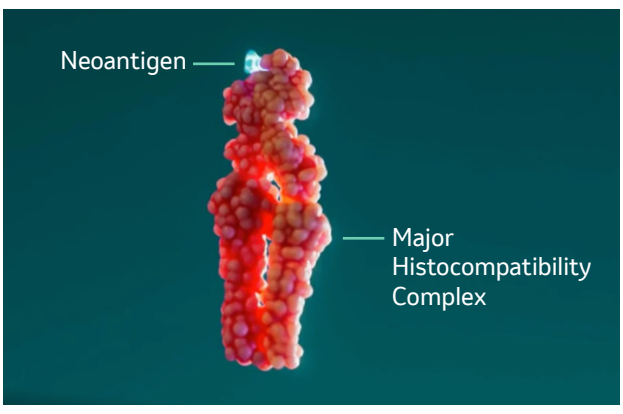
Intismeran Autogene
INTerpath late-stage clinical development program



Exploring an individualized approach to cancer care

Intismeran autogene (V940/mRNA-4157) is a novel, potential first-in-class investigational messenger RNA (mRNA)-based individualized neoantigen therapy (INT) being jointly developed by Merck and Moderna. Intismeran is designed using a patient's tumor sample to identify the unique mutational signature, or "fingerprint," of their cancer. This information is then used to create a personalized synthetic mRNA coding for up to 34 neoantigens — abnormal proteins that arise from mutations in cancer cells and are not found in healthy cells. Since these tumor-specific mutations are unique to each individual, they could provide a personalized therapy tailored to generate anti-cancer immunity.

INTs are designed to train and activate an anti-tumor immune response by generating specific T-cell responses based on the unique mutational signature of a patient's tumor. Upon administration, the mRNA-encoded neoantigen sequences are translated in the body and presented to the immune system, a key step in generating specific T-cell responses against cancer cells. The mRNA sequences are transient and are not incorporated into the DNA.

Intismeran was developed through a strategic collaboration combining Merck's established leadership in immuno-oncology with Moderna's pioneering mRNA technology and manufacturing capabilities.

INTerpath
ONCOLOGY CLINICAL TRIALS

INTerpath is Merck and Moderna's global clinical development program evaluating the safety and efficacy of intismeran in combination with pembrolizumab, with other anti-cancer therapies and as a monotherapy across multiple tumor types and stages of disease, including melanoma, non-small cell lung cancer (NSCLC), bladder cancer and renal cell carcinoma (RCC). The program currently comprises nine total Phase 2 and Phase 3 clinical trials, with plans for continued expansion.

SKIN CANCERS

	Disease setting	Study phase	Study design	Treatment arms	Primary outcome measure	Estimated enrollment	Estimated primary completion
INTerpath-001 NCT05933577	High-risk (stage IIB-IV) resected cutaneous melanoma	Phase 3	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab • Placebo + pembrolizumab	• RFS	1089	October 2029
INTerpath-012 NCT06961006	First-line advanced melanoma	Phase 2	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab • Placebo + pembrolizumab	• PFS	160	July 2028

LUNG CANCERS

	Disease setting	Study phase	Study design	Treatment arms	Primary outcome measure	Estimated enrollment	Estimated primary completion
INTerpath-002 NCT06077760	Margin negative, completely resected stage II, IIIA, IIIB (with nodal involvement) NSCLC	Phase 3	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab • Placebo + pembrolizumab	• DFS	868	June 2030
INTerpath-009 NCT06623422	Resectable stage II, IIIA, IIIB (N2) NSCLC, previously treated with chemotherapy and pembrolizumab in the neoadjuvant setting without achieving pCR	Phase 3	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab • Placebo + pembrolizumab	• DFS	680	May 2033
INTerpath-013 NCT07221474	Metastatic treatment-naïve squamous NSCLC	Phase 2	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab + chemotherapy • Placebo + pembrolizumab + chemotherapy	• PFS • OS	180	July 2029
INTerpath-014 NCT07513376	Completely resected high-risk stage I NSCLC	Phase 3	• Randomized • Placebo-controlled • Two double blind arms and one open label combination arm	• Intismeran + pembrolizumab and berahyaluronidase alfa (open-label) • Intismeran • Placebo	• DFS	876	August 2034

RENAL CANCERS

	Disease setting	Study phase	Study design	Treatment arms	Primary outcome measure	Estimated enrollment	Estimated primary completion
INTerpath-004 NCT06307431	Intermediate-high-risk, high-risk or M1 NED RCC	Phase 2	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab • Placebo + pembrolizumab	• DFS	272	April 2027

BLADDER CANCERS

	Disease setting	Study phase	Study design	Treatment arms	Primary outcome measure	Estimated enrollment	Estimated primary completion
INTerpath-005 NCT06305767	High-risk muscle-invasive urothelial carcinoma post-radical resection	Phase 1/2	• Randomized • Placebo- and active-controlled • Double-blind	• Intismeran + pembrolizumab (Phase 2) • Placebo + pembrolizumab (Phase 2) • Intismeran + pembrolizumab + enfortumab vedotin + surgery (perioperative, Phase 1)	• DFS • AEs *(Perioperative cohort only)*	230	October 2029
INTerpath-011 NCT06833073	High-risk NMIBC	Phase 2	• Randomized • Active-controlled • Open-label	• Intismeran + BCG • BCG • Intismeran (cohort B, non-comparative, exploratory arm)	• EFS	308	September 2031

Abbreviations

AE adverse event
BCG bacillus Calmette-Guérin
DFS disease-free survival
EFS event-free survival
INT individualized neoantigen therapy
mRNA messenger RNA
NED no evidence of disease
NMIBC non-muscle invasive bladder cancer
NSCLC non-small cell lung cancer
OS overall survival
pCR pathological complete response
PFS progression-free survival
RCC renal cell carcinoma
RFS recurrence-free survival