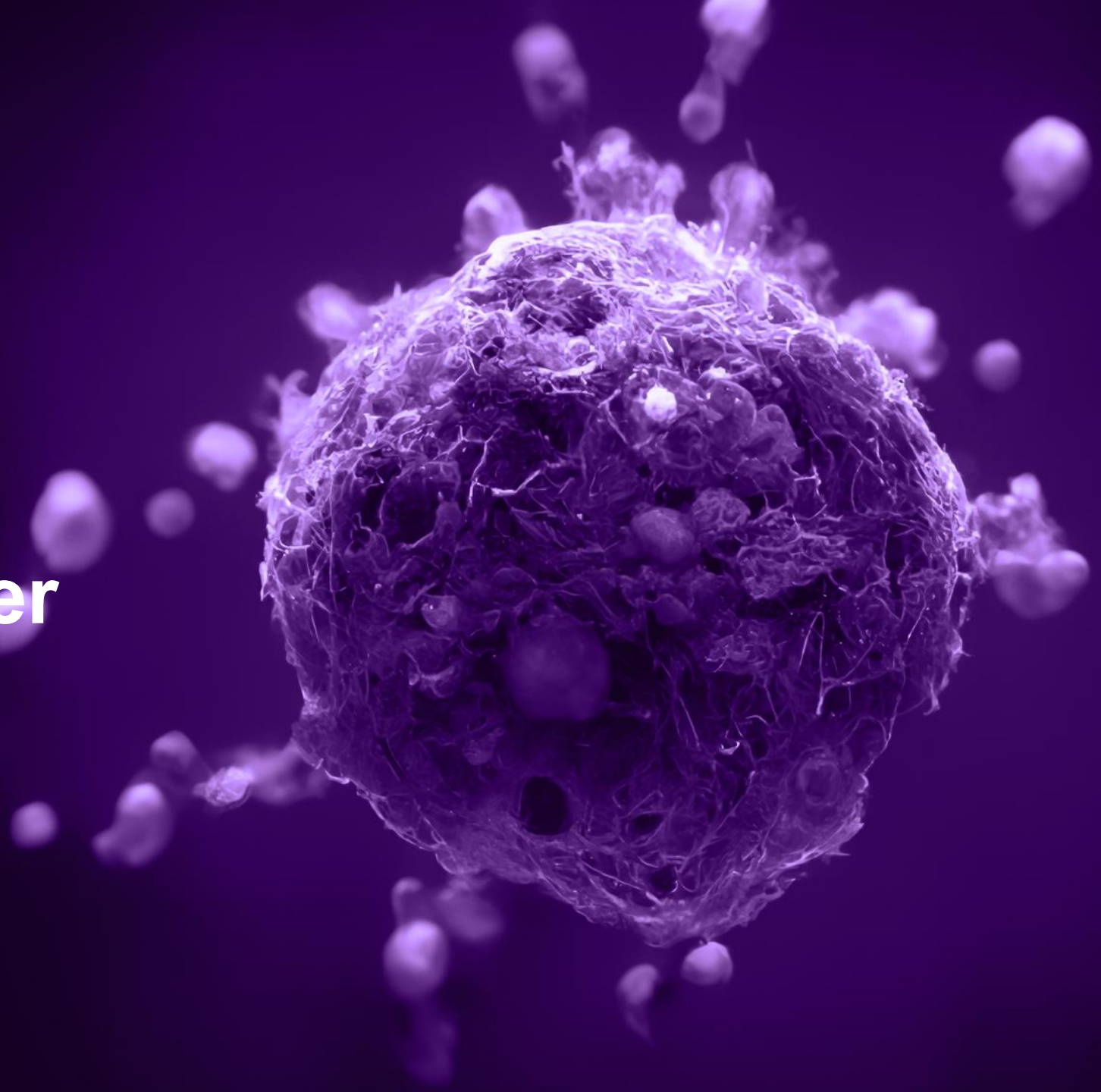
TuHURA biosciences

Overcoming Resistance to Cancer Immunotherapy

March 2026



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We are a Phase 3 immuno-oncology company developing three distinct novel technologies and therapeutics to overcome primary and acquired resistance to cancer immunotherapies

Investment Highlights

Overcoming resistance to cancer immunotherapies

IFx-2.0 in a Ph3 accelerated approval study in 1st Line Merkel Cell Carcinoma

- Top-line data expected 1H 2027
- Confirmatory trial not required
- SPA Agreement with the FDA

VISTA inhibiting Mab Ph2 study in AML, data expected in 3Q 2026

Immune modulating ADC proof-of-concept data Q2 providing partnering opportunity

Presentations at multiple scientific meetings across portfolio assets

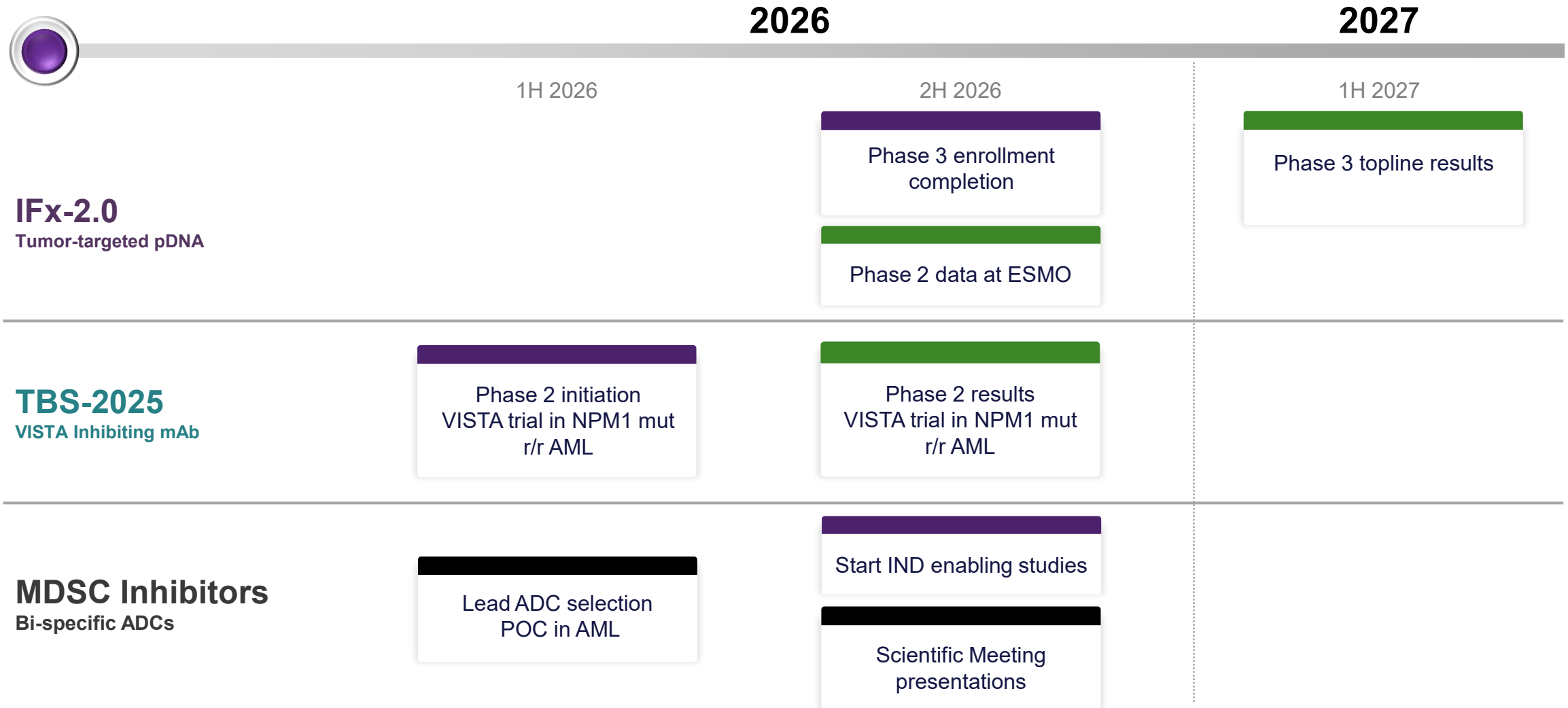
Cash balance adequate to reach key milestones in 2026

Diversified Immuno-Oncology Pipeline

PROGRAM	DRUG CANDIDATE	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	Upcoming Milestone
Innate Immune Agonists	**IFx-2.0 Tumor-targeted pDNA**	1st Line Merkel Cell Cancer Keytruda® +/- IFx-2.0 or placebo[1]					**1H 2027:** Phase 3 Topline Results
		Primary Checkpoint Inhibitor Resistant Metastatic Cancer "Basket" Trial					**Q3 2026:** Phase 1a/2b preliminary results ESMO*
TME Modulators **Negative Immune Regulators**	**TBS-2025 VISTA inhibiting mAb[1]**	*mut*NPM1 Acute Myeloid Leukemia					**Q2 2026:** Phase 2 Trial Initiation
TME Modulators **MDSC Inhibitors**	**Bi-specific ADCs**	Myelodysplasia Acute Myeloid Leukemia					**Q2- 2026** ADC *in vivo* POC studies

Trial completed under SPA agreement with U.S. Food and Drug Administration

Upcoming Milestones



Results Trial Initiation or completion Regulatory Updates

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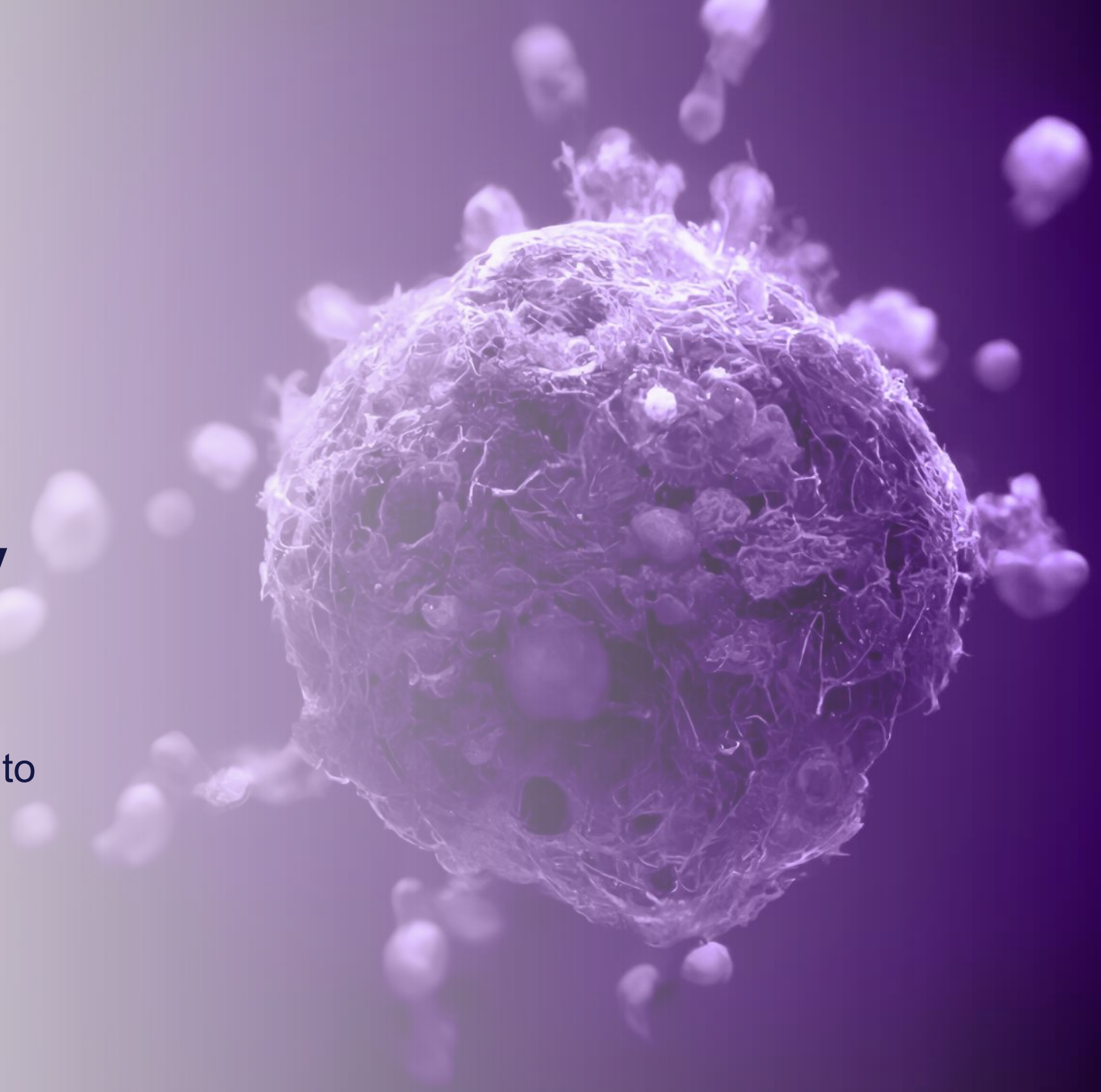
IFx Technology

Innate Immune Agonists

Designed to Overcome Primary Resistance to Checkpoint Inhibitors



IFx-2.0: Mechanism of Action

Making a Tumor Look Like a Bacterium

Initiation of an Innate Immune Response

1

Intra-tumoral injection of pDNA results in expression bacterial protein on surface of tumor – making tumor look like a bacterium

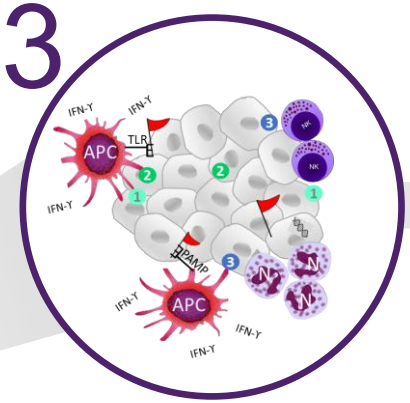
2

Molecular patterns on bacterial protein conserved through evolution, recognized by pattern recognition receptors (TLR2) on APCs

Activation of Tumor Specific T Cells

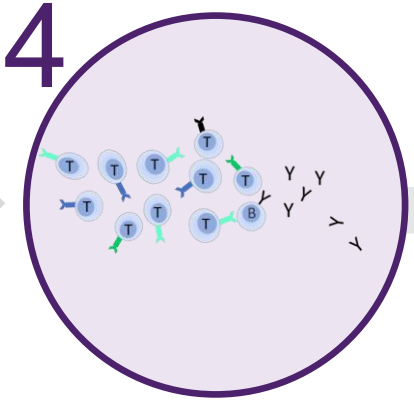
Allows CPI to work where they previously failed

3



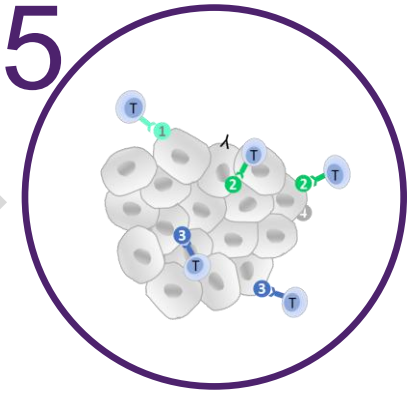
APCs 'ingest" intact tumor cell, package and present all tumor neoantigens to B and T cells leading to activation of tumor specific B and T cells (1^0 epitope spreading)

4



Tumor-reactive T and B cell activation, amplification, trafficking and antibody production (adaptive response)

5



Tumor-specific T cell killing and release of "new / different" tumor antigens (2^o epitope spreading)

Presenting full complement of neoantigens from intact tumor cell *provides optimal neoantigen presentation and inter-antigenic epitope spreading more effectively than Oncolytic Viral or Individual Neoantigen Therapy approaches.*

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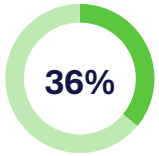
Advanced Metastatic Merkel Cell Carcinoma

50% of Patients Don't Respond to 1st Line Keytruda®

Keytruda® (pembrolizumab) is the 1st line standard of care for advanced metastatic MCC

Complete Response *(CR) rate*



Partial Response *(PR) rate*

Progressive Disease *(PD) rate*

Increasing Keytruda's Response Rate in 1L metastatic MCC is an attractive commercial opportunity

Addressable Market Size (2025-2034)

~8,167 to ~14,891 patients

US, EU4, UK*

Probability of disease progression at two years is 26%, 57% and 100% for those with CR, PR and SD, respectively

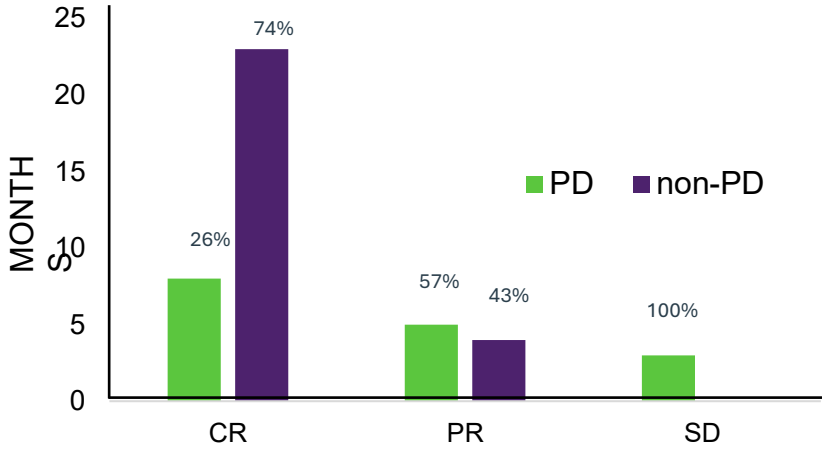


Figure 1. Rate of PD based on best ICI response

Sources: N Engl J Med 2016; 374:2542-2552 DOI: 10.1056/NEJMoa1603702 *DelveInsight Merkel Cell Carcinoma (MCC) -- Market Insight, Epidemiology, and Market Forecast – 2034

Phase 1b Study in Advanced Skin Cancer

(Merkel Cell and Cutaneous Squamous Cell Carcinoma)

Enrolled n=23

(13 MCC, 10 SCC)

Safety evaluable (n=21) TRAEs

Grade 1 35% (8)

Grade 3 4% (1)

Dose and Schedule selected: 1-3 lesions, Weekly x 3

Response evaluable MCC (n=9)

1^0 CPI resistance, no Rx between 1st line and IFx-2.0

Best Overall Response 66%

3 CR (includes 1 pCR)

3 PR

Median Duration of Response 21 months

(range 6 – 33; 4 ongoing time of data cut-off)

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Sources: N Engl J Med 2016; 374:2542-2552 DOI: 10.1056/NEJMoa1603702 *DelveInsight Merkel Cell Carcinoma (MCC) -- Market Insight, Epidemiology, and Market Forecast – 2034

Single Phase 3 Accelerated Approval Trial

Designed with OCE[1] – Utilized Project Front Runner Initiative

1st line CPI naïve, advanced/metastatic MCC
1:1 Randomization, Placebo, Injection Controlled Trial

Enrolling ~118 patients

IFx-2.0 weekly x 3 + pembrolizumab VS pembrolizumab + placebo

21of 25 U.S. clinical centers initiated, screening, enrolling patients

SPA Agreement with FDA

- Moved to 1st line indication after reviewing 2nd line results
- ORR allows for potential accelerated approval
- No requirement for post-marketing trial
- PFS converts accelerated to full approval
- Would satisfy requirement for confirmatory trial

Primary Endpoint

Overall Response Rate (ORR)

Key Secondary Endpoint

Progression Free Survival (PFS)
Stepwise hierarchal design preserves alpha allocation)

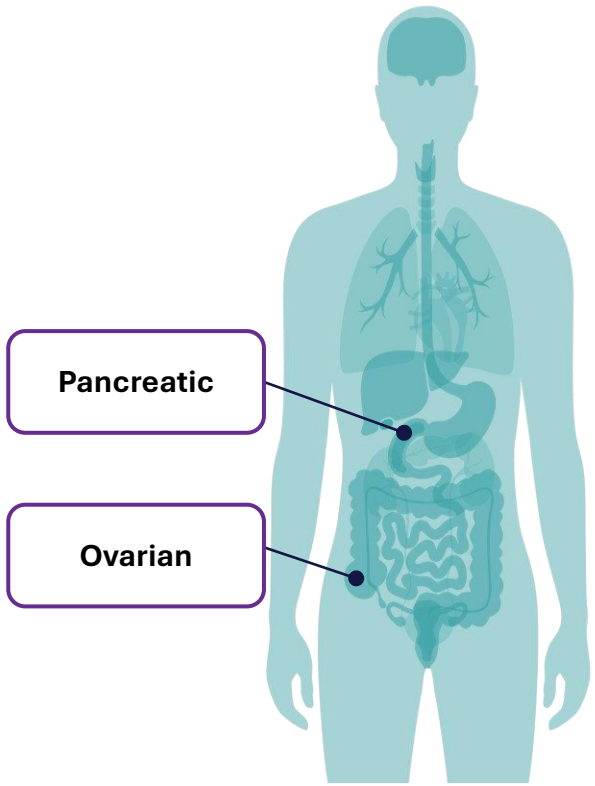
Study Timeline

FPI – first patient in LPI - last patient in TLR - topline results

[1]Oncology Center of Excellence

Phase 2 trial in MSI-low Deep-Seated Tumors Expands Commercial Opportunity Beyond Merkel Cell Carcinoma

Image Guidance for Broader Usage Through Interventional Radiology

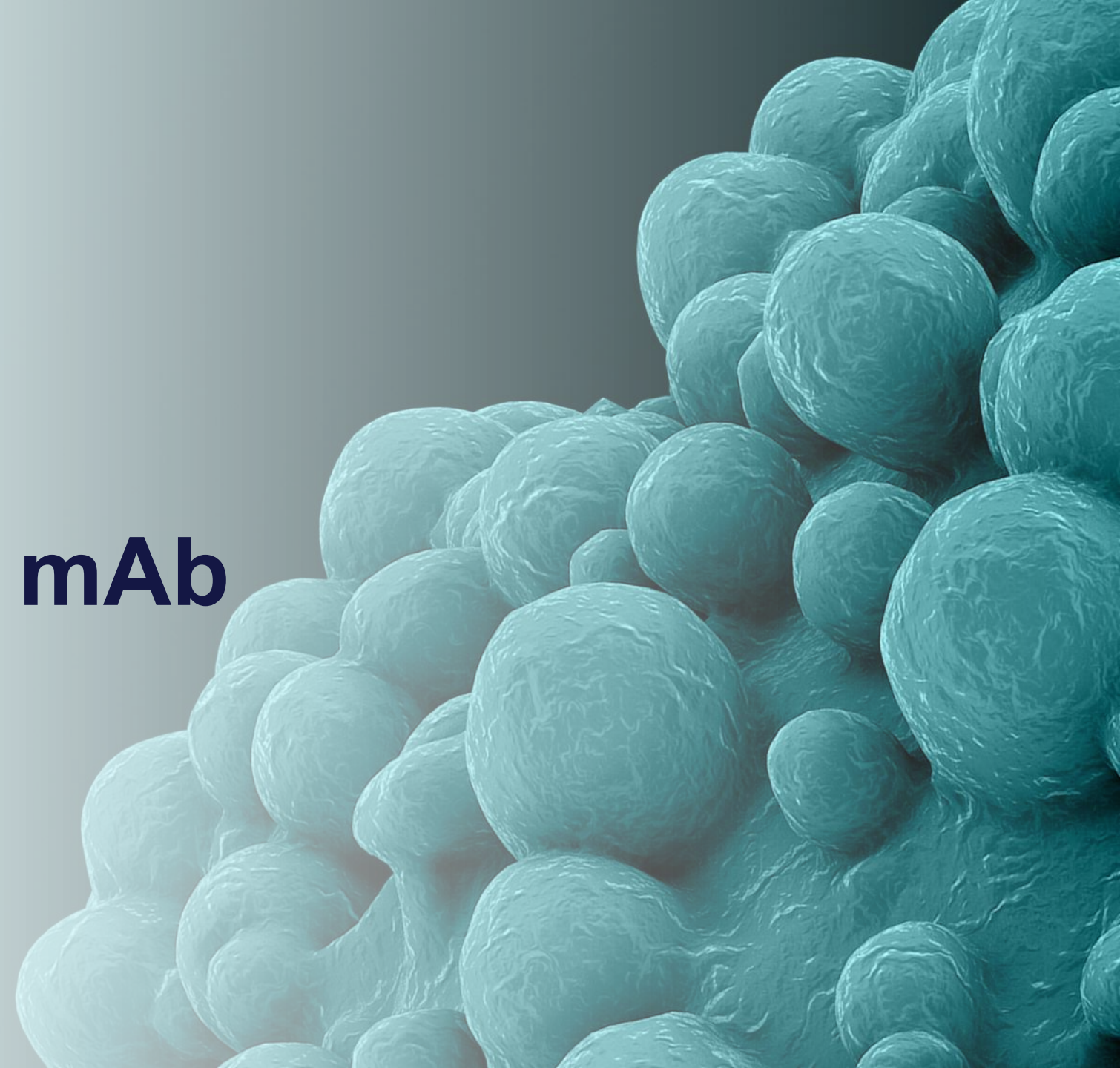


- **Biology of 1^0 resistance is common across tumor types (histology agnostic)**
  - MSI-low and MSS tumors are non-immunogenic
  - Lack activated tumor specific T cells
- **Objective: enhance tumor immunogenicity and activate tumor specific T cells**
- **IFx-2.0 patients with MSI-low/MSS cancers**
  - Safety IFx-2.0 administration via interventional radiographic technique to deep seated tumors (liver, lung, retroperitoneal) as adjunctive Rx to Keytruda®
    - Patients with deep seated MCC not eligible for P3 trial
    - Patients with demonstrated MSI-low/MSS tumors (pancreatic, ovarian)
- **Preliminary data targeted for ESMO presentation**

Sources:
1. Zhao B, et al. Ther Ady Med Oncol. 2020;12:1-22;
2. 2. Sun JY, et al. Biomark Res. 2020;8:35; 3. Zhang T, et al. Oncotarget. 2016:7(45):73068-73079.

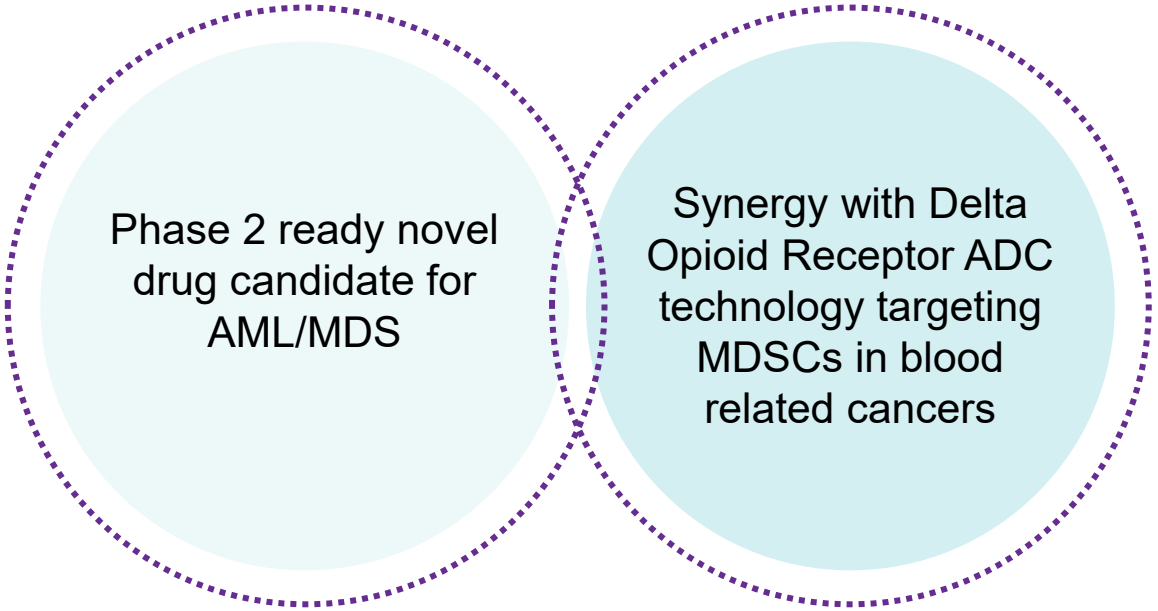
TBS-2025
VISTA Inhibiting mAb

*mut*NPM1 Acute Myeloid Leukemia (AML)



Targeting VISTA: a new checkpoint target in AML, MDS

Strategic Focus and Technology Synergies



Broad Potential in Blood Related Malignancies

VISTA is a novel checkpoint highly expressed on:

- Leukemic blasts
- Myeloid Derived Suppressor Cells (MDSCs)
- Quiescent T Cells – VISTA maintains resting state, preventing activation

VISTA plays a central role in therapy failure and relapse in both AML and MDS

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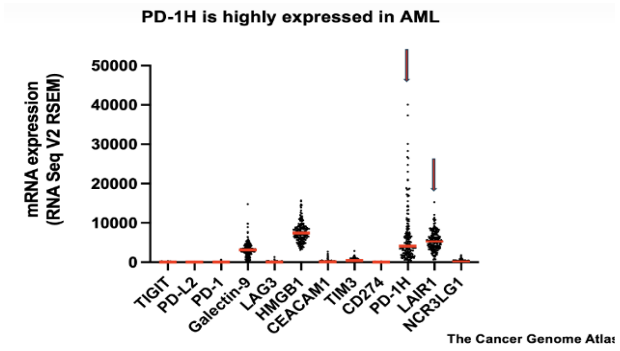
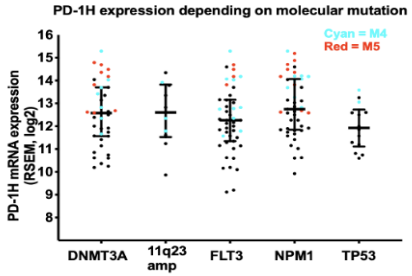
* Formerly KVA12123

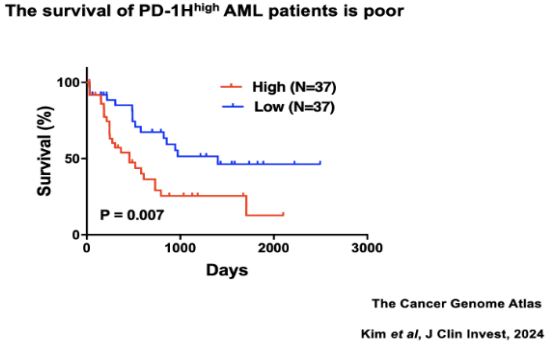
TBS2025: Scientific Rational for VISTA in AML

Strong Scientific Rational for VISTA in AML

- Only checkpoint highly expressed in AML responsible for immune evasion
- Presence on leukemic blast correlates with poor survival
- Expression driven by most common mutations in AML (DNMT3A, NPM1)
- Menin inhibitors <25% CR/CRh in mutNPM1 r/r AML , short duration 4.7 months
- Increasing CR/CRh in mutNPM1 r/r AML represents unmet medical need







Kim *et al*, J Clin Invest, 2024

PD-1H = VISTA

TBS-2025: Inhibiting VISTA in AML to improve Complete Remission

Phase 2 Trial Design[1]

Group 1
Menin inhibitor naïve *mut*NPM1 r/rAML

- Simon 2 stage design
- Stage 1
  - 14 patients TBS-2025 + menin inhibitor
  - Success ≥4 CR/CR_h to advance
- Stage 2
  - 26 patients
  - *Success CR/CRh ≥35% (14/40)

Group 2
Menin inhibitor exposed mutNPM1 r/rAML

- Exploratory design in menin inhibitor resistant AML
- Progression on or after menin inhibitor in 1st line HMA/Ven therapy

*CR/CRh 95% CI 12% to 34% in menin inhibitor trials
1Protocol design provided to FDA.

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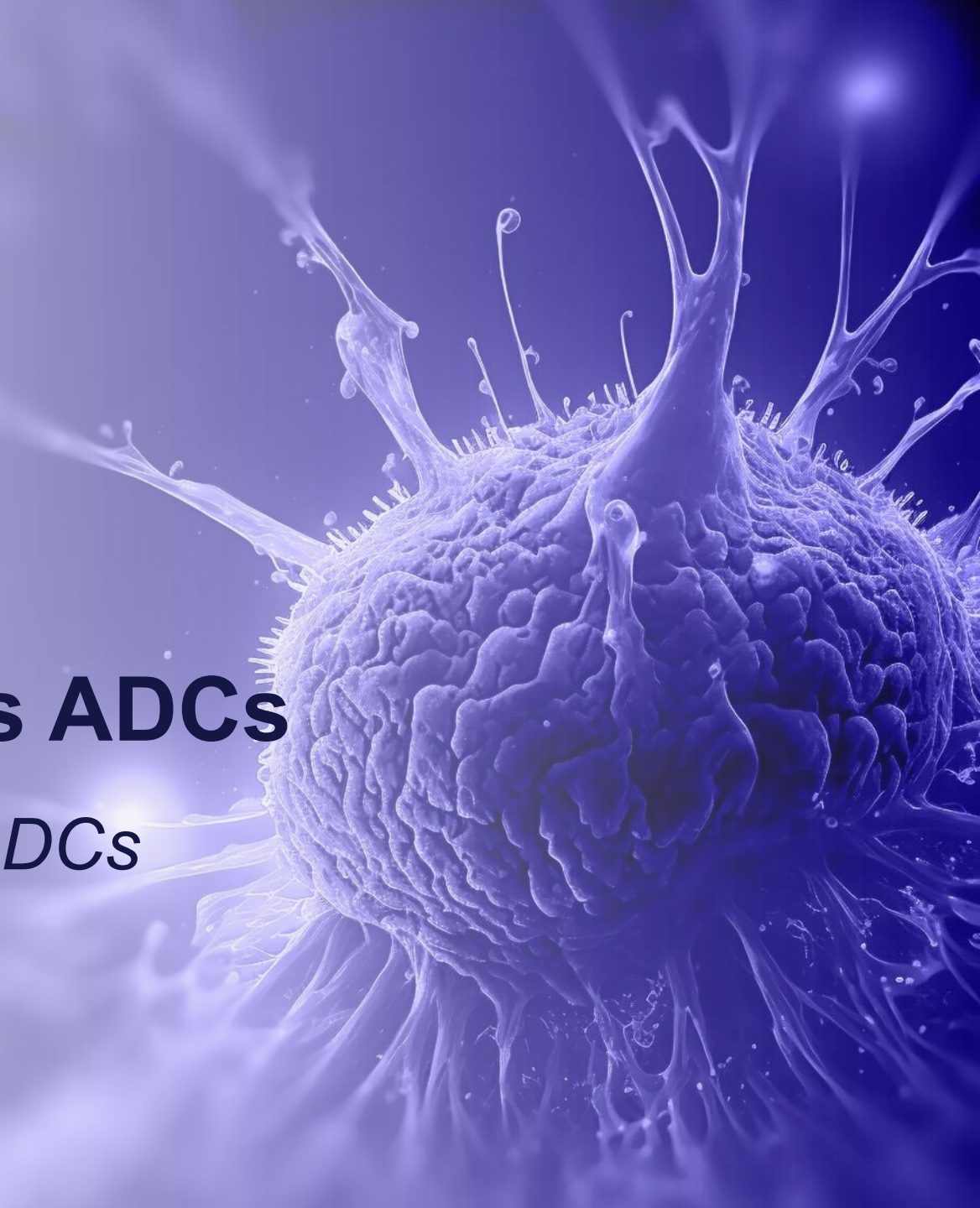
Bi-Specific, Bi-Functional Antibody Drug Conjugates ADCs

First in class immune modulating ADCs



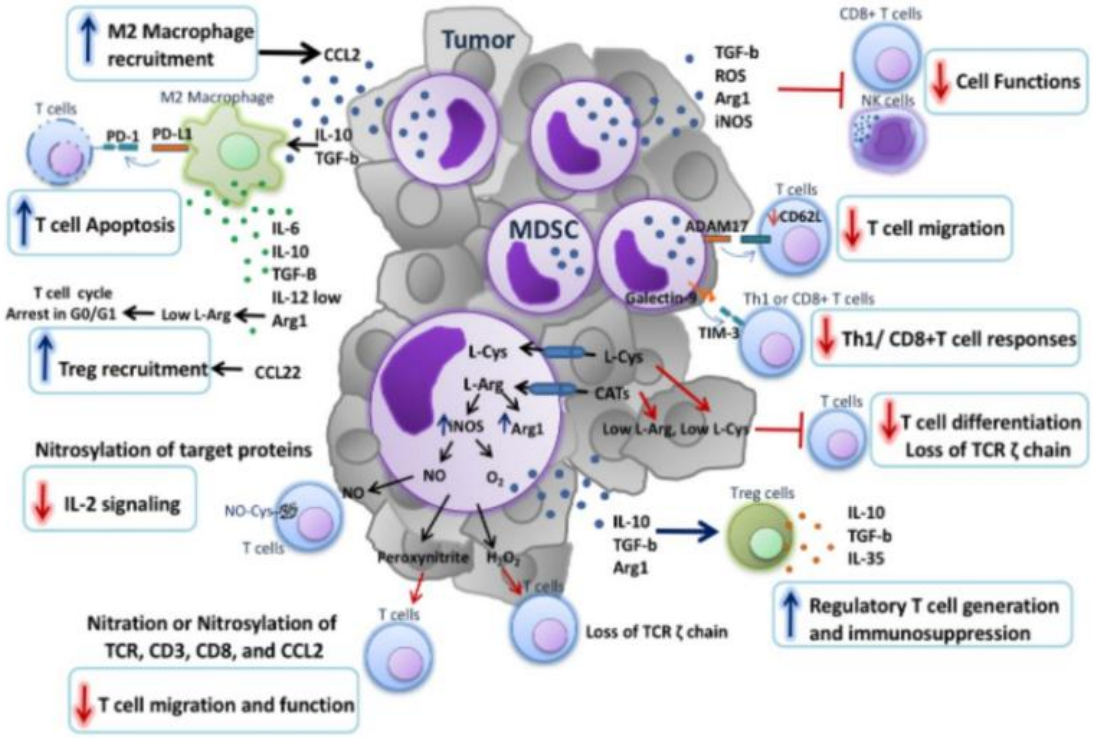
*DOR – Delta Opioid Receptor

Reprograming MDSC Immune Suppressing Functions

(Novel approach to overcome acquired resistance to cancer immunotherapies)

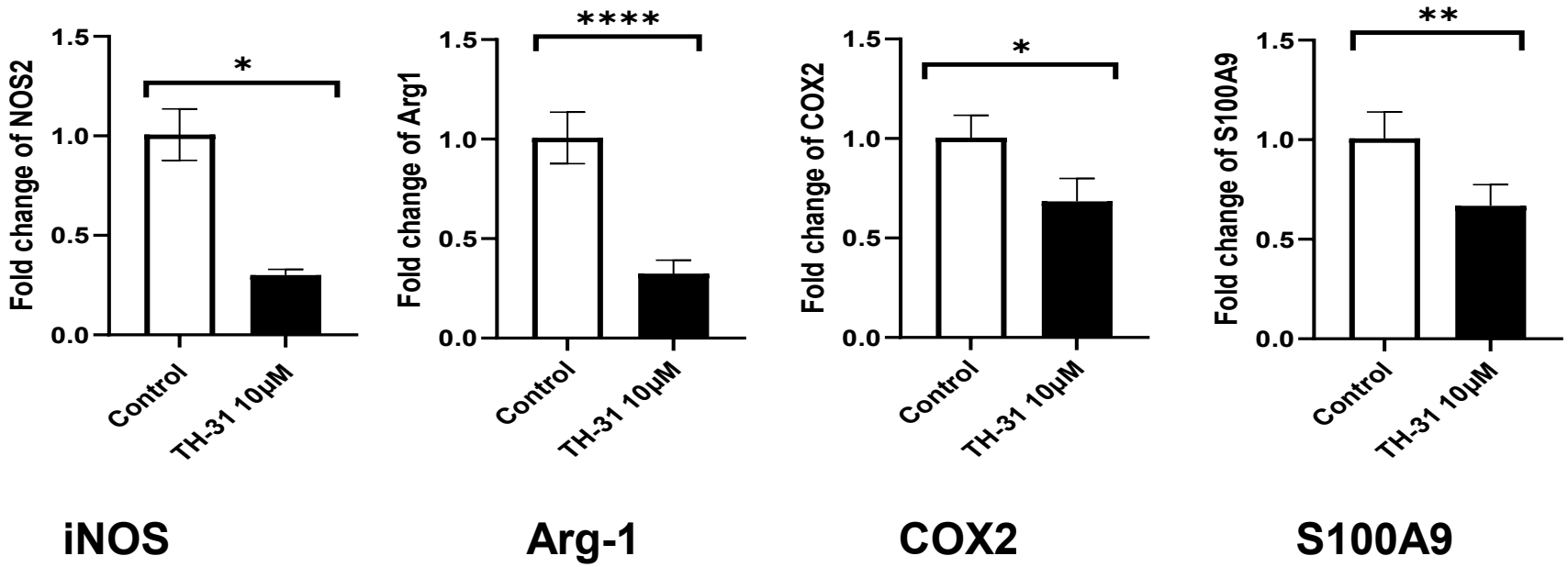
- MDSC are normally produced during pregnancy; provide immune sanctuary for fetus
- Hijacked by tumors, responsible for immunosuppression in the TME
- Tumor associated MDSCs
  - Produce multiple immune suppressing factors (Arg-1, iNOS, COX2)
  - Also express high levels of VISTA
  - Inhibit T cell proliferation, leads to acquired resistance to cancer immunotherapies

MDSC immunosuppressive activities



Delta Opioid Receptor (DOR) – a single target to control expression of multiple immune suppressing genes in MDSCs

qPCR assessment of suppressive genes in MDSCs
Before and after DOR inhibition



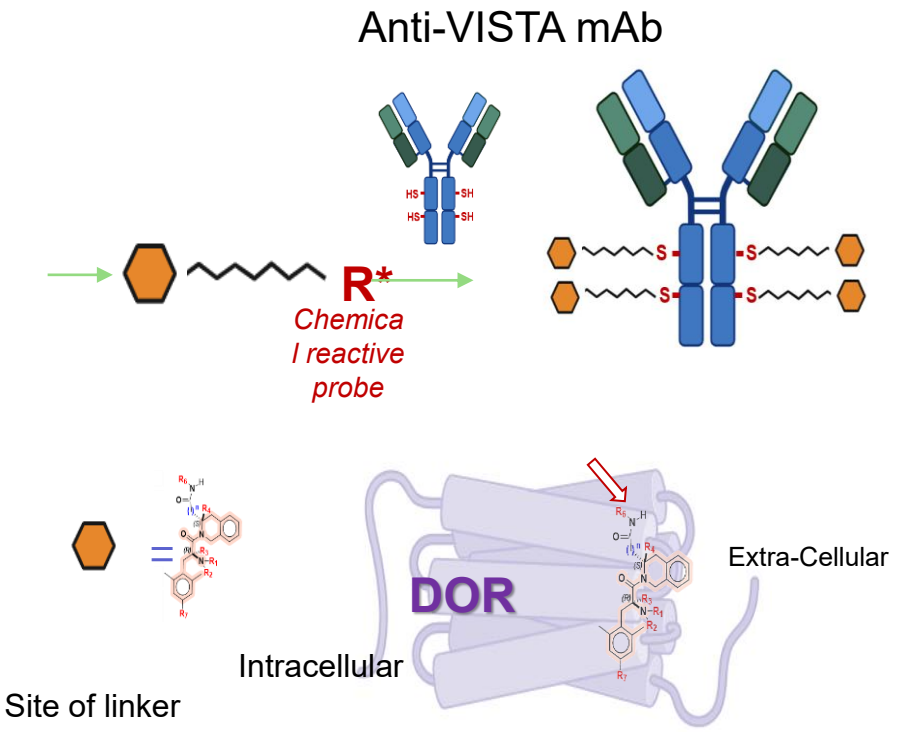
iNOS **Arg-1** **COX2** **S100A9**

* p≤0.05, and ** p≤0.001, *** p≤0.001, **** p ≤ 0.0001

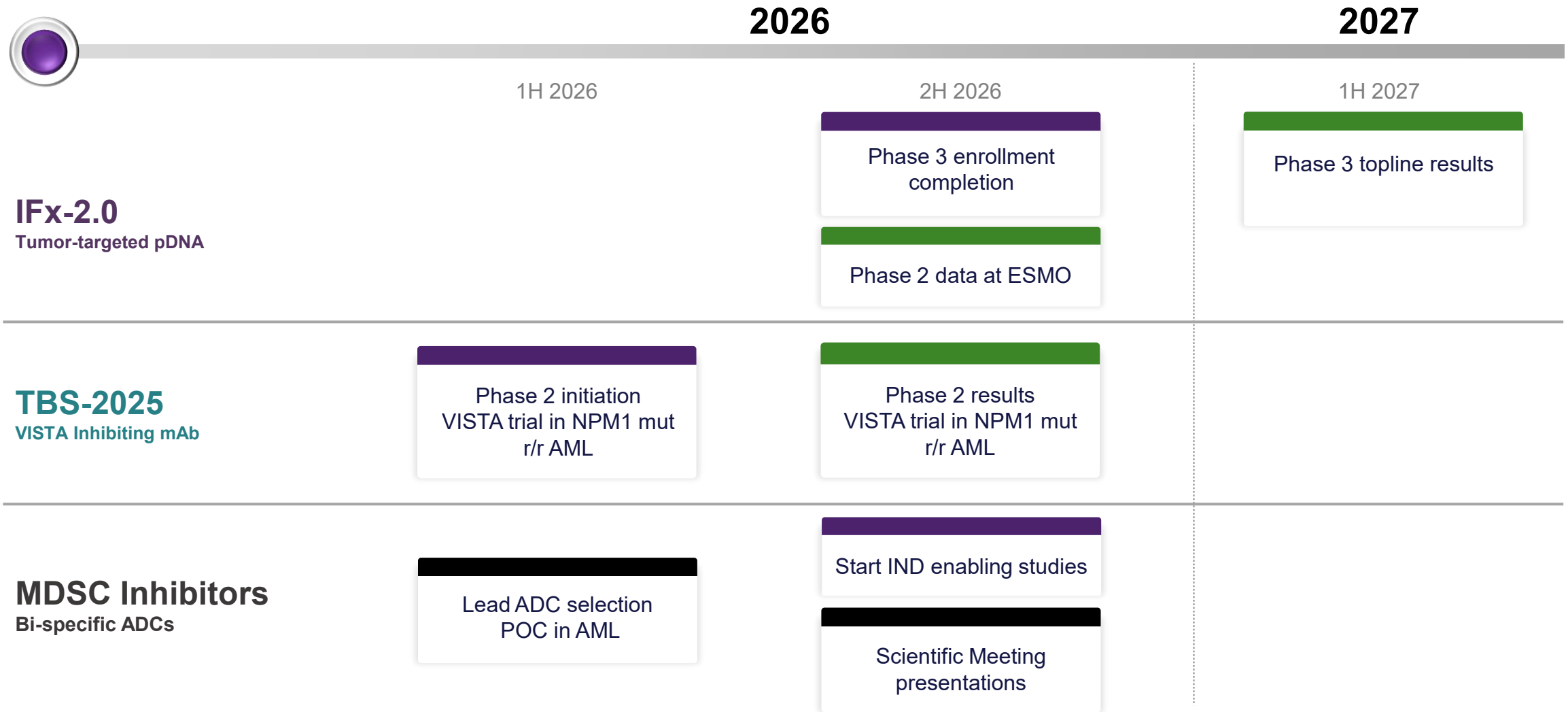
First in Class Bi-functional, Bi-specific Antibody Drug Conjugates$_{(ADC)}$

Differences from Current ADC Approaches

- Non tumor targeting, internalizing, nor cytotoxic, cell cycle targeting payloads
- Bi-specific:
- Targets both DOR and VISTA on MDSCs
- Bi-functional:
  - Antibody: TBS-2025 targets VISTA on immune suppressing cells and quiescent T cells allowing T cell activation
  - Drug : HURA-101 inhibits DOR on MDSC removing their immune suppression, reversing T cell suppression to normal proliferation levels



Upcoming Milestones



Results Trial Initiation or completion Regulatory Updates

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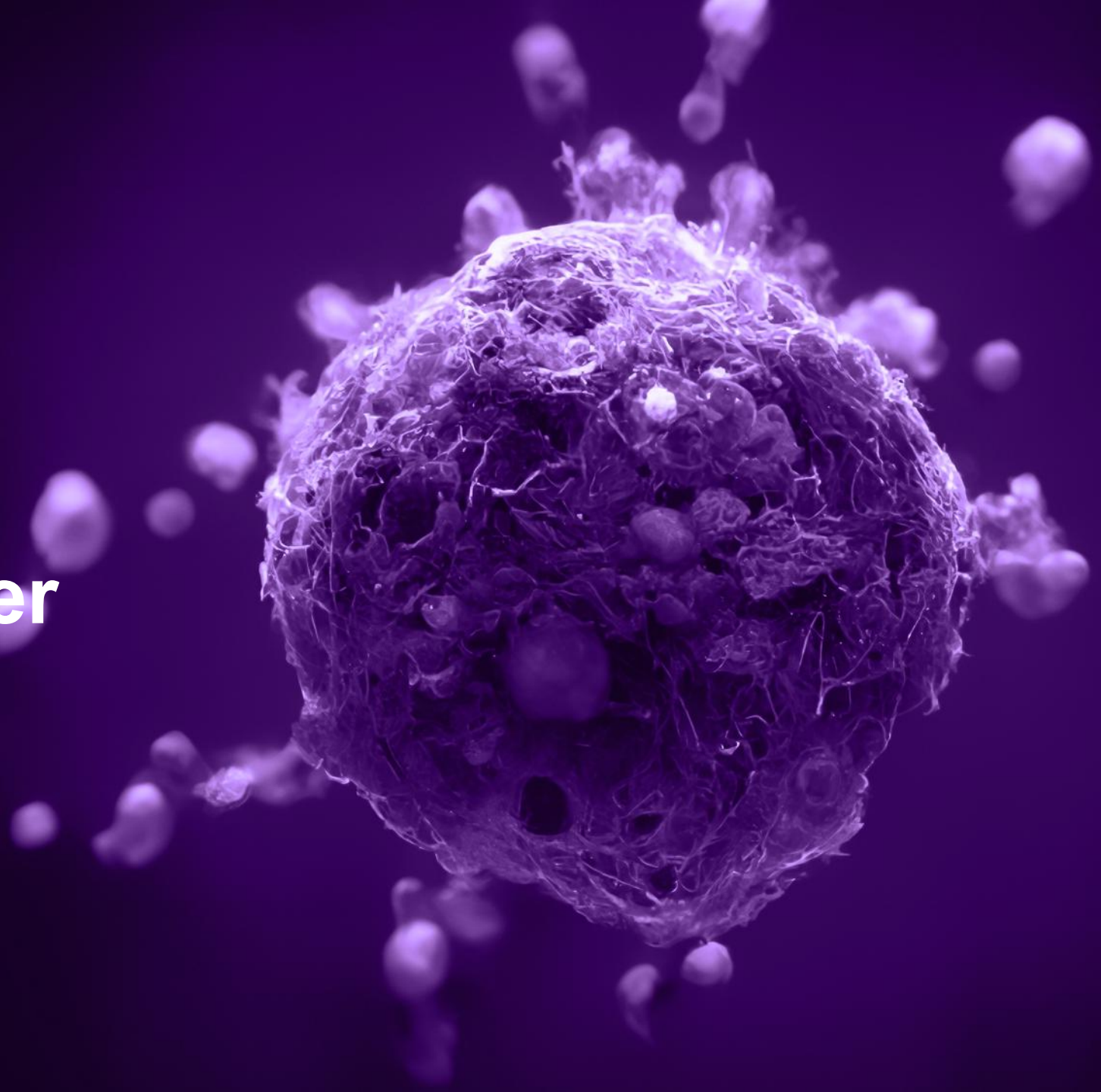

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