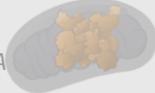


# Methylmalonic acidemia (MMA) (mRNA-3704)

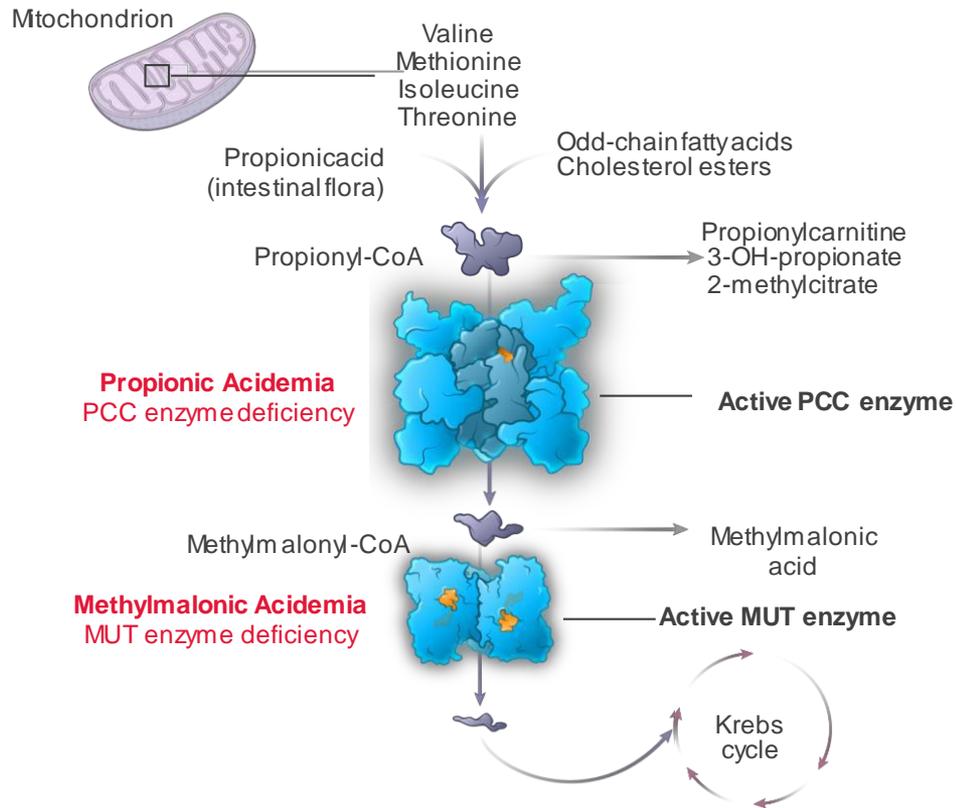
Last program update: May 7, 2020

Modality	ID #	Program Indication	Preclinical development	Phase 1	Phase 2	Phase 3 and commercial	Moderna rights
 Systemic intracellular therapeutics	mRNA-3704	MUT Methylmalonic acidemia, MMA					Worldwide
	mRNA-3927	PCCA/PCCB Propionic acidemia, PA					Worldwide
	mRNA-3283	PAH Phenylketonuria, PKU					Worldwide
	mRNA-3745	G6Pase Glycogen storage disease type 1a, GSD1a					Worldwide

**Phase 1/2 study of mRNA-3704 for Methylmalonic Acidemia paused due to COVID-19 pandemic**

# Organic acidemias

## Multiple candidates targeting same metabolic pathway



### MMA and PA

- Similar biology and disease pathology
- Shared KOLs 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\*

## mRNA advantages



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



Potential to treat during **acute** metabolic decompensations

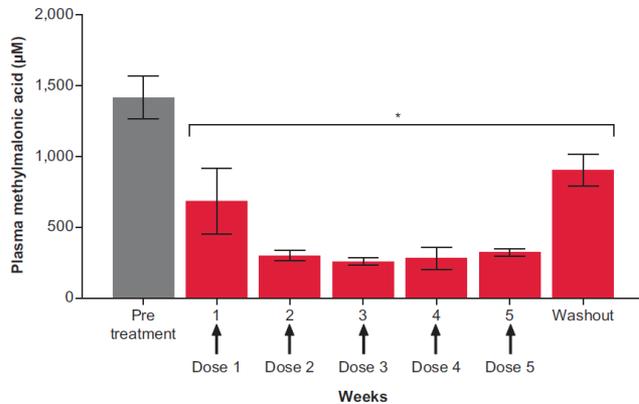
# Methylmalonic acidemia (MMA) (mRNA-3704)

## Preclinical data show restoration of enzyme activity

Species:  
Mouse

- Animals: mut<sup>0</sup>
- Dose: 0.2 mpk
- Dosing Schedule: weekly
- Injection Route: IV
- Sample Size: 6-7/group

Decrease in plasma methylmalonic acid with in 6-week study in mouse disease model



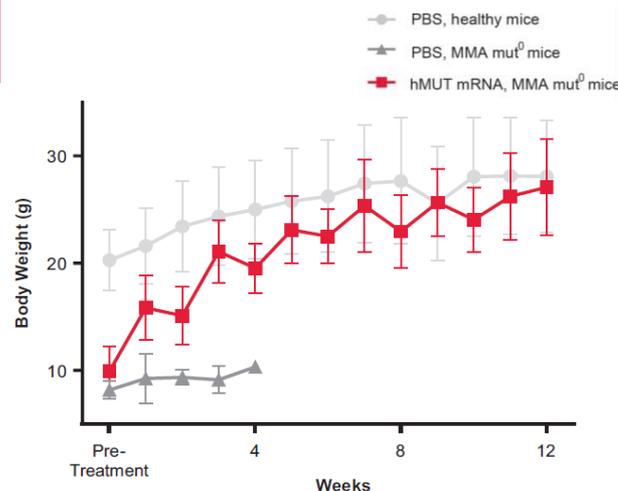
\*p<0.01 from paired t-test of post-treatment vs. pre-treatment levels

MMA mut<sup>0</sup> mice are Mut<sup>-/-</sup>; Tg<sup>INS-MCK-Mut</sup> mice

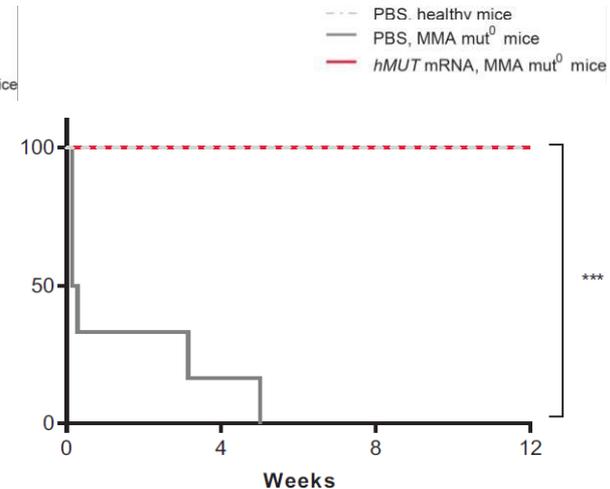
Species:  
Mouse

- Animals: mut<sup>0</sup>
- Dose: 0.5 mpk
- Dosing Schedule: every other week
- Injection Route: IV
- Sample Size: 6/group

Increase in body weight in a 12-week study in mouse disease model



Improved survival in a 12-week study in mouse disease model



\*\*\*p<0.001 hMUT mRNA v. PBS-injected MMA mut<sup>0</sup> mice from log-rank test

**We have observed pronounced improvement in survival due to mRNA treatment in an MMA mouse model**

# Clinical development plan

## Combined natural history study, and two Phase 1/2 MAD studies in pediatric MMA and PA patients

### Global natural history study:

- Enrollment in the study has been completed for MMA and PA
- Identifying and correlating clinical and biomarker endpoints
- Global, multi-center, non-interventional study:
  - Patients confirmed with MMA due to MUT deficiency or PA
  - Up to 60 MMA patients and up to 60 PA patients in the US and Europe will be followed prospectively for 1-3 years
  - Retrospective data to be collected as available

### 2 Phase 1/2 clinical trials, for mRNA-3704 in MMA and mRNA-3927 in PA:

- Open-label, multi-center, dose escalation Phase 1/2 study (US and Europe)
- **Objectives**
  - Evaluate safety and tolerability
  - Characterize the pharmacodynamic response
  - Characterize the pharmacokinetic profile
  - Assess incidence of clinical events

***mRNA-3704 (MMA) and mRNA-3927 (PA) have both received FDA Fast Track designation, FDA orphan drug designation, FDA rare pediatric disease designation and EMA orphan drug designations***

# Methylmalonic acidemia (MMA) (mRNA-3704)

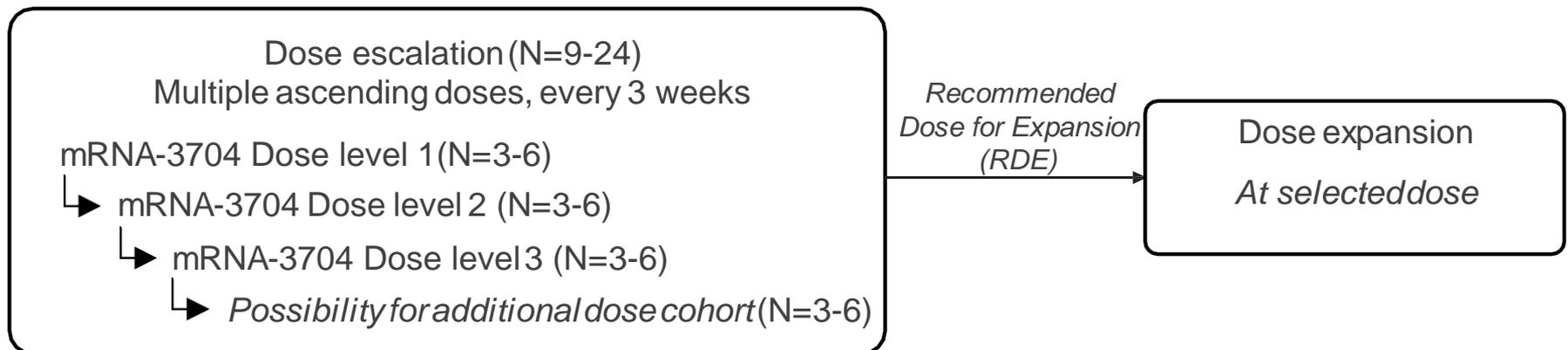
## Phase 1/2 design

### Study Objectives

- Evaluate the safety, pharmacodynamics (as assessed by changes in plasma methylmalonic acid), and pharmacokinetic profile of mRNA-3704 in patients with MMA
- Eligibility criteria: patients with isolated MMA due to MUT deficiency between 1 to 18 years of age with elevated plasma methylmalonic acid concentrations
- First dose level will enroll adolescents aged 8-18; once safety and tolerability determined we intend to enroll patients who are between the ages of 1 and 18 years old

### Due to COVID-19 pandemic, Phase 1/2 study new enrollment and new site initiation has been paused to ensure the safety of these pediatric patients and their caregivers

- No patients have been dosed to date. During the pause, the Company is implementing changes that the Company believes will help to accelerate clinical development.



# Forward-looking statements

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This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended including, but not limited to, statements concerning potential development candidate applications, development candidate activities, preclinical and clinical studies, regulatory submissions and approvals, risk management and estimates and forward-looking projections with respect to Moderna or its anticipated future performance or events. 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, among others: preclinical and clinical development is lengthy and uncertain, especially for a new category of medicines such as mRNA, and therefore Moderna’s preclinical programs or development candidates may be delayed, terminated, or may never advance to or in the clinic; no mRNA drug has been approved in this new potential category of medicines, 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 category of medicines; and 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](http://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 hereof.