Date: 23 January, 2024

REQUEST OF AUTHORIZATION FOR A NEW CLINICAL TRIAL
Submission of application dossier

EU Trial Number	2023-505712-37
Universal Trial Number	U1111-1292-3589
Protocol Code	V940-007
Protocol Title	A Phase 2/3, adaptive, randomized, open-label, clinical study to evaluate neoadjuvant and adjuvant V940 (mRNA-4157) in combination with pembrolizumab (MK-3475) versus standard of care, and pembrolizumab monotherapy in participants with resectable locally advanced cutaneous squamous cell carcinoma (LA cSCC) (INTerpath-007)
Sponsor	Merck Sharp & Dohme LLC

Dear Sir/Madam

On behalf of the Sponsor, Merck Sharp & Dohme LLC, I am hereby submitting the application dossier for the Clinical trial V940-007.

The following information related to the clinical study is provided:

- The Clinical trial will not enroll vulnerable populations as defined in Art. 10 of REGULATION (EU) No 536/2014.
- The clinical trial does NOT involve the first administration of a new active substance to humans; This information is contained within the Application dossier in Part I - *Trial information* Section.
- A scientific advice relating to the clinical trial has been given by the Agency; this information is contained within the Application dossier in Part I - *Scientific advice and Paediatric Investigation Plan (PIP)* Section.
- The clinical trial is not part and is not intended to be part of a Paediatric Investigation Plan (PIP) as referred to in Title II, Chapter 3, of Regulation (EC) No 1901/2006.
- The trial design does NOT include any investigational medicinal products that are a narcotic, psychotropic or radiopharmaceutical.

- The trial design does NOT involve the use of any investigational medicinal products which consist of or contain a genetically-modified organism or organisms.

- The trial design does NOT involve the use of any investigational medicinal product that has obtained an orphan designation.

- The trial design anticipates the use of the following investigational medicinal products:

Investigational Medicinal Product	**Regulatory Status in EEA**	**Sourcing strategy**
V940 (mRNA-4157)	not authorized	centrally sourced
Keytruda (Pembrolizumab, MK-3475)	authorized	centrally sourced

• Committee for Medicinal Products for Human Use has granted access to the PRIME scheme for V940 (mRNA-4157) and has classified it as Advanced Therapy Medicinal Product. The Committee for Advanced Therapies has ruled that an mRNA meets the definition of a gene therapy medicinal product (GTMP), which is currently the best available option for Advanced therapy classification for V940.

• IMPD Quality information for V940 is provided within a separate IMPD-Q-only application (EU CT # 2023-509999-42-00).

• The Sponsor would like to provide some additional information on the parallel submission of the investigational medicinal product dossier (IMPD) by Moderna, to explain how the Sponsor can take responsibility for the investigational medicinal product (IMP) in line with the relevant legislation (refer to Guideline on active substance master file procedure [CHMP/QWP/227/02 Rev 4/ Corr] which excludes the use of an Active Substance Master File (ASMF) for biological medicinal products).

- V940 IMP is being jointly developed by MSD and Moderna, with MSD being the study sponsor of V940-007 and Moderna being the manufacturer of the IMP. As manufacturer of V940, Moderna is responsible for the production process of the IMP.
- The IMPD has been submitted in parallel of this clinical trial application (CTA) by Moderna as IMPD-Q-only submission.
    - *In order for Moderna, the manufacturer of the IMP, to retain rights to its intellectual property and avoid broad dissemination of proprietary information, the confidential manufacturing information was submitted separately from the Sponsor's clinical trial application as foreseen in the Clinical Trials Regulation (EU) No 536/2014 Questions & Answers document version 6.4, section 2.15 (published 17-Feb-2023). The companies have jointly agreed on this submission pathway. Correspondingly, appropriate letters of cross reference to enable the health authorities to access the IMPD-Q-only submission have been supplied with the Sponsor's clinical trial application.*
- In recognition of the duty of the Study sponsor to have overall oversight of the quality and safety of the IMP being studied in the proposed trial, MSD put into place collaboration agreements with Moderna to enable review of relevant CMC information and allow for quality audit of manufacturing and testing facilities. MSD considers that this agreement allows it to fulfil all obligations for quality oversight of the IMP.

- Of note, the parallel submission for V940 of the IMPD-Q-only by Moderna (EU CT number 2023-505501-16-00) and the CTA by MSD (EU CT number: 2023-503652-27-00) was endorsed previously under the EU CTR and the CTA for Study V940-001 was fully authorized on 25 September 2023.

- The trial design does NOT anticipate the use of any medical device subject to investigation in the clinical trial.

- The *Reference Safety Information* (RSI) necessary for assessing whether an adverse reaction is a suspected unexpected serious adverse reaction, is located within Part I - *Investigator brochure for the medicinal product* Section of the application dossier:

-V940: Investigator Brochure – 13MAR2023 - version 15 - section 6.6
- Pembrolizumab: Investigator Brochure – 08NOV2023 - version 24 - section 7.2 - Appendix 7

Please note that the following documents have been already approved or are under evaluation within a previous application in the MSC as described in the table below; note that for documents approved in multiple clinical trials, only the most recent approval is indicated, while for documents under evaluation, only the first submitted application in the country is indicated:

EU Trial number	**Protocol code**	**Document name**	**Sponsor version code or number and date**	**Authorization status**	**MSC**
2023-503652-27	V940-001	V940 Investigator Brochure	Version 15 dated 13MAR2023	Approved	Belgium, France, Germany, Italy, Poland, Spain
2023-504923-20	V940-002	V940 Investigator Brochure	Version 15 dated 13MAR2023	Under evaluation	Czech Republic, Hungary, Norway

V940 Investigator Brochure Version 15 dated 13MAR2023 was never submitted to Romania.

EU Trial number	**Protocol code**	**Document name**	**Sponsor version code or number and date**	**Authorization status**	**MSC**
2023-507179-23	MK-9999-01B	Pembrolizumab Investigator Brochure	Version 24 dated 08NOV2023	Under evaluation	Belgium; Czech Republic; France; Germany; Hungary; Italy;

					Norway; Poland; Romania; Spain

EU Trial number	Protocol code	Document name	Sponsor version code or number and date	Authorization status	MSC
2022-501966-23	MK-3475-716	Pembrolizumab Q-IMPD	Version 080L74, dated 22-Apr-2022	Approved	Belgium
2023-505615-21	MK-3475-B15	Pembrolizumab Q-IMPD	Version 080L74, dated 22-Apr-2022	Approved	Czech Republic; France; Germany; Hungary; Italy; Poland; Romania; Spain
2023-504923-20	V940-002	Pembrolizumab Q-IMPD	Version 080L74, dated 22-Apr-2022	Under evaluation	Norway

Note. All Part I documents subject to redaction are provided as follows: a red line version not for publication showing the sections subject to CCI redaction. A version for publication where the redline sections are redacted. The Sponsor confirms that the investigational sites will receive a clean, unredacted version of the relevant documents.

Content of the labelling:
The labelling of the products used within the clinical trial is provided in Part I – *Content labeling* Section.
Note. The information omitted from the content of the labelling (Principal Investigator/ site and emergency unblinding contact information) complies with Annex VI since it is provided to patients with the Participant Identification Card immediately after the informed consent. This is justified in the Protocol - section 8.1.3.

The Sponsor declares that the present submission is NOT a resubmission of a previous application.

The following Ethics Committee(s) is/are proposed by the Sponsor for the following Member States:

Member State	**Proposed Ethics Committee**
Italy	National Ethics Committee for clinical trials on advanced therapies (Advanced Medicinal Therapeutic Products "ATMPs")
Spain	CEIm de la Comunidad Foral de Navarra

The relevant document to confirm Sponsor **Compliance with Regulation (EU) 2016/679**, is uploaded within the Application dossier – *Form* Section.

For country specific information, please see Annex 1 at the end of this letter.

Sincerely,

MSD EU Regional Submission Lead

Annex 1. Country specific information

Czech Republic

List of sites and principal investigators with Czech diacritics for Czech Republic

1800	Všeobecná fakultní nemocnice v Praze **Dermatovenerologická klinika** U nemocnice 499/2	Prim. MUDr. Ivana Krajsová, MBA
1802	Fakultní nemocnice Královské Vinohrady **Dermatovenerologická klinika** Šrobárova 1150/50	Prof. MUDr. Petr Arenberger, DrSc., MBA, FCMA

List of submitted docs for Czech Republic:
Protocol amendment V940-007-00 / 20NOV2023
Scientific protocol synopsis in Czech language verze 1.0_CZE_05Jan2024
Protocol Plain Language Summary v1.0 / 20Nov2023 in Czech language
MK-3475 IB ed. 24/08NOV2023
V940 IB ed. 15 /13MAR2023
O2_Proof of insurance_CZE_CS_not pub_Version 10OCT2023_10OCT2023
EUB Patient ID card Czech Republic (Czech) 1.0_00_1.2 / 29Nov2012
V940-007_eCOA Screen Report_Czech Republic (Czech)_v1.0_05DEC2023
R1_Compliance with national Data Protection_CZE_CS_not pub_Version 05JAN2024_ 05JAN2024
K1_Recruitment Arrangements and IC Procedure_CZE_CS_not pub_Version 05JAN2024_ 05JAN2024
P1_Financial and other arrangements_CZE_EN_not pub_Version 20DEC2023_ 20DEC2023
P1_Compensation for trial participants_CZE_CS_not pub_Version 05JAN2024_05JAN2024
S1_Compliance with use of biological samples_CZE_EN_not pub_Version 1-0_05JAN2024
All active (2) site´s PI´ CVs
Site Suitability for all active (2) sites
Suitability of investigator - Declaration of Interest for all active (2) sites
ICF:
1) **Main** ICF - CZE V940-007_v.00_Czech v.1_ 05JAN2024
2) **GDPR** Information for Study Subjects CZE v.3.0_01MAY22 based on Main ICF CZE V940-007
3) CZE V940-007_v.00_Addendum **Disease Progression**_Czech v.1_05JAN2024
4) CZE V940-007_v.00_**Optional-Limited Screening**_Czech v.1_05JAN2024
LABELS:

- ✓ J1_CLP IMP_MK-3475_not pub/for pub_Version 29AUG2023_29AUG2023
- ✓ J1_CLP IMP_V940 (mRNA-4157)_not pub/for pub_Version 06OCT2023_06OCT2023

Attached: Q1_Payment Details_CZE_EN_not pub_Version 05JAN2024_05JAN2024

Germany

Since we plan to notify the German Federal Office for Radiation Protection of this clinical trial, we would like to ask you to include a statement according to § 36 Para. 3 StrlSchG in the approval letter. – Thank you very much in advance!

Hungary

V940-007 List of submitted documents for Hungary / Beadott dokumentumok listája
V940-007-00_Final Protocol_20Nov2023
V940-007-00_Protocol Plain Language Summary _v.1.0_20Nov2023
MK-3475 Investigator's Brochure edition 24 08Nov2023
V940 Investigator's Brochure non-MSD edition 15 13Mar2023
V940-007 Recruitment Arrangements and IC Procedure, 19Dec2023
V940-007 Subject questionnaire ePRO v.1.00_13Dec2023
Proof of Insurance, 24Jul2023
V940-007 Compensation for trial participants, 11Dec2023
V940-007 Division of cost between Investigators and Institutions, V1.0, 21DEC2023
V940-007 Proof of payment, 13Dec2023
Patient materials
HUN_V940-007_Main_v.00_Hungarian_21DEC2023
HUN_V940-007_HG_v.00_Hungarian_09JAN2024
HUN_V940-007_Pregnant Partner_v.00_Hungarian_21DEC2023
HUN_V940-007_Addendum_Disease Progression v.00_Hungarian_21DEC2023
HUN_V940-007_Optional Limited Screening_v.00_Hungarian_21DEC2023
V940-007 Patient Brochure_Version v00.1_11JAN2024
V940-007 Master Tissue Brochure_Version v00.1_11JAN2024
Suitability of the investigator
V940-007 PI CV + GCP, Gyulai Rolland 12Dec2023
V940-007 PI CV + GCP, Lengyel Zsuzsanna 13Dec2023
V940-007 PI CV + GCP, Sipőcz István 12Dec2023
V940-007 PI CV + GCP, Barkóczi Beáta 22Dec2023
V940-007 PI CV + GCP, Emri Gabriella 20Dec2023
V940-007 PI Declaration of Interest, Gyulai Rolland 30Nov2023
V940-007 PI Declaration of Interest, Lengyel Zsuzsanna 30Nov2023
V940-007 PI Declaration of Interest, Sipőcz István 05Dec2023
V940-007 PI Declaration of Interest, Barkóczi Beáta 18Dec2023
V940-007 PI Declaration of Interest, Emri Gabriella 18Dec2023
Suitability of the facilities
V940-007 Site suitability, Gyulai Rolland 14Dec2023
V940-007 Site suitability, Lengyel Zsuzsanna 15Dec2023

V940-007 Site suitability, Sipőcz István 14Dec2023
V940-007 Site suitability, Barkóczi Beáta 20Dec2023
V940-007 Site suitability, Emri Gabriella 19Dec2023

Italy

The Ethics Committee for Italy is: National Ethics Committee for Clinical Trials on Advanced Therapies (Advanced Medicinal Therapeutic Products “ATMPs”)
The costs of stamp duty on the electronic original of this document are paid by MSD Italia srl as a result of the Revenue Agency Authorization no. 1480/2022

Poland

Please be informed that the payment to the Clinical Trials Compensation Fund was made in accordance with the recommendations for 2023 and is currently (in accordance with the amounts established for 2024) too large, therefore the difference will be refunded.