Barclays Speaking the Science: Moderna Oncology

June 16, 2025



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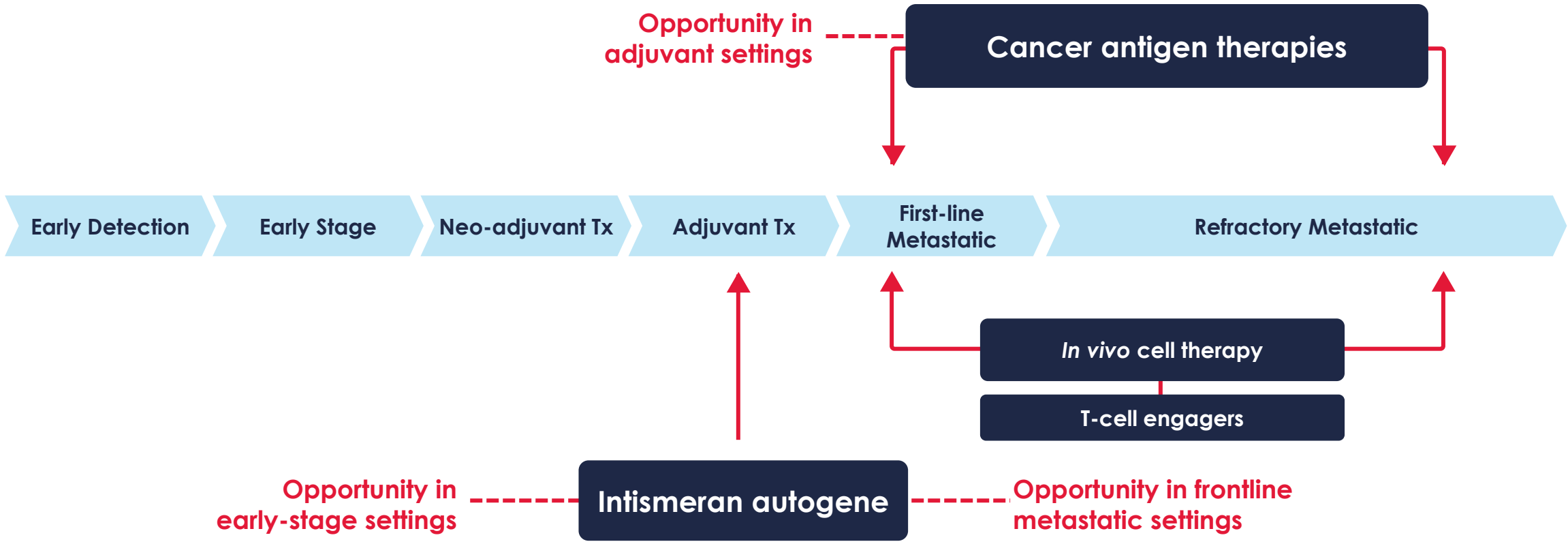
Advancing a vision to treat patients across all stages of cancer



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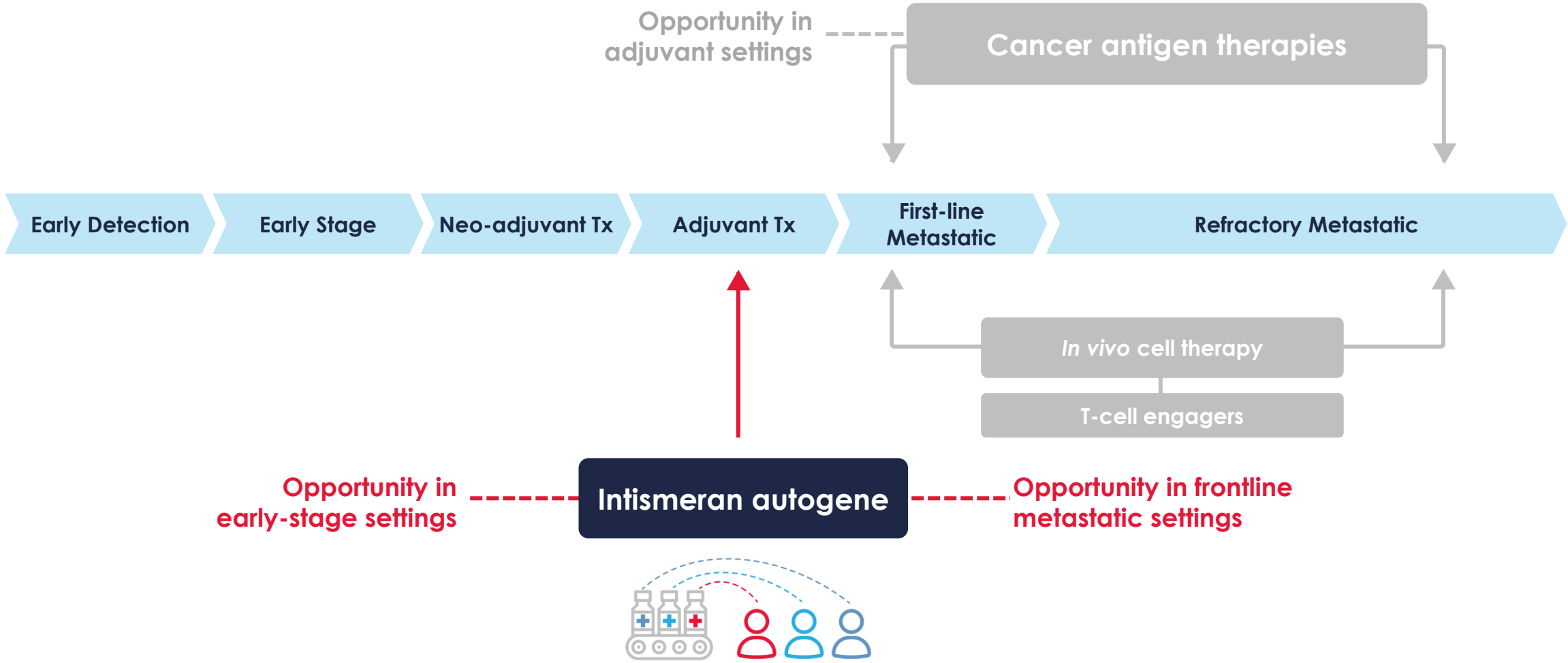

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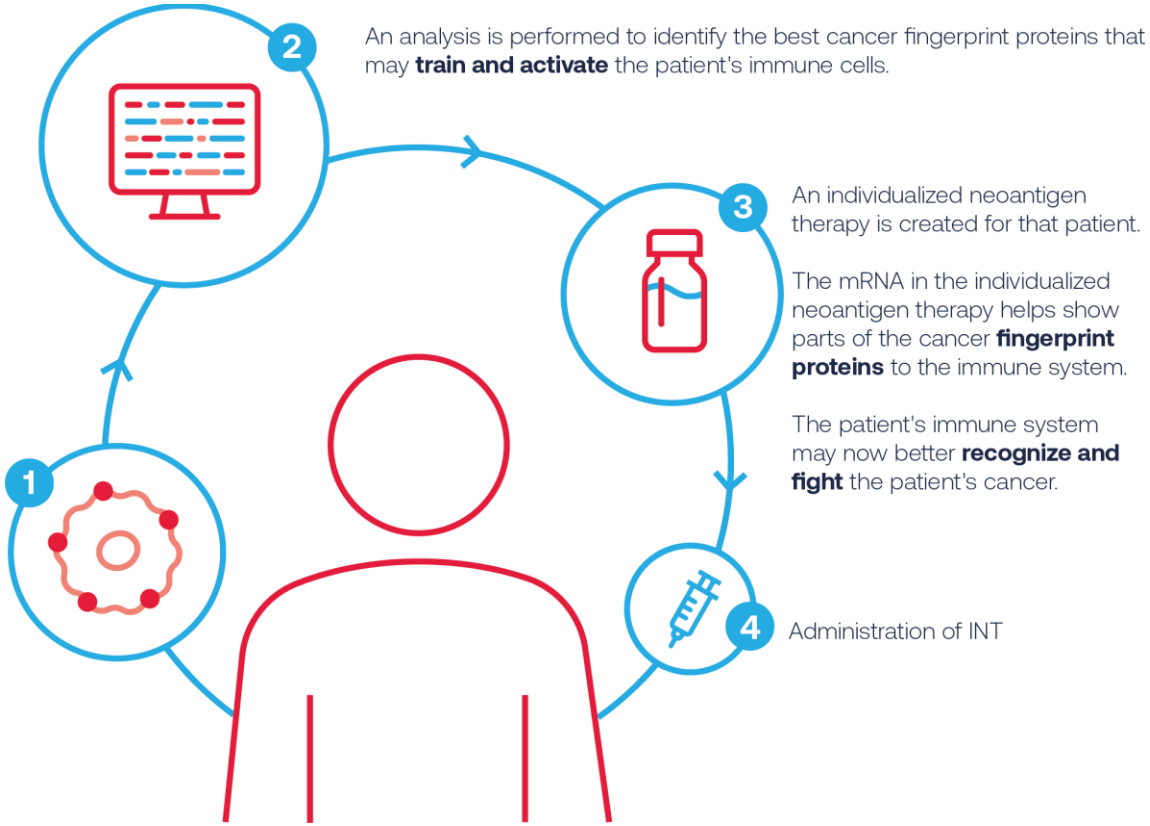
Intismeran autogene (mRNA-4157): Designed to target an individual patient's unique tumor mutation

How are individualized neoantigen therapies made?



Intismeran autogene
mRNA-4157

- **Adjuvant melanoma:** Phase 3 study fully enrolled
- **NSCLC:** in two adjuvant Phase 3 studies for those with and without prior neoadjuvant treatment
- **Adjuvant high-risk muscle invasive bladder cancer:** in randomized Phase 2 study
- **Adjuvant renal cell carcinoma**: in randomized Phase 2 study; fully enrolled
- **High-risk non-muscle invasive bladder cancer (HR NMIBC):** in randomized Phase 2 study
- **Solid Tumors: Melanoma, Gastric, PDAC, NSCLC**: In Phase 1 basket study

In collaboration with Merck

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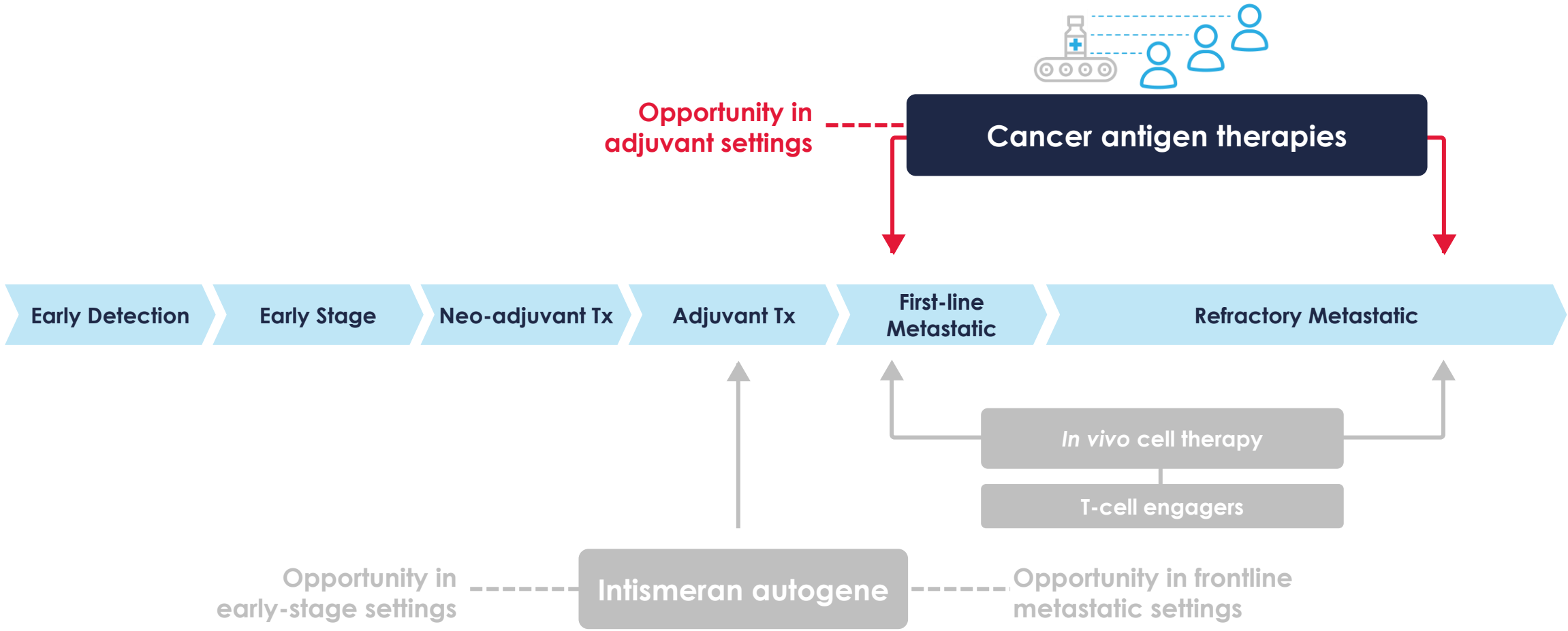

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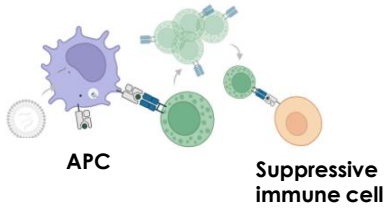
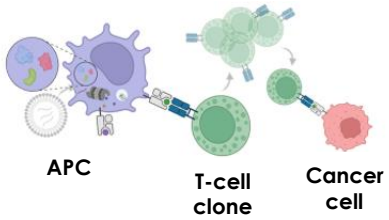
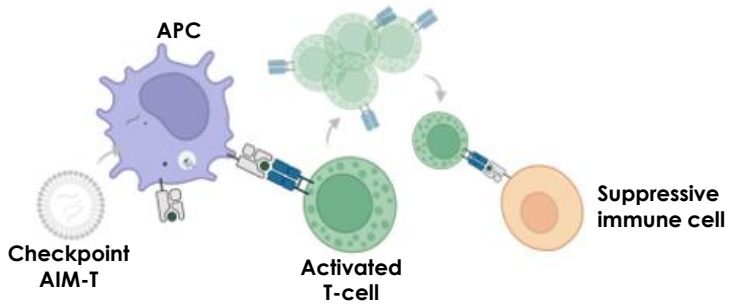
Off-the-shelf cancer antigen therapies

Cancer antigen therapies
Off-the-shelf therapies targeting shared antigens

Therapies	Development phase
 **mRNA-4359** Targets immunosuppressive cells and mechanisms	mRNA-4359 in Phase 2
 **Tumor-targeted antigen therapy** Targets tumor-specific and tumor-associated antigens shared across patients	mRNA-4106 in Phase 1

mRNA-4359 is ongoing in Phase 1/2 study; now enrolling Phase 2 with additional indications planned

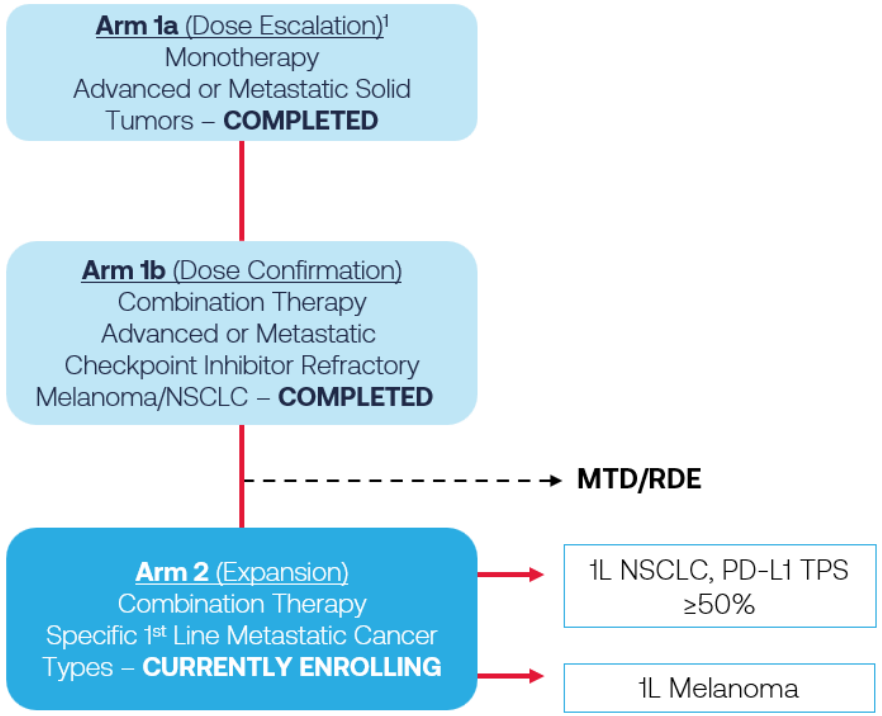
mRNA-4359



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



- **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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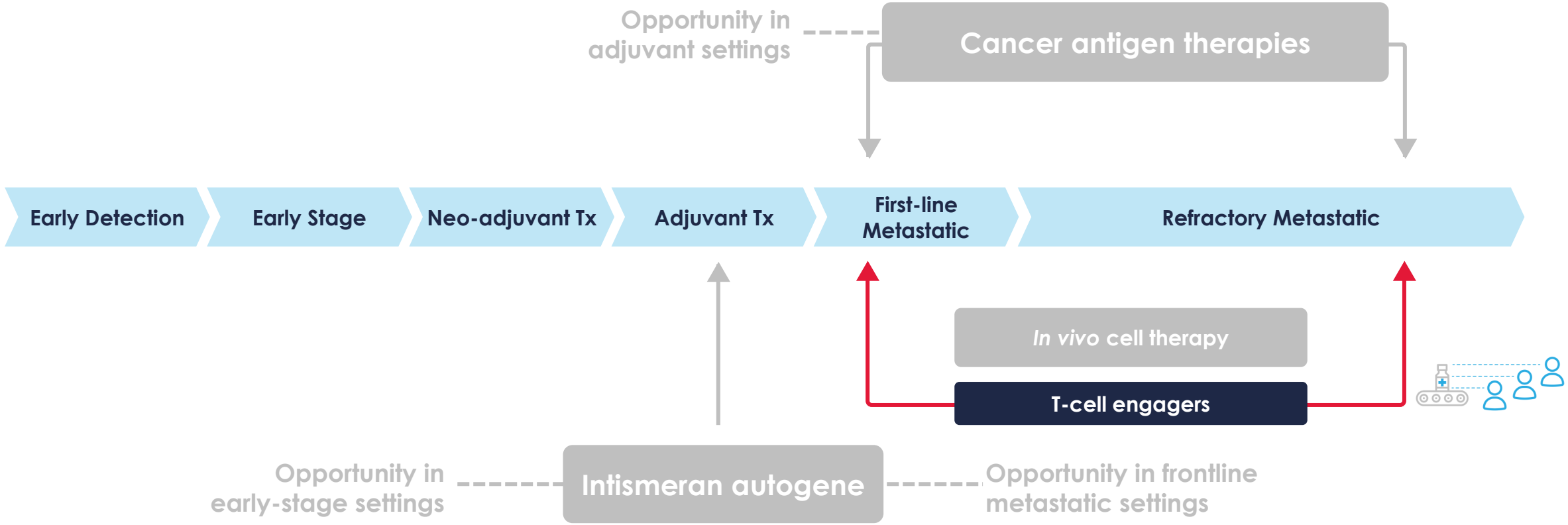

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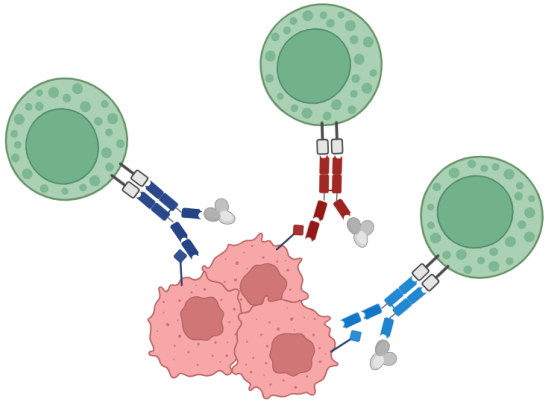
T-cell engagers: Two approaches with secreted T-cell engaging antibodies to target surface and intracellular proteins

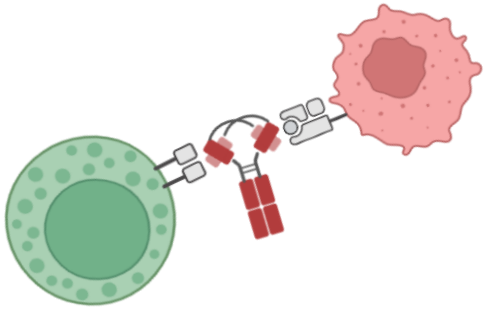
Surface Antigen T-Cell Engagers

- 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
- Potential to multiplex other T-cell targets for co-stimulation
- Defined pool of antigens with high tumor specificity



Intracellular Antigen T-Cell Engagers

- Targets T-cell CD3 and tumor-specific antigens that are processed and displayed as peptides by MHC
- Potential to multiplex to provide more coverage to intracellular proteins
- Large pool of intracellular antigens, on an HLA-specific basis



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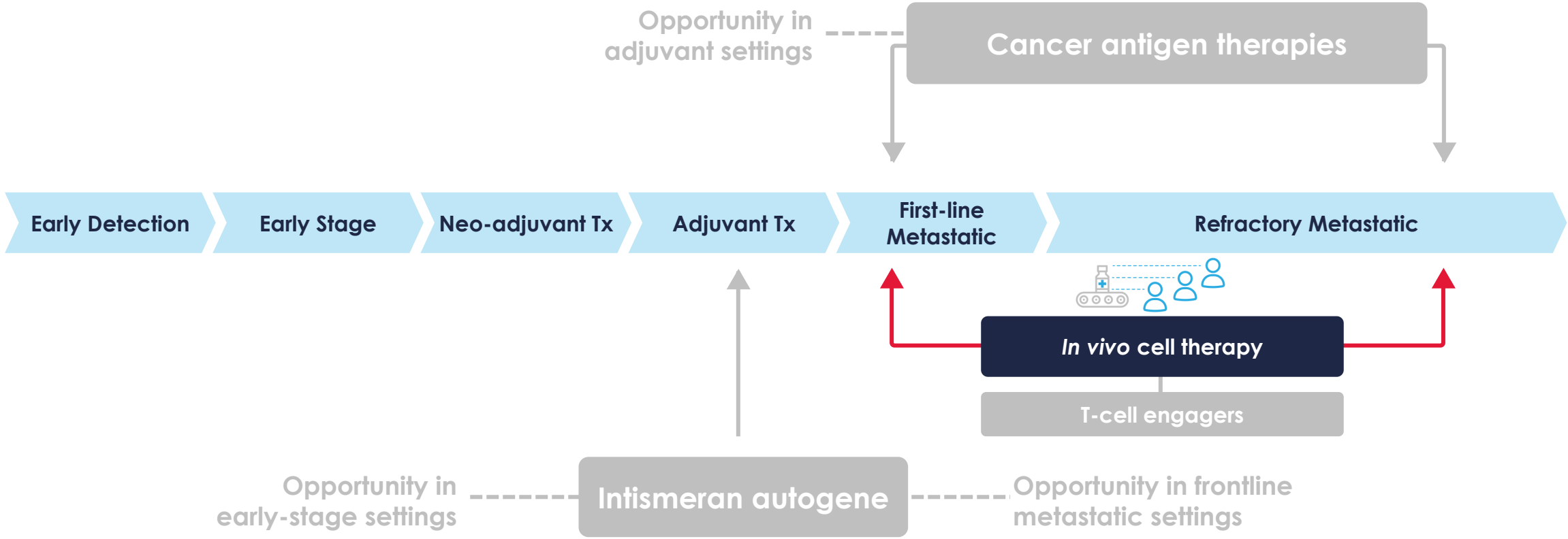

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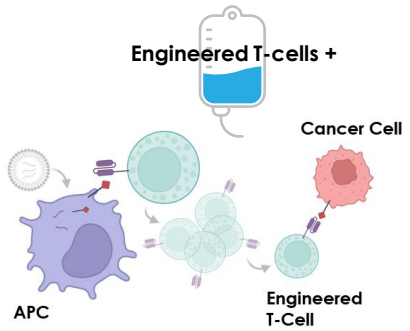
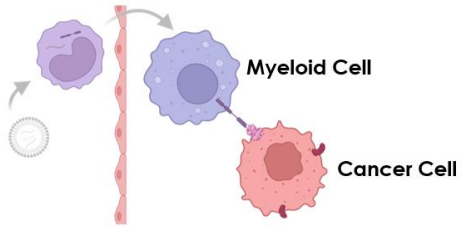
In vivo cell therapy: lead candidate entering clinic

***In vivo* cell therapy**





Therapies	Development phase
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	mRNA-4203: IND open *Partnered with Immatics*
CAR-M or CAR-T Leverages mRNA-LNP technology to transfect myeloid or T-cells for *in vivo* CAR-M / CAR-T cell therapy	Evaluating preclinical candidates

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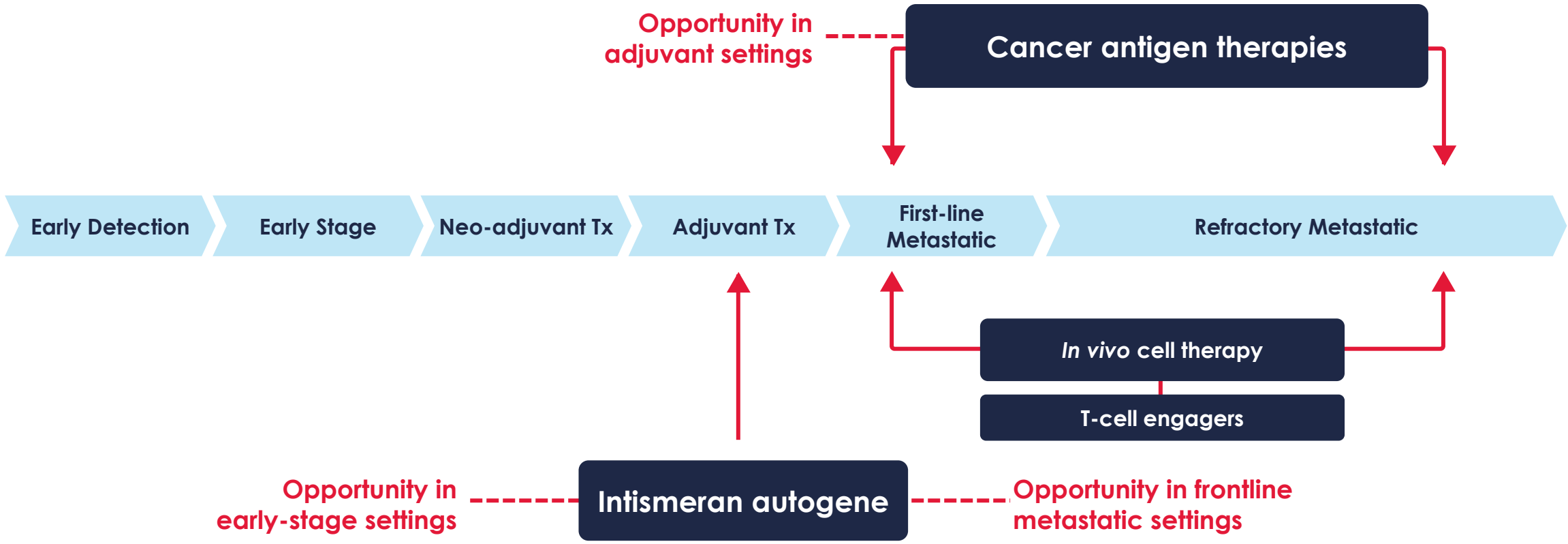

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