## Personalized cancer vaccine (PCV) (mRNA-4157)

*Last program update: May 6, 2021*

<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>
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</thead>
<tbody>
<tr>
<td>Cancer vaccines</td>
<td>mRNA-4157</td>
<td>Personalized cancer Vaccine (PCV)</td>
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<td>50-50 global profit sharing with Merck</td>
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<tr>
<td>Cancer vaccines</td>
<td>mRNA-5671/ Merck V941</td>
<td>KRAS vaccine, CRC, NSCLC, pancreatic cancer</td>
<td></td>
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<td></td>
<td></td>
<td>50-50 global profit sharing with Merck</td>
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</tbody>
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PCV (mRNA-4157) Phase 1 and Phase 2 studies ongoing
Personalized cancer vaccine (mRNA-4157)
Designed to target an individual patient’s unique tumor mutations

- First patient dosed in November 2017
- Partnered with Merck (Keytruda combo)
Modernaria’s mRNA vaccines elicit T cells required for curative cancer therapy

Neoantigen concatemers in single mRNA

Ribosome

Neoantigen protein chain

Proteasome

Neoantigen

Nucleus

ER

Vesicle

Golgi

TCR

T cell

moderna
Personalized cancer vaccine (mRNA-4157)

Phase 1 study ongoing

Key Objectives

- Part A — To assess the safety and tolerability of mRNA-4157 monotherapy in subjects with resected solid tumors, including an apheresis cohort
- Parts B, C and D — To assess the safety, tolerability, and recommended Phase 2 dose of mRNA-4157 administered in combination with pembrolizumab
- Part D — To assess the immunogenicity of mRNA-4157 with pembrolizumab from apheresis samples in certain subjects

**Part A: Dose escalation (N = approx. 18)**
- mRNA-4157 0.04 mg
- mRNA-4157 0.13 mg
- mRNA-4157 0.39 mg
- mRNA-4157 1 mg

**Part B: Dose escalation (N = approx. 18)**
- mRNA-4157 0.04 mg
- mRNA-4157 0.13 mg
- mRNA-4157 0.39 mg
- mRNA-4157 1 mg

**Part C: PD1/PDL1i naïve (N = 34)**
- MSS-CRC (N = 17)
- HPV-neg HNSCC (N = 40)

**Part D: Adjuvant melanoma (N = 10)**

MSS-CRC: Microsatellite stable colorectal cancer
HNSCC: Head and neck squamous cell carcinoma
Personalized cancer vaccine (mRNA-4157)

Early Phase 1 data shows antigen-specific T cell response

First patient with melanoma treated at the 0.13 mg dose level has shown an induction of mutation-specific T cells after the 4th cycle (week 12), as measured by ELISPOT assay.

Data as of November 9, 2018
Personalized cancer vaccine (mRNA-4157)

Phase 1 human data for PCV

Clinical & regulatory update

- Enrolling Part C checkpoint naïve HNSCC patients in Phase 1 study
- Interim safety, tolerability and preliminary efficacy data presented for Part C checkpoint naïve HNSCC and MSS-CRC cohorts at SITC 2020

Representative clinical data (from SITC 2020 poster)\(^1,2\)

Safety:

- mRNA-4157 is well tolerated at all dose levels studied with no DLTs reported. The majority of AEs were low grade and reversible.

Activity:

- No clinical responses were noted in the 17 patients with MSS CRC. Most of these tumors were immunologically ‘cold’, with microenvironments that may be impermissible to inflamed T cells, as indicated by low GEP (including low PD-L1 transcript expression) and CYT score.
- Of the ten CPI-naïve HPV(-) HNSCC patients in Part C to date, the overall response rate (ORR) to mRNA-4157 and pembrolizumab by RECIST 1.1 is 50% (2CR, 3PR), DCR is 90% (2CR, 3PR, 4SD), and mPFS is 9.8 months, which compares favorably to the published pembrolizumab ORR and mPFS of 14.6% and 2.0 months respectively [2,3]. mDOR is not yet reached. Although 4 of the 5 clinical responses started prior to vaccine administration, the current 50% response rate, prolonged mPFS, and the overall trend of further tumor burden decrease over time is encouraging and warrants further expansion of the HPV(-) HNSCC cohort.
- A general trend towards favorable clinical response in HPV(-) HNSCC patients with more inflamed tumors as indicated by a higher GEP and CYT scores was observed, while TMB was similar in responding and non-responding HPV(-) HNSCC tumors.

\(^1\) Data cutoff as of Oct 01, 2020
\(^2\) https://investors.modernatx.com/static-files/a79f9ce0-026-4ea8-8a8b-2d9fdccc531
Ten out of seventeen MSS-CRC patients progressed rapidly within 6 weeks of mRNA-4157 vaccine administration. Only one patient completed all doses of vaccine and remains on study. Six HPV(-) HNSCC patients currently remain on study.

Data cutoff as of Oct 1, 2020
Part C: CPI naïve HPV(-) HNSCC patients receiving mRNA-4157+pembrolizumab

Spider plot of tumor burden (% change from baseline)

Figure 1-1: Four out of five responding patients achieved PR after 2 doses of pembrolizumab prior to the start of vaccine administration. Two PRs converted to CR after the addition of vaccine. Patient 109's tumor burden was decreasing but then started to progress until 2 doses of vaccine were given, and then subsequently achieved a PR. Patient 067 also had started to progress until after the 5th dose of vaccine, then ultimately had a discordant CR in the neck while progressing in the lung (vaccine was manufactured from the genetic sequencing of the dermal neck disease). Patient 117 progressed on monotherapy pembrolizumab until vaccine was started and tumor burden continues to decrease.
**Best overall response in CPI naïve HPV(-) HNSCC and MSS CRC patients receiving mRNA-4157 + pembrolizumab**

<table>
<thead>
<tr>
<th>Best overall response</th>
<th>HPV(-) HNSCC (n=10*)</th>
<th>MSS CRC (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Progressive Disease (PD)</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Overall response rate (ORR)</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>Disease control rate (DCR)</td>
<td>90%</td>
<td>6%</td>
</tr>
<tr>
<td>Median progression-free survival (mPFS)</td>
<td>9.8 months</td>
<td>2.7 months</td>
</tr>
<tr>
<td>Median duration of response (mDOR)</td>
<td>Not reached</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*4 additional patients started pembrolizumab dosing but progressed and came off study prior to the start of vaccine dosing.

Data cutoff as of Oct 01, 2020
Personalized cancer vaccine (mRNA-4157)

Phase 2 study ongoing

- Randomized Phase 2, PCV + pembrolizumab vs. pembrolizumab alone in resected melanoma at high risk of recurrence

Key Objectives
- Assess whether postoperative adjuvant therapy with mRNA-4157 and pembrolizumab improves recurrence free survival compared to pembrolizumab only in patients with complete resection of cutaneous melanoma at high risk of recurrence
- Primary endpoint: recurrence free survival at 12 months

![Diagram showing study design and patient flow](image-url)
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