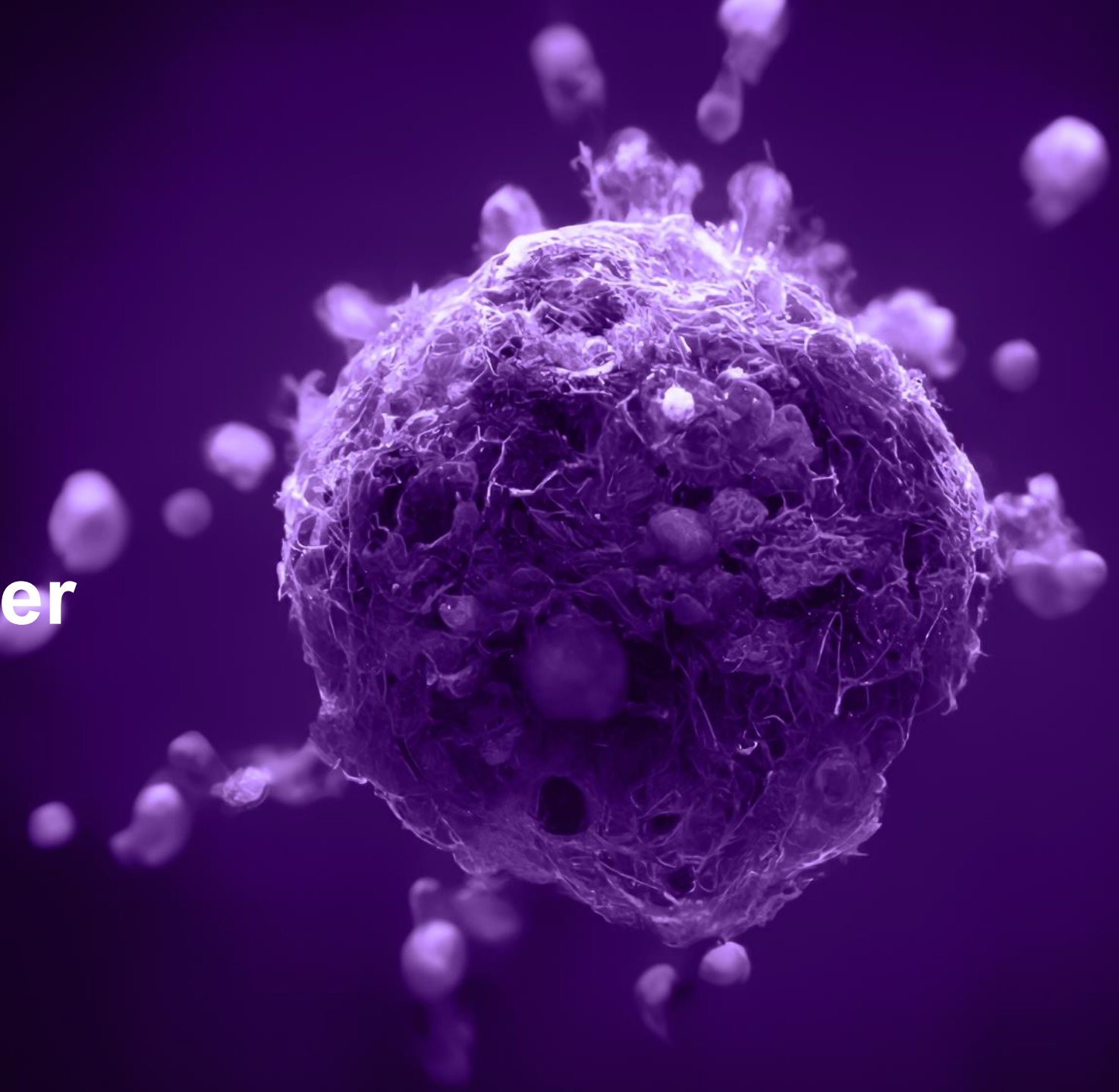
TuHURA biosciences

Overcoming Resistance to Cancer Immunotherapy

Presentation | September 2025



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Forward Looking Statements

This presentation includes “forward-looking statements” under the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, and TuHURA’s actual results may differ from its expectations, estimates and projections expressed in its forward-looking statements, and consequently you should not rely on these forward-looking statements as predictions of future events. Words such as “expect,” “estimate,” “project,” “budget,” “forecast,” “anticipate,” “intend,” “plan,” “may,” “will,” “could,” “should,” “believes,” “predicts,” “potential,” “continue,” and similar expressions are intended to identify such forward-looking statements. These forward-looking statements include, without limitation, statements about TuHURA’s IFx-Hu2.0 product candidate, its IFx-Hu3.0 preclinical program, its tumor microenvironment modulators development program, and any developments or results in connection therewith and the anticipated regulatory pathway and timing of those development programs, studies and trials. These forward-looking statements involve significant risks and uncertainties that could cause the actual results to differ materially from the expected results, including the risks set forth in the “Risk Factors” section of TuHURA's Quarterly Report on Form 10-Q for the quarter ended August 14, 2025, and the proxy statement/prospectus filed with the SEC by TuHURA with the SEC on August 14, 2025. TuHURA does not undertake or accept any obligation or undertaking to update or revise any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based.

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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 existing cancer immunotherapies

Investment Highlights:
Overcoming resistance to cancer immunotherapies

- Phase 3 study of IFx-2.0 being conducted under an SPA Agreement with the FDA
  - Enrollment completion Q4-2026 – currently anticipate no requirement for post approval confirmatory trial
- IFx-2.0 Phase 1b/2a “basket trial” with topline data expected in 1H 2026
- TBS-2025: VISTA inhibiting mAb asset moving into Phase 2 development in *mut*NPM1 r/r AML
  - TBS-2025 + menin inhibitor; Phase 2 anticipated to start early Q1 2026
- Three key clinical data readouts expected over the next 18 months
- Lean operational footprint and focused, late-stage pipeline

Milestones Achieved: 1st Half 2025

- ✓ FDA Removed CMC related Partial Clinical Hold
- ✓ Initiated Phase 3 IFx-2.0 Accelerated Approval Trial
- ✓ Closed Kineta Acquisition
- ✓ Raised $15 million

Diversified Immuno-Oncology Pipeline

PROGRAM	DRUG CANDIDATE	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	Upcoming Milestone Targets
Innate Immune Agonists	**IFx-2.0** Tumor-targeted pDNA	1st Line Merkel Cell Cancer Keytruda® + IFx-2.0 or placebo[1]					**Q1 2027:** Phase 3 Topline Results
		Primary Checkpoint Inhibitor Resistant Metastatic Cancer "Basket" Trial					**Q2 2026:** Phase 1a/2b "Basket" trial results
TME Modulators Negative Immune Regulators	**TBS-2025** VISTA inhibiting mAb[1]	*mut*NPM1 Acute Myeloid Leukemia					**Q4 2025:** Phase 2 Trial Initiation
TME Modulators MDSC Inhibitors	**Bi-specific ADCs and PACs**	Myelodysplasia Acute Myeloid Leukemia					**Q4 2025:** ADC/APC *in vivo* POC studies

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

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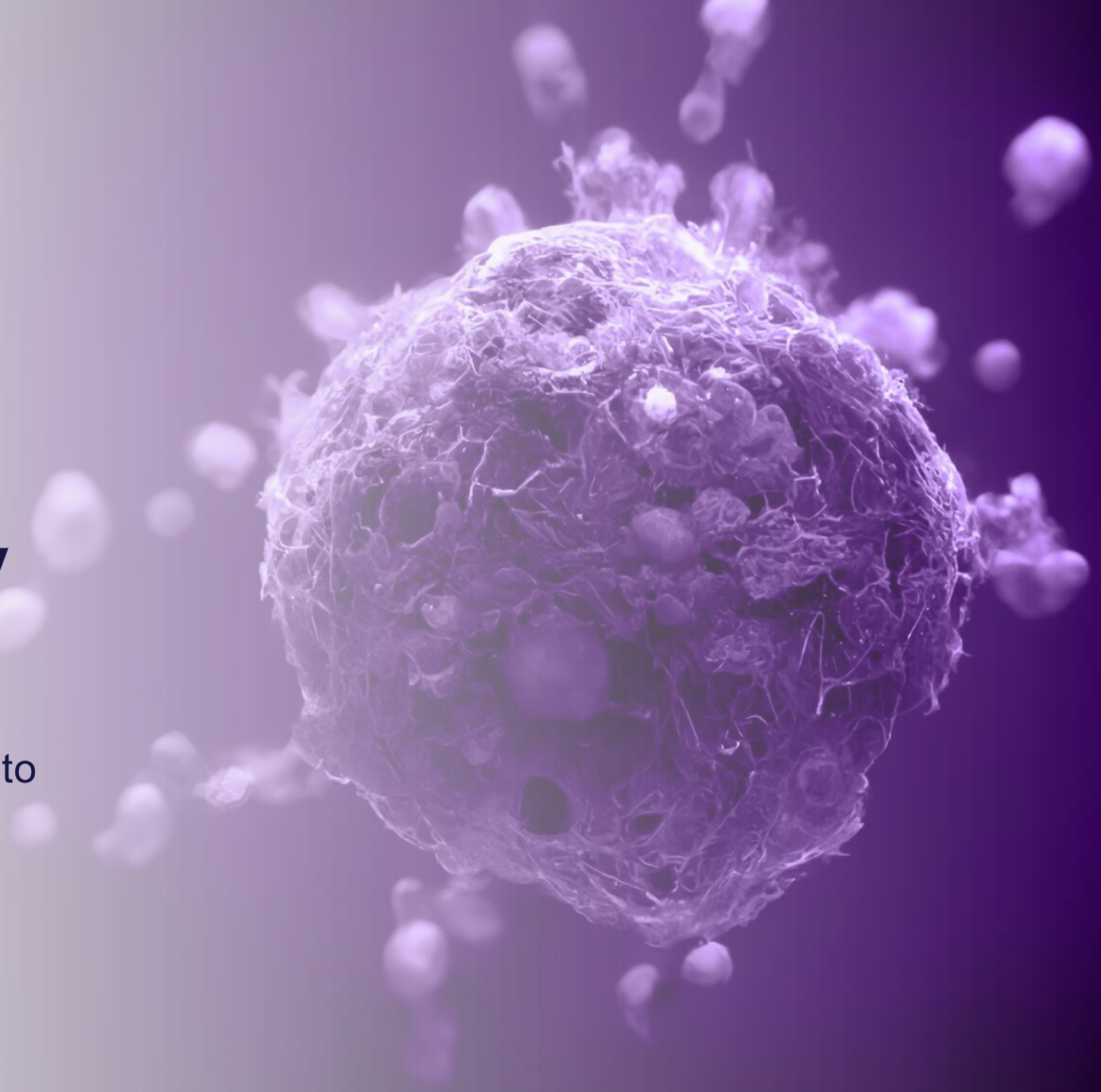
IFx Technology

Innate Immune Agonists

Designed to Overcome Primary Resistance to Checkpoint Inhibitors



IFx-2.0: Mechanism of Action

Making a Tumor Look Like a Bacterium

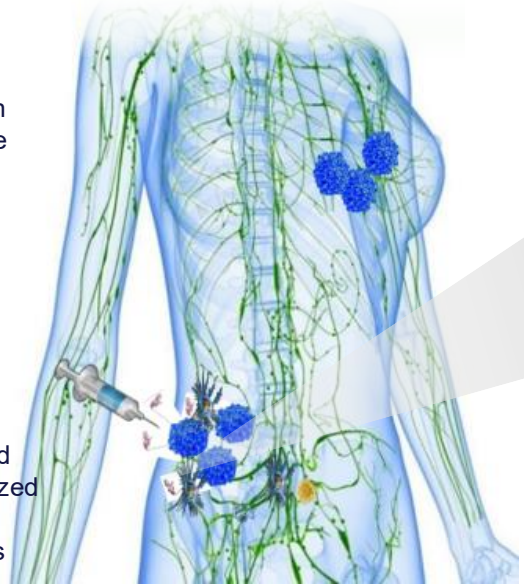
Initiation of an Innate Immune Response

1

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

2

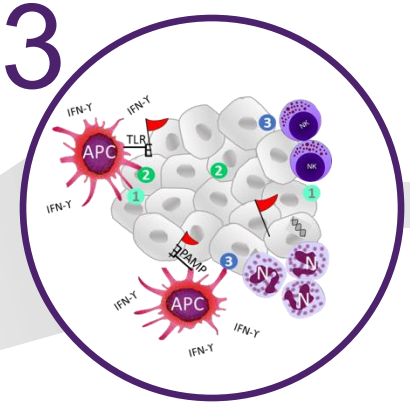
Molecular patterns on bacterial protein conserved through evolution, recognized by pattern recognition receptors (TLR2) on APCs



Activation of Tumor Specific T Cells

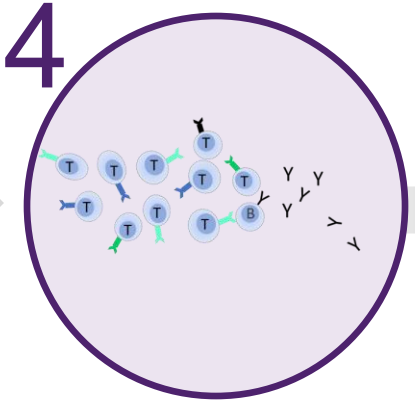
Allows CPI to work where they previously failed

3



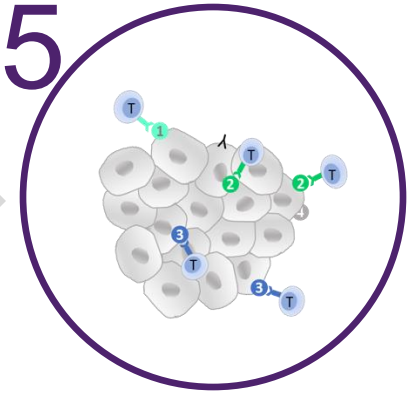
APCs 'ingest" intact tumor cell, package and present all tumor neoantigens to B and T cells leading to activation of tumor specific B and T cells (1^0 epitope spreading)

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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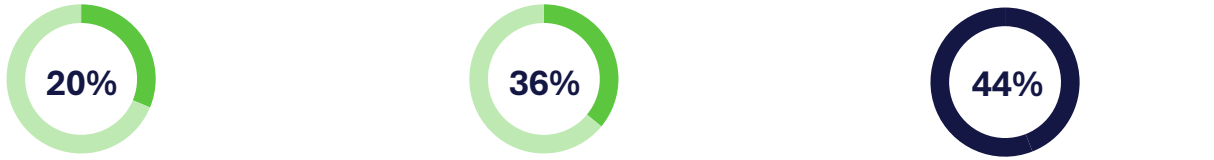
Advanced Metastatic Merkel Cell Carcinoma

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 is an attractive commercial opportunity

2020 Incidence:
~8,167

2034 Incidence:
~14,891
US, EU4, UK*

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

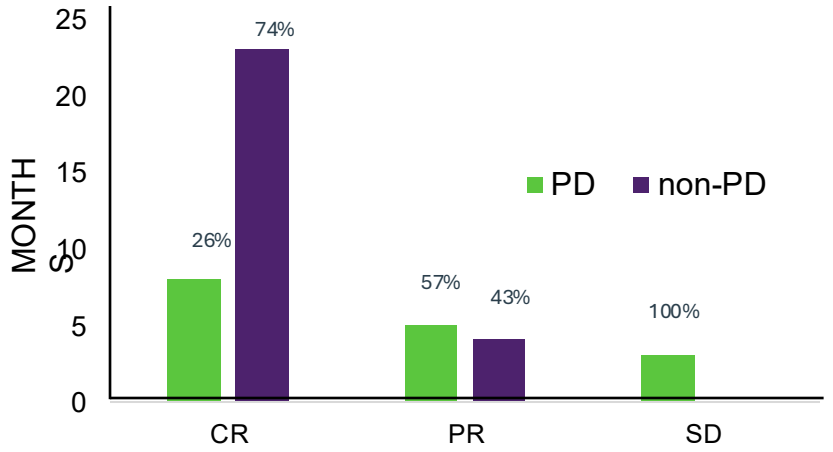


Figure 1. Rate of PD based on best ICI response

Phase 1b Study in Advanced Skin Cancer
(Merkel Cell and Cutaneous Squamous Cell Carcinoma)

Phase 1b

- Advanced MCC (5) Squamous Cell (4) patients
- Three dosing cohorts:
- IFx-2.0 weekly for one, two or three weeks
- Up to 3 accessible lesions injected
- N=9

Objectives (on/off protocol)

- Assess safety of 3 dosing schedules for IFx-2.0
- Determine optimal dose / schedule for maximizing immune response
- Explore tumor response to rechallenge with checkpoint inhibitor post IFx-2.0

Expanded Trial

- IFx-2.0 weekly x 3
- CPI naive patients who progressed on 1st line Rx with anti-PD-(L)1
- Post protocol anti-PD-(L)1 rechallenge
- N=8 MCC*

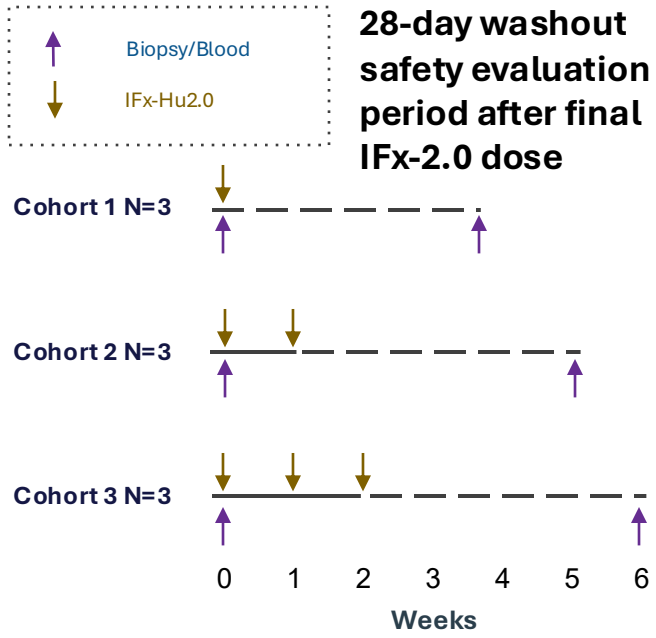
23 pts enrolled 21 safety 19 response

Enrolled 23
Safety evaluable 21
Response evaluable 19

SAFETY: TRAEs
Grade 1 8(35%)
Grade 3 1(4%)

POST CPI RECHALLENGE
MERKEL CELL n=13
CR - 3
PR - 4
PD - 4
N/A - 2
MEDIAN DOR> 21 months

Dose & Schedule Design



DANA-FARBER CANCER INSTITUTE
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USC UNIVERSITY OF SOUTHERN CALIFORNIA
MOFFITT CANCER CENTER

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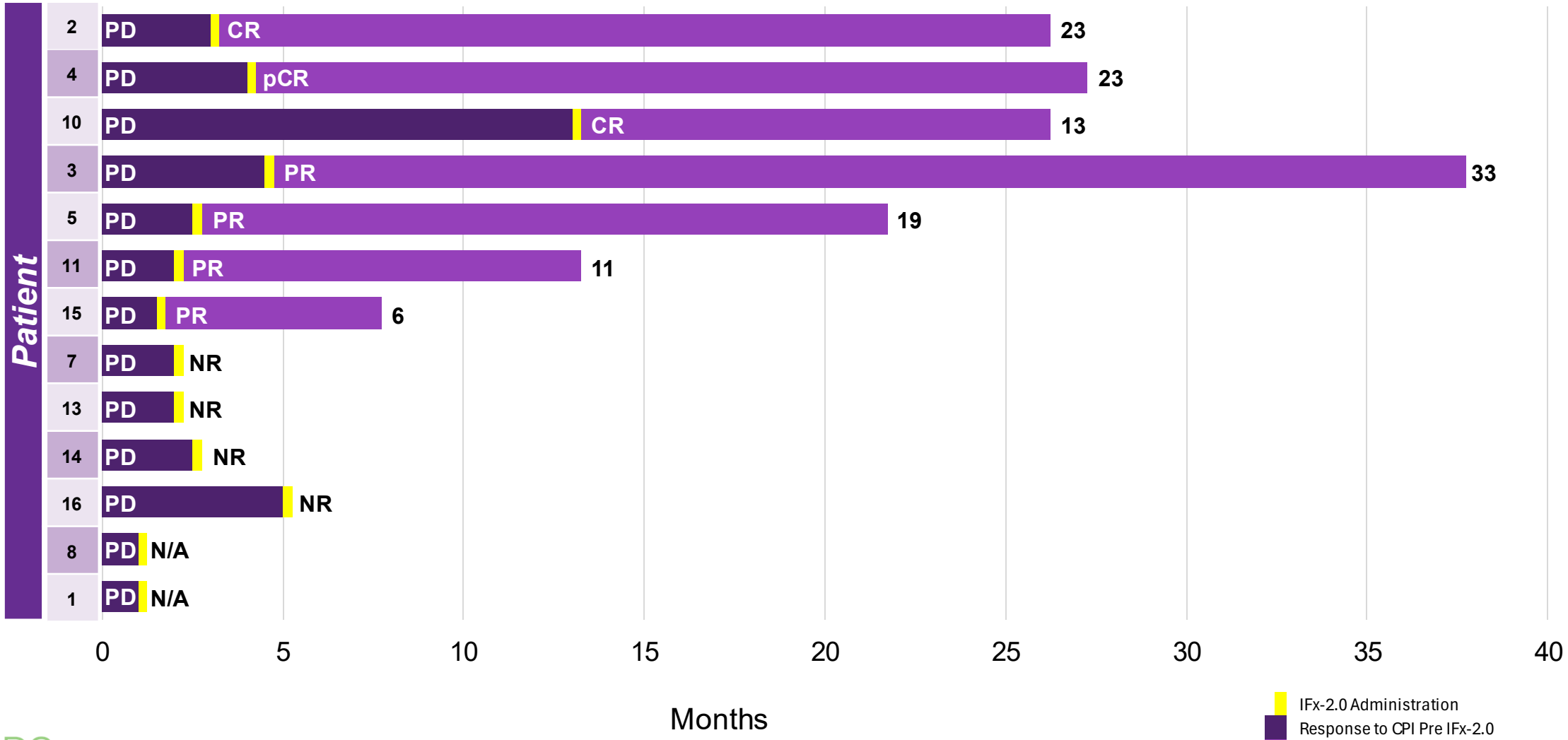
ASCO 2024. Abstract #9592: Phase 1b trial of IFx-Hu2.0, a novel in situ cancer vaccine, in checkpoint inhibitor-resistant Merkel cell carcinoma and cutaneous squamous cell carcinoma

IFx-2.0 MCC Phase 1b Results Suggest Encouraging Efficacy with Durable Responses

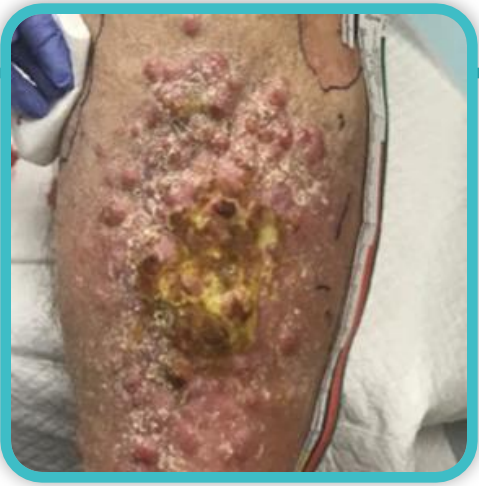


IFx-2.0 Phase 1b trial advanced, metastatic Merkel Cell Carcinoma

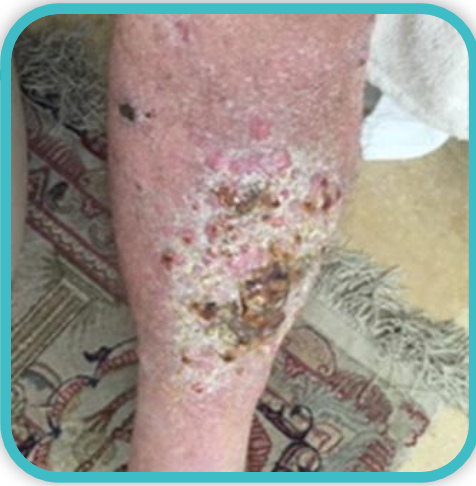
IFx-2.0 Weekly x3 – Followed by Keytruda® (pembrolizumab)

Progression

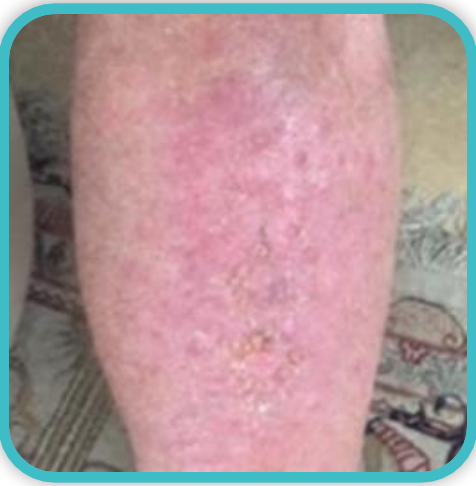
Three months on avelumab, a checkpoint inhibitor



IFx-2.0 Weekly x3
Injected Lesion Not Shown



Checkpoint Inhibitor Keytruda® Rechallenge
Following IFx-2.0



Partial Response (PR)
33 Months

Overcomes 1^0 Resistance to Anti-PD-(L)1 Therapy (pembrolizumab or avelumab) in MCC

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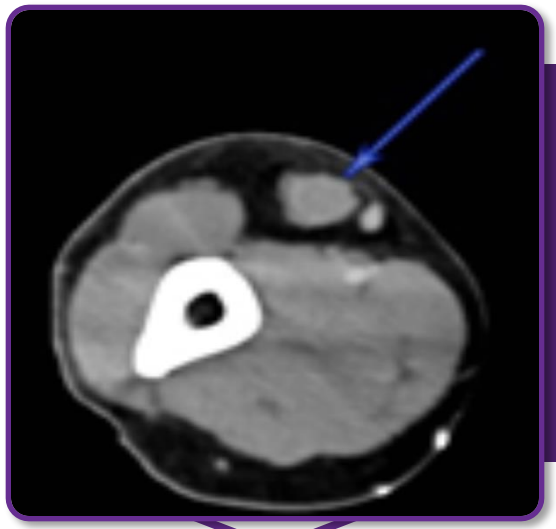
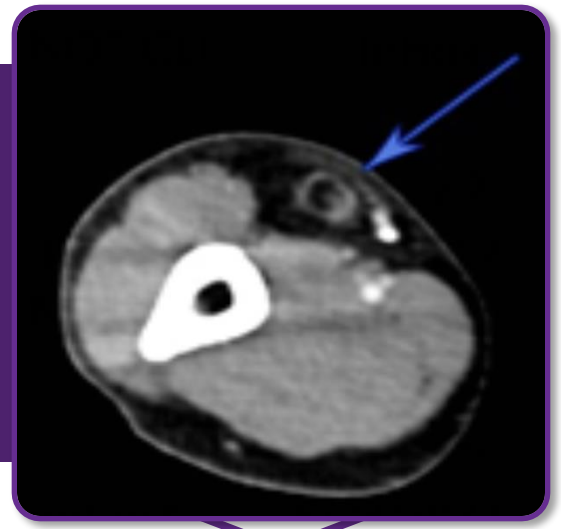
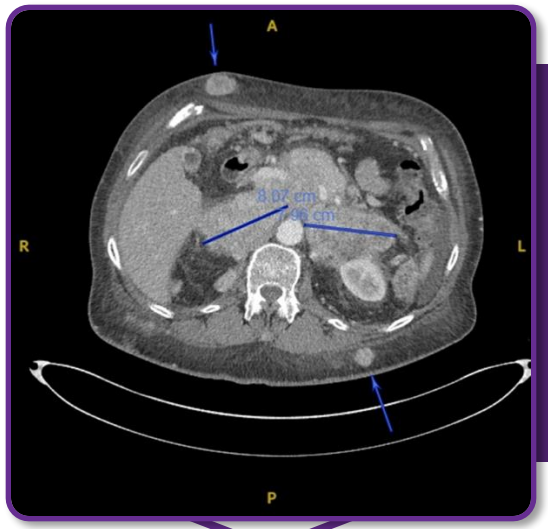
IFx-2.0 Phase 1b Trial in Advanced Metastatic Merkel Cell Carcinoma



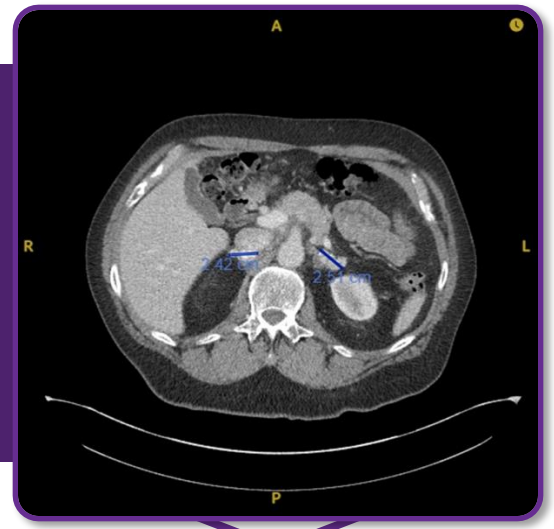
Progressed through 3 months of Keytruda® (pembrolizumab). Large sub-dermal metastatic deposit IFx-2.0 weekly x2 injected into dermal lesions (blue arrows)



Post IFx-2.0 Keytruda® (pembrolizumab) rechallenge. Cavitation of lesion radiographically a PR when excised demonstrated necrotic tissue, no tumor; re-classified as pathologic CR. Response ongoing 23+ months



Progressed through 2 months of Keytruda®. Large bulky abdominal masses (blue) IFx-2.0 weekly x2 injected into dermal lesions (blue arrows)



Post IFx-2.0 rechallenged with checkpoint inhibitor, Bavencio ® (avelumab). Complete disappearance of subcutaneous nodules and ~80% reduction (Partial Response) in abdominal masses. Responses are ongoing 19+ months

Overcomes 1^0 Resistance to Anti-PD-(L)1 Therapy (pembrolizumab or avelumab) in MCC

Single Phase 3 Accelerated Approval Trial

Designed with OCE[1] - Project Front Runner

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

Enrolling ~118 patients

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

20-25 U.S. clinical centers

SPA Agreement with FDA

- ORR allows for potential accelerated approval
- No requirement for post-marketing trial
- PFS converts accelerated to full approval
- Would satisfy requirement for confirmatory trial

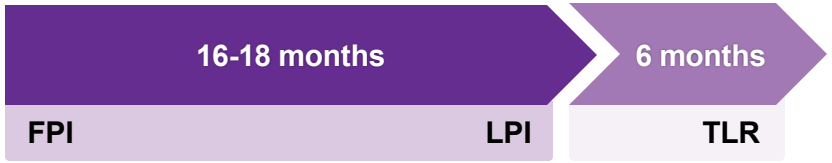
Primary Endpoint

Overall Response Rate (ORR)

Key Secondary Endpoint

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

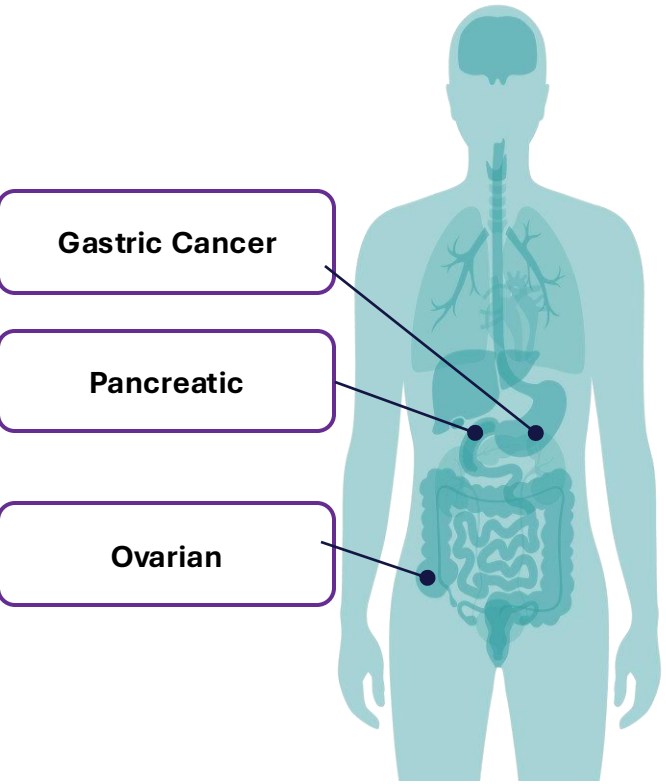
Study Timeline



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

Phase 2 Basket Trial Expands Commercial Opportunity Beyond Merkel Cell Carcinoma

Only 20% of Patients Respond to CPIs on Average



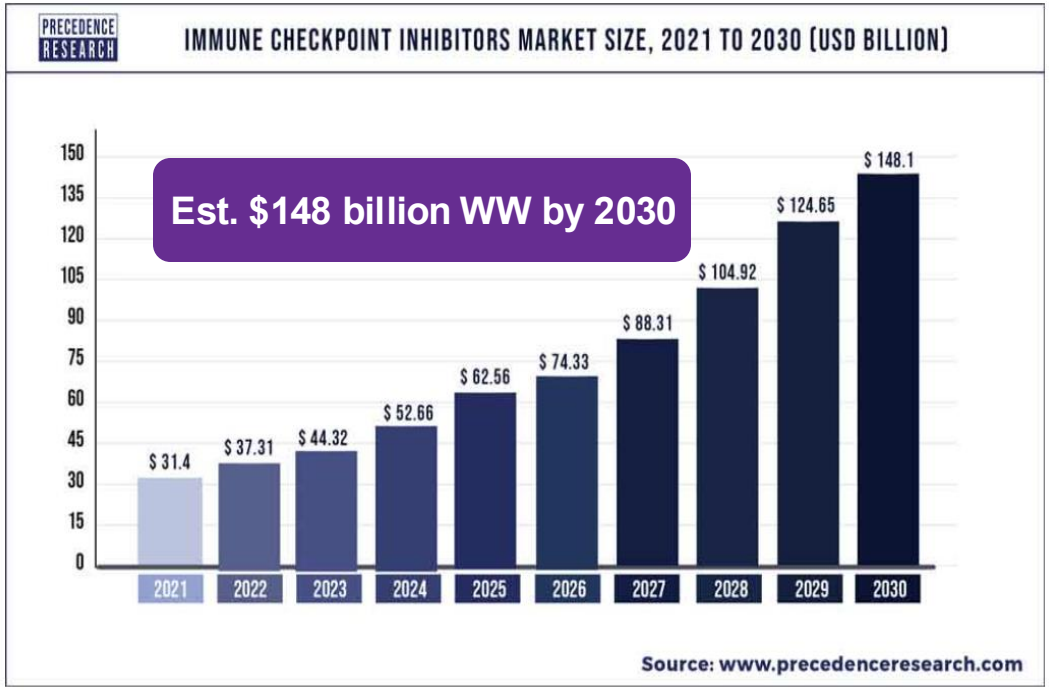
- **Biology of 1^0 resistance is common across tumor types (histology agnostic)**
  - MSI-low and MSS tumors are non-immunogenic
  - Lack activated tumor specific T cells
- **Objective: enhance tumor immunogenicity and activate T cells**
  - PARP inhibitors inhibit DNA repair – activating cGAS-STING
  - Oncolytic viral therapy disperse tumor neoantigens into TME
  - ***Innate immune agonists (IFx-2.0) PAMP activated TLR-2 neoantigen presentation and epitope spreading generates MHC restricted activated tumor specific T cells***
- **IFx-2.0 "basket trial" 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 who are not eligible for P3 trial
    - Patients with demonstrated MSI-low/MSS tumors (pancreatic, CRC, ovarian)

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.

Overcoming Resistance to Checkpoint Inhibitors is an Attractive Commercial Opportunity

Approximately 20% of patients with cancer respond to checkpoint inhibitors like Keytruda®

Company	Marketed Name	Class Of Checkpoint	2025 WW Sales Est.	FDA Approval
Merck	Keytruda[1]	PD-1	$30.0 Billion	2016
Bristol Myers	Opdivo[2]	PD-1	$11.3 Billion	2014
Bristol Myers	Yervoy	CTLA-4	$5.4 Billion	2011
Bristol Myers	Opdualag	LAG-3	$1.0 Billion	2022
EMD Serono	Bavencio	PD-L1	$0.5 Billion	2017



Keytruda's loss of exclusivity in December 2028 (U.S.) and January 2031 (Europe).
Opdivo's loss of exclusivity in 2028 (U.S.) and 2030 (Europe).

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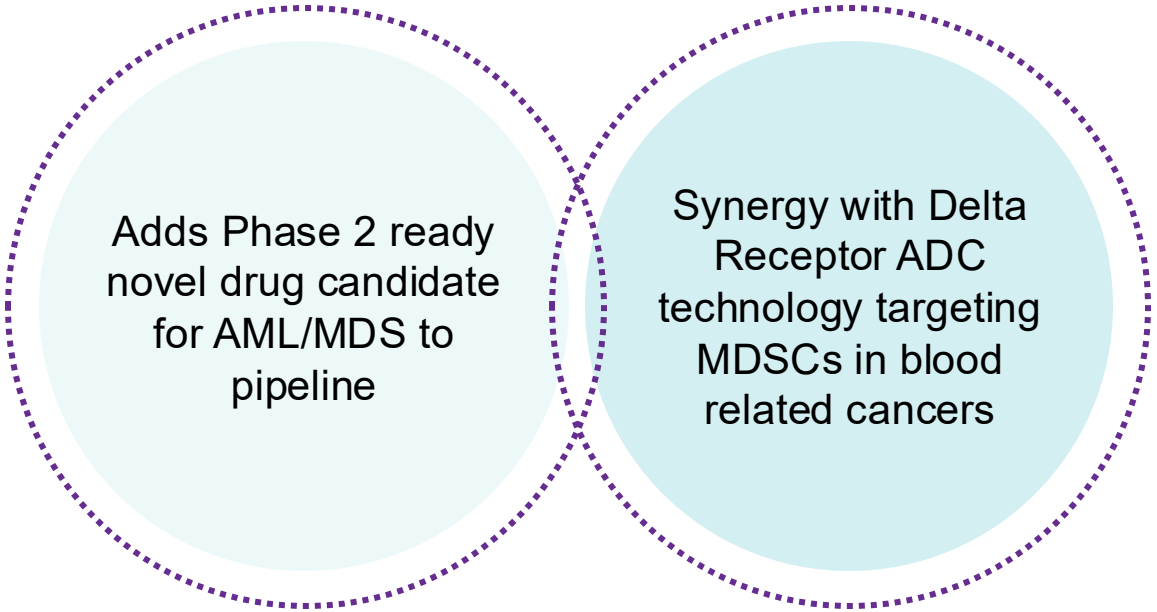
Tumor Microenvironment Modulators

Negative Immune Regulators

VISTA Inhibiting mAb TBS-2025

Targeting VISTA to Overcome Acquired Resistance to Cancer Immunotherapy

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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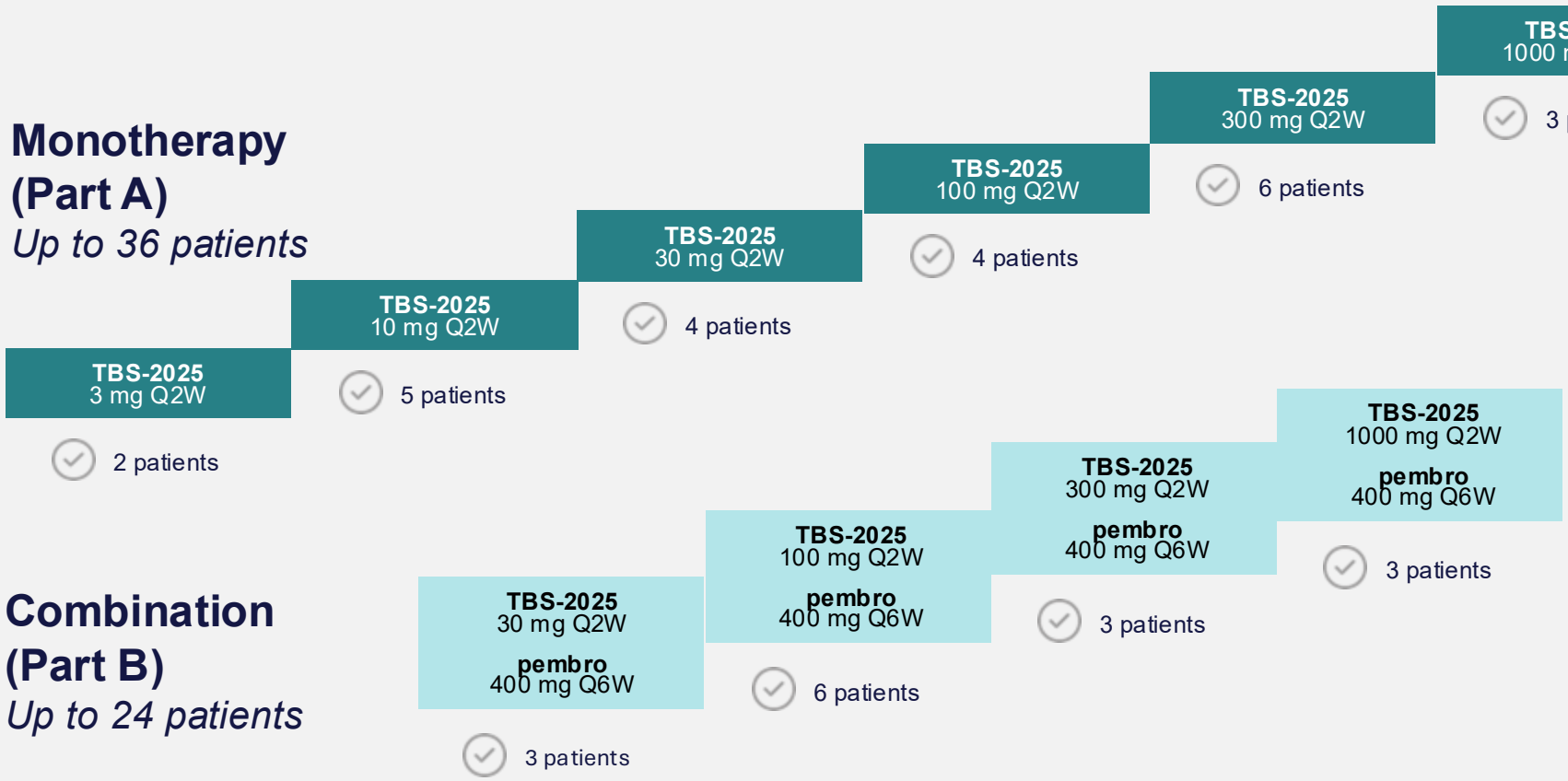
* Formerly KVA12123

TBS-2025 Phase 1b Dose Escalation Trial[1]

Modified BOIN Design with Accelerated Titration



Safety

- No DLT, CRS cytokines (IL-6, TNFα & IL-10) detected at 1,000mg dose
- **100% VISTA receptor occupancy at 1,000mg dose**, PK/PD supports 750mg q2w or 1000mg q3w

Monotherapy Arms n=24

- 13 of 19 patients achieved SD as best overall response (68%)

Combination Arms n=15

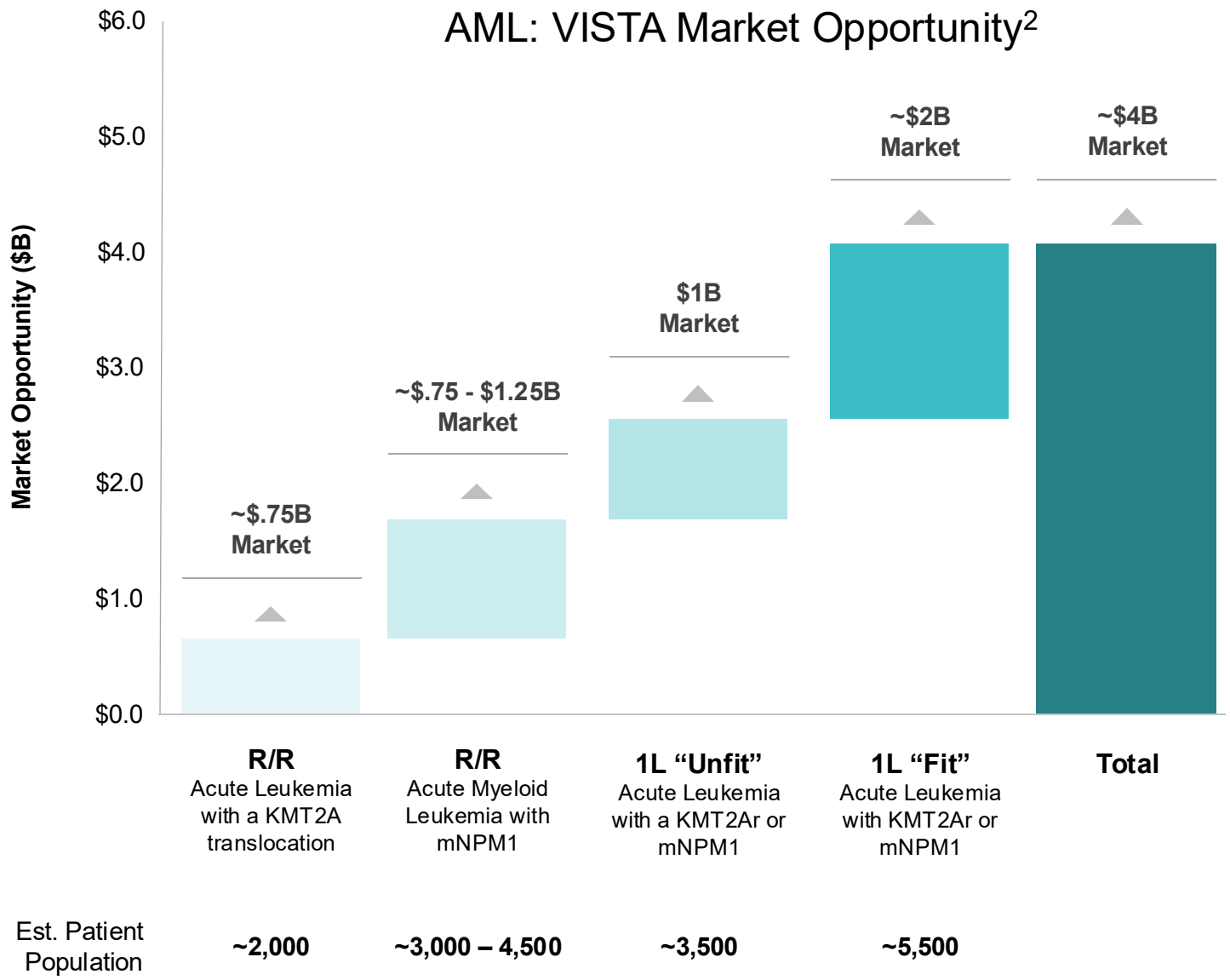
- 12 patients received baseline and at least one follow up scan
- 1 evaluable patient achieved a **PR**, 1 patient achieved SD

1. Phase 1 dose escalation conducted by Kineta, Inc., evaluating TBS-2025 in patients with advanced solid tumors, data cutoff as of 11-21-24.

VISTA linked to Most Common Mutations in AML & MDS

Primary mechanism for leukemic blasts to escape immune recognition[1]

- Three mutations that are expressed or co-expressed in AML and MDS: NPM1, DNMT-3A, FLT3-ITD
- Co-expression associated with poor outcome, low response rates, high rate of relapse
- *mut*NPM1 interacts with menin to drive downstream expression linked to leukemogenesis
- Menin inhibitors can salvage ~25-30% of patients with *mut*NPM1 r/r AML
- **Initial proof of concept trial:**
  - TBS-2025 + menin inhibitor vs menin inhibitor alone
  - Approximately 60 patients, interim data at 30 patients
  - Estimated six months to interim data



1. VISTA As a Mediator of Immune Suppression in AML Initiated By DNMT3A and NPM1 mutations. Blood 2024; 144 (Supplement 1): 4100.
2. Source: Data on file; Redbook 2023

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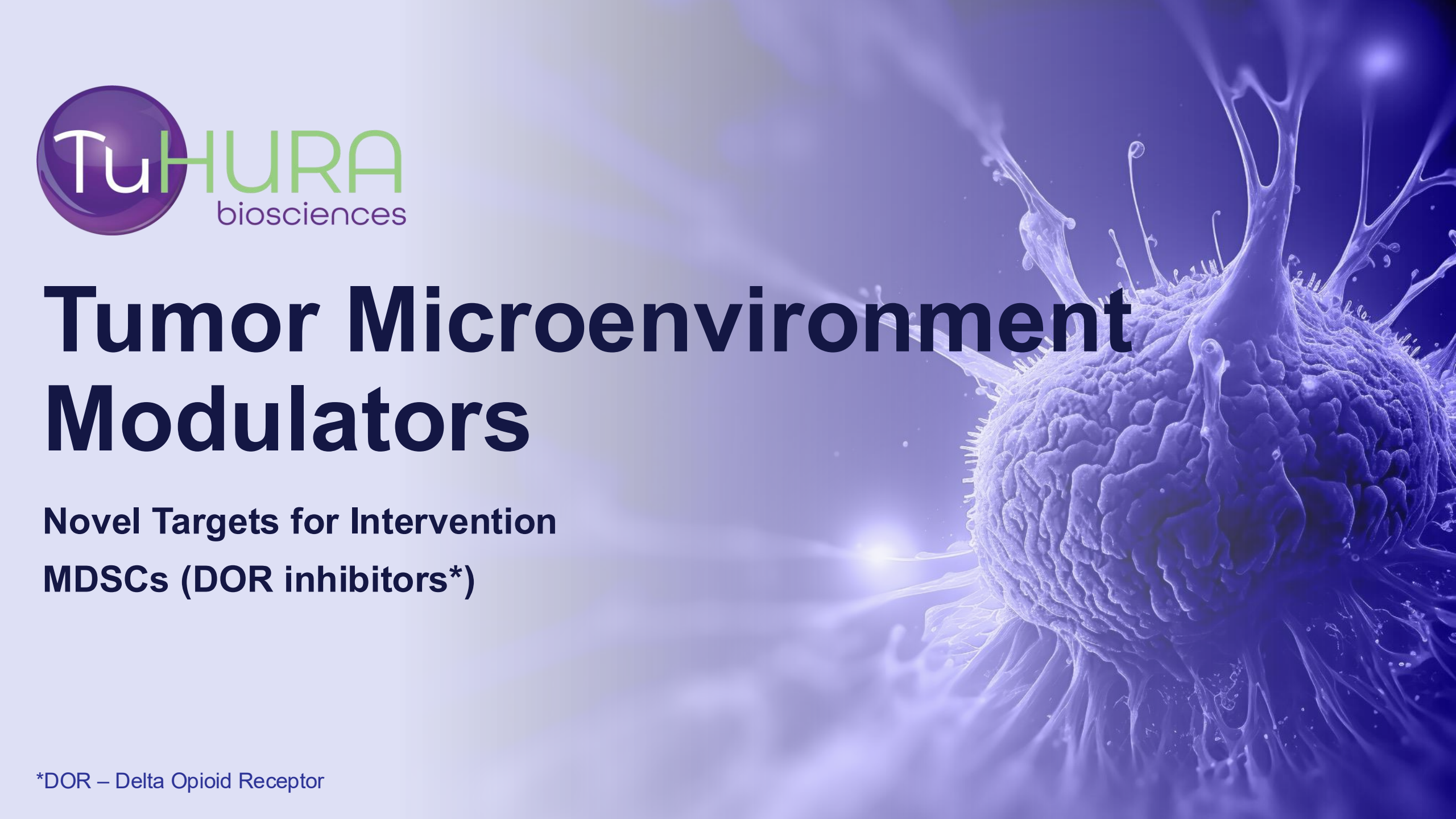
Tumor Microenvironment Modulators

Novel Targets for Intervention

MDSCs (DOR inhibitors*)

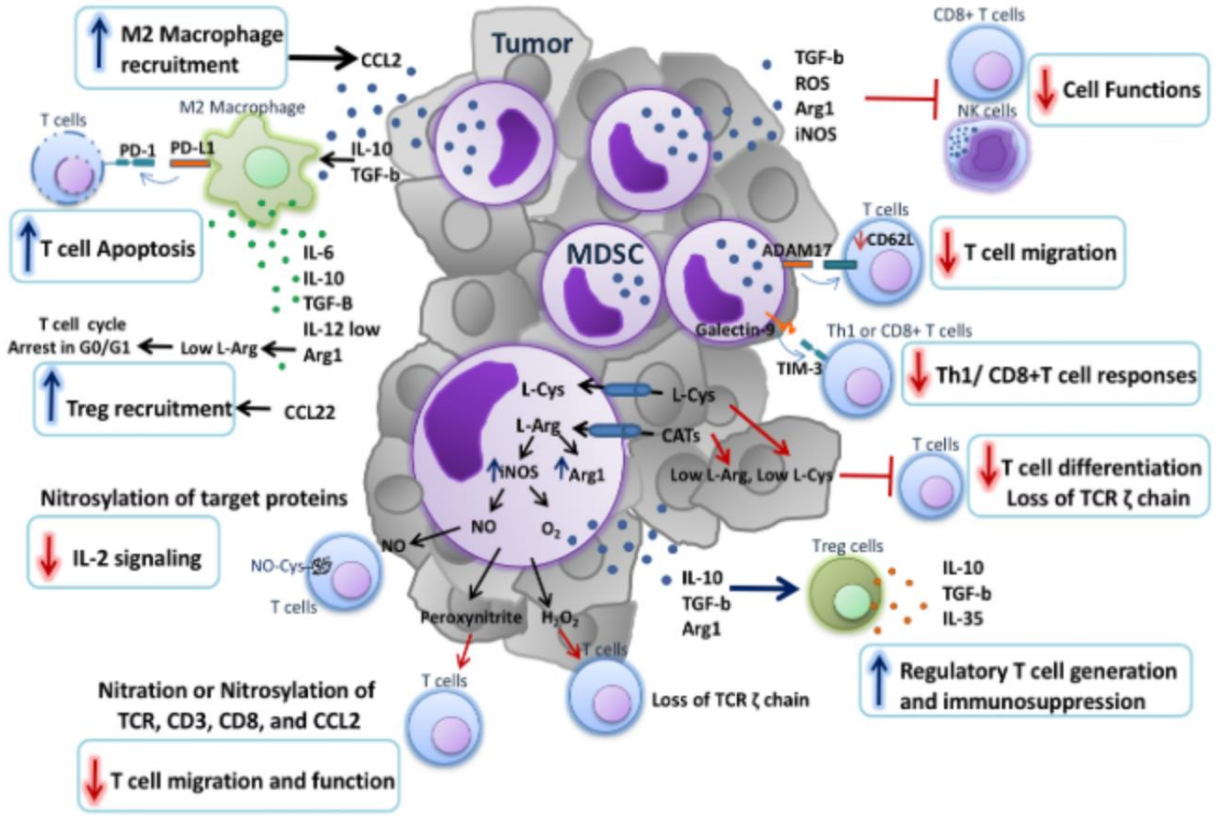


*DOR – Delta Opioid Receptor

MDSCs Create Immune Sanctuary for Tumors Causing Checkpoint Inhibitors and T Cell Therapies to Stop Working

- MDSCs are normally produced during pregnancy; provide immune sanctuary for fetus
- Hijacked by tumors, responsible for immunosuppression in TME
- Tumor associated MDSCs produce multiple immune suppressing factors (Arg-1, iNOS, TGFb,)
- VISTA highly expressed on MDSCs
- Inhibit T cell proliferation and activation
- TuHURA and Moffitt scientists first to report expression of Delta Opioid Receptor on tumor associated MDSCs

Mechanism of MDSC Derived Immunosuppression



First-in-Class Immune Modulating Bi-Specific/Bi-functional Antibody Drug or Antibody Peptide* Conjugates

Single receptor target controls multiple pathways coupled to TME immune suppression

Delta Opioid Receptor (DOR)

- Well characterized class of G-protein-coupled receptors (GPCRs)
- TuHURA and Moffitt Cancer Center scientists first to report
  - High expression (80%) on tumor associated MDSCs
  - Association with expression multiple suppressive factors
  - Inhibition of T cell proliferation

HUR-009: DOR Specific Antagonists**

- Decreases tumor associated MDSC production of multiple immunosuppressive factors (Arg-1, iNOS, IDO-1, VISTA, TGF-β)
- Blocks tumor associated MDSC suppression of T cell proliferation
- Restores T cell proliferation
- Restore HSPC activity from MDS patient derived tumor MDSCs

First-in-Class Immune Modulating APCs & ADCs

- Conjugates peptidomimetic or small molecule or DOR inhibitor to a VISTA inhibiting mAb
- Dual modality for inhibiting immunosuppressive phenotype of tumor microenvironment
- Lead selection Q4-2025
- Preclinical POC Q2-2026
- Targeting FIH Q1-2027

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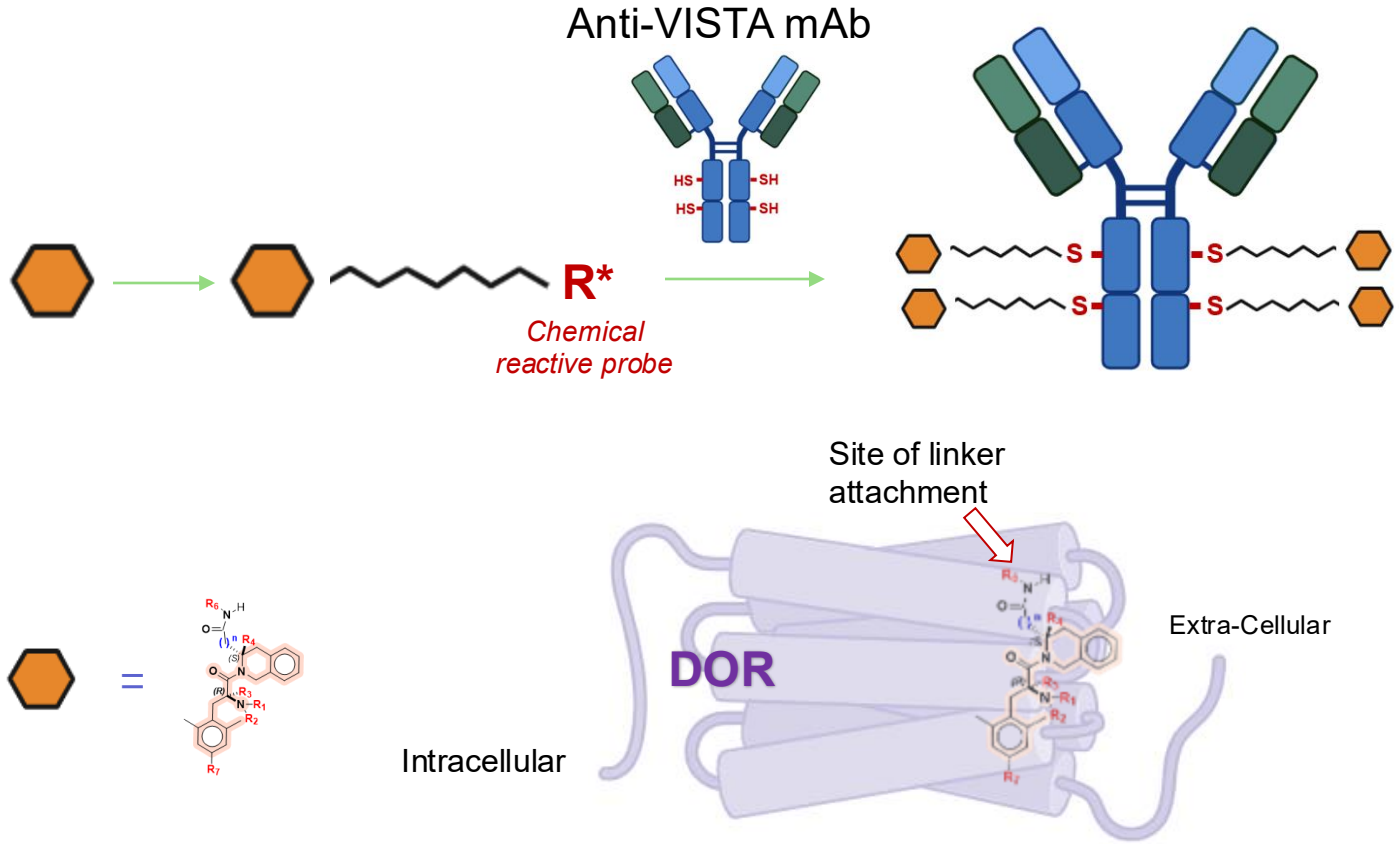
* Peptidomimetic Delta Opioid Receptor specific inhibitor.
** McLaughlin, Rodriguez, Moffitt Cancer Center

DOR-VISTA APC-ADC Design

Multiple Factors to Consider when Designing DOR-VISTA ADCs

- Bioconjugation site
- Bioconjugation method: stochastic vs site-specific conjugation
- Cleavable or non-cleavable linker
- High drug loading (DAR) vs hydrophobicity
- Heterogeneous vs homogeneous ADC population
- PK profile of ADC and various components: Payload-Linker, Ab-Linker, free Payload
- Safety profile of ADC & Payload



DAR: Drug-Antibody Ration; FIH: First-in-Human

Upcoming Anticipated Milestones

2025 | **2026** | **2027**

2H 2025 | 1H 2026 | 2H 2026 | 1H 2027

IFx-2.0
Tumor-targeted pDNA

- End of Phase 3; start of rolling BLA submission (2H 2026)
- Phase 3 topline results & potential BLA filing (1H 2027)

TBS-2025
VISTA Inhibiting mAb

- Initiate Phase 2 VISTA trial in NPM1 *mut r/r AML* (2H 2025)
- Phase 2 results VISTA trial in NPM1 mut r/r AML (1H 2026)

MDSC Inhibitors
Bi-specific ADCs and APCs

- In vivo POC data (2H 2025)

Results | Trial Initiation | Regulatory Updates

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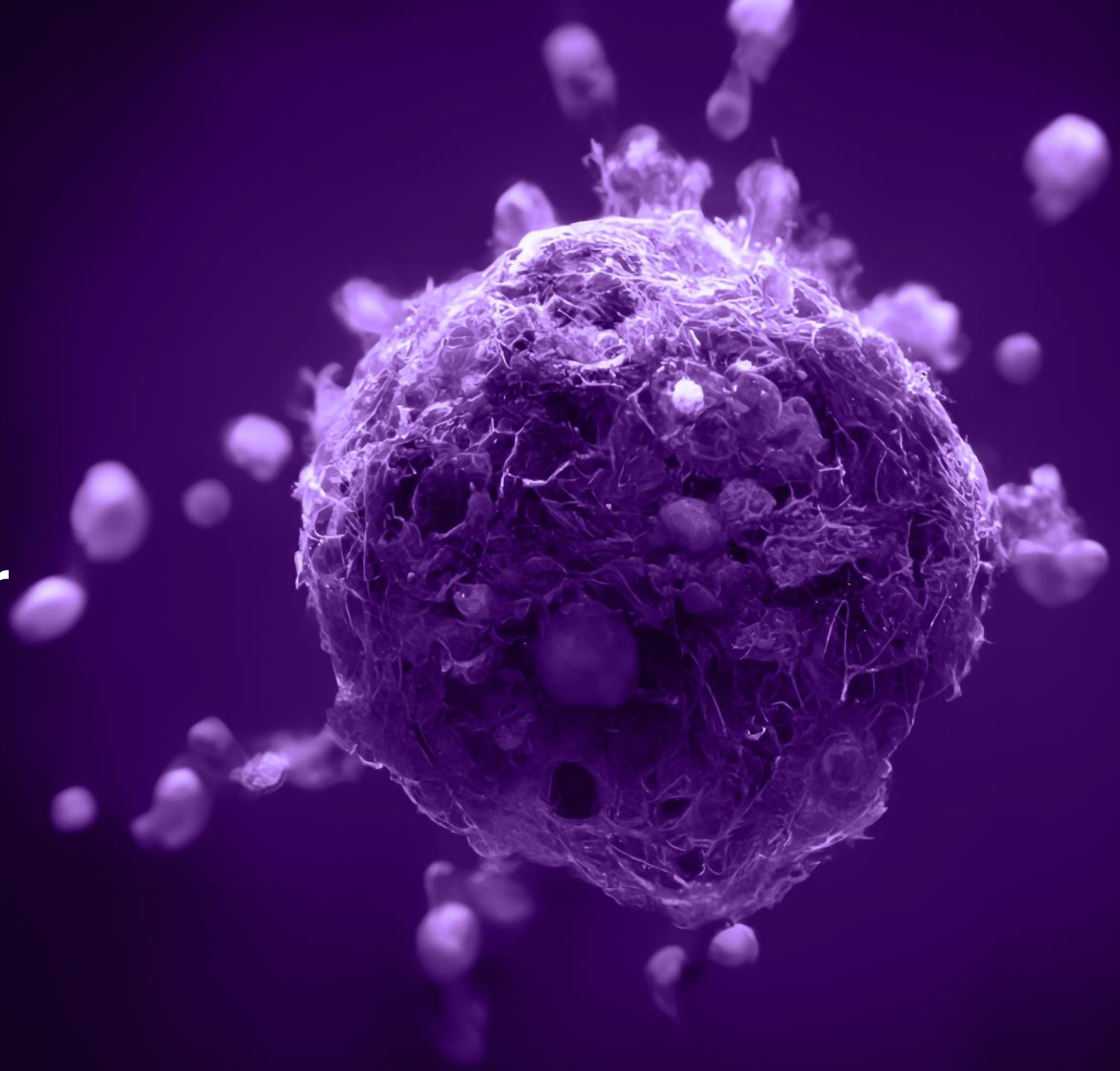
Overcoming Resistance to Cancer Immunotherapy



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