=trend. Accessed 16 Sep 2020.
3. Our World in Data. Available at: http://ourworldindata.org/coronavirus-data. Accessed 04 Aug 2020.
4. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. Published online July 27, 2020.
5. Advisory Board: it's not just lungs: COVID-19 may damage the heart, brain, and kidneys(2020). www.advisory.com/daily-briefing/2020/04/17/organ-damage.

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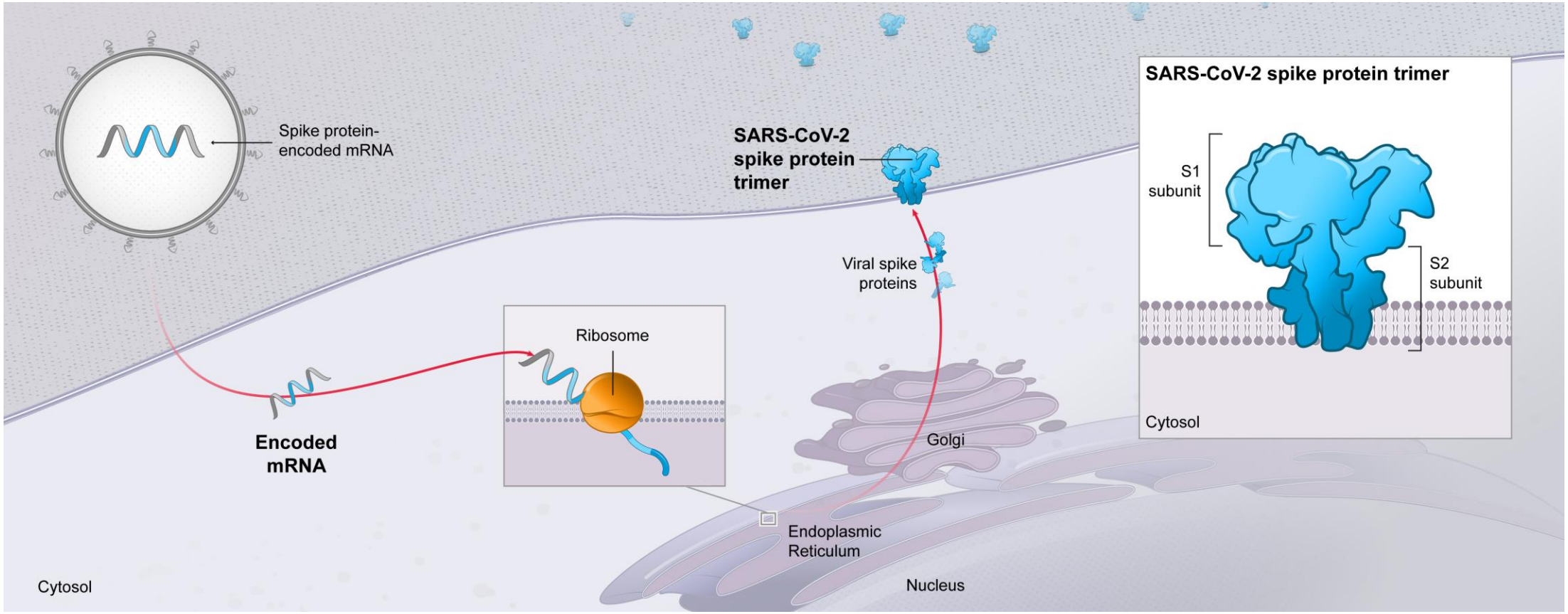
SARS-CoV-2 vaccine (mRNA-1273)

Encodes for the full spike S protein



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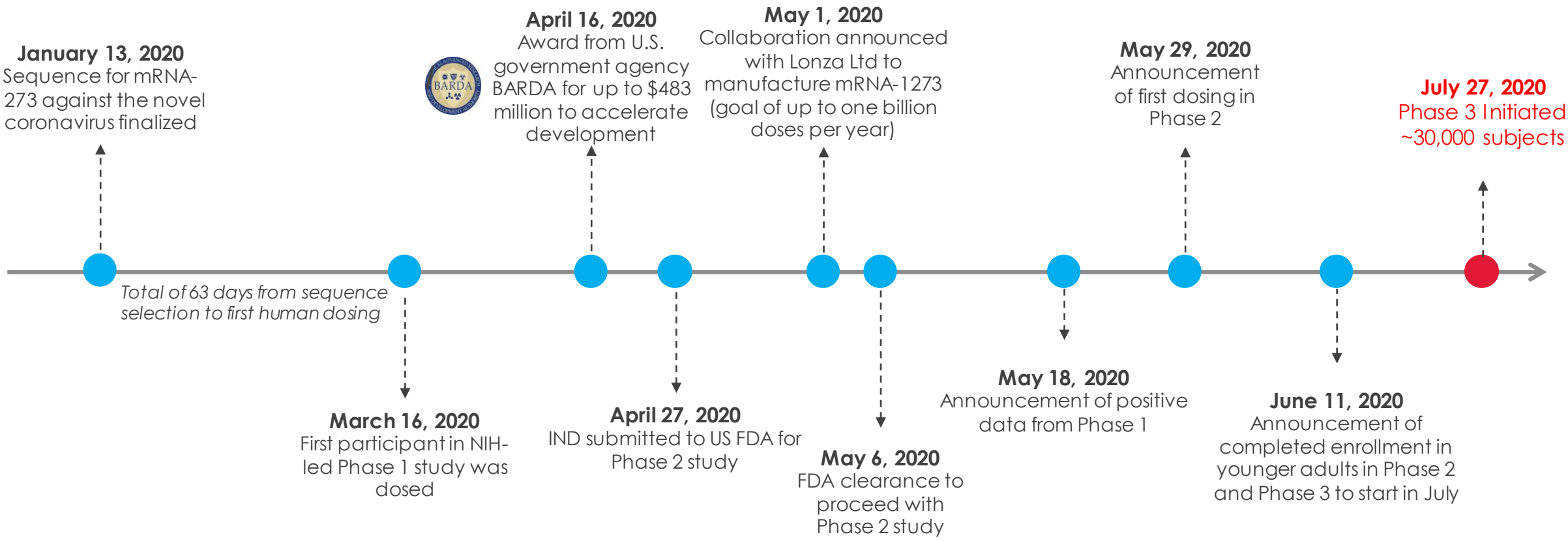
mRNA-1273 program timeline

mRNA-1273 timeline: Research and development of SARS-CoV-2 vaccine



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Phase 1 trial overview

Led by the National Institutes of Health (NIH)

Key objective:

- To assess the safety, reactogenicity and immunogenicity of mRNA-1273

Study design:

- Phase 1, open-label dose ranging clinical trial in healthy adults
- Subjects received an intramuscular (IM) injection (0.5 milliliter [mL]) of mRNA-1273 on Days 1 and 29 in the deltoid muscle and will be followed through 12 months post second vaccination (Day 394)

Primary endpoint:

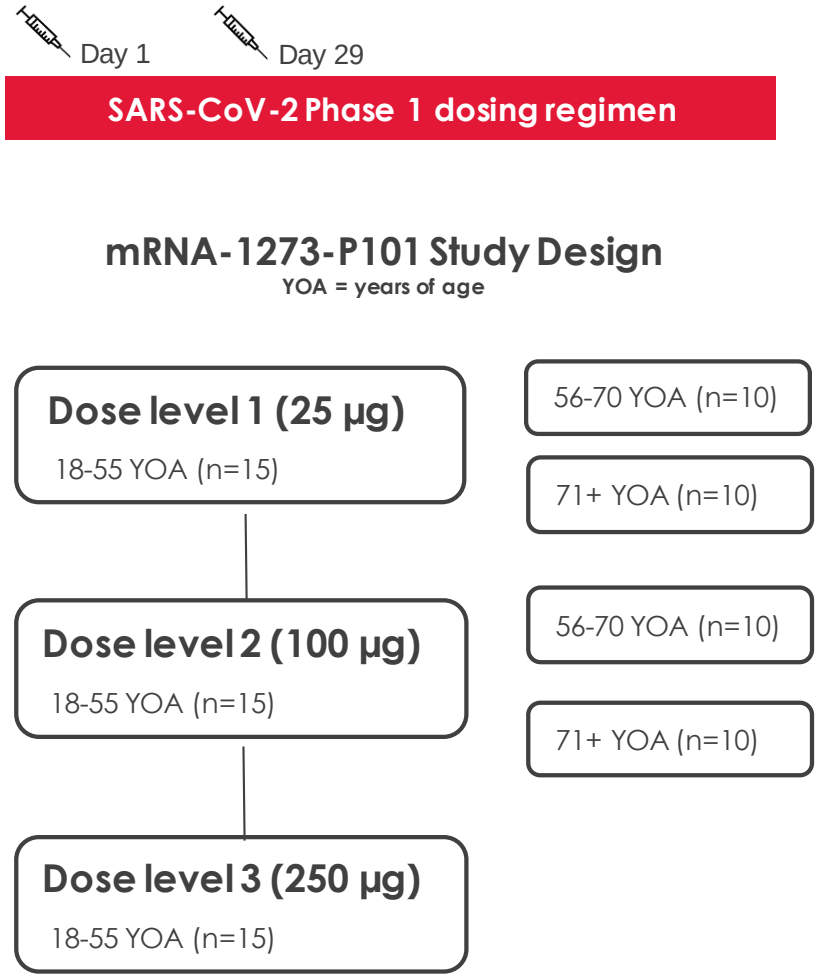
- Safety and reactogenicity of a 2-dose vaccination schedule of mRNA-1273, given 28 days apart

Secondary endpoint:

- Evaluate the immunogenicity to the SARS-CoV-2 S protein following a 2-dose vaccination schedule of mRNA-1273 at Day 57

Trial progress/details:

- Original 3 dose cohorts 25 µg, 100 µg and 250 µg (18-55 years old) Day 57 data published in *The New England Journal of Medicine*[1]
- Interim analysis of the 100 µg dose for the 56-70 and 71+ age cohorts presented at ACIP Meeting
- 50 µg dose across three age cohorts (18-55, 56-70 and 71+) are fully enrolled



1. Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483 Interim Immunogenicity Report

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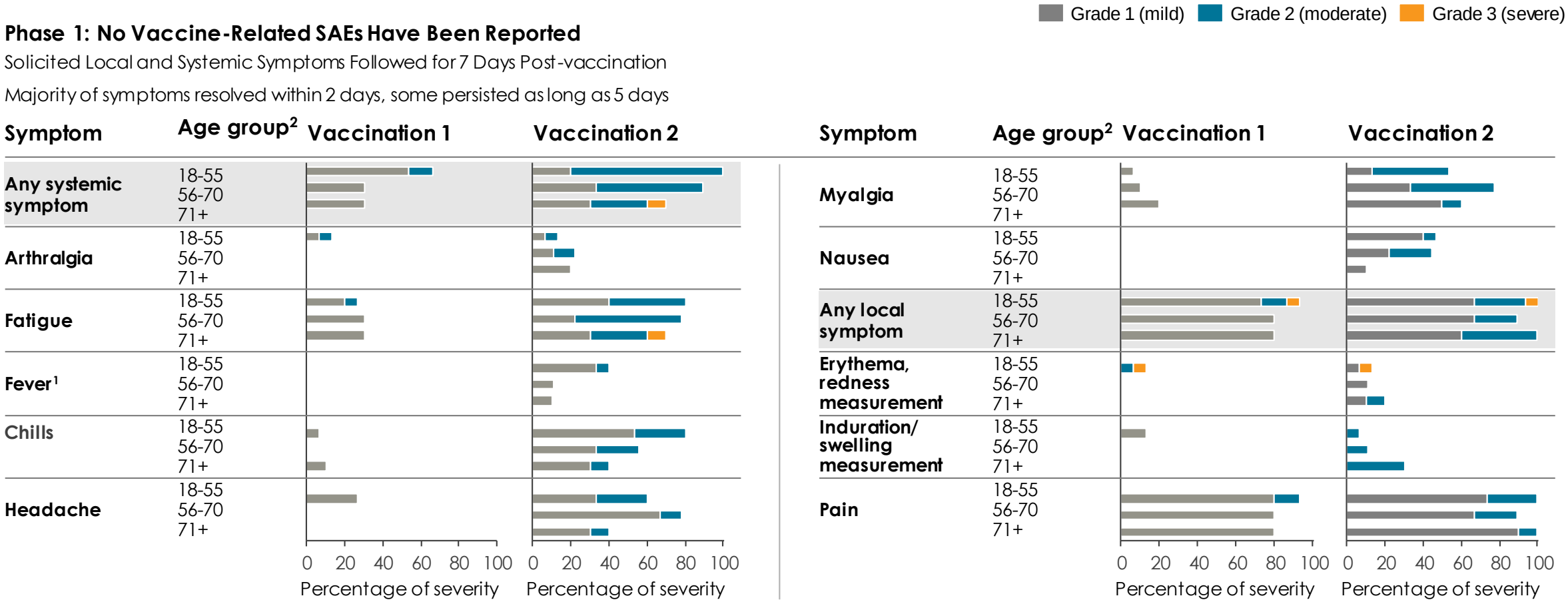
100 µg mRNA-1273 well-tolerated across age groups

Phase 1: No Vaccine-Related SAEs Have Been Reported

Solicited Local and Systemic Symptoms Followed for 7 Days Post-vaccination

Majority of symptoms resolved within 2 days, some persisted as long as 5 days



1. Fever percentages reflect the number of subjects with at least one measurement available in the data system as the denominator. This denominator may differ from other systemic symptoms, which are solicited in-clinic at the post-dose assessment
2. 18-55: N=15; 56-70: N=10; 71+: N=10; N = All subjects receiving Dose 1 with any solicited event data recorded in the database

Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483

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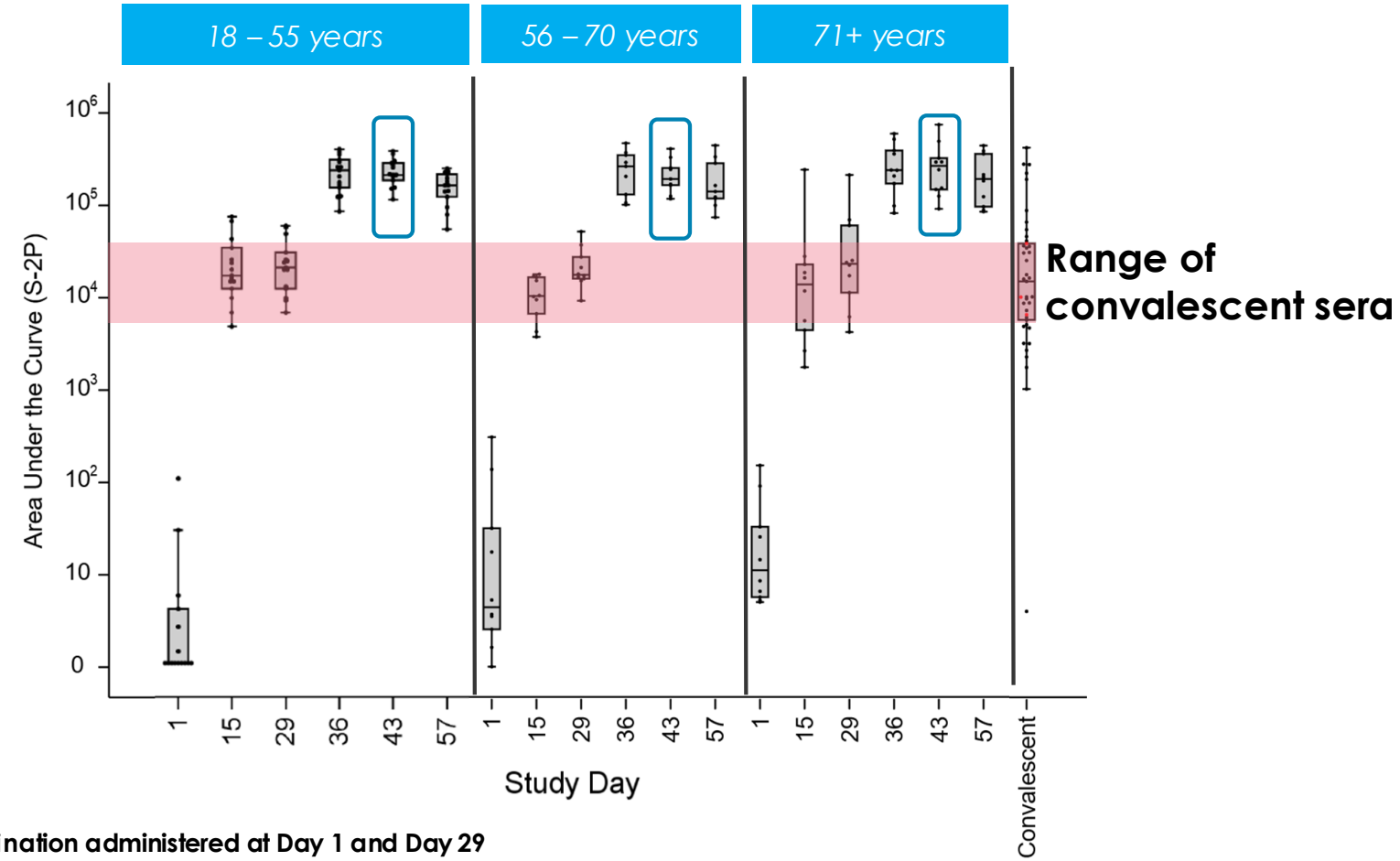
Binding antibodies comparable across age groups

S-2P binding antibodies (ELISA)- 100 µg at Day 1 and Day 29



Vaccination administered at Day 1 and Day 29

- 100 µg two-dose series seroconverted all participants after the first vaccination
- After the first vaccination, AUC for all age groups exceeded the median of convalescent sera
- After two vaccinations, all age groups are equivalent to high-titer convalescent sera (i.e., upper quartile)

Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483
Interim Immunogenicity Report

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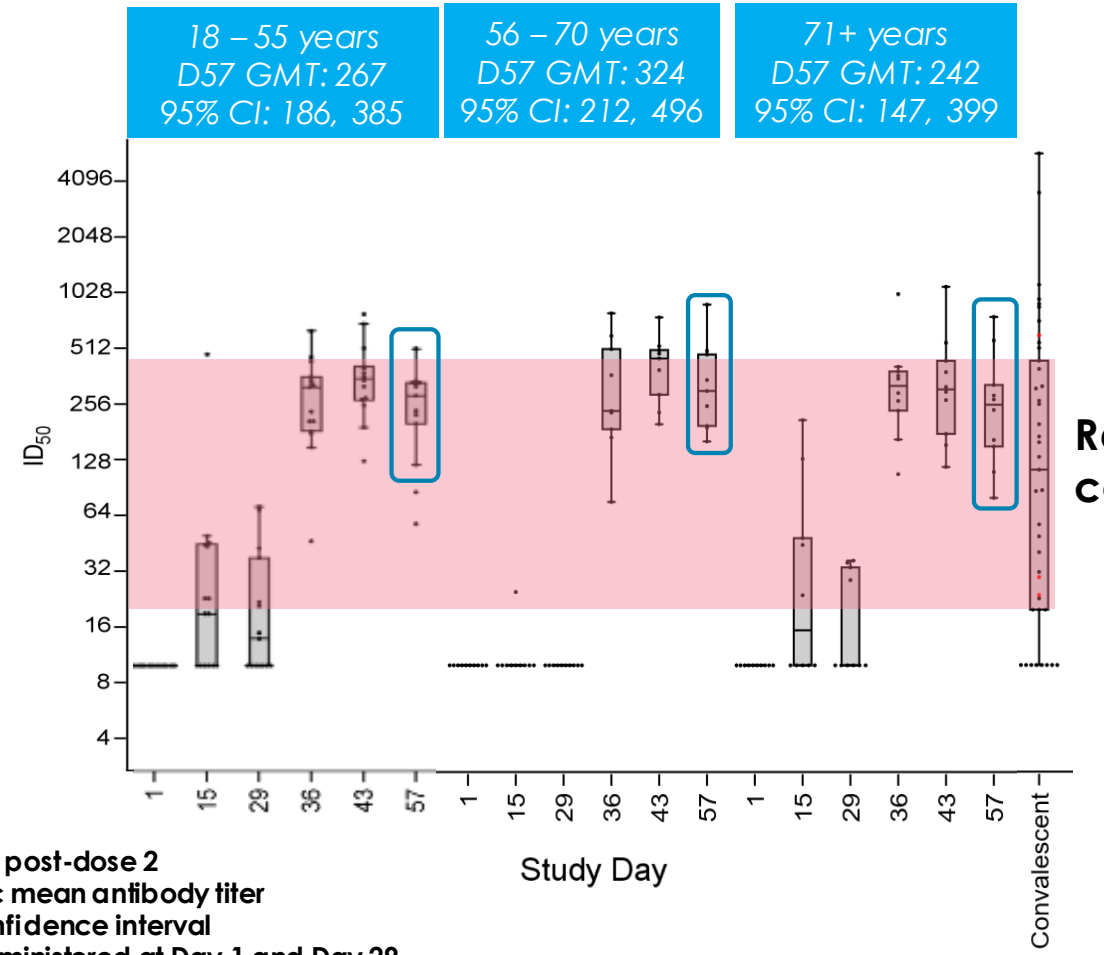
Distribution of antibody titers in pseudovirus neutralization assay comparable across age groups

Pseudovirus neutralization assay titers (ID_{50})- 100 µg at Day 1 and Day 29



Range of convalescent sera

D57: one month post-dose 2
GMT: geometric mean antibody titer
95% CI: 95% confidence interval
Vaccination administered at Day 1 and Day 29

- After second vaccination, pseudovirus neutralization responses were detected in all participants
- Pseudovirus neutralization titers were comparable across age groups
- Pseudovirus neutralization titer for 56-70 and 71+ YOA above convalescent sera median titer at Day 57

Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483
Interim Immunogenicity Report

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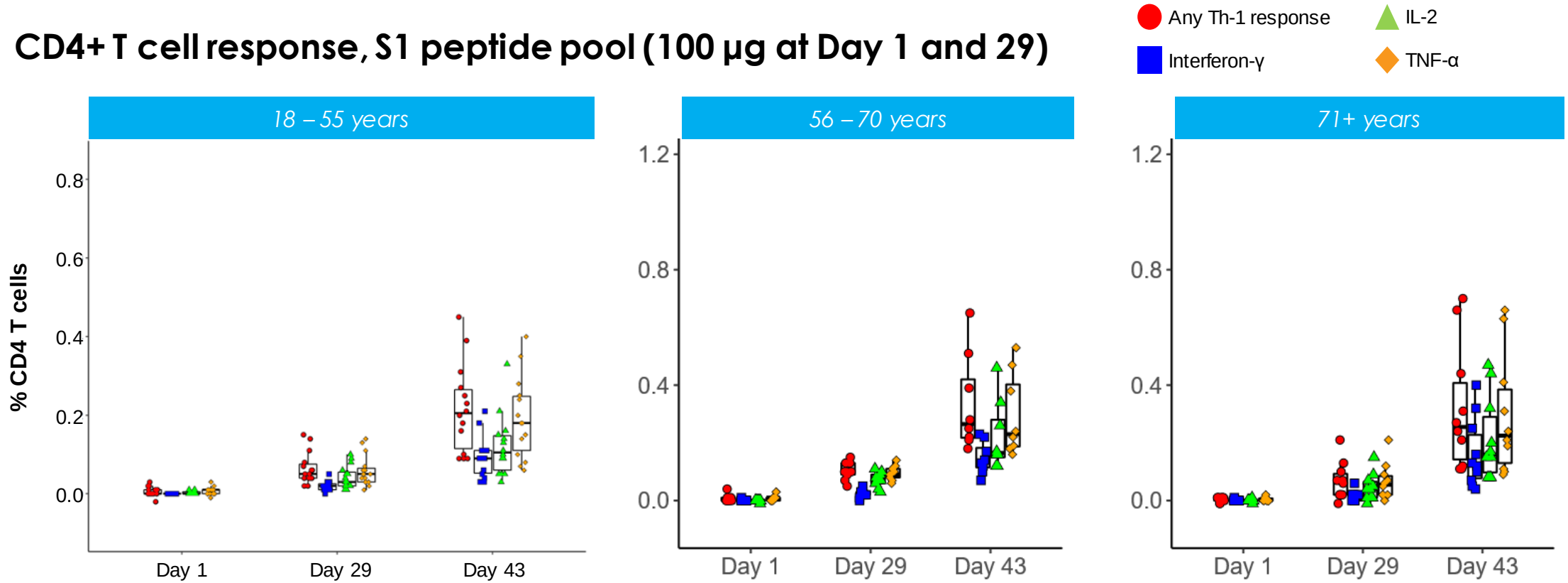
mRNA-1273 elicited Th1-biased CD4 T cell responses in all participants

Th1 CD4+ T cell response, S1 peptide pool (100 µg at Day 1 and 29)



- Vaccination with 100 µg mRNA-1273 led a Th1-biased CD4+ T-cell response across all age groups
- Th2 phenotype was rare (data not shown)

Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483
Interim Immunogenicity Report

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mRNA-1273 vaccine against COVID-19

Data generated to date

- **Phase 1 clinical data**
  - Neutralizing antibody titers were observed in 100% of evaluated participants
  - In the pseudovirus (ID_{50}) neutralization assay, at the 100 µg dose, mRNA-1273 induced consistently high levels of neutralizing antibody titers in all participants in the young adult and older adult cohorts
  - In the live SARS-CoV-2 ($PRNT_{80}$) neutralization assay in the younger adult cohort, the Day 43 geometric mean titer levels at the Phase 3 selected dose of 100 µg were above those seen in reference convalescent sera[1]

- **Nonhuman primate data publication[2]**
  - Two-dose vaccination schedule of mRNA-1273 led to rapid protection against SARS-CoV-2 infection in both the lungs and nose of non-human primates

1. Jackson L, Anderson EJ, Rouphael NG, et al. An mRNA vaccine against SARS-CoV-2- preliminary report. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483 Interim Immunogenicity Report
2. Corbett K, Flynn B, Foulds L, et al. Evaluation of the mRNA-1273 vaccine against SARS-CoV-2 in nonhuman primates. N Engl J. Med. 28 Jul 2020; DOI: 10.1056/NEJMoa2024671

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mRNA-1273 Phase 2 Study will Evaluate Safety and Immunogenicity of 50 µg and 100 µg (N=600)

Phase 2 trial overview (NCT04405076)

Protocol Title

A Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Finding Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older

Study Groups

Cohorts	Age groups	Dosage IM (D1, D29) 1:1:1	Sample size	Enrollment status
Cohort 1	18 to <55	50 µg, 100 µg, placebo	300	Fully enrolled (300/300)
Cohort 2 Sentinel	≥55	50 µg, 100 µg, placebo	50	Fully enrolled (50/50)
Cohort 2 Full	≥55	50 µg, 100 µg, placebo	250	Fully enrolled (250/250)

Participant Population

Healthy males and females at or above 18 years of age

"All-comers" with regard to SARS-CoV-2 serostatus (baseline serology will be collected)

Study Endpoints

Safety (solicited AR x 7 days post each injection; unsolicited AE to day 57; SAE and MAAE throughout the study); assessment of any cases of Covid-19; potential assessment for asymptomatic infection

Immunogenicity (ELISA, nAb)

Study Duration

Approximately 13 months for each participant corresponding to a 12-month follow up after the last vaccine administration

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Pivotal Phase 3 Efficacy, Safety and Immunogenicity Study (N=30,000)

Phase 3 trial overview (NCT04470427)

Protocol Title	A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older			
Study Groups	**Strata**	**Dosage IM (D1, D29) 1:1**	**Sample Size**	**Enrollment status**
	≥ 65 years	100 µg, placebo	25-40%	Started July 27
	< 65 years at increased risk for complication of COVID-19 ("at risk")	100 µg, placebo		Started July 27
	< 65 years and not at risk	100 µg, placebo	60-75%	Started July 27
Participant Population	Approximately 30,000 participants (case driven) whose locations or circumstances put them at appreciable risk of acquiring COVID-19 and/or SARS-CoV-2 infection "All-comers" with regard to SARS-CoV-2 serostatus (baseline serology will be collected)			
Study Objectives	To demonstrate the efficacy of mRNA-1273 to prevent COVID 19 To evaluate the safety and reactogenicity of 2 injections of the mRNA-1273 vaccine given 28 days apart			
Study Duration	Approximately 25 months for each participant corresponding to a 24-month follow up after the last vaccine administration			

COVE D&I Advisory Committee

Remit and Role of Advisory Committee:

1. Review enrollment, race, and ethnicity demographics on a weekly basis
2. Review current outreach activities and outcomes
3. Review strategies to ensure participation of individuals from communities significantly impacted by COVID-19
4. Support the development and implementation of retention strategies

Cove
DIVERSITY & INCLUSION ADVISORY COMMITTEE

MODERNA

NATIONAL INSITITUTES OF HEALTH

- National Institute on Allergy and Infectious Diseases
- National Institute on Minority Health and Health Disparities
- NIH, Tribal Health Research Office
- NHLBI

OPERATION WARP SPEED

COVPN

US DEPARTMENT OF VETERAN AFFAIRS

FAITH COMMUNITY

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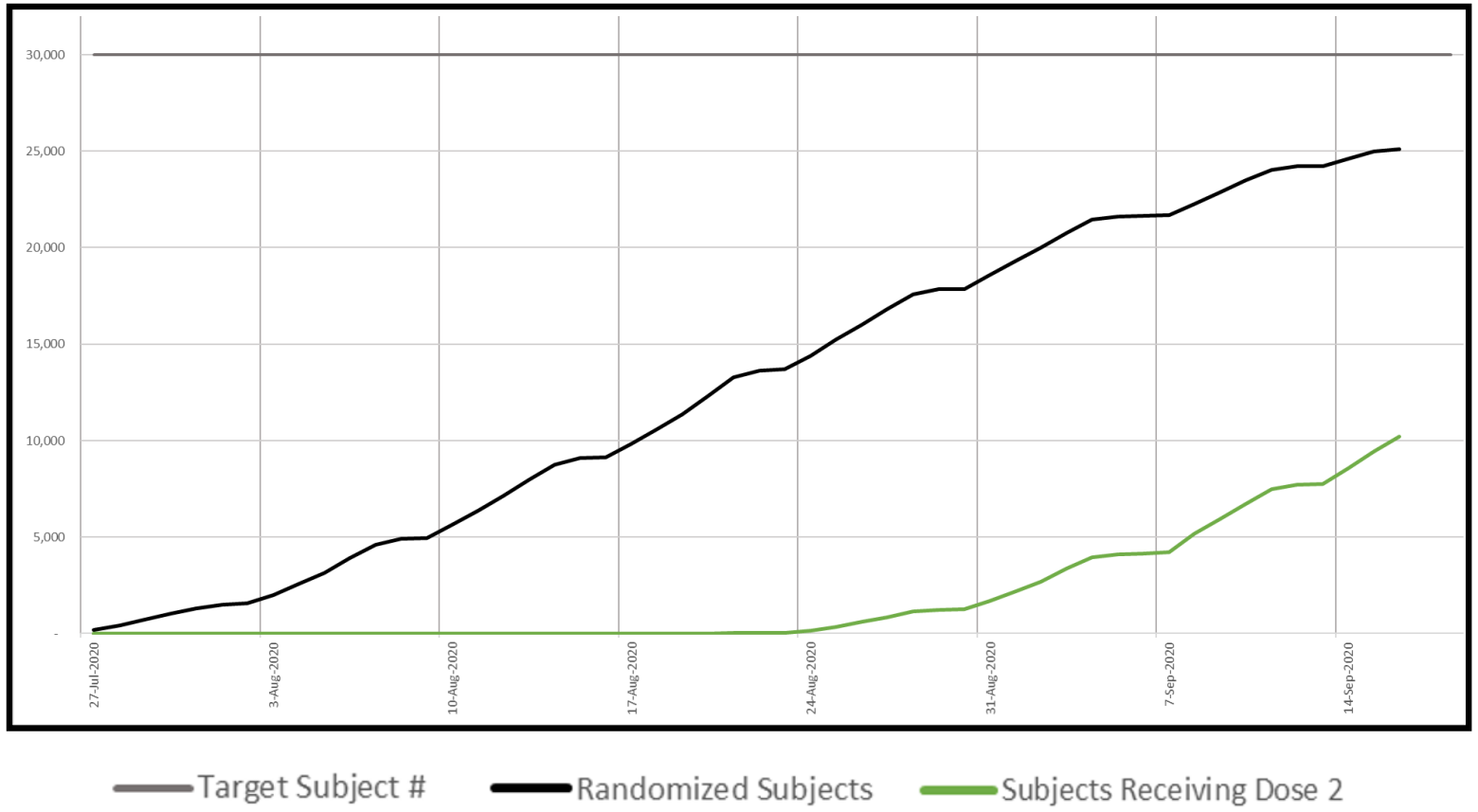
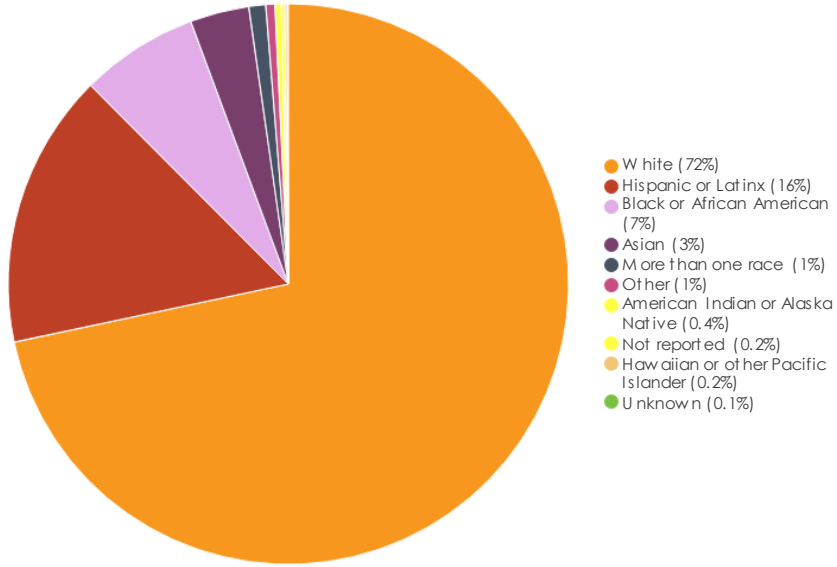
Phase 3 COVE study has enrolled 25,296 participants[1]

Phase 3 Enrollment Status



Phase 3 Diversity Status



*Approximately **28% of participants** enrolled to date are from **diverse communities***

1. As of September 16, 2020

Primary Efficacy Endpoint: COVID-19 Disease Case Definition

To be considered a case of COVID-19 for the evaluation of the Primary Efficacy Endpoint, two criteria must be met:

1. The participant must have experienced:
   - At least **TWO** of the following systemic symptoms: fever (≥ 38°C), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s)

OR

   - At least **ONE** of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia

AND

2. The participant must have at least one NP swab, nasal swab or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR

Primary analysis set is seronegative and negative NP swab at baseline without major PD (Per Protocol)

An independent Data and Safety Monitoring Board (DSMB) ensures continuous data monitoring and enhances participant safety

Independent review of data

Deliberation on best course of action

Independent regulatory review

Independent DSMB → Oversight group → Moderna (sponsor) → FDA

NIH National Institute of Allergy and Infectious Diseases

BARDA

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- A **fully independent Data and Safety Monitoring Board** reviews unblinded data
- Established and supported by NIAID
- Experts in infectious disease, epidemiology, and ethics
- Monitors event rates; at pre-defined analyses unblinds and **DSMB makes a formal recommendation**

- Oversight group receives recommendation, which **includes NIAID and BARDA for transparency**
- Sponsor (Moderna) reviews the DSMB recommendation, and discusses plans with Oversight group (NIAID, BARDA)
- Sponsor determines whether to submit the data to the FDA for review

- FDA conducts independent review
- Seeks **external advisory committee** (VRBPAC) input

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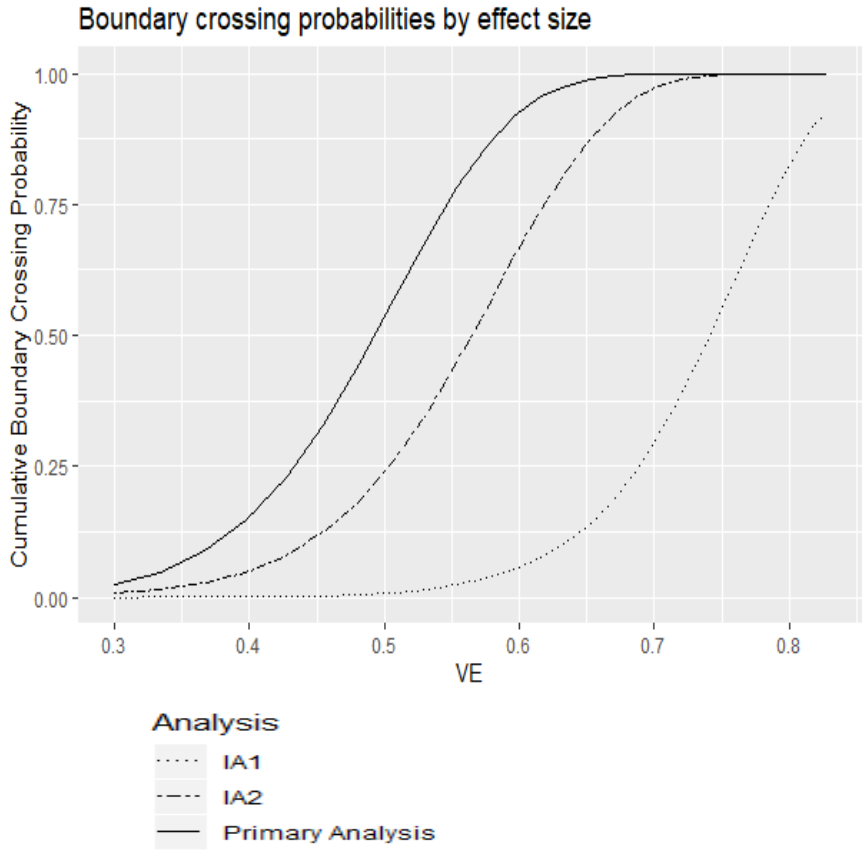
Overview of primary efficacy endpoint

Interim Boundaries Using O'Brien-Fleming Spending Function

	Approximate # of cases (% of total cases)	VE: Efficacy bound
Interim analysis #1	• 53 (35%)	• ~0.74
Interim analysis #2	• 106 (70%)	• ~0.57
Primary analysis	• 151 (100%)	• ~0.50

Boundary Crossing Probabilities by Effect Size



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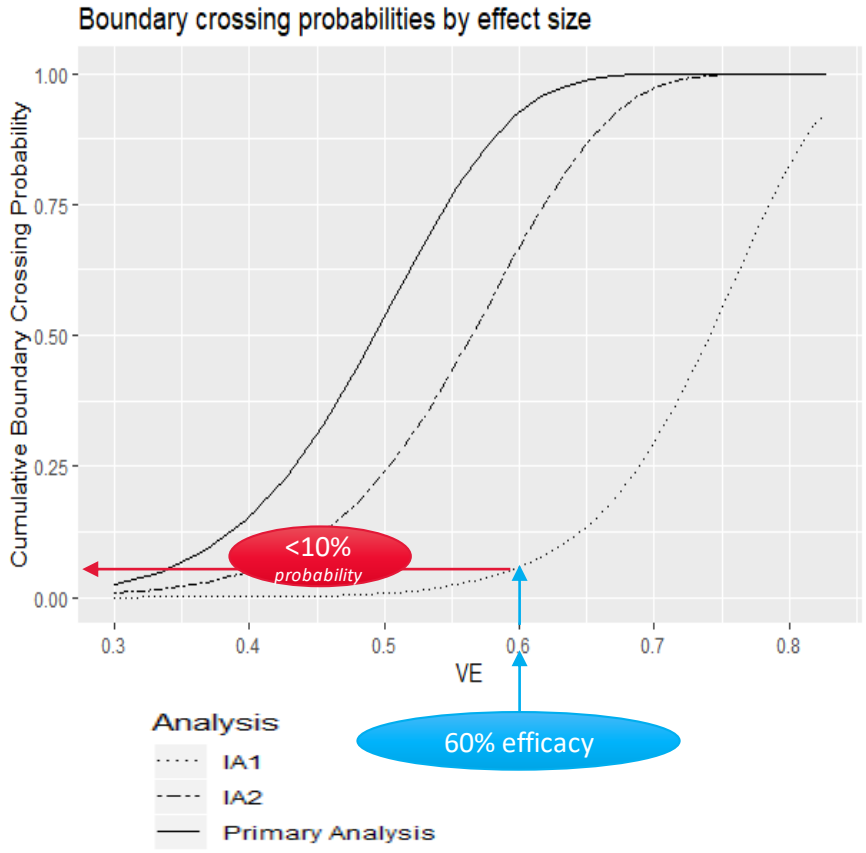

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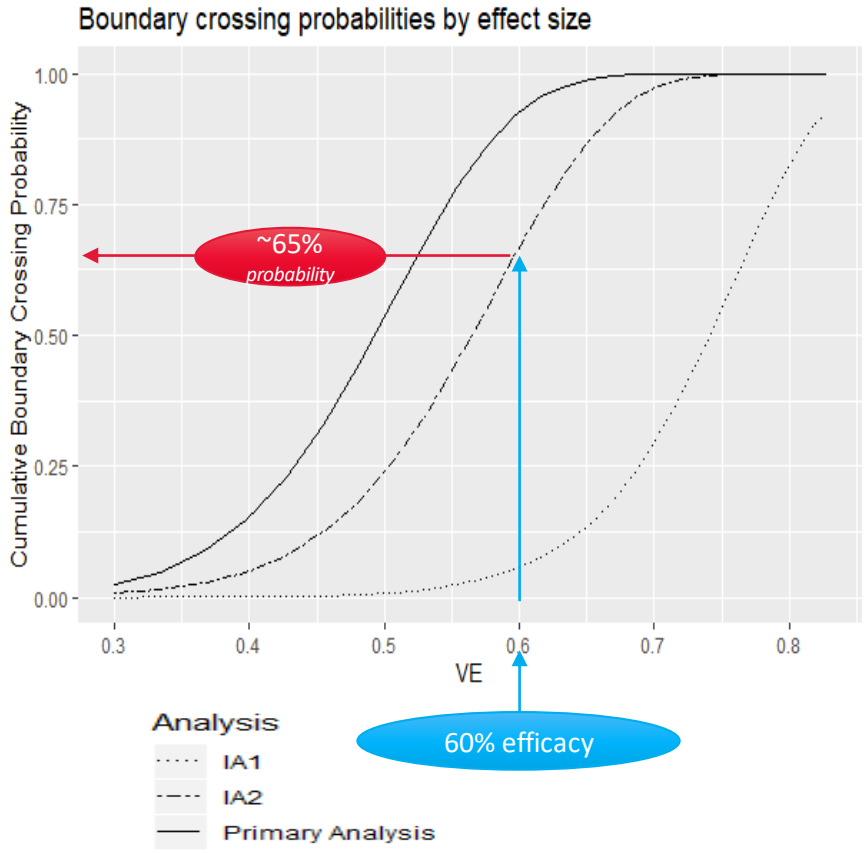

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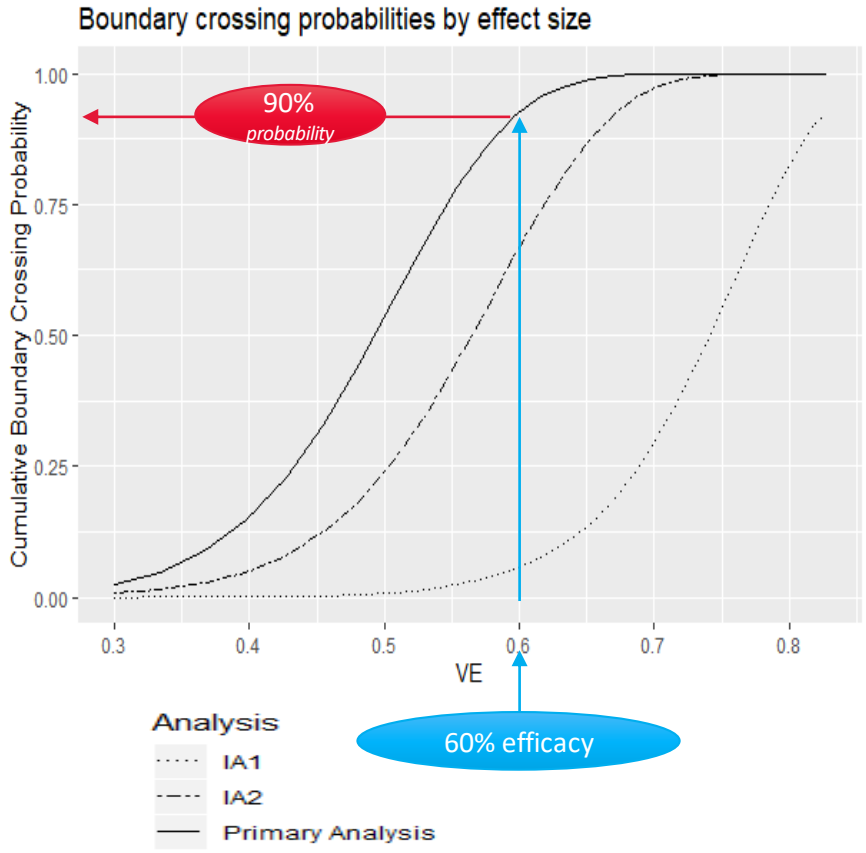

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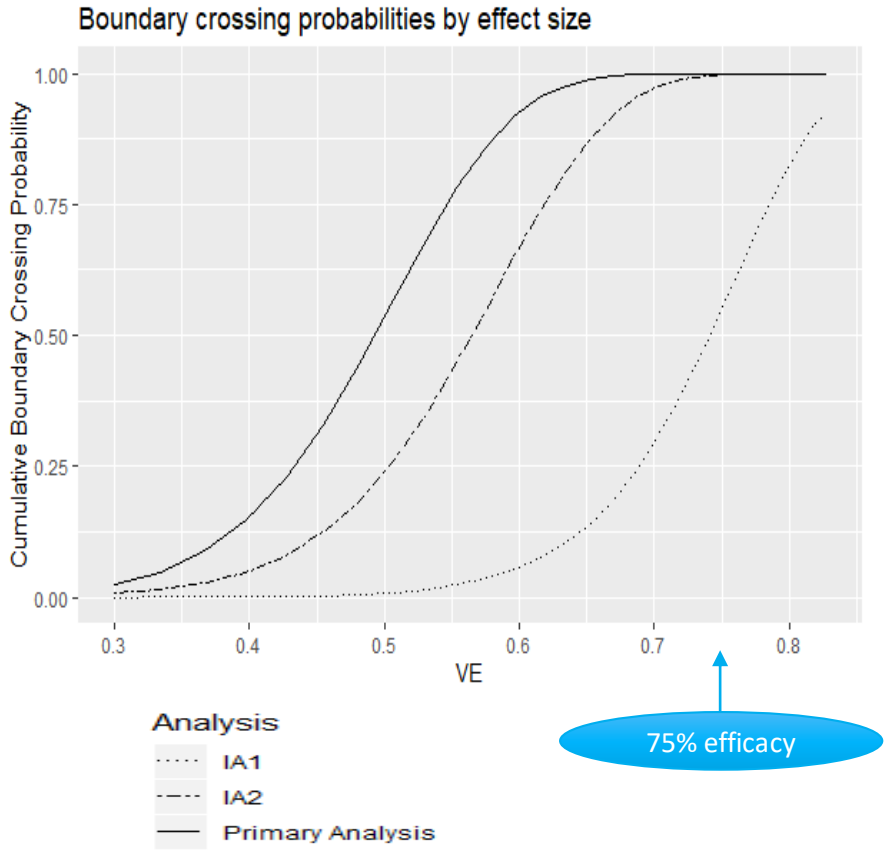

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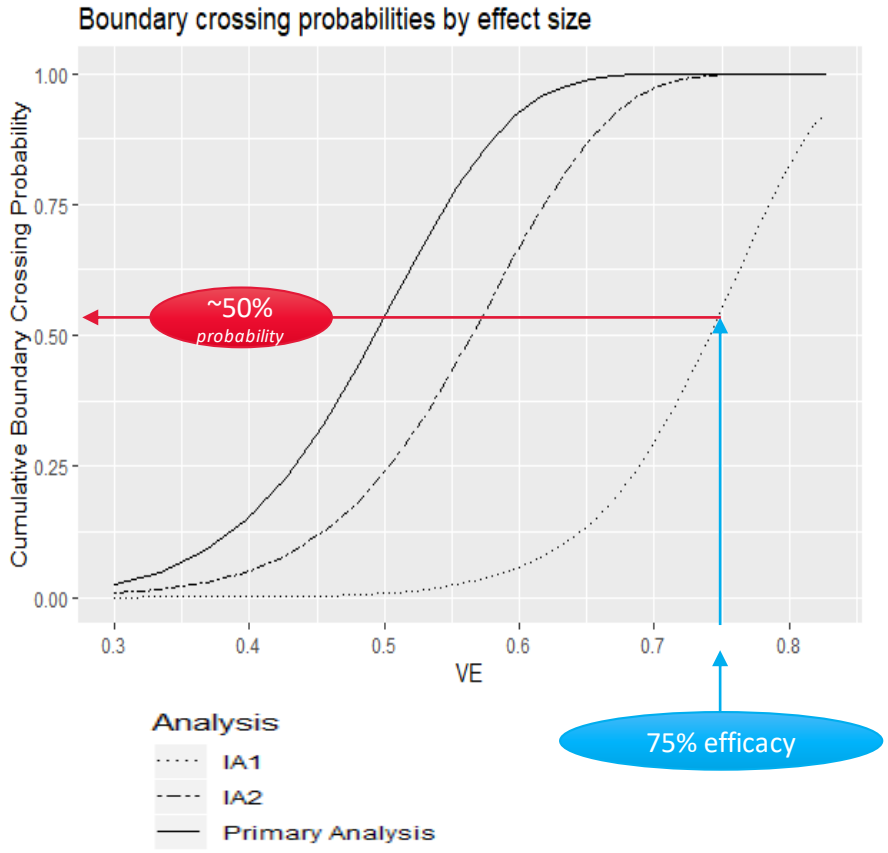

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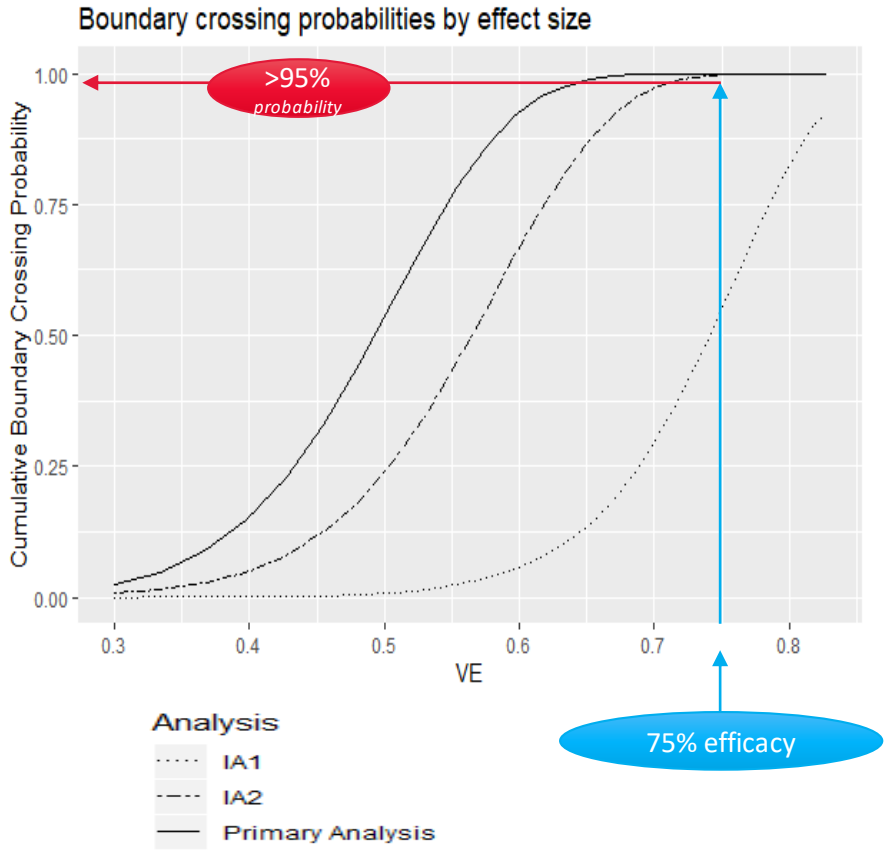

Juan Andres
Chief Technical Operations and Quality Officer

COVID-19 Manufacturing and Distribution Update

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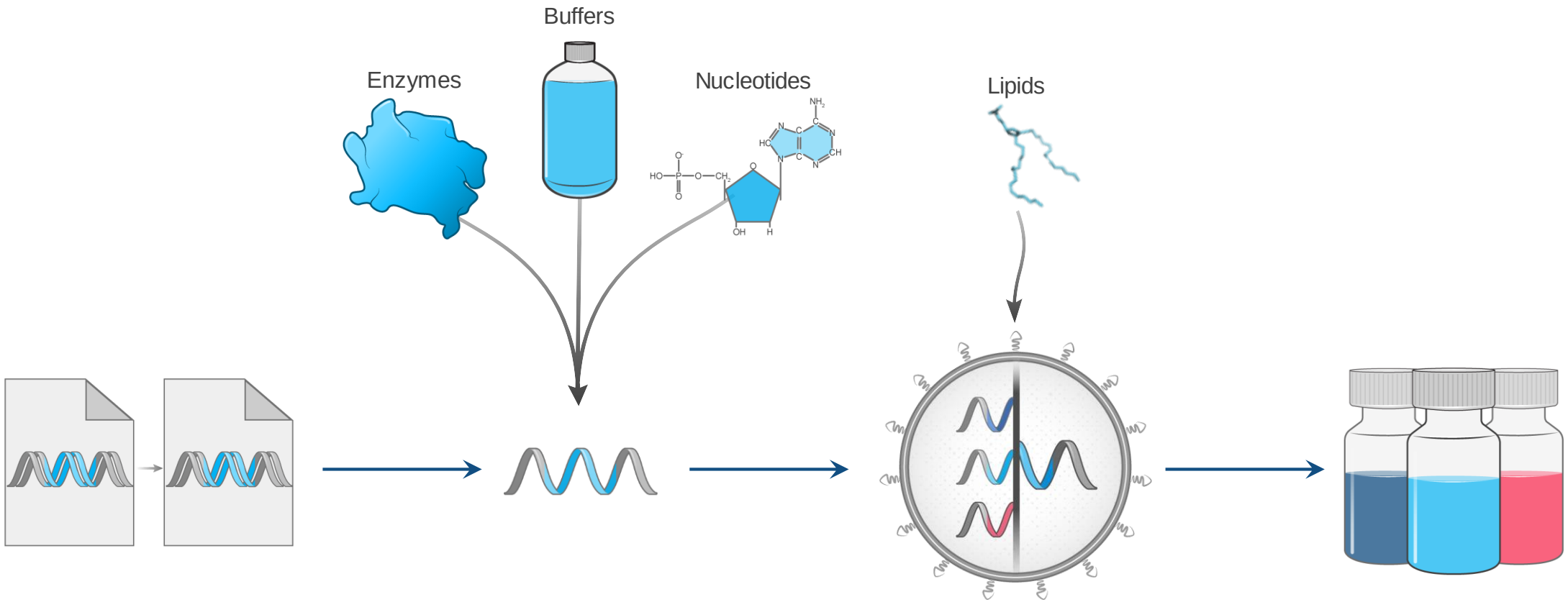
We are a platform…



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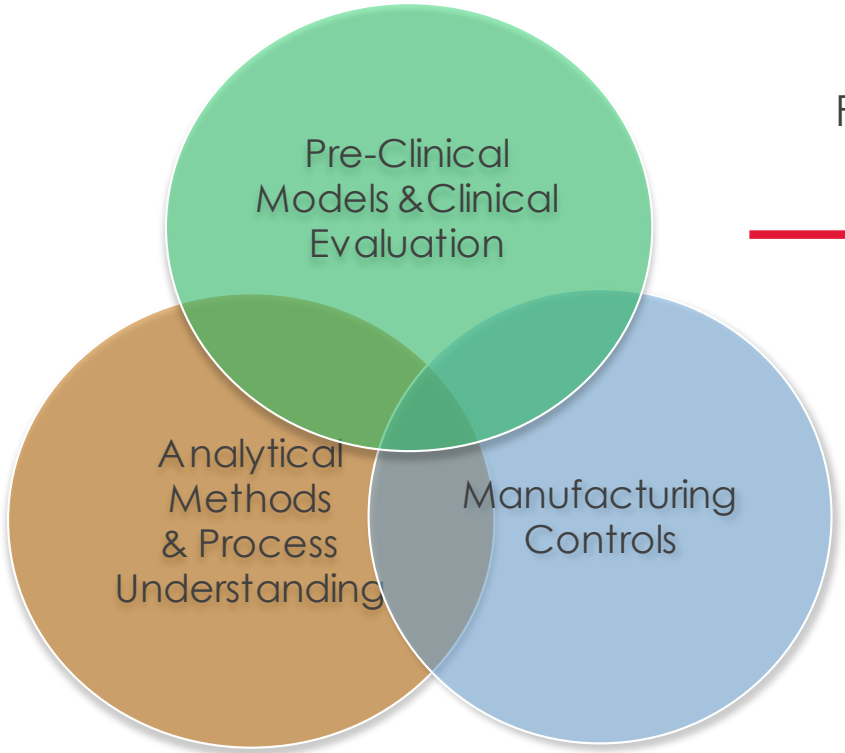
Platform investments resulted in improved pharmaceutical properties

Investments



Fundamental Product Understanding

Product Optimization

Pharmaceutical Properties

Shelf-life ✓
Storage Temperature ✓
Safety/Tolerability ✓
Potency ✓
Consistency of Manufacture ✓

10 Years of R&D Investment

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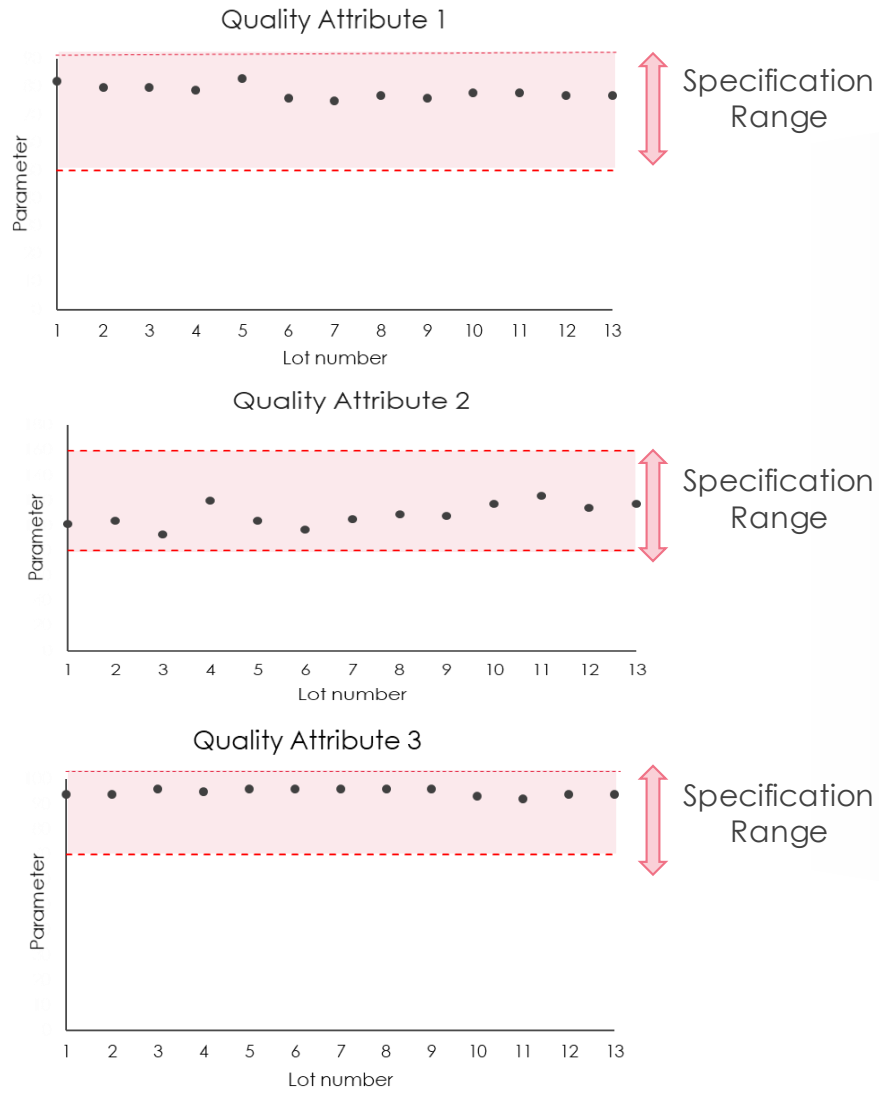
Pharmaceutical development has enabled consistent manufacture across multiple scales (mRNA-1273)



As shown by these important Drug Product Characteristics.

mRNA-1273 has demonstrated a high level of consistency across manufacturing scales (small, mid, large)

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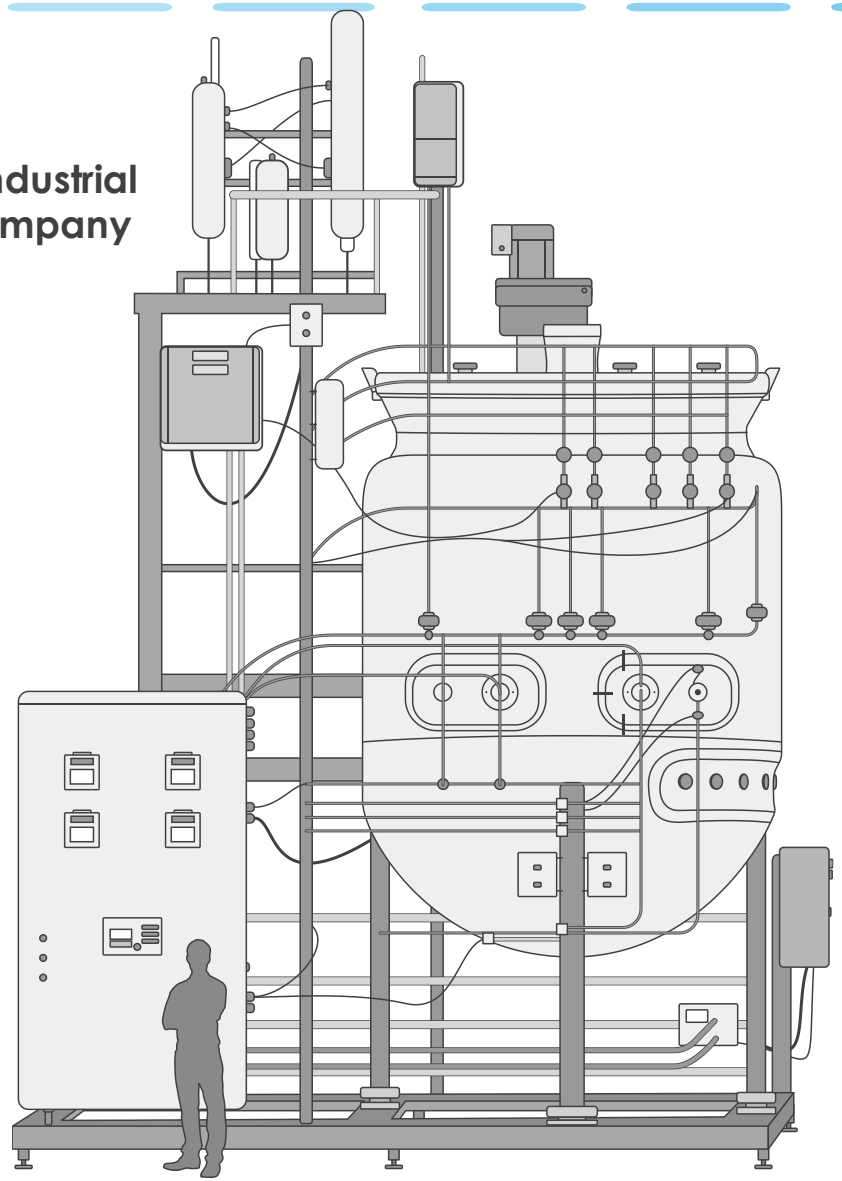
Integrated Manufacturing

Plasmid » mRNA » LNP » Fill/Finish » QC

Our manufacturing site is scalable and flexible

Standard Industrial Biotech Company



- Cell free manufacturing
- Non product dedicated plants
- Lower capex requirements
- Smaller footprint

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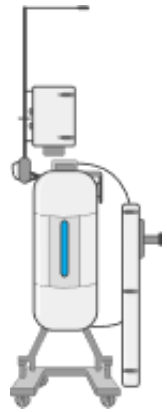
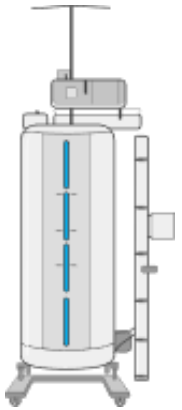
Clinical Manufacture

Commercial Manufacture





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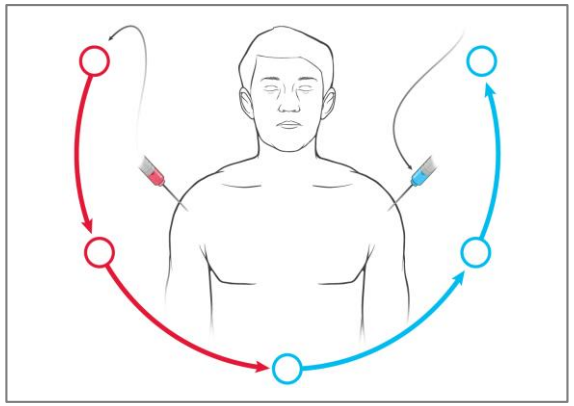
Now 4 manufacturing engines…

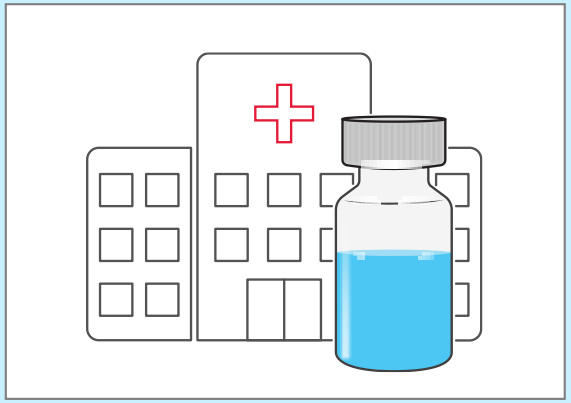
PRECLINICAL

PERSONALIZED VACCINE UNIT



CLINICAL

COMMERCIAL



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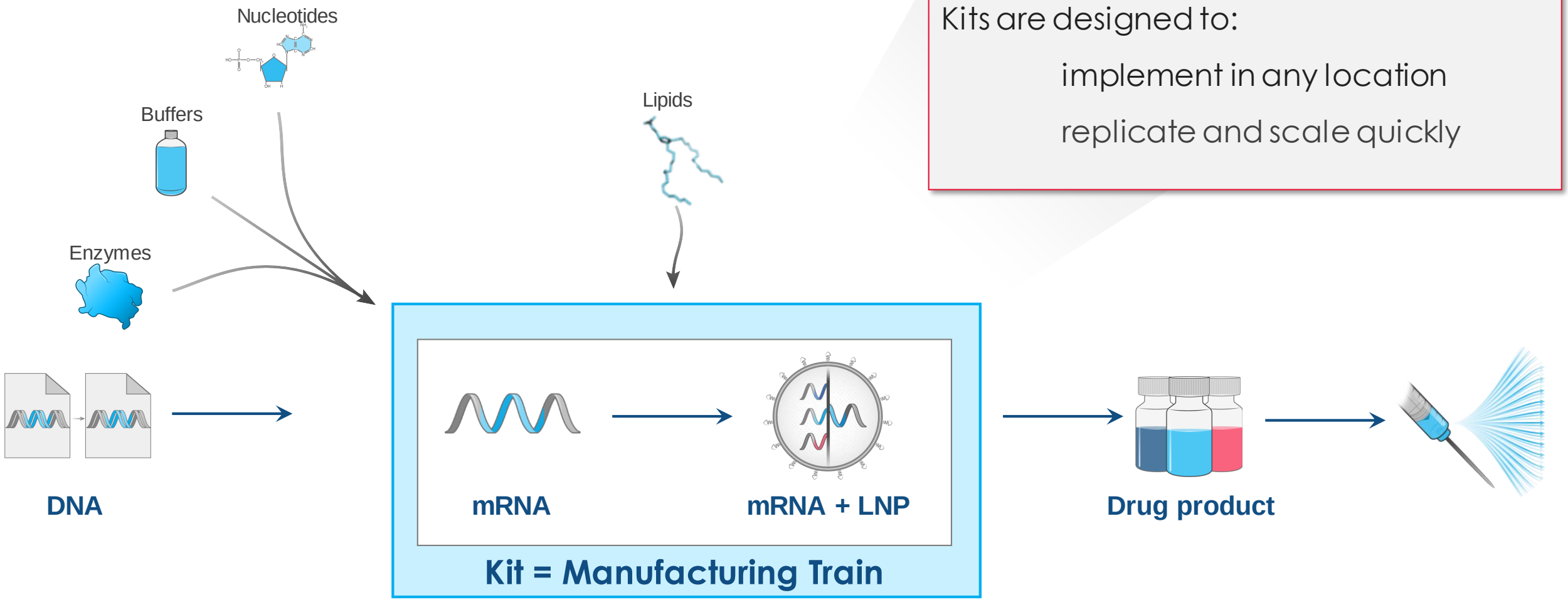
Modular manufacturing "kits" enable scalability and consistency

Kits are designed to:

implement in any location

replicate and scale quickly



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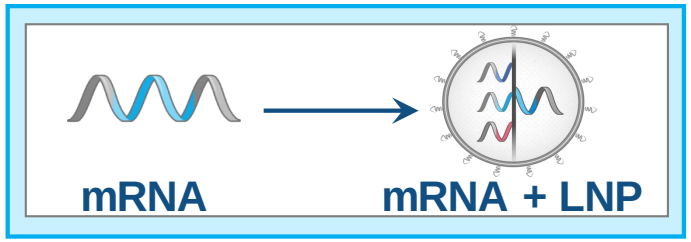
Moderna manufacturing collaborations

United States

moderna + Lonza (US)

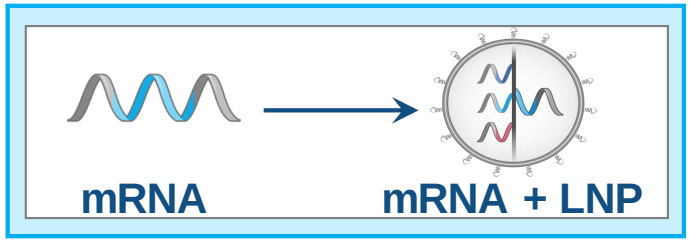
Pharma & Biotech

Catalent



Independent supply chains

Manufacturing scale up to supply 500 million to 1 billion doses per year



International

Lonza (Switzerland)

Pharma & Biotech

ROVI (Spain)

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Working with experienced partners

Digitally integrated site including Plasmid, Buffer Prep, QC and sterile filling capacity

US

US

State-of-the-art, barrier-isolated filling lines

Global Manufacturing with NH and VISP sites using the same digital platforms

US + International

International

Presence in 65 countries with diversified marketing portfolio of more than 40 products

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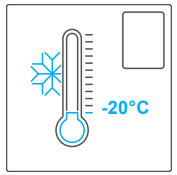
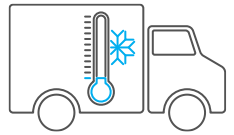
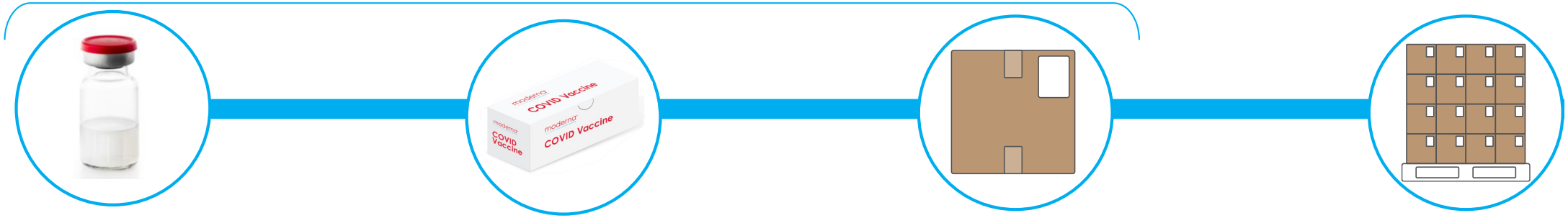
From manufacturing to distribution

Pre-conditioned -20°C shipper



-20°C Temp controlled truck for full loads





Multi-dose vial
(10 doses per vial)

10-vial cartons
(100 doses)

Full cases
(1,200 doses)

Full or partial pallets
(up to 230,400 doses)

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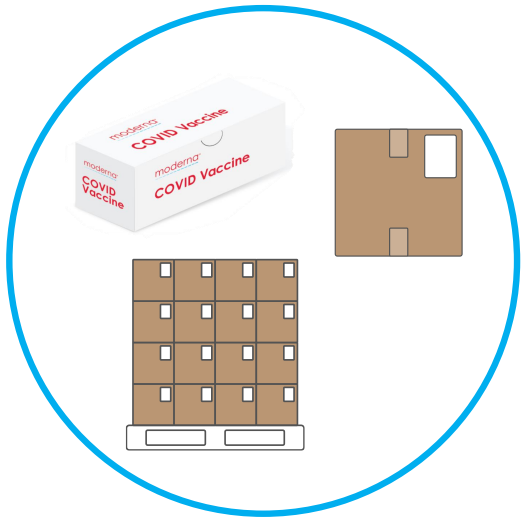
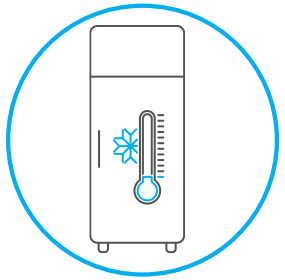
Distribution to any immunization locations using existing infrastructure



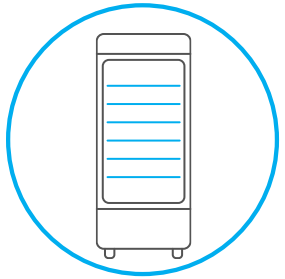
Ship any configuration using existing infrastructure

Storage Conditions*



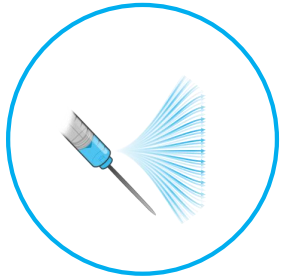
Freezer: -20°C/-4°F for 6 months

+



Fridge: 2-8°C/~36-46°F for up to 7 days

+



Room temperature: 12 hours post thaw

Flexible and adaptable supply chain

Uses standard existing vaccination infrastructure

No dilution required

*Shelf life is expected based on current data available; Product characteristics subject to regulatory review and approval

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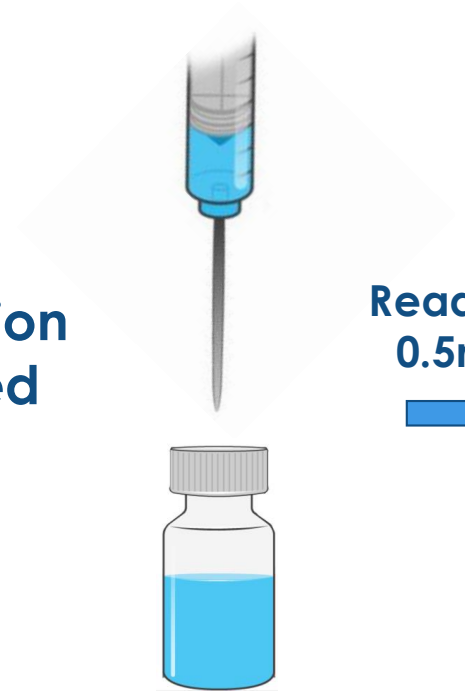
Standard 0.5 mL liquid administration provided in multi-dose vials

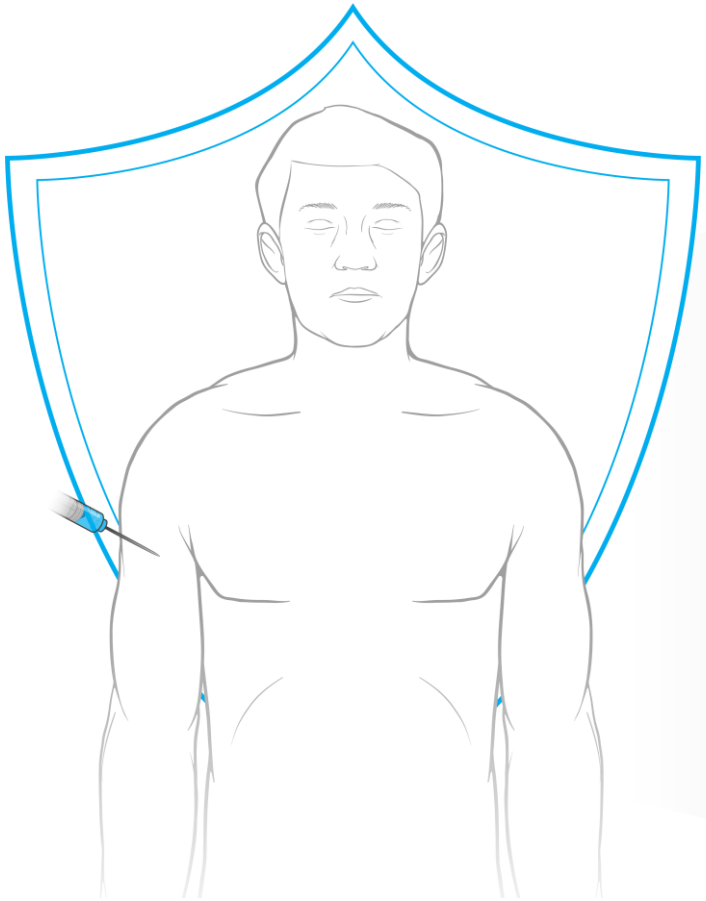
Standard needles & syringes



No dilution required

10 dose vials

Ready to use, draw 0.5mL and inject



Can be deployed in any setting:

Hospitals

Doctors' offices

Nursing homes

Immunization centers

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Moderna's vaccine franchise

Prophylactic Vaccines		Likely Commercial Drug Product Profile*
COVID-19 vaccine (mRNA-1273)		Liquid, Multi-Dose Vial (10 doses), -20°C storage ≥6 months shelf-life
CMV vaccine (mRNA-1647)		Lyophilized, Single-Dose (0.5mL), 5°C storage ≥ 18months shelf-life
Zika vaccine (mRNA-1893)		Lyophilized, Single-Dose (0.5mL), 5°C storage ≥ 18months shelf-life
hMPV/PIV3 vaccine (mRNA-1653)		Lyophilized, Single-Dose (0.5mL), 5°C storage ≥ 18months shelf-life

*Shelf life is expected based on current data available; Product characteristics subject to regulatory review and approval

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CMC BLA/Emergency Use Authorization (EUA) readiness

Experienced CMC leadership team

- Product development ✓
- BLA launch ✓
- Commercial operation ✓

Expert commercial manufacturing partner, i.e. Lonza with more than 45 BLA's/MAA's

Scale validation

- Commercial scale ✓
- Next scale in progress

Extensive operational experience with greater than 100 GMP batches produced over the last few years

Realtime and constructive dialogue with regulators

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We are on target

Kits able to produce 500 million to 1 billion doses with independent supply chains

Started manufacturing for market use

Scale up and documentation on track

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Thank you

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Stephen Hoge, M.D.
President

New Research & Development

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Moderna and Vertex Establish New Collaboration to Treat Cystic Fibrosis Using Gene Editing

Three-Year Collaboration Overview

- Aimed at the discovery and development of lipid nanoparticles (LNPs) and mRNAs for the delivery of gene-editing therapies for the treatment of cystic fibrosis (CF)
- Initially will focus on the discovery and optimization of novel LNPs and mRNAs that can deliver gene-editing therapies to cells in the lungs, enabling functional cystic fibrosis transmembrane conductance regulator (CFTR) protein to be produced

Collaboration details:

- Moderna will conduct research activities to discover and optimize novel LNPs and mRNAs for the delivery of gene-editing therapies to lung cells for the treatment of CF
- Vertex will be responsible for providing other components of the gene-editing therapies to be formulated into LNPs, as well as subsequent preclinical and clinical development and potential commercialization efforts
- Moderna will receive $75 million upfront and will be eligible to receive up to $380 million in development, regulatory and commercial milestones, plus tiered royalties on future gross profits on any products that result from the collaboration

VERTEX®

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Vertex collaborations to address Cystic Fibrosis

Two parallel approaches to addressing the unmet need

(Approximately 10% of Cystic Fibrosis patients are not addressable with a CFTR modulator)

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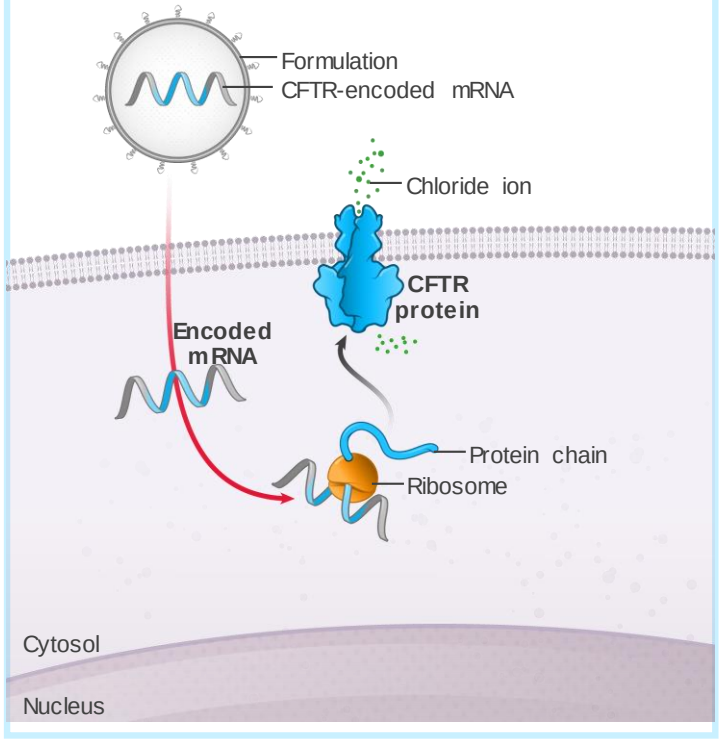
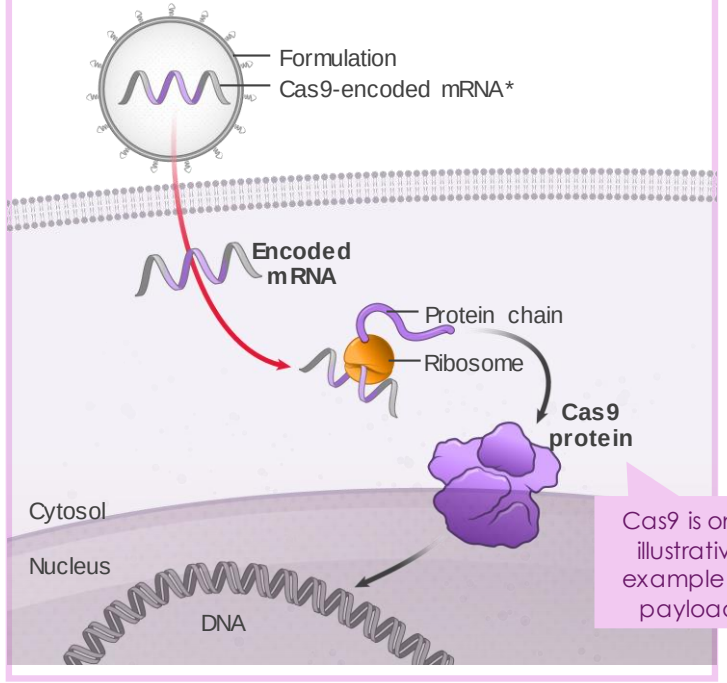
Existing Collaboration: mRNA for CFTR



New Collaboration: mRNA for gene therapy



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Moderna and Chiesi Group establish collaboration to discover and develop mRNA therapeutics for pulmonary arterial hypertension (PAH)

Collaboration Overview

- Announced a collaboration with Chiesi Farmaceutici S.p.A, an international research-focused healthcare group (Chiesi Group)
- Aimed at the discovery and development of mRNA therapeutics for the treatment of PAH, a rare disease with an incidence of 2-5 per million adults[1]
  - PAH is a progressive disorder characterized by high blood pressure in the arteries of the lungs with concomitant right heart failure[2]
  - There is an unmet medical need for novel treatments that could delay, or reverse, the disease progression in patients

Collaboration details:

- Moderna will lead discovery efforts and Chiesi Group will lead development and worldwide commercialization activities and will fund all expenses related to the collaboration
- Moderna will receive $25 million upfront and is eligible for more than $400 million in development, regulatory, and commercial milestones, as well as tiered double-digit royalties on net sales

Chiesi
People and ideas for innovation in healthcare

1. Lancet Resp Medicine, Vol. 4, issue 4, p. 306-322, 2016
2. "Understanding the Subpopulations of Pulmonary Hypertension," AMJC; https://www.ajmc.com/view/subpopulations-pulmonary-hypertension

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Stéphane Bancel
Chief Executive Officer

Conclusion

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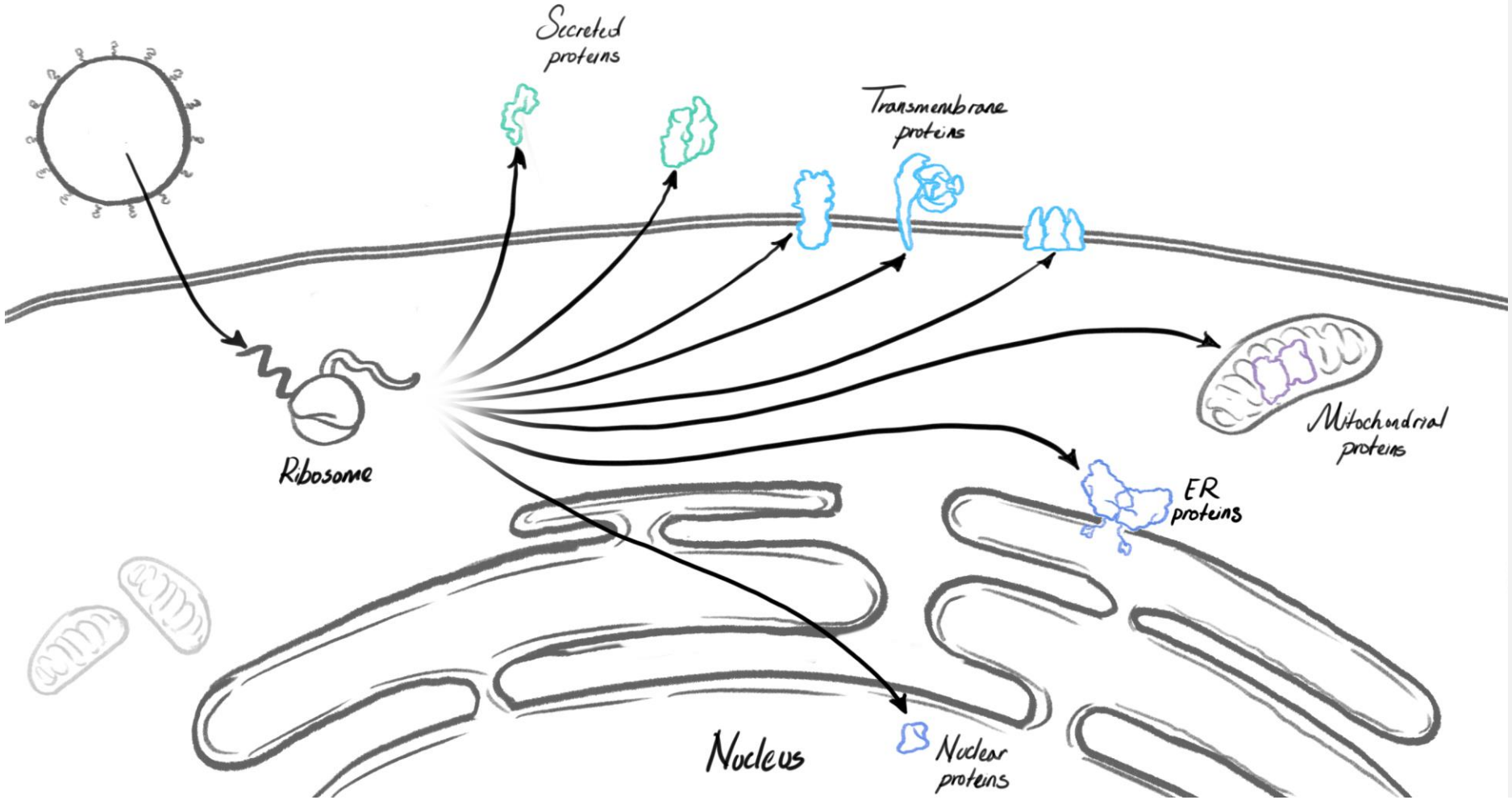
This was our vision: mRNA as a potential new class of medicines



1. Large product opportunity
2. Higher probability of technical success
3. Accelerated research and development timelines
4. Greater capital efficiency over time vs. recombinant technology

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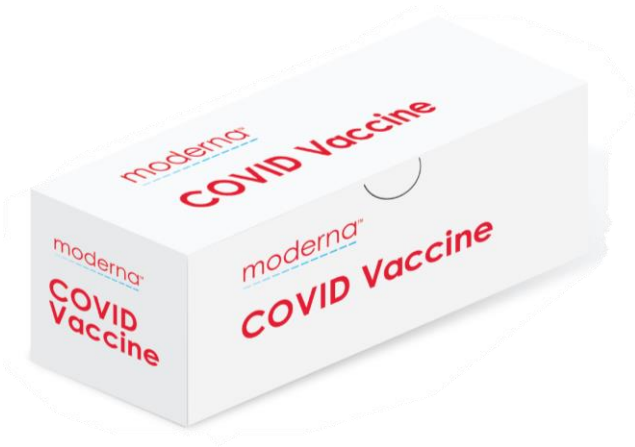
This is how far we have come



Product subject to regulatory review and approval

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Moderna has, and will continue, to expand in two dimensions

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Development pipeline

September 2020

		Preclinical *(incl. Open IND)*	Phase 1	Phase 2	Phase 3	Commercial
Core modalities	Prophylactic vaccines	EBV; *Pediatric RSV (Open IND)*	Flu (Pandemic); Adult RSV *(mRNA1172)*; Zika; Adult RSV *(mRNA1777)*; hMPV/PIV3	*Phase 2 preparations Zika*; CMV	COVID-19; *Phase 3 preparations CMV*	*Launch preparation COVID-19*
	Systemic secreted & cell surface therapeutics	Relaxin; PD-L1; IL-2	Chikungunya antibody			
	Cancer vaccines		KRAS	Personalized Cancer Vax		
Exploratory modalities	Intratumoral immuno-oncology		IL-12; OX40L/IL-23/IL-36γ	OX40L		
	Localized regenerative therapeutics			VEGF		
	Systemic intracellular therapeutics	MMA; PA *(open IND)*; PKU; GSD1a				

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Moderna in September 2020

Pipeline

Phase 3
COVID-19 vaccine

Phase 2
CMV vaccine
PCV, OX40L
VEGF

Phase 1
8 programs

12
Positive Phase 1 readouts: 8 vaccines, PCV, OX40L, VEGF, anti-Chikungunya antibody

Programs in development

7
Vaccines for major unmet needs

- COVID-19 Phase 3 ongoing
- CMV in Phase 2, Phase 3 preparation
- hMPV/PIV3 started Phase 1b age de-escalation study
- RSV and Zika in Phase 1
- Pediatric RSV open IND, EBV in preclinical

5
Immuno-Oncology

- PCV in Phase 2
- OX40L in Phase 2
- Triplet, IL-12, KRAS in Phase 1

4
Rare disease

- PA open IND
- MMA, PKU, GSD1a in preclinical

2
Autoimmune disease

- IL-2 and PD-L1 in preclinical

Foundations

>27,000
Healthy volunteers and patients enrolled

>1,100
Employees

A fully-integrated **GMP site** in Massachusetts

Lonza

Leading biopharma partners

MERCK
AstraZeneca
VERTEX

$3.1 bn
of cash and investments[1]

1. As of June 30, 2020; Cash and investments denotes cash, cash equivalents and investments; Excludes restricted cash of $12 mm at June 30, 2020

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A few closing thoughts

- Moderna could receive Emergency Use Authorization (EUA) for mRNA-1273 in 2020
- Moderna could receive a Biologics License Application (BLA) approval for mRNA-1273 in 2021
- mRNA-1273 could validate the entire vaccine portfolio because mRNA is an information molecule
- Phase 3 success in mRNA-1273 has implications for:
  - All vaccines in the development pipeline
  - All the vaccines in the research pipeline
  - All the vaccines that we are not yet working on in the labs
- With a manufacturing base plan of 500 million doses/year, potentially going up to 1 billion doses/year, Moderna could have a multi-billion dollar revenue line in 2021
- A strong balance sheet comprised of $3.1B of cash as of June 30, 2020 and multi-billion dollars of potential revenue in 2021 will allow Moderna to invest in R&D to scale the development pipeline and maximize what we could do for patients

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Our strategic priorities

1. Maximize value generation by mRNA-1273 between now and year-end 2021
2. Accelerate vaccine developments
3. Generate multiple human proof of concepts (POCs) in Oncology/Rare Disease/Auto-immune diseases
4. Continue to invest to expand the breadth of mRNA: mRNA technology, delivery technology, lung delivery, gene editing…

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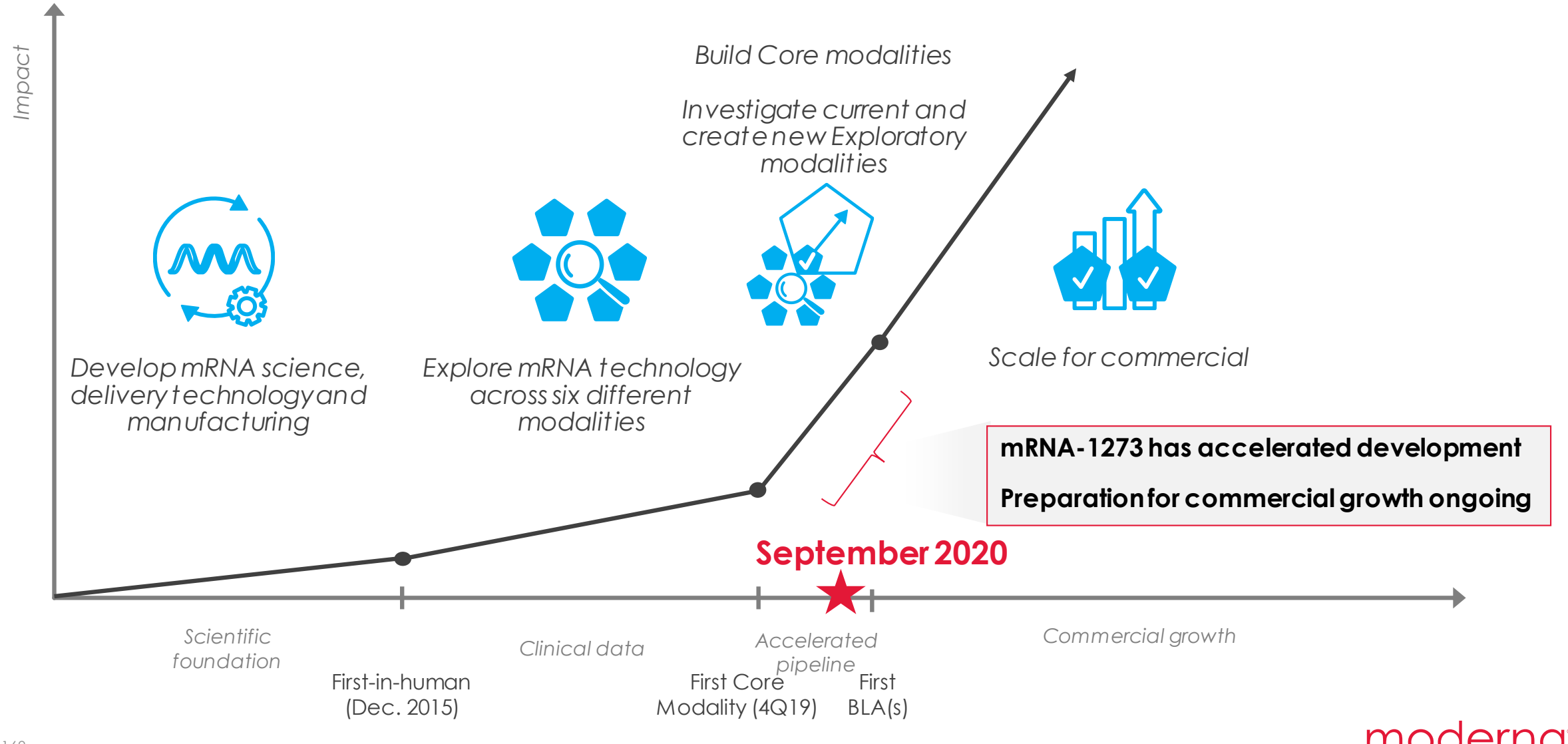
Moderna is close to an historic inflection point



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Q&A