Moderna Oncology Event

October 17, 2025



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Agenda

Precision Immunotherapy pipeline	**Kyle Holen, M.D.** Senior Vice President, Head of Development, Oncology and Therapeutics, Moderna
Intismeran autogene Phase 2 adjuvant melanoma data review and development plan	**Kyle Holen, M.D.** Senior Vice President, Head of Development, Oncology and Therapeutics, Moderna
Overview of advanced melanoma treatment landscape	**Ryan Sullivan, M.D.** Massachusetts General Hospital, Associate Professor of Medicine, Harvard Medical School
Precision immunotherapy: mRNA-4359	**Kyle Holen, M.D.** Senior Vice President, Head of Development, Oncology and Therapeutics, Moderna
MRNA-4359 ESMO Presentation reprise	**David J. Pinato, M.D., PhD.** Director of Developmental Cancer Therapeutics, Imperial College, London
Precision immunotherapy pipeline overview	**Kyle Holen, M.D.** Senior Vice President, Head of Development, Oncology and Therapeutics, Moderna

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Precision Immunotherapy pipeline

Kyle Holen, M.D.
Senior Vice President, Head of Development,
Oncology and Therapeutics, Moderna

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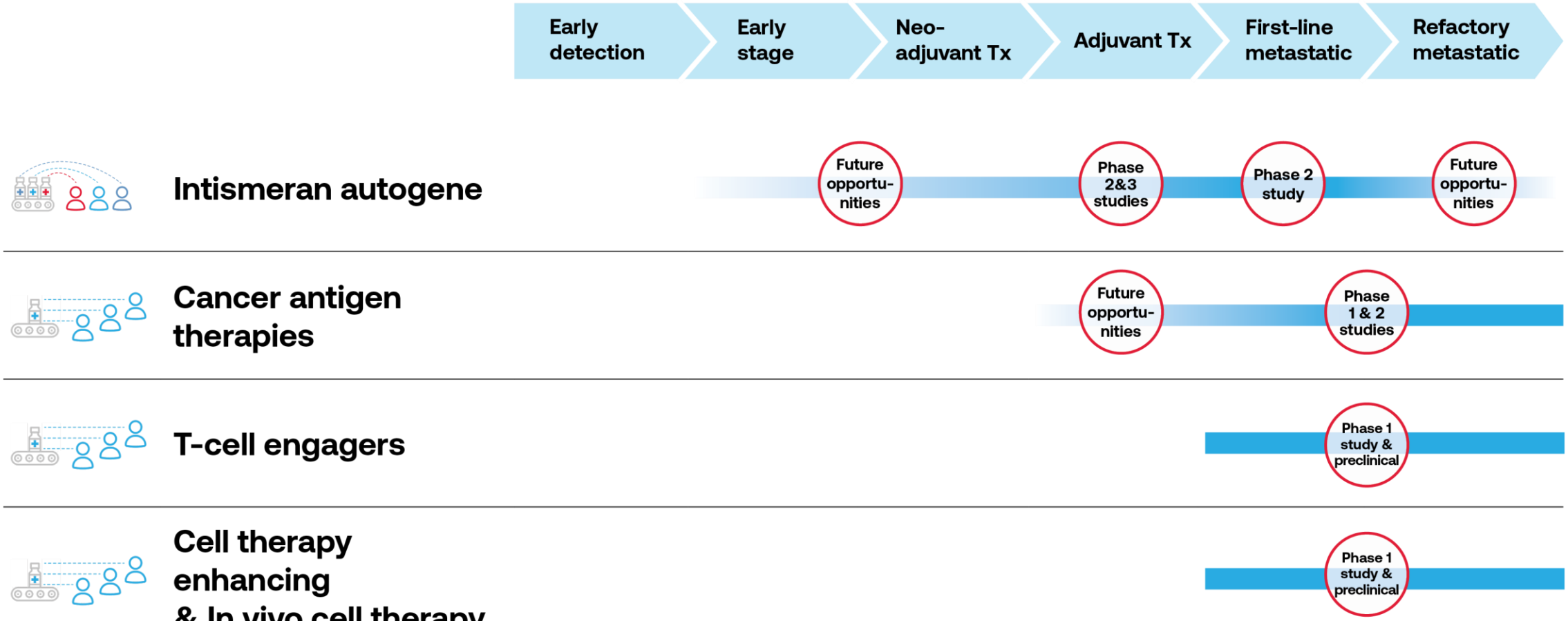
Moderna oncology research and development programs across cancer disease stages



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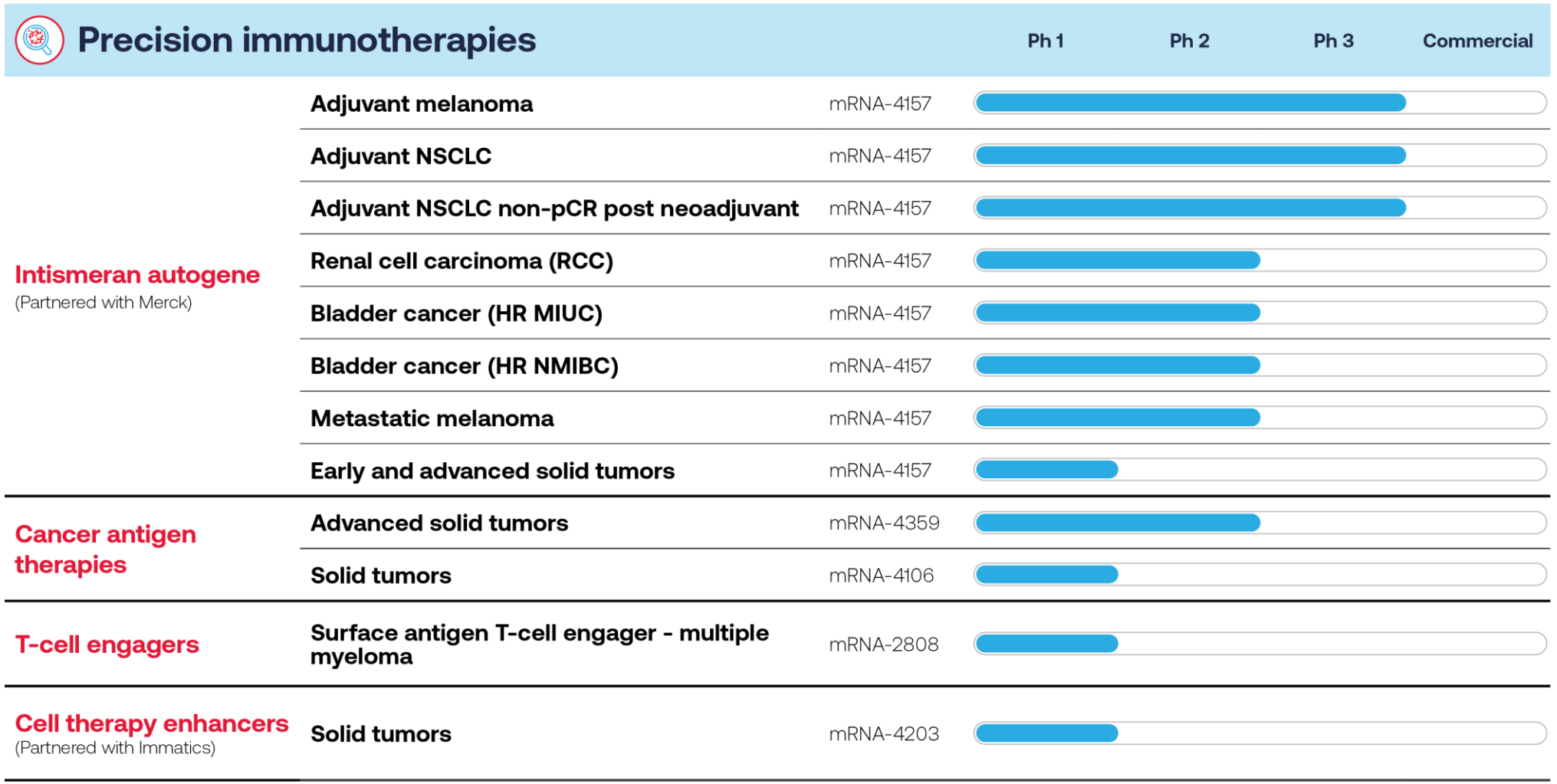
Moderna oncology clinical pipeline



Abbreviations: NSCLC, non-small cell lung cancer; pCR, non-pathological complete response; RCC, renal cell carcinoma; HR MIUC, high-risk muscle-invasive urothelial carcinoma; HR NMIBC, high-risk non-muscle invasive bladder cancer

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Intismeran autogene overview

Kyle Holen, M.D.
Senior Vice President, Head of Development,
Oncology and Therapeutics, Moderna

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Intismeran autogene (mRNA-4157/V940): Designed to target an individual patient's unique tumor mutation

How are individualized neoantigen therapies made?

An analysis is performed to identify the best cancer fingerprint proteins that may **train and activate** the patient's immune cells.

An individualized neoantigen therapy is created for that patient.

The mRNA in the individualized neoantigen therapy helps show parts of the cancer **fingerprint proteins** to the immune system.

The patient's immune system may now better **recognize and fight** the patient's cancer.

First, doctors take a sample of a patient's tumor and blood so they can identify the **unique genetic mutations** of that patient's cancer.

Administration of INT

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Phase 2b intismeran autogene adjuvant melanoma study: 3-year follow-up data

Reprise of ASCO 2024 presentation

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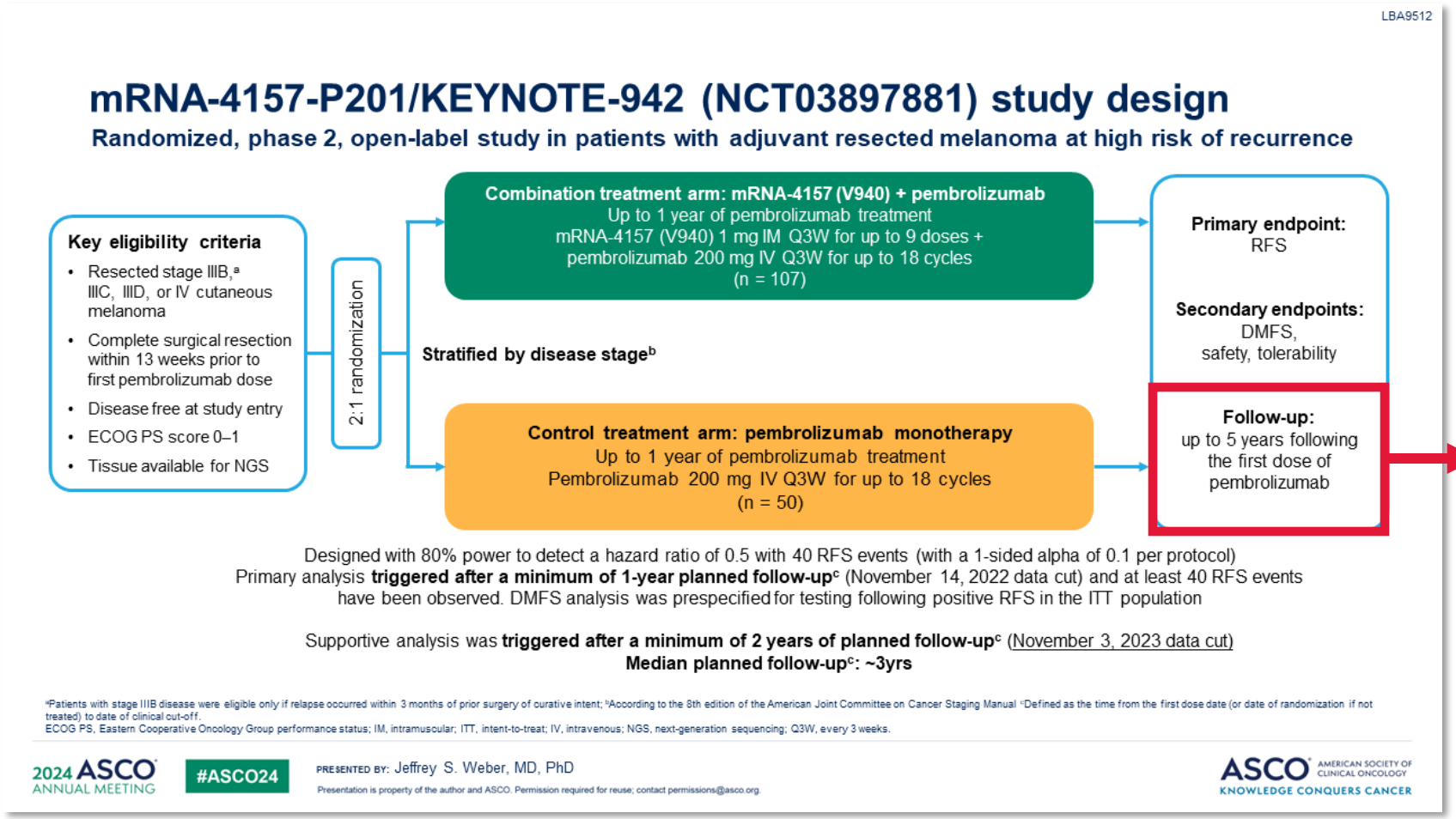
Randomized Phase 2 trial design comparing mRNA-4157/V940 in combination with KEYTRUDA to KEYTRUDA alone in adjuvant melanoma



Results from this trial at ~2 years of follow-up and ~3 years of follow-up were presented at the American Society of Clinical Oncology in 2023 and 2024, respectively

5 year follow-up from this Phase 2 study is expected in 2026

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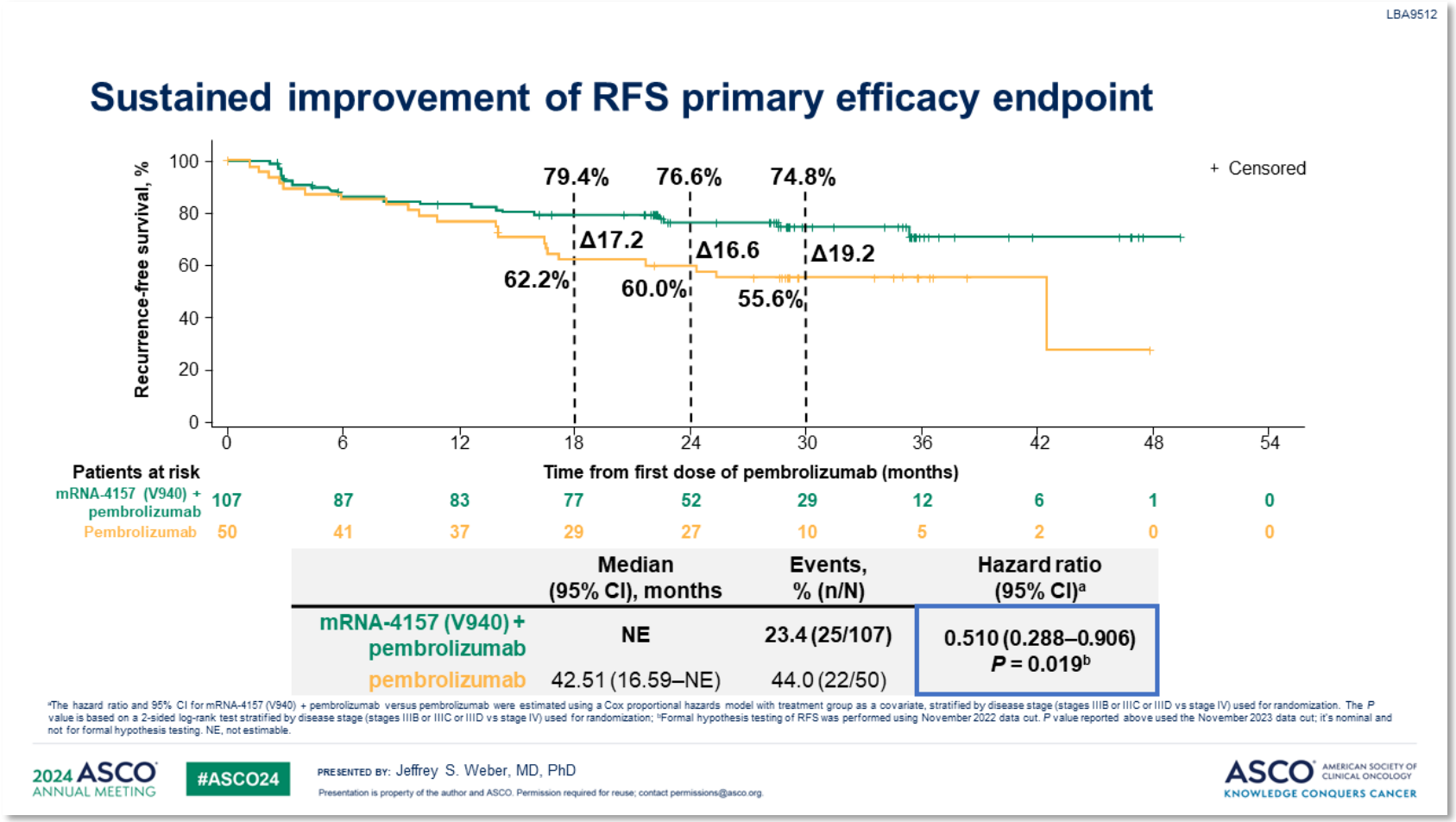
Recurrence free survival rate of mRNA-4157/V940 in combination with KEYTRUDA was 74.8% as compared to 55.6% for KEYTRUDA alone, at ~3 years of follow-up



At a median planned follow-up of the Phase 2 study at 34.9 months, **mRNA-4157/V940 in combination with KEYTRUDA reduced the risk of recurrence or death by 49%**

(n=157)

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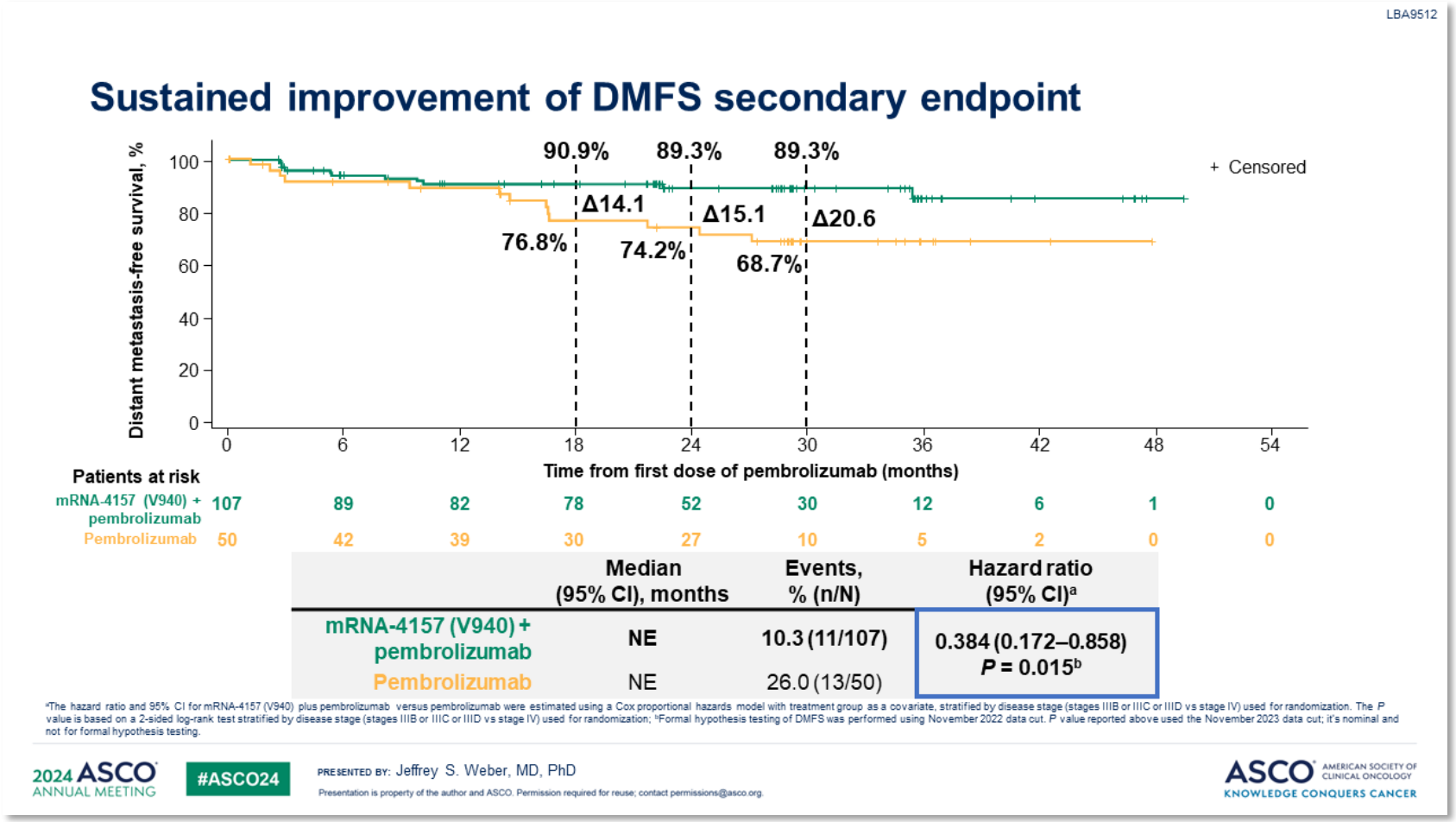
Distant metastasis-free survival is a key secondary endpoint of the Phase 2 study



At ~ 3 years of follow-up, mRNA-4157/V940 in combination with KEYTRUDA also continued to demonstrate a meaningful improvement in distant metastasis-free survival (DMFS) compared with KEYTRUDA alone, reducing the risk of developing distant metastasis or death by 62%.

(n=157)

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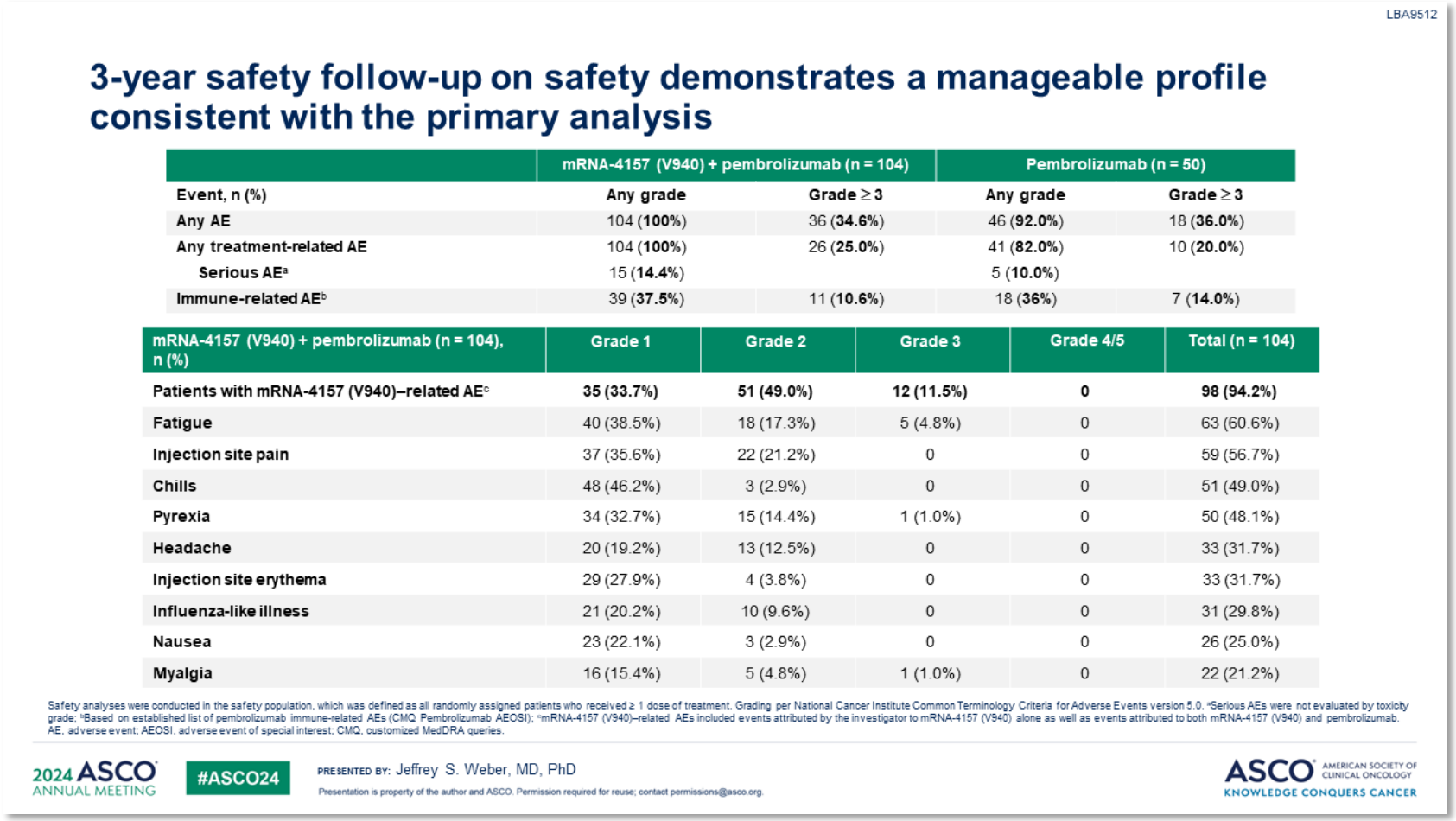
Safety and tolerability from the Phase 2 adjuvant melanoma trial



LBA9512

3-year safety follow-up on safety demonstrates a manageable profile consistent with the primary analysis

	mRNA-4157 (V940) + pembrolizumab (n = 104)		Pembrolizumab (n = 50)	
Event, n (%)	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Any AE	104 (**100%**)	36 (**34.6%**)	46 (**92.0%**)	18 (**36.0%**)
Any treatment-related AE	104 (**100%**)	26 (**25.0%**)	41 (**82.0%**)	10 (**20.0%**)
Serious AE[a]	15 (**14.4%**)		5 (**10.0%**)	
Immune-related AE[b]	39 (**37.5%**)	11 (**10.6%**)	18 (**36%**)	7 (**14.0%**)

mRNA-4157 (V940) + pembrolizumab (n = 104), n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5	Total (n = 104)
Patients with mRNA-4157 (V940)–related AE[c]	**35 (33.7%)**	**51 (49.0%)**	**12 (11.5%)**	**0**	**98 (94.2%)**
Fatigue	40 (38.5%)	18 (17.3%)	5 (4.8%)	0	63 (60.6%)
Injection site pain	37 (35.6%)	22 (21.2%)	0	0	59 (56.7%)
Chills	48 (46.2%)	3 (2.9%)	0	0	51 (49.0%)
Pyrexia	34 (32.7%)	15 (14.4%)	1 (1.0%)	0	50 (48.1%)
Headache	20 (19.2%)	13 (12.5%)	0	0	33 (31.7%)
Injection site erythema	29 (27.9%)	4 (3.8%)	0	0	33 (31.7%)
Influenza-like illness	21 (20.2%)	10 (9.6%)	0	0	31 (29.8%)
Nausea	23 (22.1%)	3 (2.9%)	0	0	26 (25.0%)
Myalgia	16 (15.4%)	5 (4.8%)	1 (1.0%)	0	22 (21.2%)

Safety analyses were conducted in the safety population, which was defined as all randomly assigned patients who received ≥ 1 dose of treatment. Grading per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. [a]Serious AEs were not evaluated by toxicity grade; [b]Based on established list of pembrolizumab immune-related AEs (CMQ Pembrolizumab AEOSI); [c]mRNA-4157 (V940)–related AEs included events attributed by the investigator to mRNA-4157 (V940) alone as well as events attributed to both mRNA-4157 (V940) and pembrolizumab. AE, adverse event; AEOSI, adverse event of special interest; CMQ, customized MedDRA queries.

2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Jeffrey S. Weber, MD, PhD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

mRNA-4157/V940 in combination with KEYTRUDA was well tolerated without potentiation of immune-related adverse events compared to KEYTRUDA alone

(n=157)

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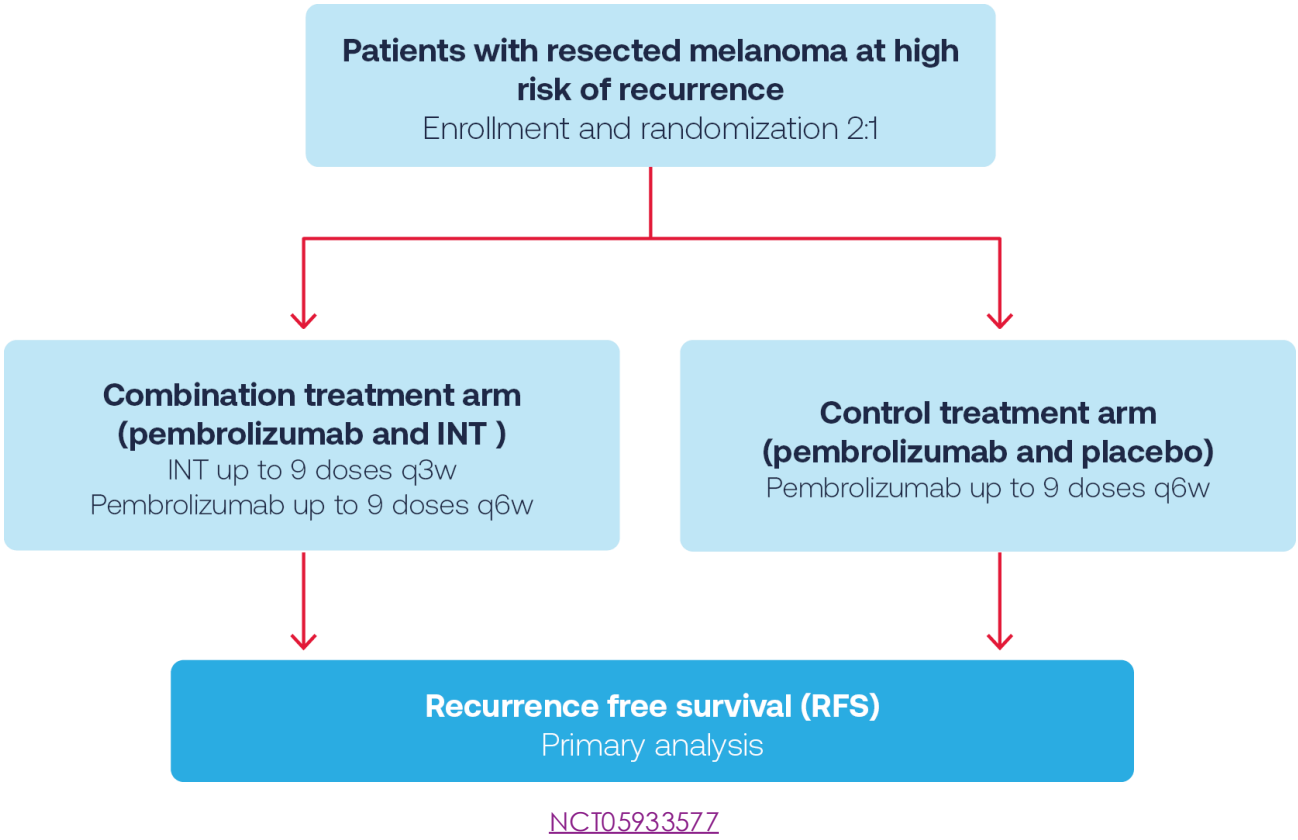
Adjuvant melanoma Phase 3 (mRNA-4157 / V940) trial design

Primary endpoint is recurrence free survival compared to KEYTRUDA



NCT05933577

Randomized, double-blind placebo controlled, mRNA-4157 + pembrolizumab (KEYTRUDA®) vs. placebo + pembrolizumab (2:1) (INTerpath-001)

Resected melanoma patients: stage IIB or IIC, III, IV

Primary endpoint: recurrence free survival (RFS)

Secondary endpoints: Distant Metastasis-Free Survival (DMFS), Overall-Survival (OS)

Number of participants: ~1,089

Phase 3 trial is fully enrolled

Intismeran autogene is in multiple clinical studies across tumor types and disease stages

Intismeran autogene

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Adjuvant melanoma	mRNA-4157					
Adjuvant NSCLC	mRNA-4157					
Adjuvant NSCLC non-pCR post neoadjuvant	mRNA-4157					
Renal cell carcinoma (RCC)	mRNA-4157					
Bladder cancer (HR MIUC)	mRNA-4157					
Bladder cancer (HR NMIBC)	mRNA-4157					
Metastatic melanoma	mRNA-4157					
Early and advanced solid tumors	mRNA-4157					

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Overview of advanced melanoma treatment landscape

Ryan Sullivan, MD
Head, Melanoma Center
Massachusetts General Hospital

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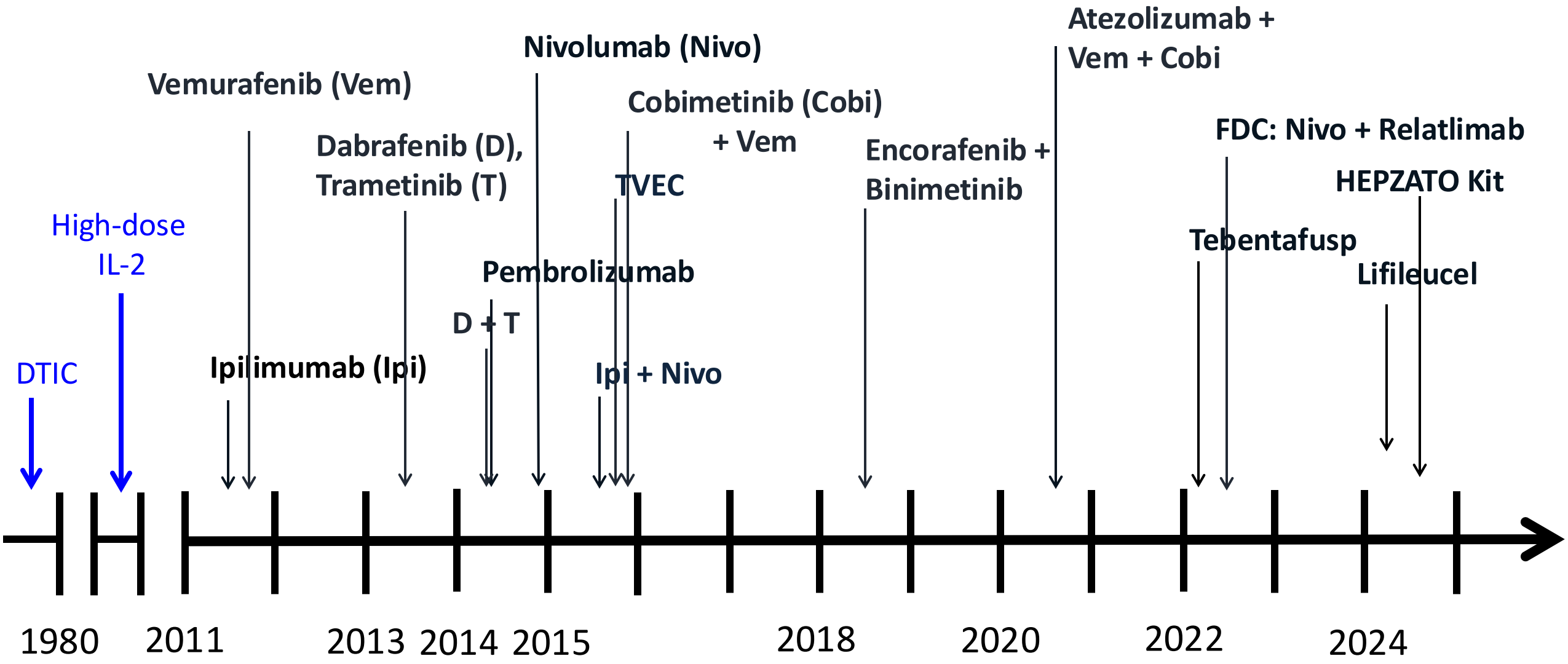
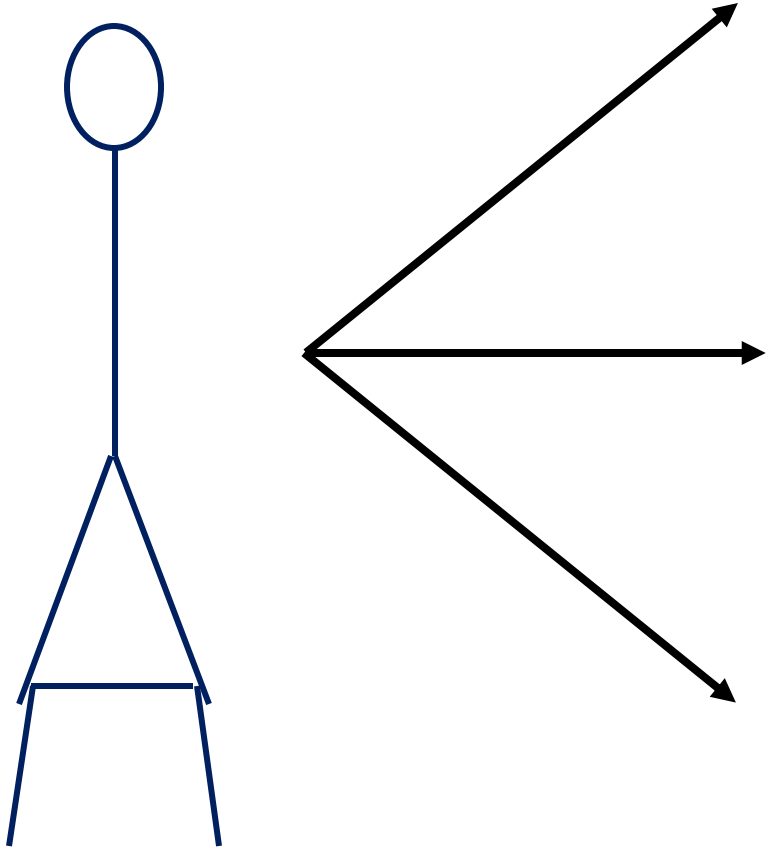
Advanced Melanoma Treatment Landscape 2025



The SOC 1st line options

New patients with advanced,
BRAF MT or BRAF WT melanoma



Single-agent anti-PD-1

Anti-PD-1/anti-LAG3

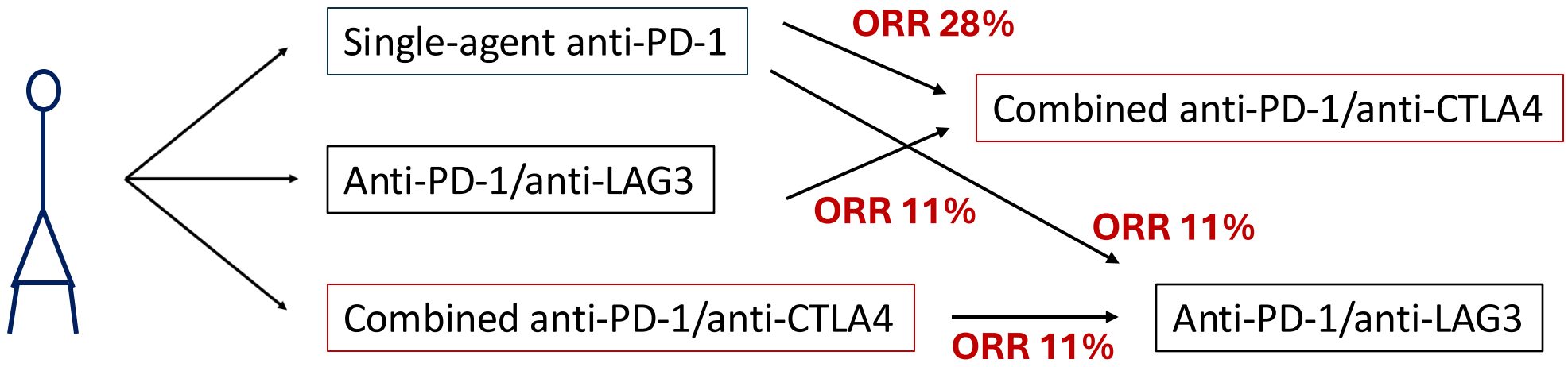
Combined anti-PD-1/anti-CTLA4

Agent(s)	Pembro[1,2] (front-line)	Nivo[3-6]	Nivo/Rela[4,5]	IPI/Nivo[3-6]
ORR (%)	46	34 – 45	44	58
10-yr PFS*# (%)	22 (~33)	27 (32)	32	65 (39)
10-yr OS* (%)	34 (~48)	37 (48-51)	55	43 (58)
10-yr MSS* (%)	45 (~54)	44 (54-55)	63	52 (63)
Gr3+ TRAE (%)	17	11 – 23	21	59

*3-yr for RELATIVITY 047 (NIVO/RELA; 3-yr for other therapies in parentheses)
#10-yr for Checkmate 067 (NIVO, IPI/NIVO)

1. Robert et al. Lancet Oncol 2019
2. Robert et al. ESMO 2024; Annal Oncol 2024
3. Larkin et al. ESMO 2024; Wolchok NEJM 2024
4. Hodi et al. ASCO 2024
5. Long et al. NEJM Evid 2023
6. Tawbi et al. ASCO 2024

Is anti-PD-1 resistance transferrable to other subsequent immune checkpoint inhibition?

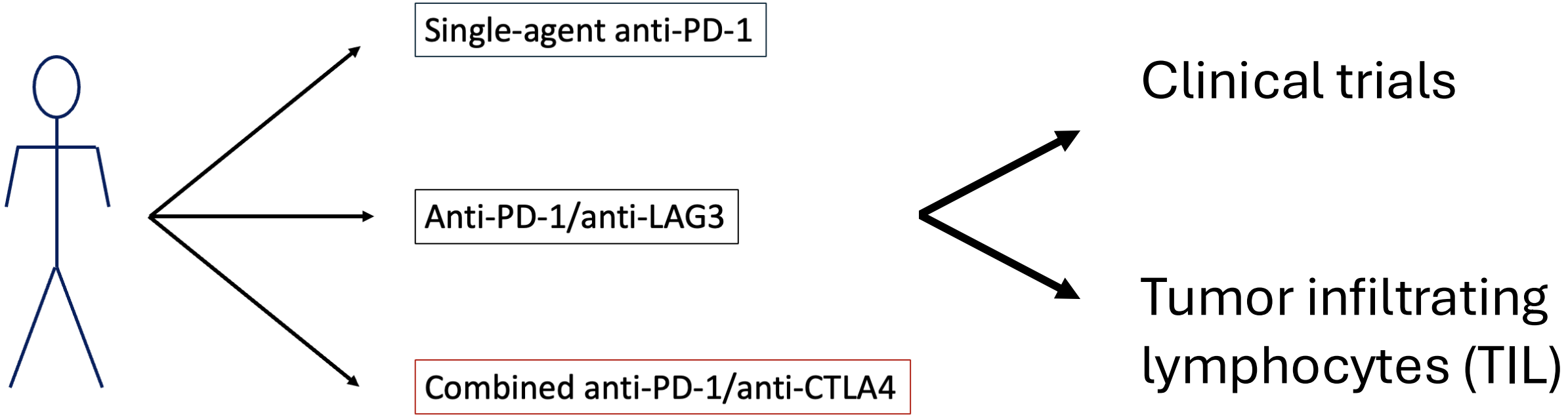


VanderWalde et al. Nat Med 2023

Menzies et al. New Engl J Med 2022

Ascierto et al. J Clin Oncol 2023

Limited options in post-PD-1 setting



TIL Data in Melanoma

- Wide range of response rates in pre-/early days of ICI (25-53%)
- Impressive ORR and DOR with lifileucel in post-PD-1 (30-35%)
- Randomized data demonstrating improved ORR (almost 50%!!) and PFS compared to ipilimumab in patients previously treated with anti-PD-1
- Lifileucel FDA-approved in February 2024
- Randomized, frontline trial ongoing
  - Lifileucel + pembrolizumab vs pembrolizumab
- OBX-115 avoids IL-2 by incorporating a carbonic anhydrase drug responsive domain which leads to membrane-bound IL-15 expression
  - Early data with OBX-115 suggests different (better) toxicity profile that lifileucel

Precision immunotherapy: mRNA-4359

Kyle Holen, M.D.
Senior Vice President, Head of Development,
Oncology and Therapeutics, Moderna

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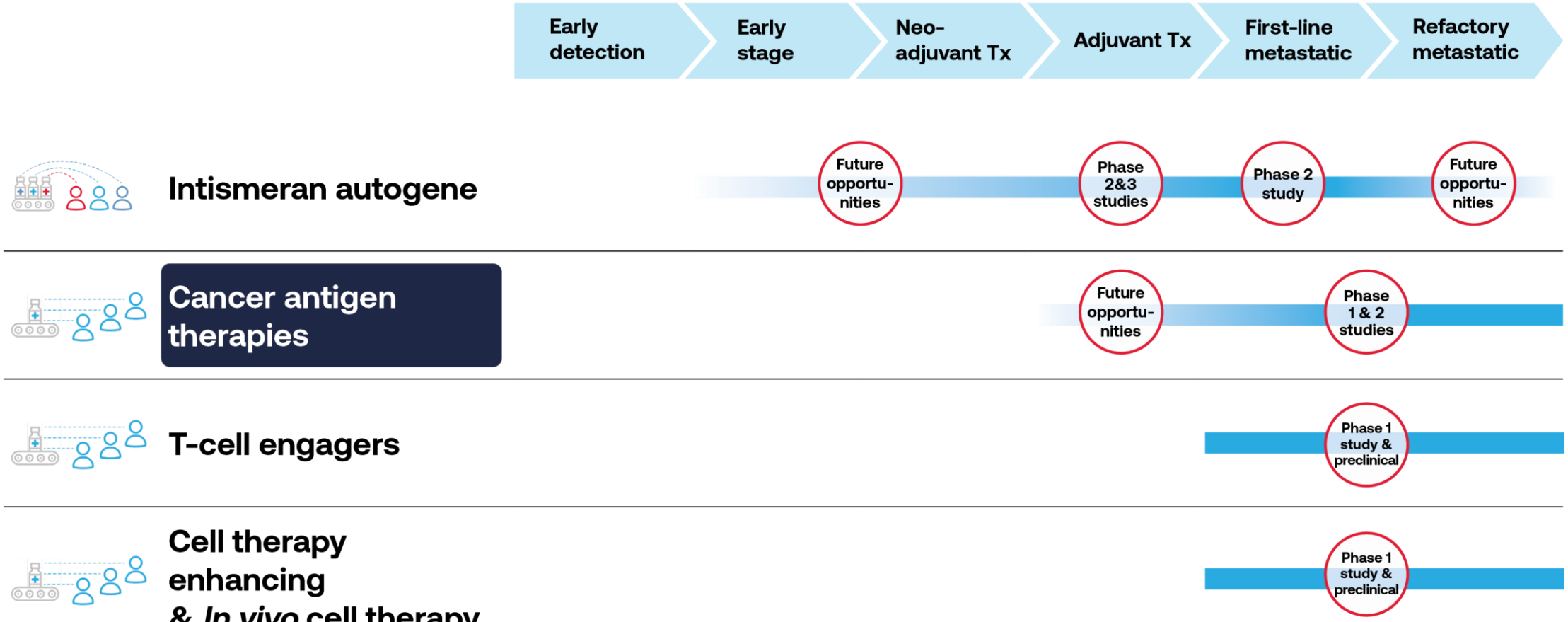
Moderna oncology research and development programs across cancer disease stages



Two investigational off-the-shelf cancer antigen therapy candidates currently in clinical trials

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					

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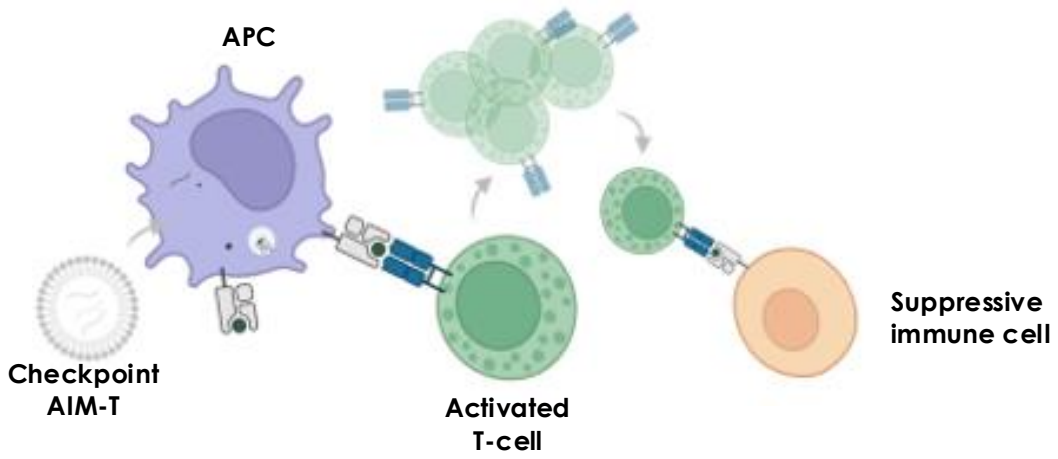
mRNA-4359 targets both immunosuppressive and cancer cells that overexpress PD-L1 and IDO

mRNA-4359



Harnessing T-cells with off-the-shelf cancer antigen therapies

- Encodes for PD-L1 and IDO
- Targets both immunosuppressive cells and cancer cells
- Applicable to many different cancer types

Study design and key objectives

Arm 1a presented at ESMO 2024

Arm 1a (Dose escalation)
Monotherapy
Advanced or metastatic solid tumors
COMPLETED

Arm 1b presented today at ESMO 2025

Arm 1b (Dose confirmation)
Combination therapy
Advanced or metastatic Checkpoint Inhibitor refractory melanoma/NSCLC
ONGOING

- **Safety and tolerability** of mRNA-4359 alone and in combination with pembrolizumab
- **Antitumor activity** of mRNA-4359 alone and in combination with pembrolizumab (ORR, DCR, DOR, PFS)
- **T-cell profile changes** (peripheral and tumor) after treatment of mRNA-4359 alone or in combination with pembrolizumab

Note: for more information about mRNA-4359, see the Checkpoint AIM-T Program Pack
1. Link to 2024 ESMO presentation

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mRNA-4359: Phase 1b study results

Reprise of ESMO 2025 presentation

David Pinato, MD
Director, Developmental Cancer Therapeutics
Imperial College, London

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Clinical Outcomes and PD-L1 Expression Analyses from a Trial of mRNA-4359 Plus Pembrolizumab in Checkpoint Inhibitor–Resistant/Refractory Melanoma

D.J. Pinato,[1,2] R.J. Sullivan,[3] A. Khattak,[4] D. Sarker,[5] T. Medina,[6] I. Karydis,[7] G. W. Middleton,[8] P. Spiliopoulou,[9] A. Rohatgi,[10] M. Gutierrez,[11] A. Daud,[12] V. Boni,[13] M.R. Middleton,[14] R.F. Sweis,[15] J.E. Bauman,[16] X. Mao,[17] H.N. Daghestani,[17] M. Abadier,[17] F. Barlaskar,[17] G.V. Long[18]

[1]Imperial College London, Hammersmith Hospital, London, UK; [2]University of Piemonte Orientale, Novara, Italy; [3]Massachusetts General Hospital, Boston, MA, USA; [4]One Clinical research, Hollywood Private Hospital and Edith Cowan University, Perth, WA, Australia; [5]Guy's Hospital, King's College London, London, UK; [6]University of Colorado, Aurora, CO, USA; [7]University Hospital Southampton NHS Trust and University of Southampton, Southampton, UK; [8]University of Birmingham, Birmingham, UK; [9]University of Glasgow, Glasgow, UK; [10]Washington University in St Louis, St Louis, MO, USA; [11]John Theurer Cancer Center - Hackensack Meridian Health, Hackensack, NJ, USA; [12]UCSF, San Francisco, CA, USA; [13]NEXT Madrid, University Hospital Quiron Salud, Madrid, Spain; [14]NIHR Biomedical Research Centre, Oxford, UK; [15]The University of Chicago, Chicago, IL, USA; [16]The George Washington University, Washington, DC, USA; [17]Moderna, Inc., Cambridge, MA, USA; [18]Melanoma Institute Australia, The University of Sydney, Sydney, Mater and Royal North Shore Hospitals, NSW, Australia

Dr David James Pinato

Friday, October 17, 2025

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Declaration of Interests

- **Presenter David James Pinato**: consultant/advisory role for Eisai, Mina Therapeutics, Roche, H3 Biomedicine, Da Volterra, AstraZeneca, Ipsen. Speakers' Bureau for Bayer, ViiV Healthcare, Falk Pharma, Roche. Travel, Accommodations, Expenses for Bristol Myers Squibb, Bayer, MSD Oncology. Honoraria from Roche/Genentech, Bristol Myers Squibb, Da Volterra, Avammune, Mursla Bio, Starpharma, Lift Biosciences, Boston Scientific, Parabilis Medicines, Galapagos NV, TERUMO. Research Funding from MSD Oncology, Bristol Myers Squibb, GlaxoSmithKline
- This study was funded by Moderna, Inc.
- Medical writing support was provided by Young-A Heo, PhD, of ICON plc (Blue Bell PA, USA), funded by Moderna, Inc.

Presented by: David J. Pinato

Background

- Checkpoint inhibition has revolutionized treatment of advanced melanoma; however, despite improvements in outcomes, the majority of patients will experience disease progression[1,2]
- mRNA-4359 is a lipid nanoparticle–encapsulated mRNA-based immune evasion–targeted cancer antigen therapy encoding epitopes of PD-L1 and IDO1 antigens[3]
- mRNA-4359 is designed to elicit T-cell responses against both tumor and immunosuppressive cells, resulting in direct tumor killing and rebalancing of the tumor microenvironment[3]
- An ongoing phase 1/2 trial (NCT05533697) is evaluating mRNA-4359 as monotherapy or in combination with pembrolizumab in patients with advanced solid tumors[3,4]
- We present clinical, safety, and translational data of mRNA-4359 plus pembrolizumab in the fully enrolled CPI-R/R melanoma cohort from the dose-confirmation portion of this ongoing study

CPI-R/R, checkpoint inhibitor–resistant/refractory; IDO1, indoleamine 2,3-dioxygenase 1; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

1. Haist M, et al. *Cancer Metastasis Rev*. 2023;42:481–505; 2. Tiersma JF, et al. *Cancer Treat Rev*. 2024;129:102802; 3. Powderly JD, et al. *J Clin Oncol*. 2023;41:TPS2676; 4. Khattak MA, et al. *Ann Oncol*. 2024;35(Supplement 2):S521–S522.

Presented by: David J. Pinato

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Study Design, Patient Disposition, and Baseline Characteristics

Arm 1b (dose confirmation) and pharmacodynamic arms

mRNA-4359 plus pembrolizumab[a]

- Previously treated, histologically confirmed locally advanced or metastatic **CPI-R/R melanoma** or NSCLC, with primary refractory or acquired resistance to CPI[b] (≥1 prior line of a PD-1/PD-L1 containing regimen), and with a tumor lesion amenable to biopsy at screening

29 participants with CPI-R/R melanoma enrolled

mRNA-4359 400 µg Q3W + pembro 400 mg Q6W	**mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W**
14 received treatment	15 received treatment
1 completed both treatments **9 discontinued both treatments** PD (n = 6) AE (n =1) Death[c] (n = 1) Physician decision (n = 1)	**0 completed both treatments** **13 discontinued both treatments** PD (n = 12) Participant withdrawal (n = 1)
4 treatment ongoing Completed mRNA-4359 and pembro ongoing (n = 3) Pembro and mRNA-4359 ongoing (n = 1)	**2 treatment ongoing** Completed mRNA-4359 and pembro ongoing (n = 2)

Median follow-up time[a]: 19.9 (range 2.0–84.1) wk

	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 14)	**mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 15)**
Follow-up,[d] median (range), wk	22.5 (3.3–84.1)	10.4 (2.0–62.7)
Age, median (range), y	67 (49–83)	65 (29–79)
Male, n (%)	10 (71)	6 (40)
ECOG PS, n (%)		
0	9 (64)	12 (80)
1	5 (36)	3 (20)
PD-L1 TPS,[e] n (%)		
≥1%	6 (43)	4 (27)
<1%	6 (43)	7 (47)
Missing	2 (14)	4 (27)
CPI-R/R disease, n (%)	14 (100)	15 (100)
No. of prior therapy, median (range)	3 (1–8)	3 (1–7)

TPS, tumor proportion score. [a]Patients received treatment for 9 cycles, and afterwards, patients could continue with pembrolizumab for up to 2 years of total therapy. [b]Primary refractory resistance was defined as PD occurring within 6 months after the first dose of anti–PD-(L)1antibody; acquired resistance was defined as PD in setting of ongoing treatment occurring in patients who had confirmed objective response or prolonged SD. [c]Per autopsy, cause of death was mostly likely due to arrhythmia secondary to undiagnosed hypertrophic cardiomyopathy; melanoma disease response was pathologic complete response. [d]Defined as treatment initiation to earliest non-missing date of last known alive, death, or data cutoff. [e]PD-L1 testing was assessed centrally using PD-L1 IHC 22C3 pharmDx (Agilent, Santa Clara, CA). Data cutoff: February 28, 2025.

Presented by: David J. Pinato

mRNA-4359 + Pembrolizumab Demonstrated a Manageable Safety Profile

- mRNA-4359-related AEs were mostly grade 1/2 injection site reactions and self-limited systemic AEs (eg, fatigue, pyrexia, chills)
- Pembrolizumab AEs were consistent with its known safety profile
  - Pembrolizumab-related AEs occurred in 66% of patients (grade 3, 10%)
  - Pembrolizumab-related AEs with >10% incidence were fatigue (28%), diarrhea, (10%), pruritus (10%), and vomiting (10%)
- 13.8% of patients experienced immune-related AEs (eg, colitis, pancreatitis, gastritis, nephritis, and secondary adrenocortical insufficiency)
- No DLTs occurred for either dose level
- No grade 4 or 5 treatment-related AEs occurred

	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 14)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 15)
Duration of mRNA-4359 therapy, median (range), wk	12.5 (0.1–81.1)	6.1 (0.1–29.6)
Duration of pembro therapy, median (range), wk	10.1 (0.1–80.6)	5.9 (0.1–60.4)
mRNA-4359–related AEs, n (%)	14 (100)	12 (80)
Grade 3[a]	1 (7)[b]	1 (7)[c]
mRNA-4359–related AEs with incidence ≥20% in either cohort, n (%)		
Injection site pain	10 (71)	8 (53)
Fatigue	7 (50)	7 (47)
Pyrexia	7 (50)	4 (27)
Injection site erythema	4 (29)	1 (7)
Chills	3 (21)	2 (13)
Influenza-like illness	3 (21)	5 (33)
Vomiting	2 (14)	5 (33)
Decreased appetite	2 (14)	3 (20)
Nausea	2 (14)	3 (20)

[a]There were no grade 4 or 5 treatment-related AEs. [b]1 patient experienced grade 3 pulmonary embolism. [c]1 patient experienced grade 3 fatigue and increased blood lactic acid. Data cutoff: February 28, 2025.

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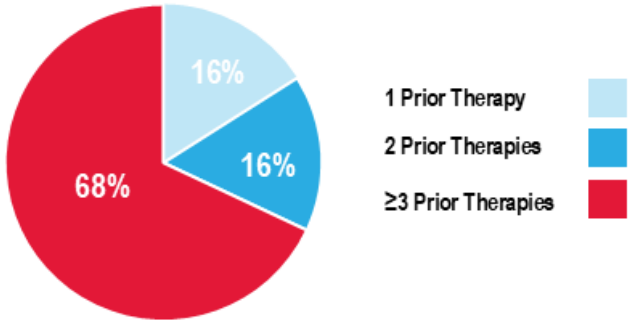
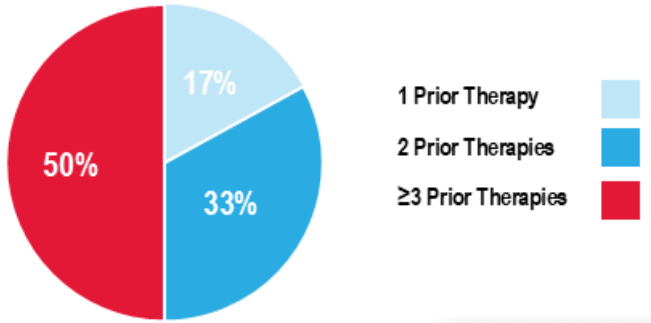
mRNA-4359 + Pembrolizumab Showed Antitumor Activity in Patients With CPI-R/R Melanoma

Evaluable patients	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 13)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 12)	All patients (N = 25)
ORR, % (95% CI)[a]	38 (14–68)	8 (0–39)	24 (9–45)
Best overall response, n (%)			
CR	0	1 (8)	1 (4)
PR	5 (38)	0	5 (20)
SD	5 (38)	4 (33)	9 (36)
PD	3 (23)	7 (58)	10 (40)
DCR, % (95% CI)[a]	77 (46–95)	42 (15–72)	60 (39–79)
DOR, median (95% CI),[b,c] wk	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)

Number of Prior Therapies Among 25 Evaluable Patients



Number of Prior Therapies Among 6 Responders



CR complete response, NR, not reached. PR, partial response. [a]Based on the Clopper-Pearson exact test. [b]Based on Brookmeyer and Crowley methodology, using log-log transformation for calculating CIs. [c]The median follow-up duration of the 6 responders was 71 (range 38–84) wk by the data cutoff date. Data cutoff: February 28, 2025.

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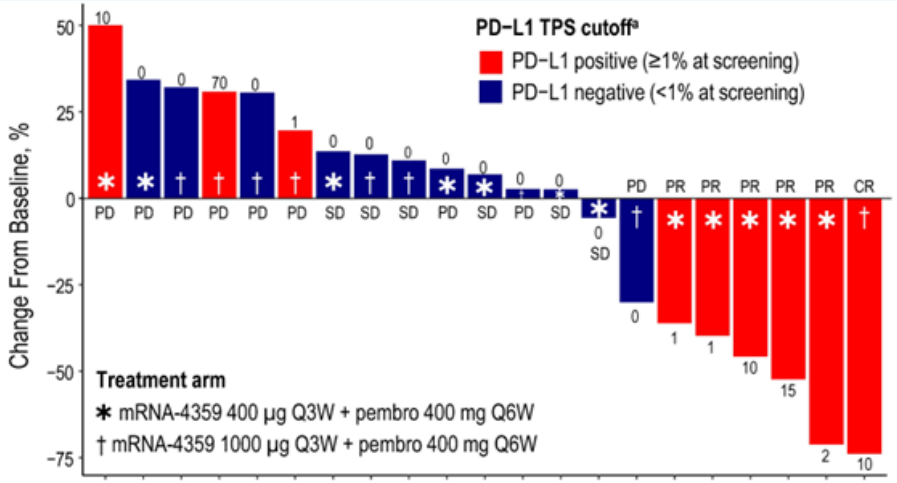
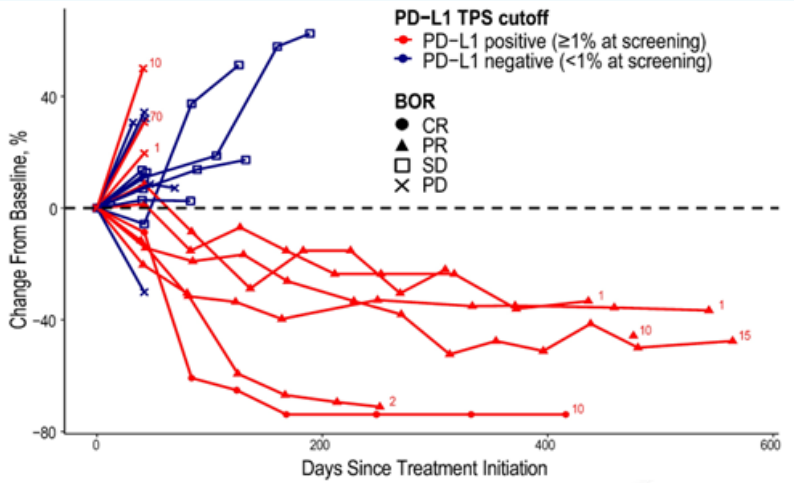
Responses Were Enriched in PD-L1–Positive Tumors (ORR, 67%), With Median Duration of Response Not Yet Reached, Indicating Encouraging Durability

Evaluable patients	Baseline PD-L1 TPS ≥1%			Baseline PD-L1 TPS <1%		
	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 6)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 3)	All patients (N = 9)	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 6)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 6)	All patients (N = 12)
ORR, % (95% CI)	83 (36–100)	33 (1–91)	67 (30–93)	0	0	0
DCR, % (95% CI)[b]	83 (36–100)	33 (1–91)	67 (30–93)	67 (22–96)	33 (4–78)	50 (21–79)

Best Percent Change From Baseline in Target Tumor Size



Tumor Responses Over Time[b]



BOR, best overall response. [a]Baseline PD-L1 TPS scores are displayed above or below each bar. [b]Baseline PD-L1 TPS scores in patients with PD-L1 positive tumors are displayed at the end of the line.
Data cutoff: February 28, 2025.

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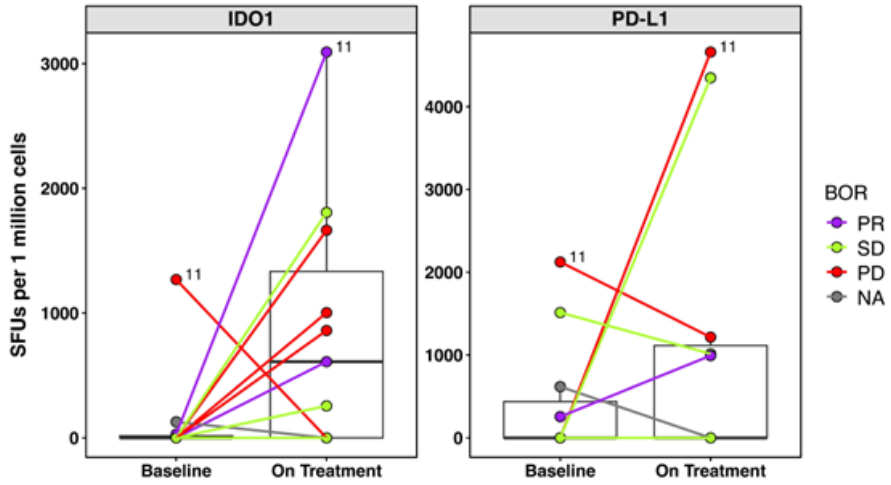
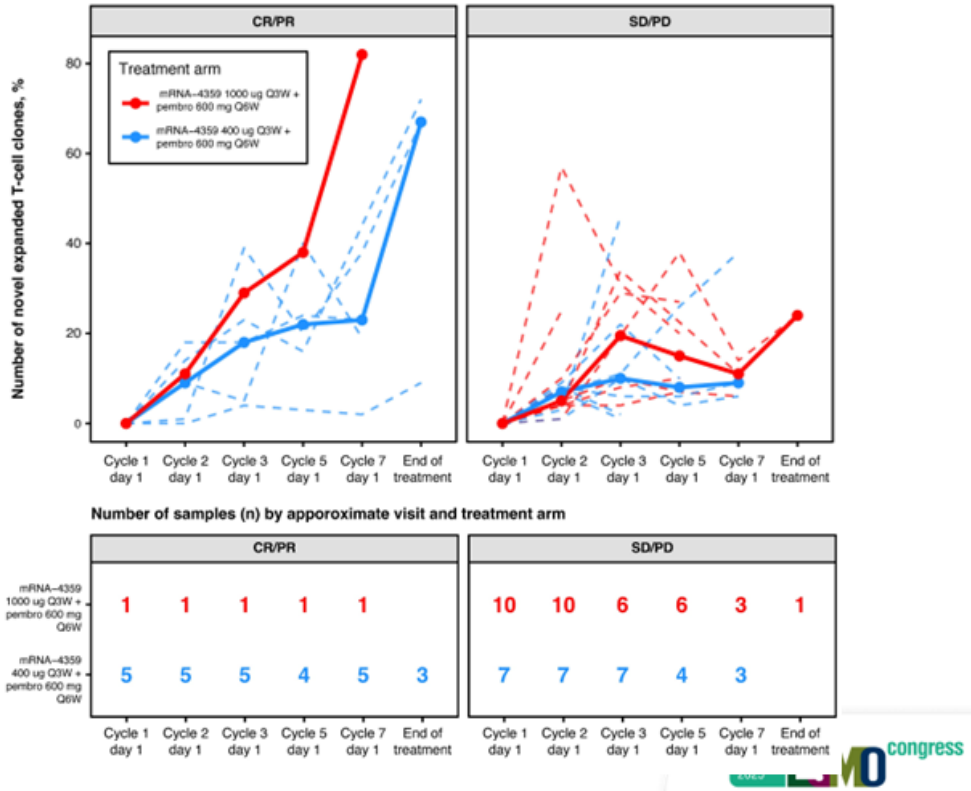
mRNA-4359 Demonstrated Biological Activity Through Specific T-Cell Responses and Novel Clonal Expansion in the Periphery

mRNA-4359 Elicited PD-L1- and IDO1-Specific T cell Responses in the Periphery[a]



Increase in Number of Novel Expanded TCR Clones in the Periphery with mRNA-4359 Treatment



SFU, spot-forming unit; TCR, T cell receptor.

[a]On treatment responses were selected from the 'best' ELISpot response at different time points for each patient.

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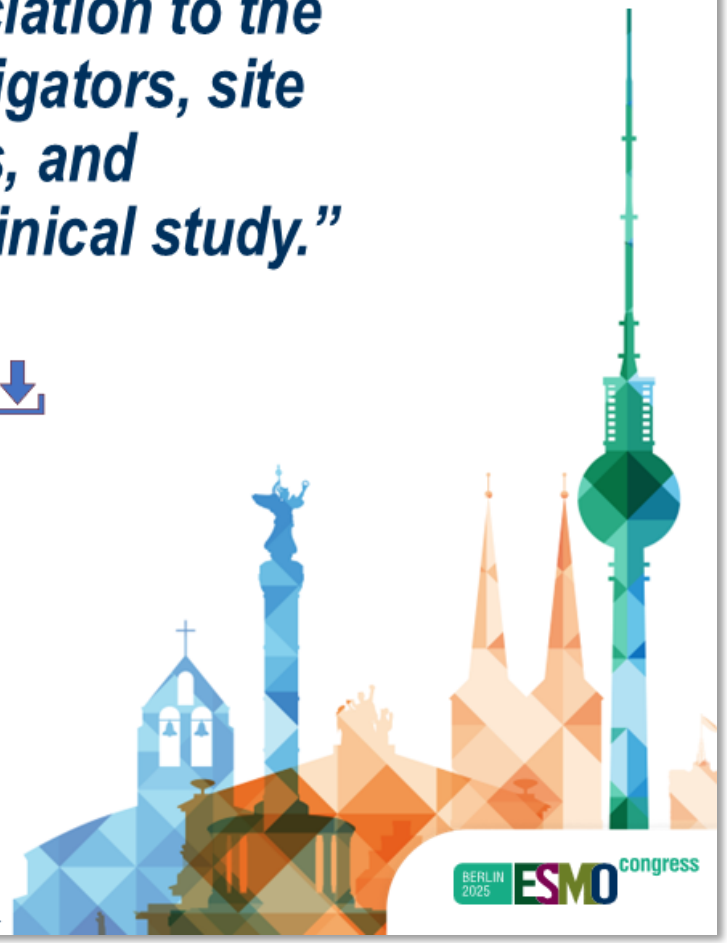
"We wish to express our sincere appreciation to the study patients, their families, the investigators, site personnel, research teams, our vendors, and collaborators who contributed to this clinical study."

To download a copy of today's presentation



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Precision immunotherapy pipeline development

Kyle Holen, M.D.
Senior Vice President, Head of Development,
Oncology and Therapeutics, Moderna

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Two investigational off-the-shelf cancer antigen therapy candidates currently in clinical trials

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					

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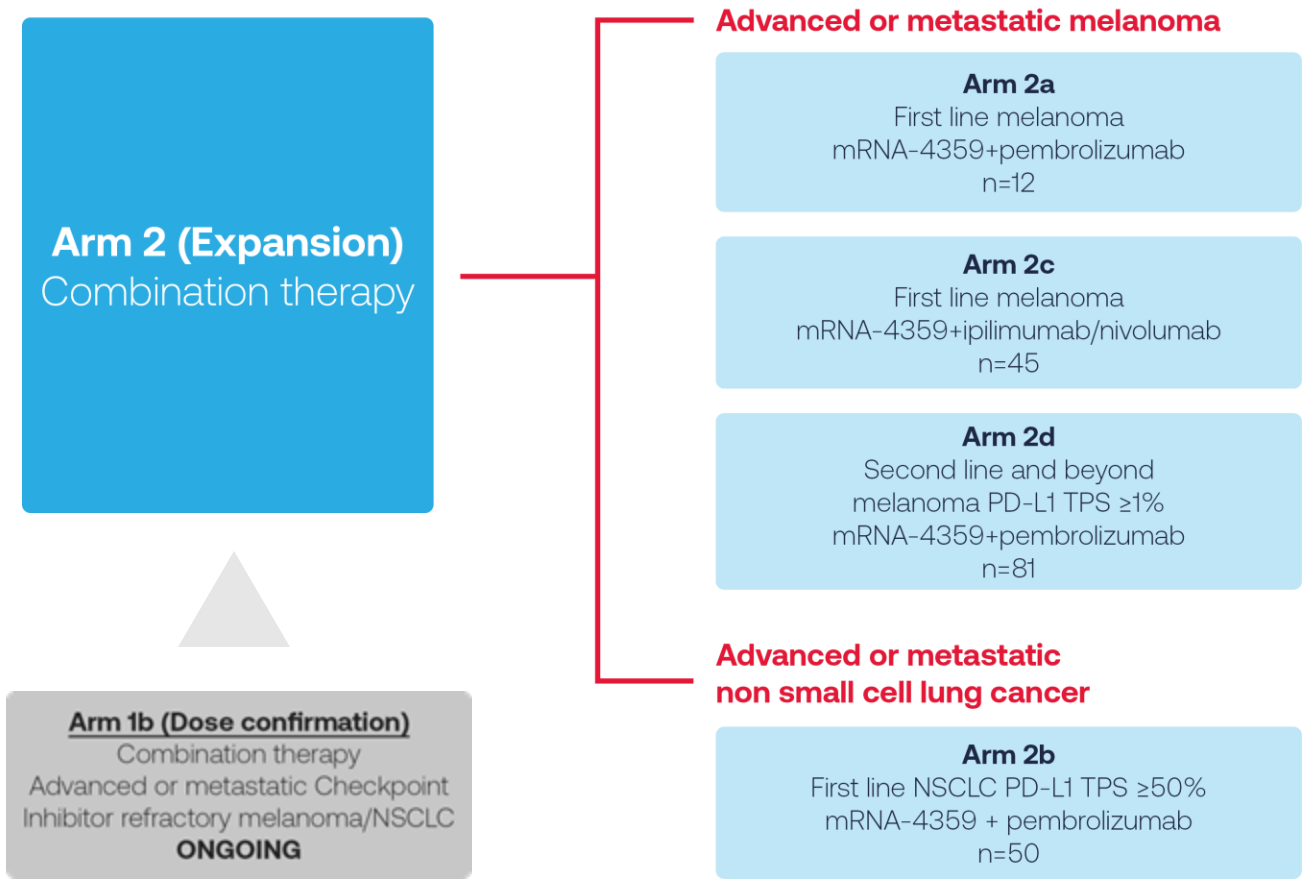
mRNA-4359 has advanced into a Phase 2 study with arms in metastatic melanoma and metastatic NSCLC



Key objectives

Primary endpoints

- Arms 2a-2c: Safety and tolerability of mRNA-4359
- Arm 2d: Objective response rate based on BICR per on RECIST v1.1

Secondary endpoints

- Arms 2a-2c: Objective response rate, disease control rate, duration of response, progression-free survival, all based investigator assessment per RECIST v1.1
- Arms 2a-2c: Percent change from baseline in T Cell profile in the tumor
- Arm 2d: Safety and tolerability of mRNA-4359
- Arm 2d: Duration of response, disease control rate, progression-free survival, all based on BICR per RECIST v1.1
- Arm 2d: Overall survival
- Arm 2d: Quality of Life

Abbreviations: BICR, Blinded Independent Central Review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1

Two investigational off-the-shelf cancer antigen therapy candidates currently in clinical trials

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					

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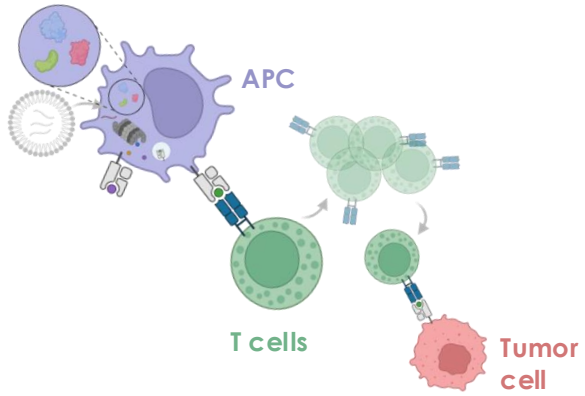
mRNA-4106 is a cancer antigen therapy offering broad coverage across tumor types

mRNA-4106



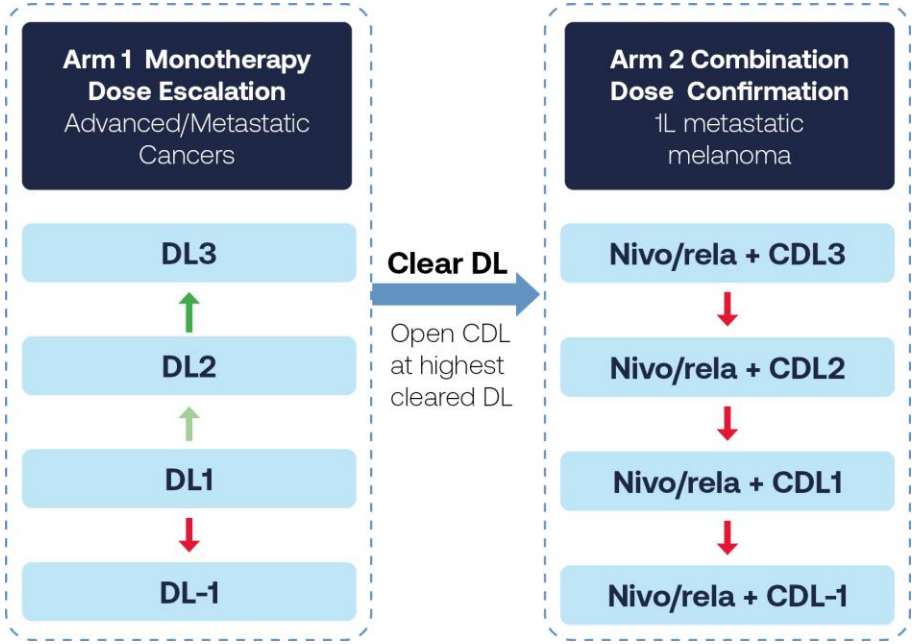
Harnessing T-cells with off-the-shelf cancer antigen therapies

- Encodes for multiple tumor targets
- Designed to broaden coverage across and within patients
- Applicable to multiple cancer types

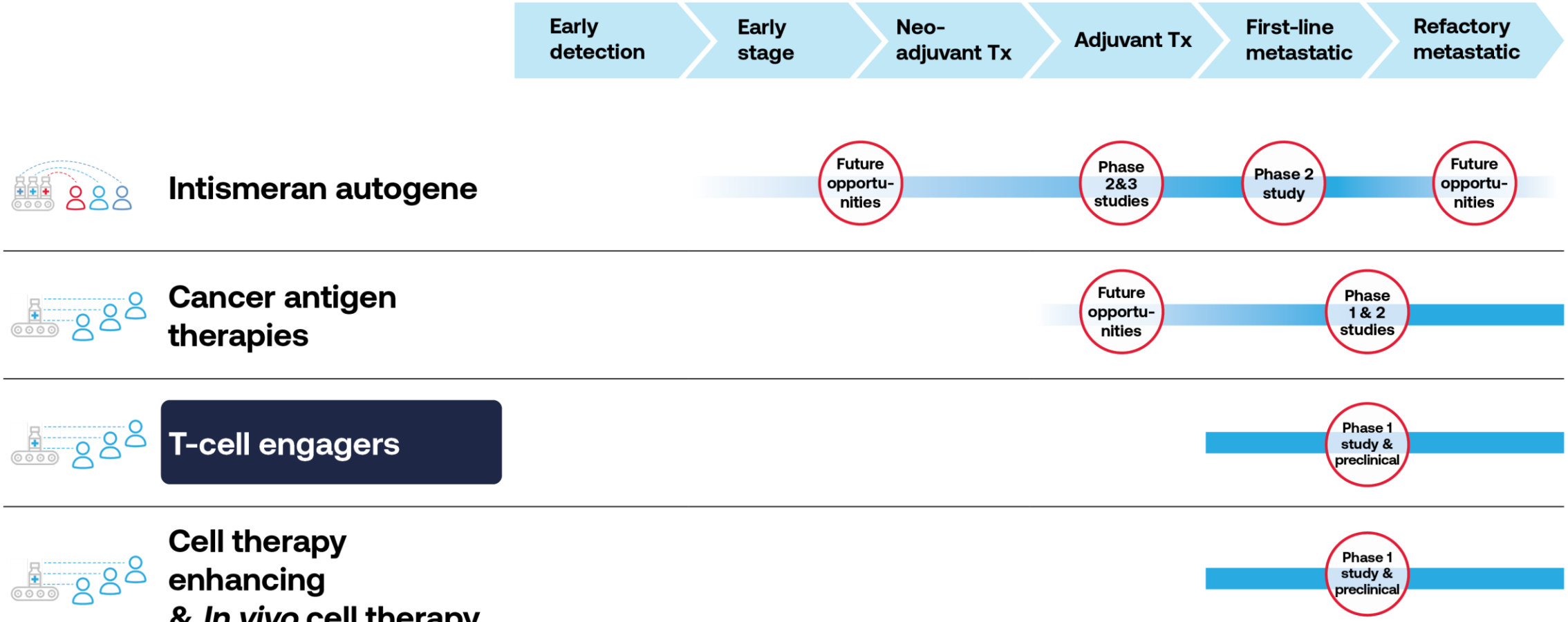
Study design and key objectives

Primary Objective: safety/tolerability as monotherapy and in combination with checkpoint inhibitor therapy

Exploratory Objectives: Anti-tumor activity



Moderna oncology research and development programs across cancer disease stages



T cell engagers bind T cells and tumor antigens together to activate killing of cancer cells

T-cell engagers

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Surface antigen T-cell engager - multiple myeloma	mRNA-2808					

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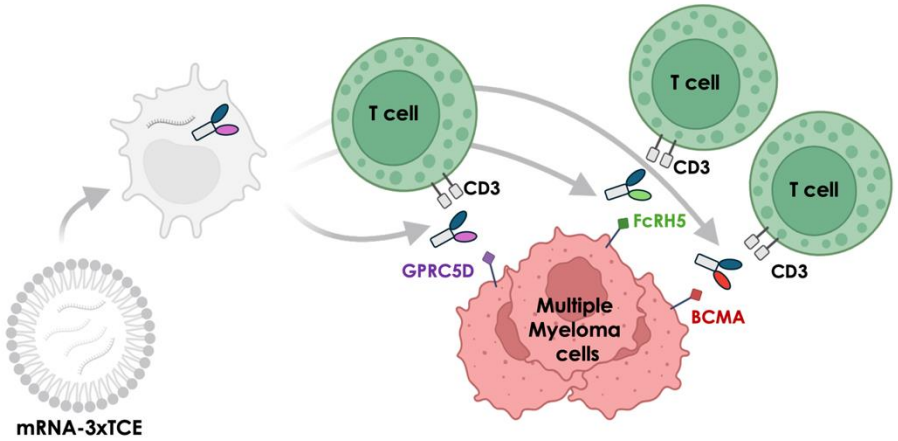
mRNA-2808 is a T-cell engager targeting surface antigens in multiple myeloma in a Phase 1/2 study

mRNA-2808

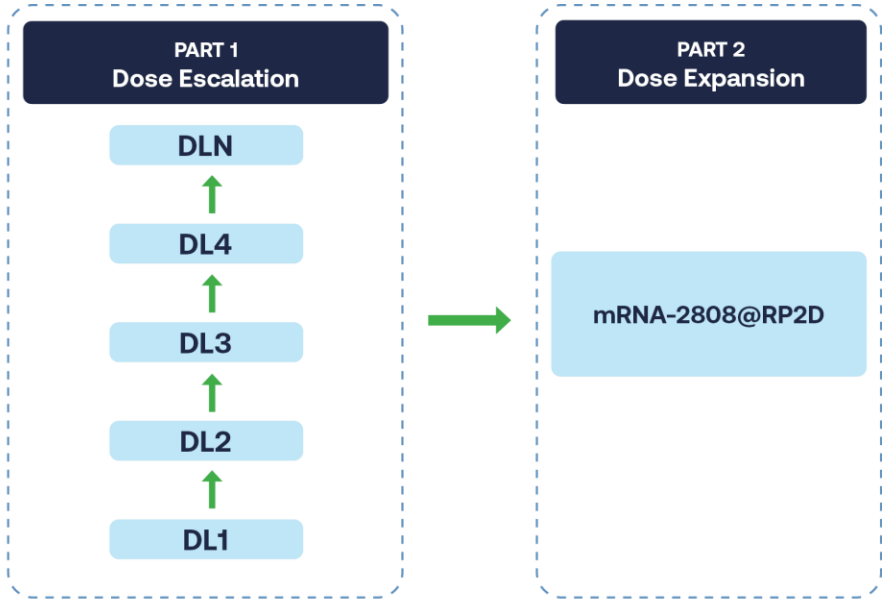


- Targets T-cell CD3 and tumor associated antigens (TAAs) that are present on the surface of the tumor
- Multiplexes to overcome antigen escape, well-established resistance mechanism
- Ability to multiplex other T-cell targets for co-stimulation

Phase 1/2 study design and key objectives

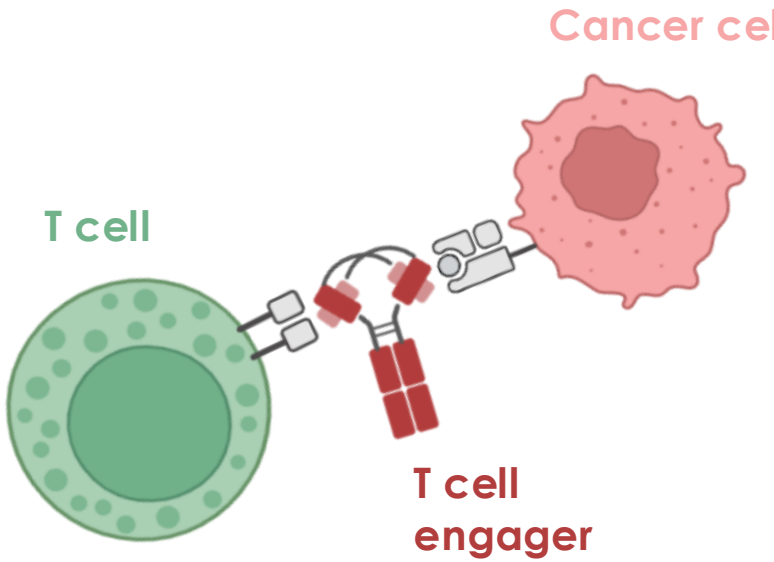
Primary endpoints: Safety, number of participants with dose limiting toxicity, number of participants with treatment-emergent adverse events

Secondary endpoints: Pharmacokinetics, pharmacodynamics, overall response rate by International Myeloma Working Group (IMWG), duration of response, progression-free survival



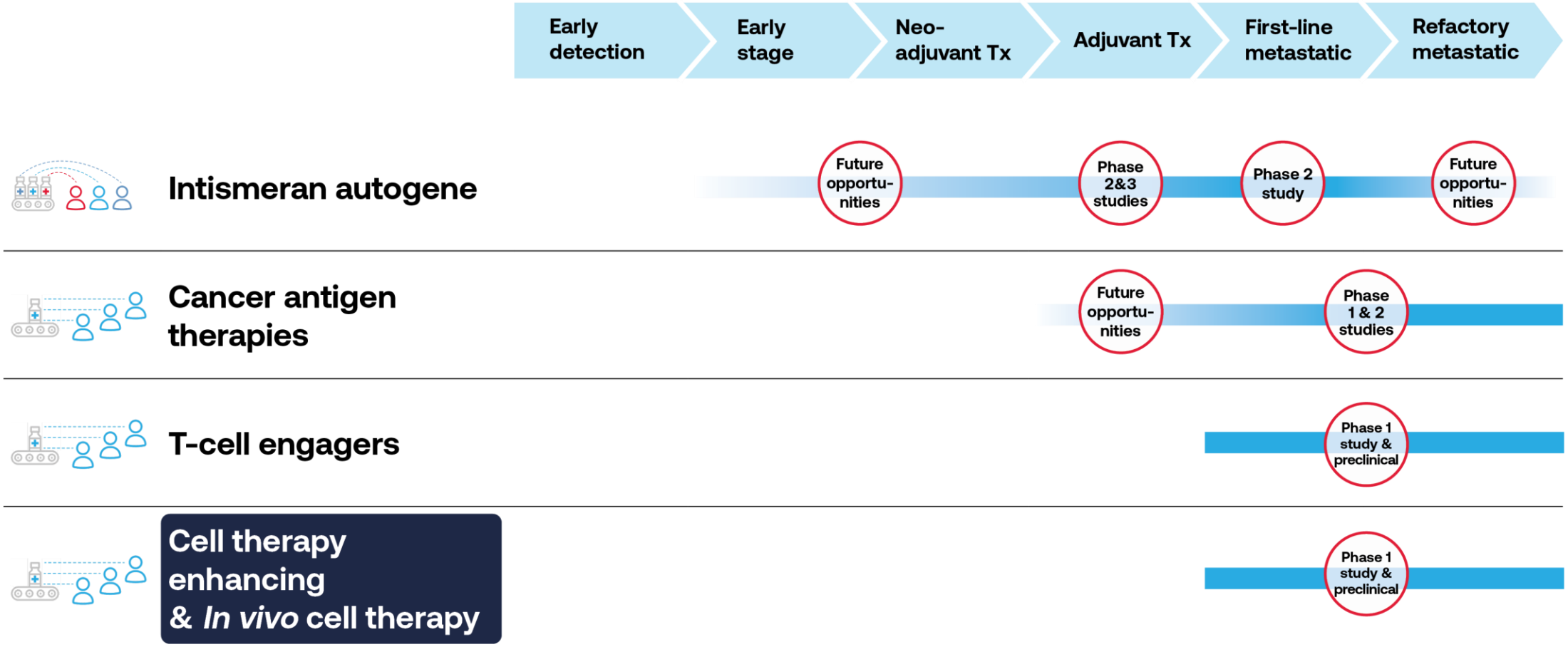
DL: dose level

Intracellular antigen T-cell engagers in preclinical development



- Targets T-cell CD3 and tumor-specific antigens that are processed and displayed as peptides by MHC
- Ability to multiplex to provide more coverage of intracellular proteins as well as across different HLA subtypes

Moderna oncology research and development programs across cancer disease stages



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Cell therapy enhancing candidate mRNA-4203 entering clinic

Cell-therapy enhancers + *In vivo* cell therapy

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Solid tumors (Partnered with Immatics)	mRNA-4203					
CAR-T/CAR-M	Preclinical					

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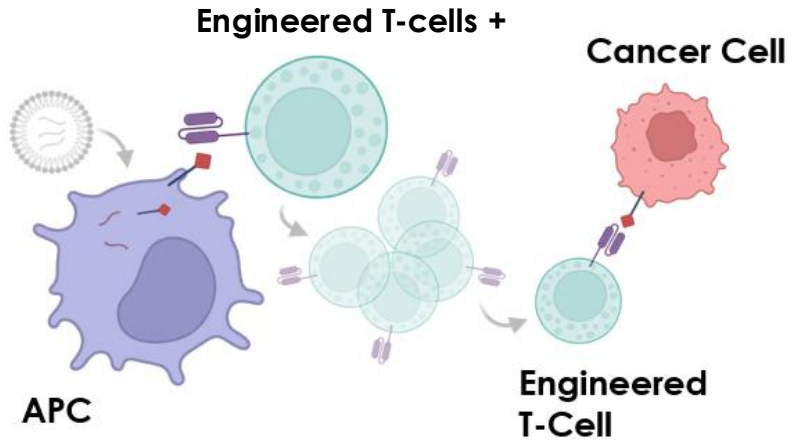
mRNA-4203 is a cell therapy enhancer in a Phase 1 study

mRNA-4203

In partnership with Immatics



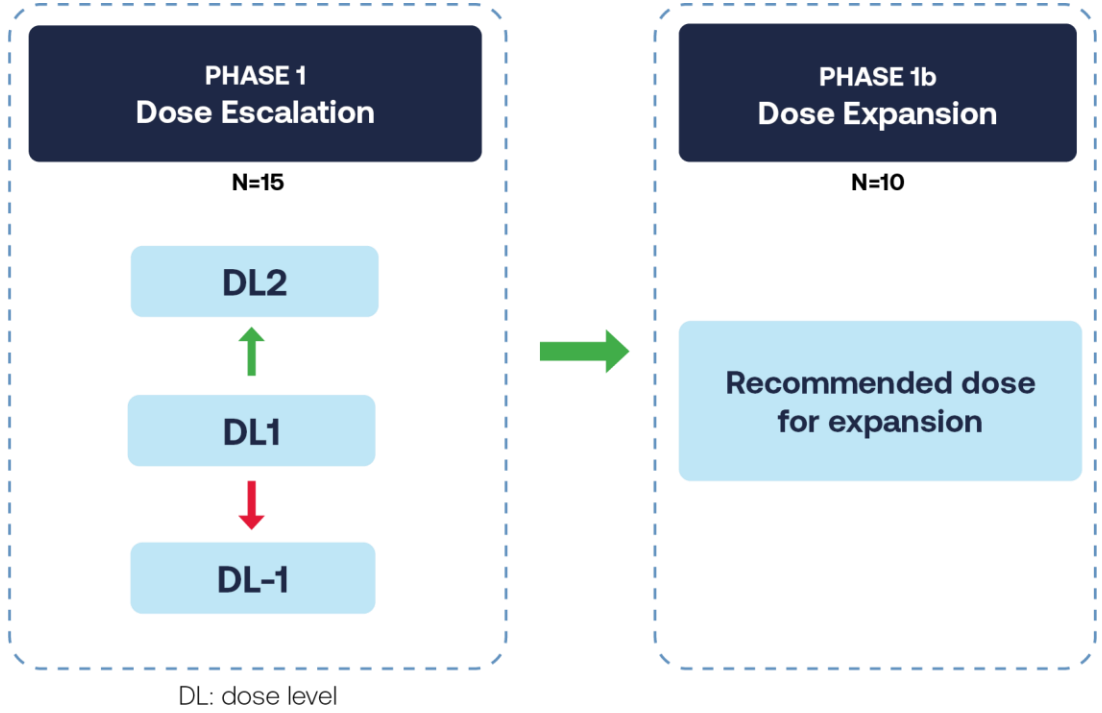
Cell therapy-enhancing antigen therapy

Encodes for the target of an *ex vivo* cell therapy to enhance the persistence and efficacy of the cell therapy

Phase 1 study design and key objectives

Primary endpoints: Safety, determine recommended dose expansion

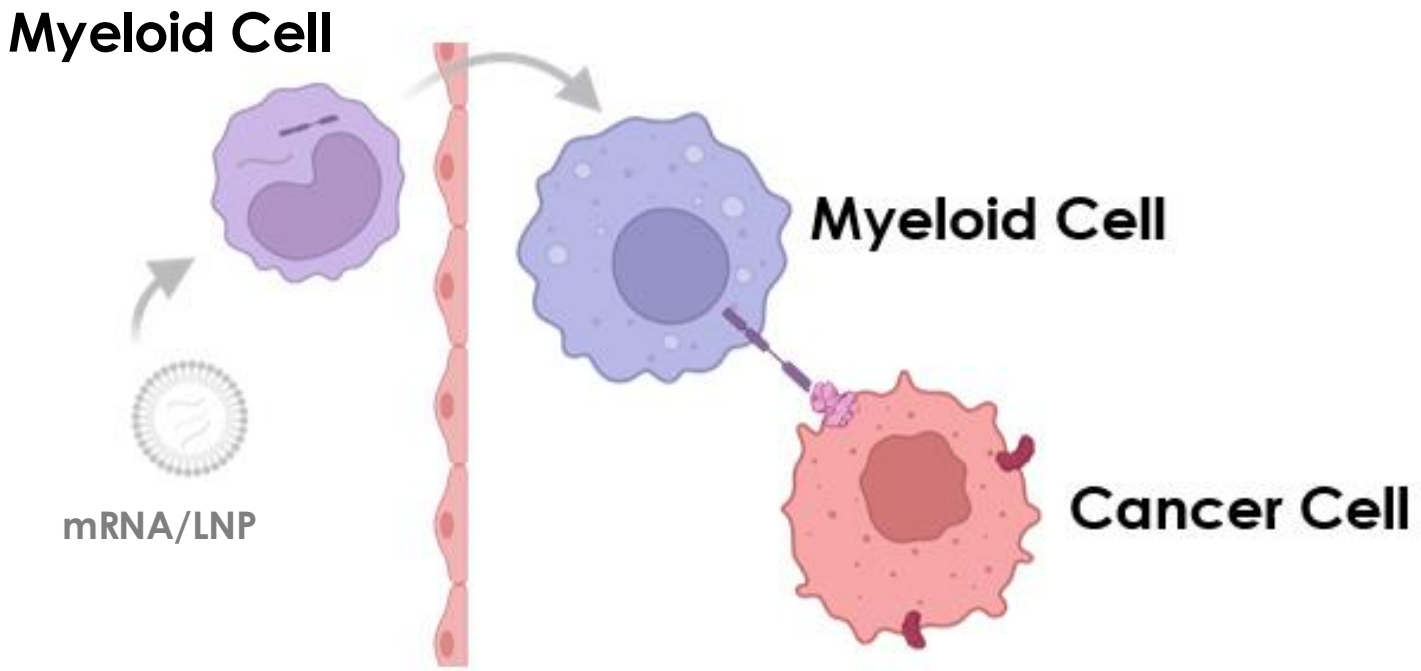
Secondary endpoints: Evaluate anti-tumor activity of IMA203 in combination with mRNA-4203 and evaluate the pharmacokinetics of TCR-engineered T cells in combination with mRNA-4203



DL: dose level

CAR-M/CAR-T candidates currently in preclinical development

Leverages mRNA-LNP technology to transfect myeloid or T-cells for in vivo CAR-M / CAR-T cell therapy



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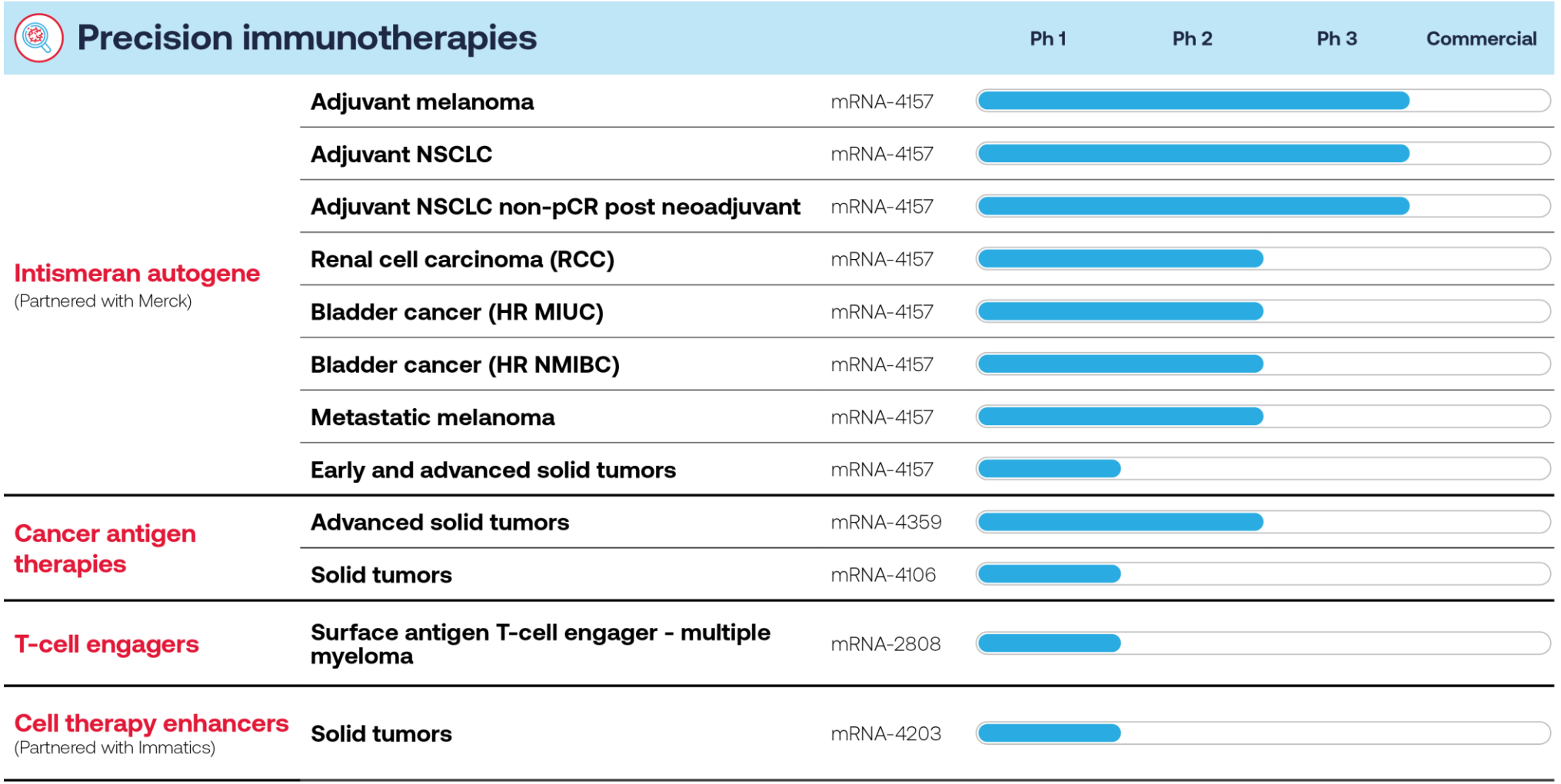
Moderna oncology clinical pipeline

Precision immunotherapies



Intismeran autogene (Partnered with Merck)	Adjuvant melanoma	mRNA-4157	Potential Phase 3 data readout in 2026
	Adjuvant NSCLC	mRNA-4157	
	Adjuvant NSCLC non-pCR post neoadjuvant	mRNA-4157	
	Renal cell carcinoma (RCC)	mRNA-4157	
	Bladder cancer (HR MIUC)	mRNA-4157	
	Bladder cancer (HR NMIBC)	mRNA-4157	
	Metastatic melanoma	mRNA-4157	
	Early and advanced solid tumors	mRNA-4157	
Cancer antigen therapies	Advanced solid tumors	mRNA-4359	Potential Phase 2 data readout in 2026
	Solid tumors	mRNA-4106	
T-cell engagers	Surface antigen T-cell engager - multiple myeloma	mRNA-2808	
Cell therapy enhancers (Partnered with Immatics)	Solid tumors	mRNA-4203	

Abbreviations: NSCLC, non-small cell lung cancer; pCR, non-pathological complete response; RCC, renal cell carcinoma; HR MIUC, high-risk muscle-invasive urothelial carcinoma; HR NMIBC, high-risk non-muscle invasive bladder cancer

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Moderna oncology research and development programs across cancer disease stages

	Early detection	Early stage	Neo-adjuvant Tx	Adjuvant Tx	First-line metastatic	Refactory metastatic
Intismeran autogene			Future opportu-nities	Phase 2&3 studies	Phase 2 study	Future opportu-nities
Cancer antigen therapies				Future opportu-nities	Phase 1 & 2 studies	
T-cell engagers					Phase 1 study & preclinical	
Cell therapy enhancing & In vivo cell therapy					Phase 1 study & preclinical	

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Thank you

Q&A