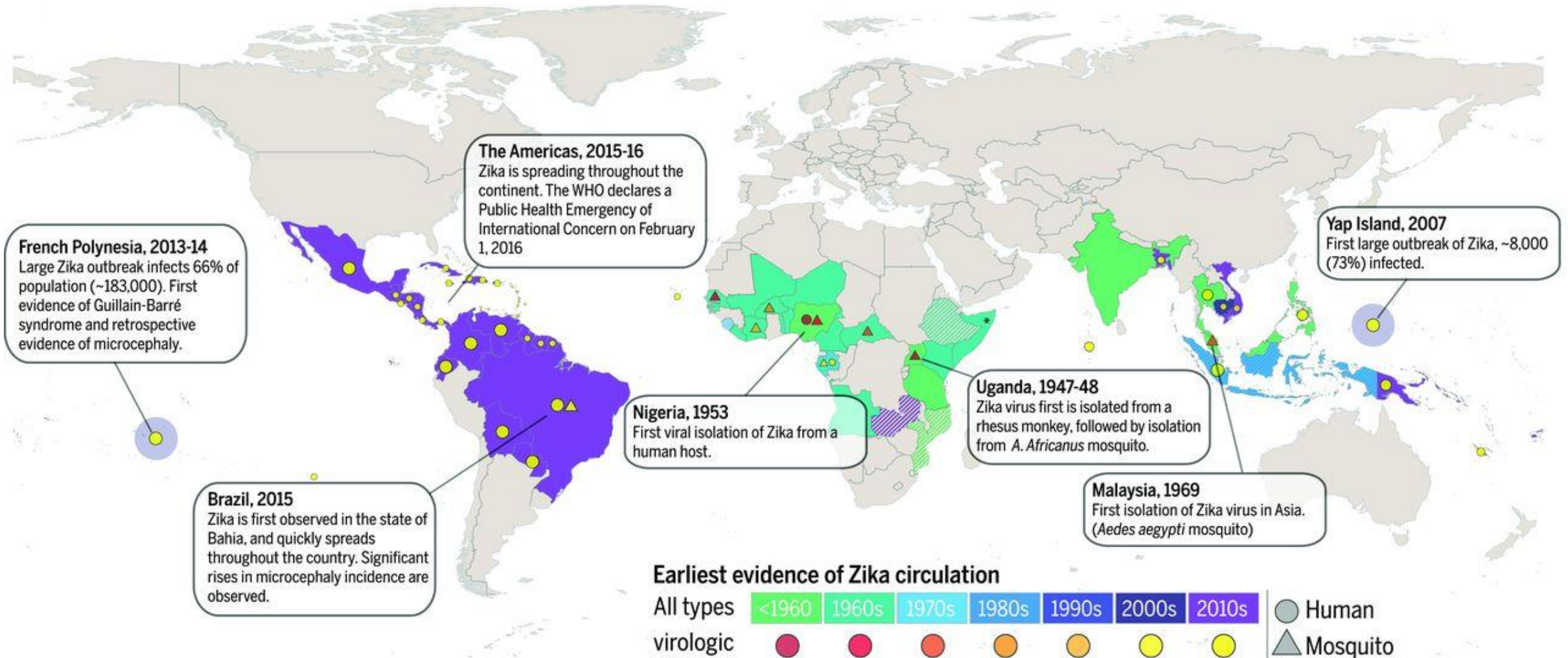


Program Pack

Zika (mRNA-1893)

Zika is an arbovirus and member of the Flaviviridae family



Zika virus overview

Zika virus (ZIKV): The primary source of ZIKV infection in humans is from bites of infected mosquitoes

- There have also been cases of sexual, perinatal, and suspected blood-transfusion transmission

In 2015 and 2016, large outbreaks of Zika virus occurred in the Americas

- Travel-associated cases in US states, widespread transmission in Puerto Rico and the US Virgin Islands, and limited local transmission in Florida and Texas
- **Disease burden:** Zika can be passed from a pregnant woman to her fetus
 - Increased risk of Guillain-Barré syndrome
 - Microcephaly was the first fetal abnormality to be recognized
 - Increasing evidence that ZIKV may be responsible for other fetal sequelae, such as intracranial calcifications, ventriculomegaly, ocular impairment, brainstem, hypoplasia, intrauterine growth restriction (IUGR), and fetal demise
- **Unmet need:** No approved Zikavaccine

Zika infection sequelae

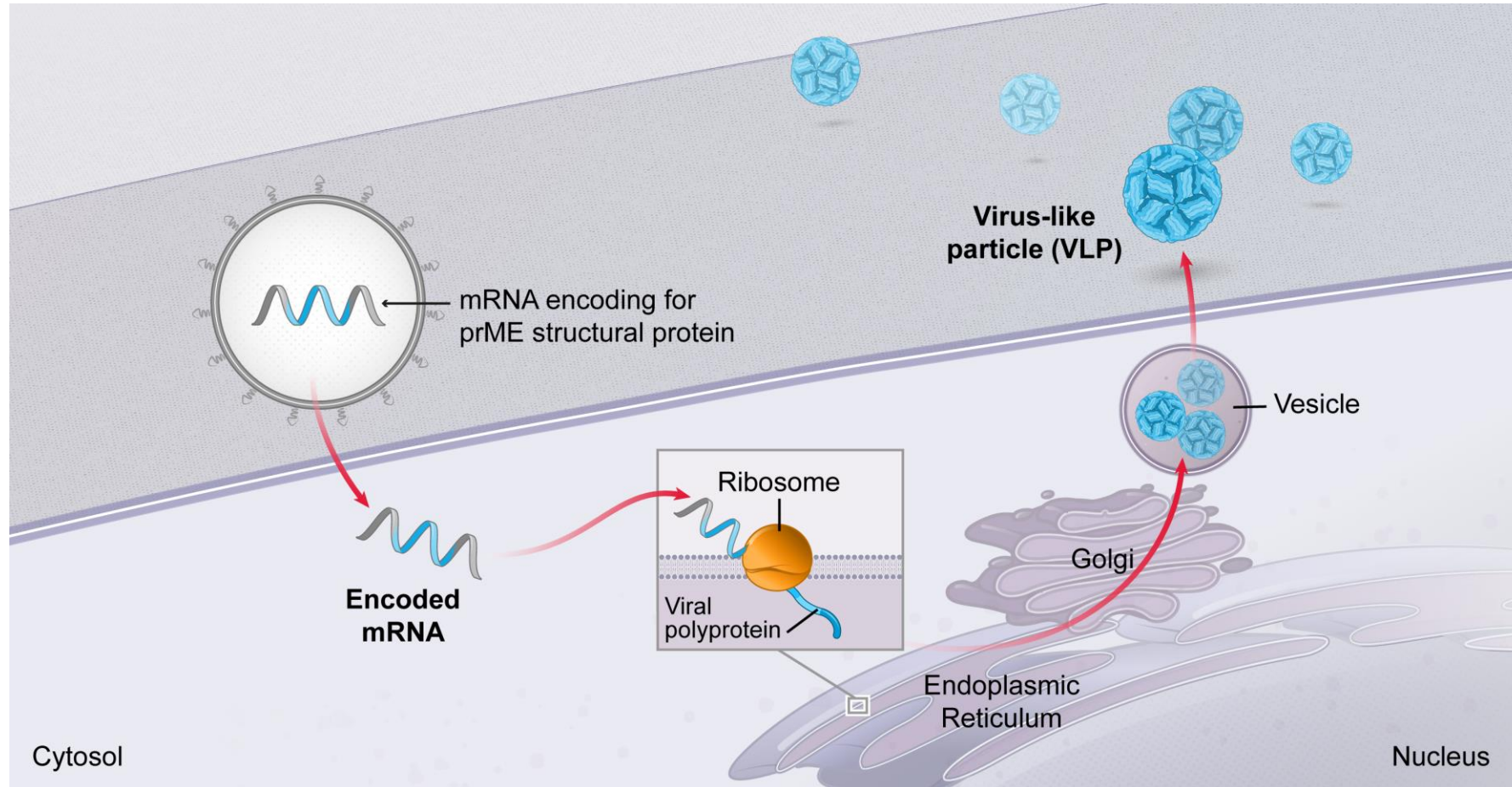
Neonatal period

Microcephaly
Other severe brain defects

Infancy, childhood, adulthood

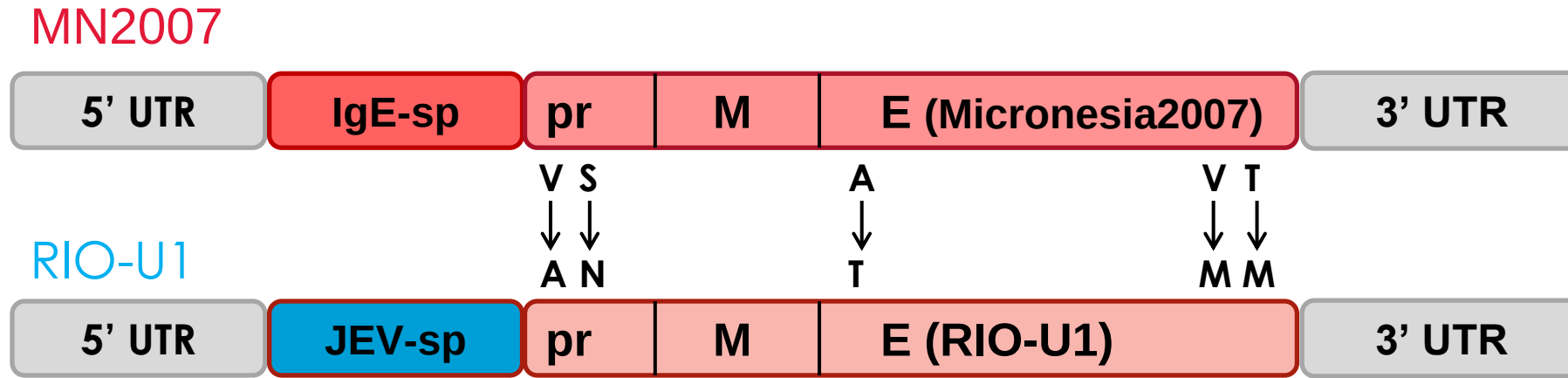
Fever
Rash
Headache
Joint pain
Red eyes
Muscle pain

Zika vaccine (mRNA-1893) : Expression of the prME can give rise to non-infectious, virus-like particles



Signal peptide and amino acid difference in the prME ORF

Between the mRNA-1325 (MN2007) and mRNA-1893 (RIO-U1) mRNA constructs



- Rio strain sequence was not available at the time of initial sequence selection
- Once additional sequences became available, the RIO-U1 strain was used for **RIO-U1** mRNA as it reflected the most current circulating strain
- Five amino acid differences in the pr and E sequences between **MN2007** and **RIO-U1**
- JEV-sp was selected for **RIO-U1** based upon the potential for improved processing of flavivirus VLPs¹

Zika vaccine (mRNA-1893): Phase 1 trial design

Key objective:

- To assess safety, reactogenicity, and immunogenicity of several dose levels of mRNA-1893 given with a 2-dose regimen at 28-day interval

Primary endpoint: Safety

Secondary endpoints:

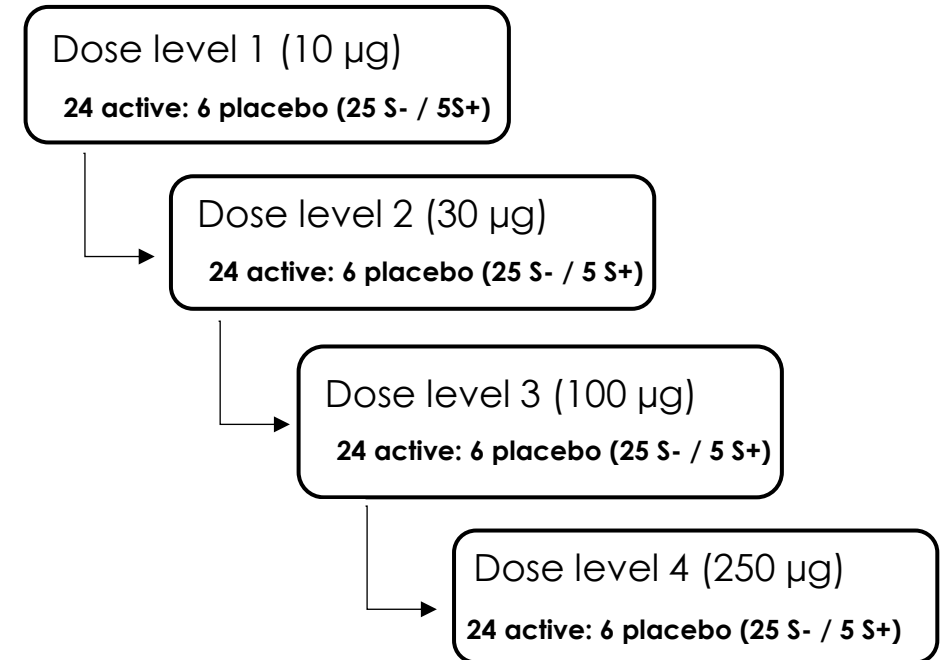
- ZIKV-specific neutralizing antibodies as measured by Plaque Reduction Neutralization Test at D29, D57, 7 months and 13 months post-last vaccine administration

Exploratory endpoints:

- ZIKV-specific neutralizing antibodies as measured by Microneutralization (MN), Reporter Virus Particle neutralization (RVP) at D29, D57, 7 Months and 13 Months



mRNA-1893-P101 Study Design



Zika vaccine (mRNA-1893): Safety profile

	Solicited ARs post-Dose 1 (solicited safety set)						Solicited ARs post-Dose 2 (solicited safety set)					
		Placebo N=24 N(%)	10µg N=24 N(%)	30µg N=24 N(%)	100µg N=24 N(%)	250µg N=24 N(%)		Placebo N=24 N(%)	10µg N=23 N(%)	30µg N=23 N(%)	100µg N=24 N(%)	250µg N=24 N(%)
Local reactions	Pain	1/23 (4.3%) —	12/24 (50%) —	12/23 (52.2%) —	17/24 (70.8) —	14/24 (58.3) —	Pain	2 /22 (9.1%) —	8/23 (34.8%) —	11/22 (50%) —	15/24 (62.5) 1 (4.2)	14/23 (60.9) 1 (4.3)
	Redness	—	—	—	1/24 (4.2) —	2/22 (9.1) —	Redness	—	—	1/20 (5.0) 1 (5.0)*	2/24 (8.3) —	2/23 (8.7) —
	Swelling	—	—	—	—	1/22 (4.5) —	Swelling	—	—	2/20 (10) 1 (5.0)*	1/24 (4.2) —	3/23 (13.0) —
Systemic reactions	Fever	—	1/24 (4.2) —	—	1/24 (4.2) —	—	Fever	1/23 (4.3) 1 (4.3)	1/23 (4.3) —	3/22 (13.6) —	7/24 (29.2) 2 (8.3)	11/23 (47.8) 3 (13.0)
	Headache	4/22 (18.2) —	7/24 (29.2) —	5/23 (21.7) 1 (4.3)*	3/24 (12.5) —	3/24 (12.5) 1 (4.2)	Headache	4/22 (18.2) —	5/23 (21.7) —	8/22 (36.4) —	9/24 (37.5) —	13/23 (56.5) 1 (4.3)
	Fatigue	3/22 (13.6) —	8/24 (33.3) —	5/23 (21.7) —	3/24 (12.5) —	4/24 (16.7) —	Fatigue	3/22 (13.6) —	6/23 (26.1) —	10/22 (45.5) —	10/24 (41.7) 2 (8.3)	13/23 (56.5) 1 (4.3)
	Myalgia	2/22 (9.1) —	5/24 (20.8) —	3/23 (13) —	1/24 (4.2) —	6/24 (25.0) —	Myalgia	1/22 (4.5) —	7/23 (30.4) —	4/22 (18.2) —	10/24 (41.7) 2 (8.3)	15/23 (65.2) 3 (13.0)
	Arthralgia	1/22 (4.5) —	2/24 (8.3) —	2/23 (8.7) —	—	—	Arthralgia	2/22 (9.1) —	4/23 (17.4) —	4/22 (18.2) —	9/24 (37.5) 2 (8.3)	7/23 (30.4) 3 (13.0)
	Nausea	—	4/24 (16.7) —	2/23 (8.7) —	3/24 (12.5) —	—	Nausea	2/22 (9.1) —	2/23 (8.7) —	1/22 (4.5) —	4/24 (16.7) —	5/23 (21.7) —
	Chills	—	1/24 (4.2) —	—	—	2/24 (8.3) —	Chills	3/22 (13.6) 1 (4.5)	1/23 (4.3) —	5/22 (22.7) —	11/24 (45.8) 2 (8.3)	14/23 (60.9) 2 (8.7)
	Rash	—	1/24 (4.2) —	—	—	—	Rash	—	—	—	1/24 (4.2)	—

N: number of participants in solicited safety set. The denominator of the rate is the number of participants who submitted any data for the respective event

Red text = grade 3 ARs

One participant experienced a Grade 4 Prothrombin Test increase at Day 29 with no clinical manifestations, this was considered not related to mRNA-1893 administration

* Updated data since Vaccines Day presentation on April 14, 2020

- Both the 100 and 250 µg dose levels were generally well tolerated
- There was a trend towards more observations of local erythema and swelling/induration at the injection site with higher dose levels, in particular after the 2nd vaccine administration
- There was a trend of more solicited systemic adverse events with the 250 µg, after the second administration

Zika vaccine (mRNA-1893) Phase 1 interim analysis: Immunogenicity in flavivirus baseline seronegative participants

Immunogenicity in Flavivirus Baseline Seronegative Participants (Per-Protocol Set)					
PRNT ₅₀					
	Placebo N=20	10µg N=20	30µg N=19*	100µg N=20	250µg N=20
Baseline GMT	8.0	9.5	8.0	8.0	8.0
GMT post-dose 1	8.0	8.5	14.4*	45.9	27.6
GMT post-dose 2	8.0	195.6	303.4	454.2	273.6
Seroconversion rate Post-dose 1; Post-dose 2	0%; 0%	5%; 94.4%	42.1%*; 100%	70%; 100%	65%; 98.7%
Immunogenicity in Flavivirus Baseline Seronegative Participants (Per-Protocol Set)					
MN					
	Placebo N=15	10µg N=20	30µg N=19	100µg N=20	250µg N=20
Baseline GMT	14.0	14.0	14.0	14.0	14.0
GMT post-dose 1	14.0	58.9	145.8*	354.7	440.4
GMT post-dose 2	14.0	1,195.3	1,478.0	1,459.3	1,415.0
Seroconversion rate Post-dose 1; Post-dose 2	0%; 0%	75%; 100%	89.5%*; 100%	95%; 100%	100%; 100%

Reporter Virus Particle neutralization (RVP) data are pending

Seroconversion is defined as a change in PRNT₅₀ from below the lower limit of quantification to a PRNT₅₀ equal to or above LLOQ, or a multiplication by at least 4 in subjects with pre-existing PRNT₅₀ titers; Seroconversion is defined as a change in MN from below the lower limit of quantification to a MN equal to or above LLOQ, or a multiplication by at least 4 in subjects with pre-existing MN titers.

* Updated data since Vaccines Day presentation on April 14, 2020

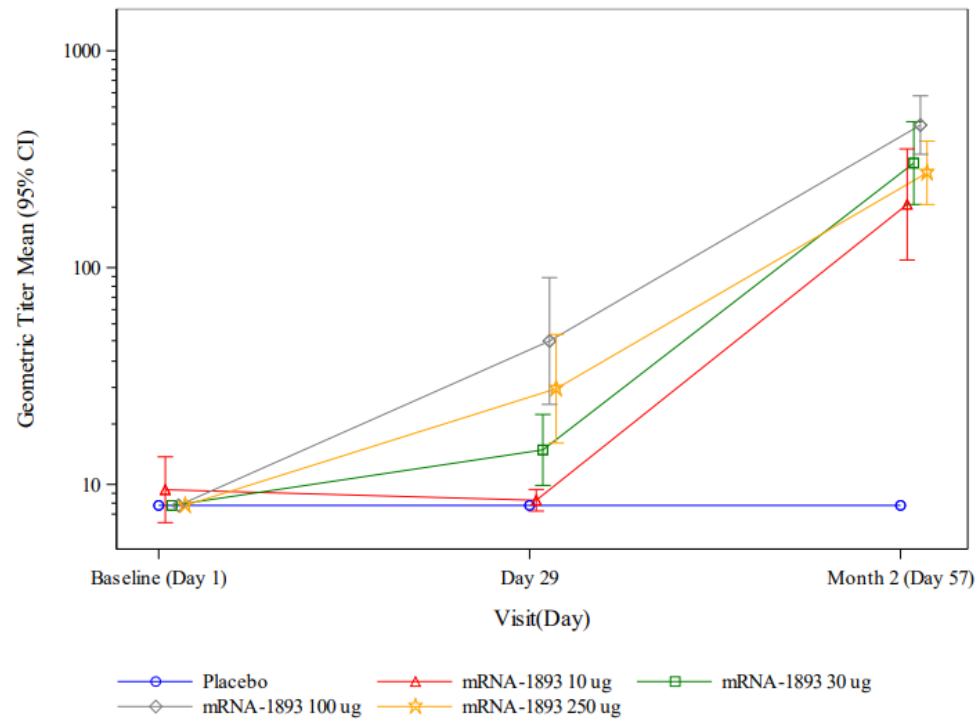
Zika vaccine (mRNA-1893) Phase 1 interim analysis: Immunogenicity in flavivirus baseline seropositive participants

Immunogenicity in Flavivirus Baseline Seropositive Participants (Per-Protocol set)					
PRNT ₅₀					
	Placebo N=4	10µg N=4	30µg N=4	100µg N=4	250µg N=4
Baseline GMT	18.3	41.5	12.3	16.1	19.4
GMT post-dose 1	17.8	147.9	88.1	130.6	38.2
GMT post-dose 2	18.6	224.1	150.9	190.5	100.9
Seroconversion rate Post-dose 1; Post-dose 2	0%; 0%	50%; 50%	75%; 75%	100%; 100%	50%; 75%
Immunogenicity in Flavivirus Baseline Seropositive Participants (Per-Protocol set)					
MN					
	Placebo N=4	10µg N=4	30µg N=4	100µg N=4	250µg N=4
Baseline GMT	31.7	54.0	39.4	40.3	44.9
GMT post-dose 1	31.9	375.0	226.7	1055.9	442.8
GMT post-dose 2	33.8	645.9	578.5	1295.0	389.3
Seroconversion rate Post-dose 1; Post-dose 2	0%; 0%	100%; 75%	75%; 75%	75%; 75%	75%; 75%

Seroconversion is defined as a change in PRNT₅₀ from below the lower limit of quantification to a PRNT₅₀ equal to or above LLOQ, or a multiplication by at least 4 in subjects with pre-existing PRNT₅₀ titers; Seroconversion is defined as a change in MN from below the lower limit of quantification to a MN equal to or above LLOQ, or a multiplication by at least 4 in subjects with pre-existing MN titers.

Zika vaccine (mRNA-1893) Phase 1 interim analysis: Immunogenicity (PRNT₅₀) at Day 57 by baseline flavivirus serostatus (per-protocol set)

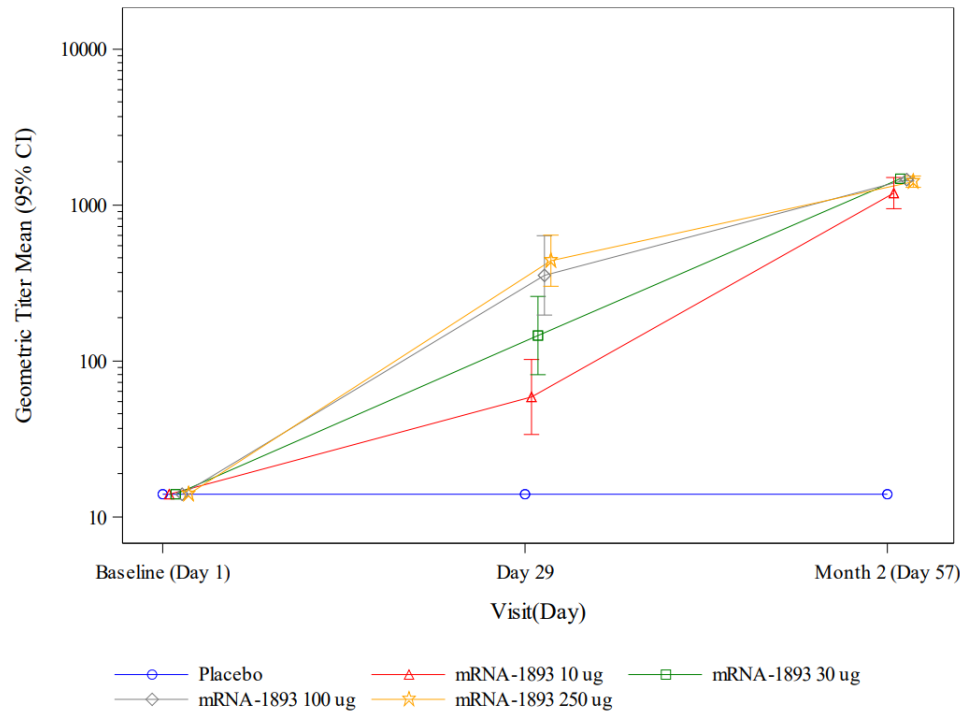
Flavivirus Baseline Seronegative Participants



- In seronegative participants, there was a clear advantage of a second vaccine administration in terms of ZIKV-specific neutralizing antibody response
- In seronegative participants, a dose response was observed after first vaccine administration
- In seropositive participants, mRNA-1893 was able to mount a ZIKV-specific neutralizing antibody response, compatible with a specific booster response

Zika vaccine (mRNA-1893) Phase 1 interim analysis: Immunogenicity (MN) at Day 57 by baseline flavivirus serostatus (per-protocol set)

Flavivirus Baseline Seronegative Participants



- MN data are consistent with the PRNT₅₀ data
- MN titers are higher compared to those reported by PRNT₅₀; consistent with the known differences between the assays

Zika vaccine (mRNA-1893) Phase 1 interim analysis: Safety and immunogenicity at Day 57 – conclusions

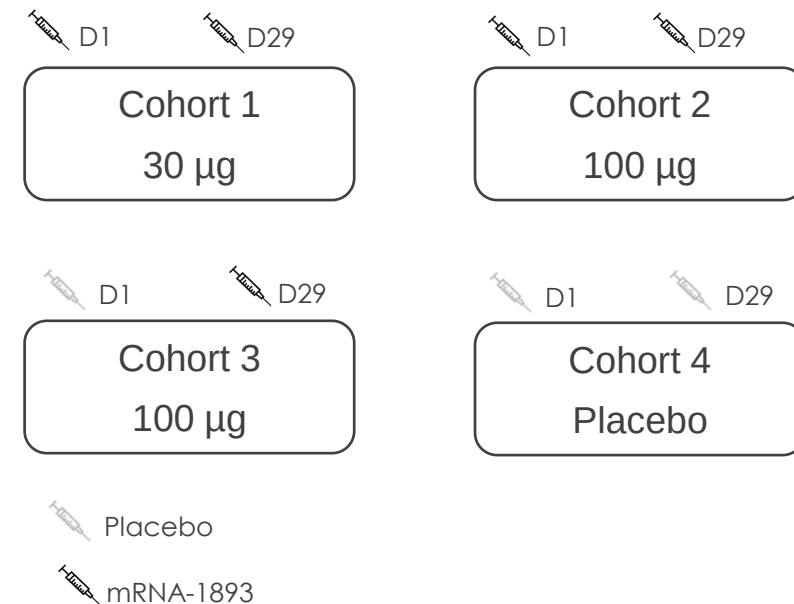
- Indication of a dose-related increase in solicited AEs that started to be observed with the 100 µg dose level became clear with the 250 µg dose level, in particular with the second dose administration
- All dose levels induce a strong neutralizing ZIKV-specific antibody response in both flavivirus infection naïve participants and in participants with pre-existing flavivirus antibodies as shown by the GMTs and the seroconversion rates
- The mRNA-1893 100 µg dose level induces a strong neutralizing ZIKV-specific antibody response in both flavivirus infection naïve participants and in participants with pre-existing flavivirus antibodies
- Notably, the 100 µg dose level is sufficient to seroconvert (PRNT) baseline flavivirus seronegative subjects following only a single vaccine administration. The trend was initially observed in the 30 µg dose level; however it is stronger in the 100 µg dose level
- When compared with the 100 µg dose level, the 250 µg dose level does not show a higher neutralizing antibody response (PRNT) in terms of GMTs at Day 29 (after one dose) or at Day 57 (after the second dose)
- Both MN and PRNT₅₀ assays provide equivalent guidance for data interpretation in terms of ZIKV-specific neutralizing immune response

Zika vaccine (mRNA-1893) Phase 2 in the United States & Puerto Rico

Phase 2 Study Overview (N=800)

- Randomized, placebo-controlled study
- Each cohort to have 100 baseline flavivirus seronegative participants and 100 baseline seropositive participants
- **Primary objectives:**
 - Evaluate the safety, tolerability and reactogenicity of mRNA-1893 compared to placebo
 - Evaluate the immunogenicity of 2 dose levels of mRNA-1893 (1-dose or 2-dose schedule) compared to placebo

Phase 2 Study Design



Medical and scientific presentations

ASTMH 2024 (Phase 2 results)

https://s29.q4cdn.com/435878511/files/doc_presentations/2024/Nov/16/mRNA1893_P201_Mainstudy_Poster_ASTMH-2024-Read-Only.pdf

Forward-looking statements

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