# Glycogen storage disease type 1a (GSD1a) (mRNA-3745)

Last program update: August 5, 2020

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

*mRNA-3745 nominated as fourth systemic intracellular therapeutics DC*
Glycogen storage disease type 1a (GSD1a) overview

**New intracellular therapeutics DC – mRNA-3745**

- **GSD1a** is a rare inherited metabolic disease resulting from a deficiency in the metabolism of glucose, due to mutations within the enzyme glucose 6-phosphatase, G6Pase.

- **Disease burden:** Life-threatening hypoglycemia, long-term liver & kidney damage.

- **Target population:** Incidence of ~1:100k live births —2,500 patients in US¹, and >4,000 patients in the EU¹

- **Standard of care:**
  - Strict diet control
  - Frequent consumption of uncooked cornstarch to improve hypoglycemia

**Moderna concept:** IV-administered mRNA encoding G6Pase enzyme to restore deficient or defective intracellular enzyme activity

¹. Based on estimated incidence of 1:100,000
Glycogen storage disease type 1a (GSD1a) overview

Defect in G6PC gene disrupts glucose metabolism pathways

- Missing or defective G6Pase leads to:
  - Hypoglycemia
  - Lactic acidemia
  - Hyperlipidemia

- Metabolite buildup associated with hepatomegaly, hepatocellular adenomas, and higher risk of liver cancer

- Restoring G6Pase activity should increase blood glucose levels, decrease uric acid, lactic acid, triglyceride levels
Glycogen storage disease type 1a (GSD1a) (mRNA-3745)
mRNA-encoded enzyme localized to endoplasmic reticulum
Glycogen storage disease type 1a (GSD1a) (mRNA-3745)

Preclinical data – restoration of enzymatic activity

**Study Design**

**Species:** Mouse

- Animals: Liver-Specific G6PC Knockout (L.G6PC -/-)
- Dose: 0.2, 0.5, 1.0 mpk
- Dosing Schedule: single dose
- Injection Route: IV
- Sample Size: 5-8

**Study Design**

**Species:** Mouse

- Animals: Liver-Specific G6PC Knockout (L.G6PC -/-)
- Dose: 0.25 mpk
- Dosing Schedule: approx. every other week
- Injection Route: IV
- Sample Size: 7-9

**Serum biomarkers after single dose of G6Pase mRNA**

- Fasting glucose
- Total cholesterol

**Reduction in liver weight 24 hours after IV administration of G6Pase mRNA**

Not at: eGFP is a negative control. Asterisks based on one-way ANOVA test post-treatment vs. eGFP levels:

* p<0.05
** p<0.001

We have demonstrated preclinical proof-of-concept for G6Pase mRNA therapy in in vivo studies.
Forward-looking statements

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. 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.