Protocol Plain Language Summary

A clinical study of V940 plus pembrolizumab in people with high-risk melanoma (V940-001)

Protocol Title: A Phase 3, Randomized, Double-blind, Placebo- and Active-Comparator-Controlled Clinical study of Adjuvant V940 (mRNA-4157) Plus Pembrolizumab Versus Adjuvant Placebo Plus Pembrolizumab in Participants with High-risk Stage II-IV Melanoma (INTerpath-001)

Why is this study needed?

Researchers are looking for new ways to treat people with high-risk **melanoma. Melanoma** is a serious type of skin cancer. Most people with melanoma have surgery to remove it. After surgery, people who have a high chance (risk) of cancer returning (coming back) receive more treatment.

Researchers want to know if pembrolizumab and V940 (study treatment) can help prevent cancer from returning in people with high risk melanoma. Pembrolizumab is an immunotherapy, which is a treatment that helps the immune system fight cancer. V940 is designed to help a person's immune system attack their specific cancer.

The goal of this study is to learn if V940 with pembrolizumab, is better than receiving placebo with pembrolizumab at preventing the cancer from returning. A placebo looks like the study treatment but does not contain any active treatment. Using a placebo helps researchers better understand if the study treatment works.

Who will take part in this study?

About 1,089 people with high-risk melanoma will be in the study. They will be 18 years old and older and:

- Have not received treatment for melanoma other than surgery
- Do not currently have melanoma following surgery

What treatments are being given during the study?

People will be assigned by chance into the following groups:

- **V940** plus pembrolizumab
- Placebo plus pembrolizumab

V940 or placebo will be given as an injection (shot) into the muscle every 3 weeks for up to 9 doses. **Pembrolizumab** will be given through a needle into a vein as an infusion every 6 weeks for up to 9 infusions.

How is this study designed?

Two out of 3 people will receive the V940 plus pembrolizumab and 1 out of 3 people will receive placebo plus pembrolizumab. This means that twice as many people will get the V940 plus pembrolizumab than placebo plus pembrolizumab. Neither the people in the study nor the researchers will know what group they are assigned to (called a **double-blind study**). During the

study, people will give tumor, blood, and urine samples, have imaging tests and physical examinations, and answer sets of questions about their health. People may be in this study for up to 8 years.

What are the goals of this study and how will they be measured?

Main goal	How it will be measured
To learn if people who receive **V940** plus pembrolizumab have better **recurrence-free survival (RFS)** compared to people who receive placebo plus pembrolizumab.	**RFS** is the length of time from when the person starts the study until either the cancer comes back, or the cancer spreads, or death due to any cause.

Other goals	How they will be measured
To learn if people who receive **V940** plus pembrolizumab have better **distant metastasis-free survival (DMFS)** compared to people who receive placebo plus pembrolizumab. A **distant metastasis** is cancer that has spread from the original (primary) tumor to distant organs or distant lymph nodes. Lymph nodes are small organs that are part of the immune system.	**DMFS** is the length of time from when the person starts the study until either the cancer spreads from where it started to other parts of the body, or death due to any cause.
To learn if people who receive **V940** plus pembrolizumab have longer **overall survival (OS)** compared to those who take placebo plus pembrolizumab.	**OS** is the length of time that people are alive after joining the study.
To learn if **V940 plus pembrolizumab** is safe and how well people manage (tolerate) the study treatment.	The number of people who: • Had an **adverse event (AE)** – An AE is a health problem that happens or worsens during a study. • Stopped treatment due to an AE.
To learn how **V940** plus pembrolizumab affects people's **health-related quality of life (HRQoL)** compared to placebo plus pembrolizumab.	People will answer sets of questions to measure their **HRQoL**, including questions about their overall health and their ability to carry out daily tasks. The change in the scores will be measured during the study.

What are the possible benefits and risks?

People in this study may or may not have cancer come back after receiving the treatment in this study. This study has an external group of experts that will oversee the study's overall risk and benefit. If this committee decides that the study treatment is not safe or does not show benefit, the study can be stopped. More information about the benefits and risks is in the Investigator Brochure, Protocol, and Informed Consent documents.