



*A transformational approach bringing
peptide nanotechnology and artificial
intelligence together.*

Dr. Anthony Maida
Co-Founder, Chairman and CEO

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Transformational Nano Immuno-Engager (NIE)

Efficacy of immune checkpoint blockade therapy is currently limited by:

- (1) ineffective infiltration of effector T cells to tumors
- (2) immunosuppressive tumor micro-environment

NIE overcomes existing cancer treatment limitations with:

- **Enhanced efficacy** of checkpoint inhibitors via 3-pronged mechanism:
 - ✓ prolong the retention of the immunomodulatory agent within the tumor micro-environment (“TME”)
 - ✓ capture the immune cells at the TME
 - ✓ activate the immune system
- **Superior safety profile** by sparing healthy tissues and organs

➤ **100% cure** in syngeneic lung and breast cancers in mice

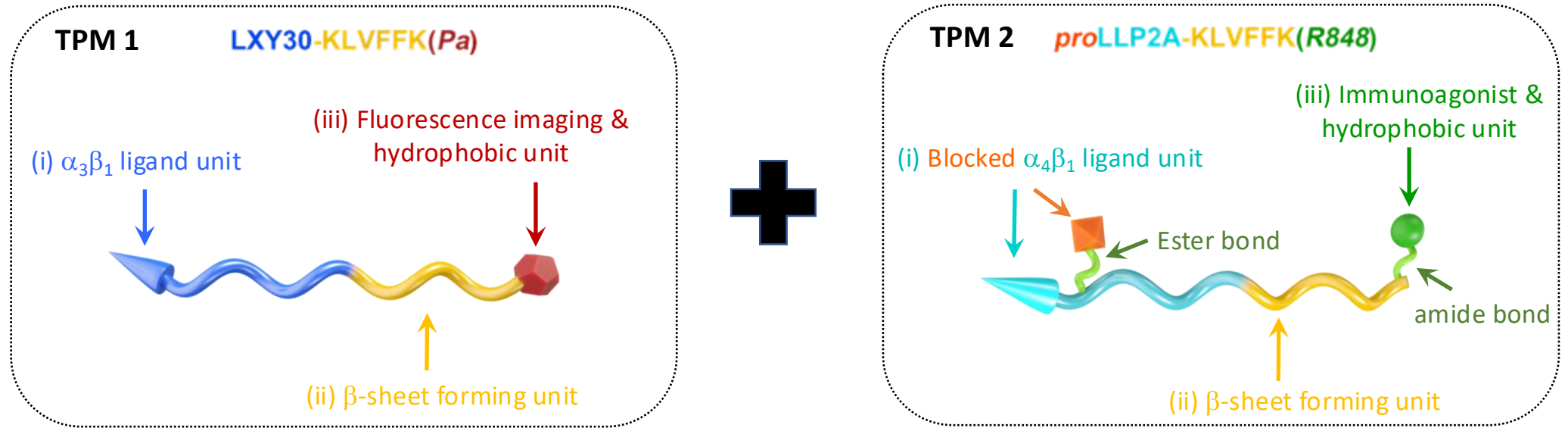


Flexibility to Design Therapeutics for a Wide Range of Uses

- **Modular design** provides ability to customize NIE for a particular application
 - **Proprietary ligand** targets tumor-specific cell surface antigen
 - **Cargo** could be immunomodulator or therapeutic agent
- **Any solid tumor type** could be targeted with NIE
- **Beyond oncology**, future therapeutic applications include
 - inflammatory diseases
 - infectious diseases
 - others

Lead asset = 1st-in-class NIE immunomodulator combined with anti-PD1 in lung cancer and other solid tumors

Nano Immuno-Engager: Drug Composition



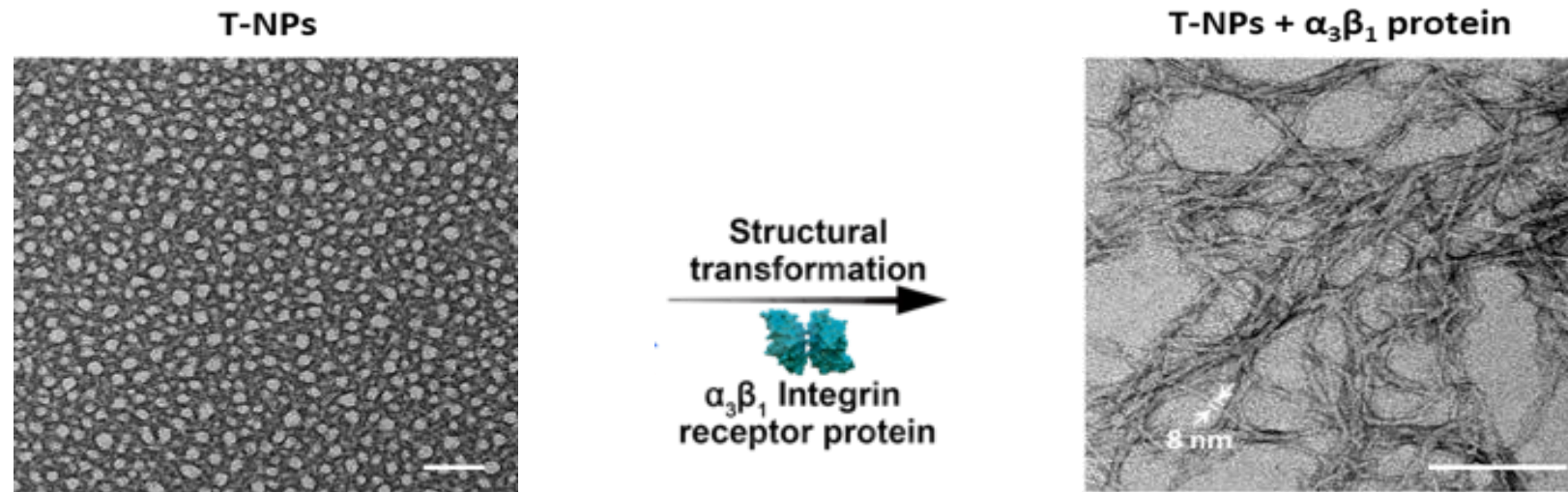
Our therapeutic **drug** consists of two peptides: Transformable Peptide Monomers (“TPM”) 1 and TPM 2, that contain molecules targeting cancer; and molecules that aggregate the peptides together to form a nanoparticle.

Key Domains:

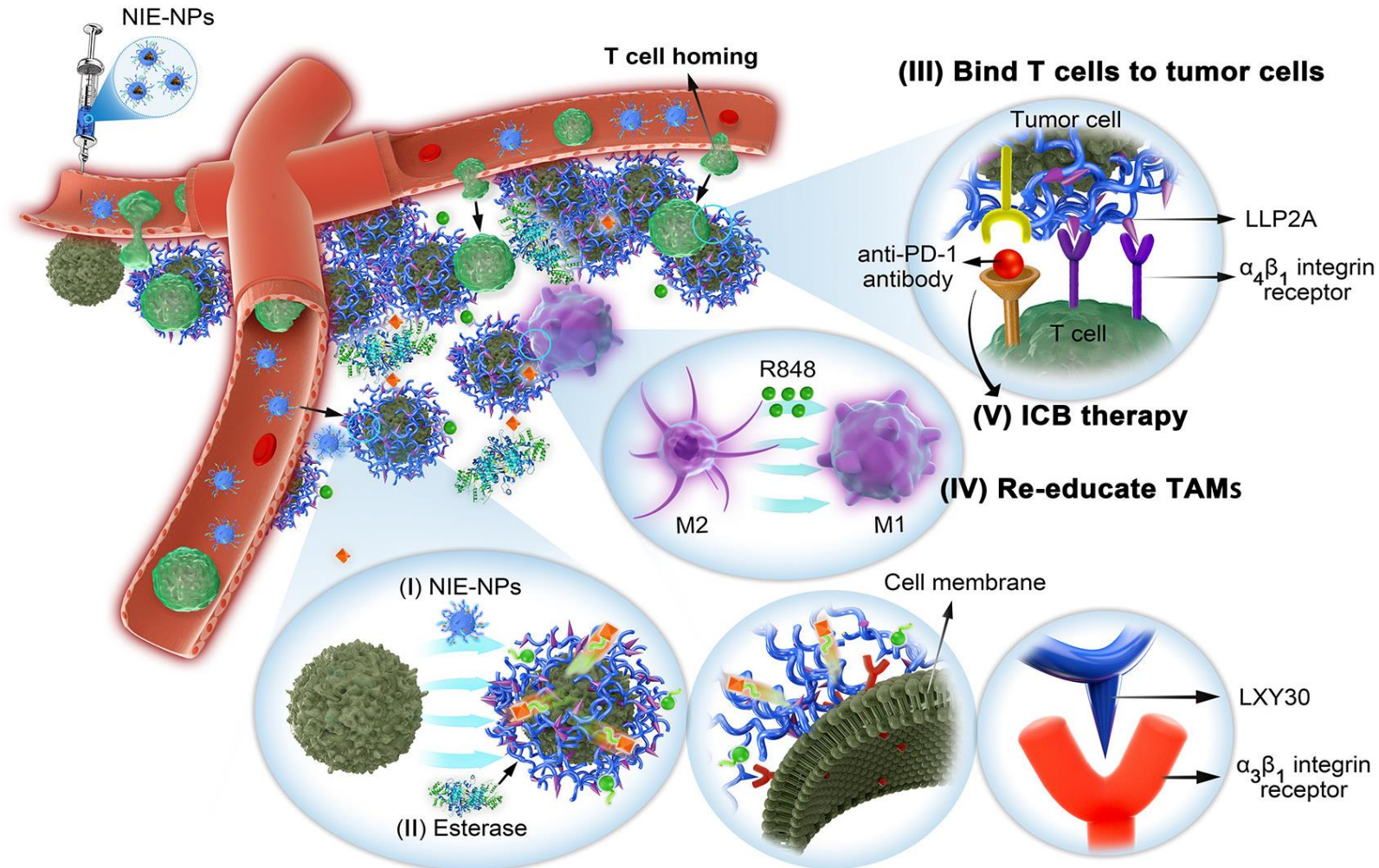
- **KLVFFK**: Proprietary structure required to aggregate the peptides together to form a nanoparticle
- **R848**: Resiquimod cargo is a potent immuno-stimulant
- **LLP2A**: Proprietary ligand to capture the immune cells
- **LXY30**: Proprietary ligand that targets the $\alpha_3\beta_1$ integrin heterodimeric transmembrane receptor expressed by many epithelial tumors with high metastatic potential

Transformation of Nanoparticles into a Nanofibril Network

Upon interaction with $\alpha_3\beta_1$ integrin receptor protein



Our NIE: Activation of the Tumor Microenvironment



Target Market – Solid Tumors

A significant opportunity remains to benefit Patients on ICI

Immune Checkpoint Inhibitors:

Foundation of Immuno-Oncology Treatment

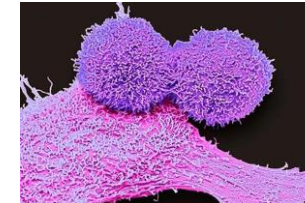
- **44%** of US cancer patients are **eligible** for Immune Checkpoint Inhibitors (“ICI”)*
- Nearly **half** of all patients with metastatic cancer in economically developed countries are **eligible** to receive ICI**
- **32%** five-year **overall survival** rate for Non-Small Cell Lung Cancer (“NSCLC”) patients***

Annual Diagnosed Cases



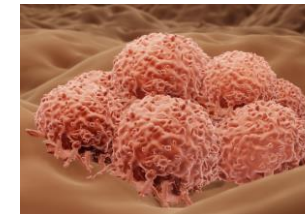
NSCLC

- US: >190K†
- Global: >1.75M††



Breast

- US: 300K†
- Global: >2.25M††



Melanoma

- US: 97K†
- Global: 325K††

*JAMA Netw Open. 2020;3(3):e200423. doi:10.1001/jamanetworkopen.2020.0423

** Immune-checkpoint inhibitors: *Nature Rev Clin Oncol* 19, 254–267 (2022)

***Journal of Clinical Oncology: Abstract KEYNOTE 024

† American Cancer Society 2023

†† Cancer.net 2020 data,



The Technology: Contributing to Better Patient Outcomes

Addressing Unmet Immuno-Oncology Needs

Lead Program / First-in-Class: Nano Immuno-Engager (“NIE”)

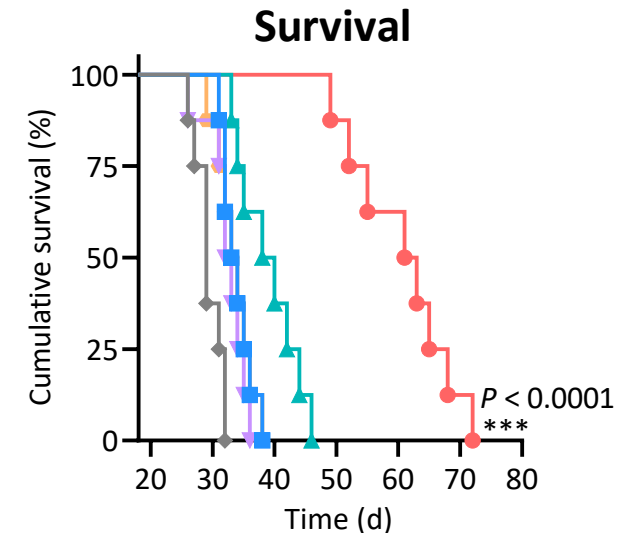
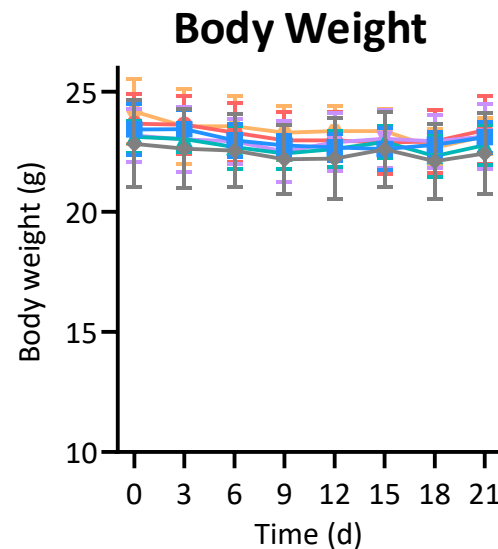
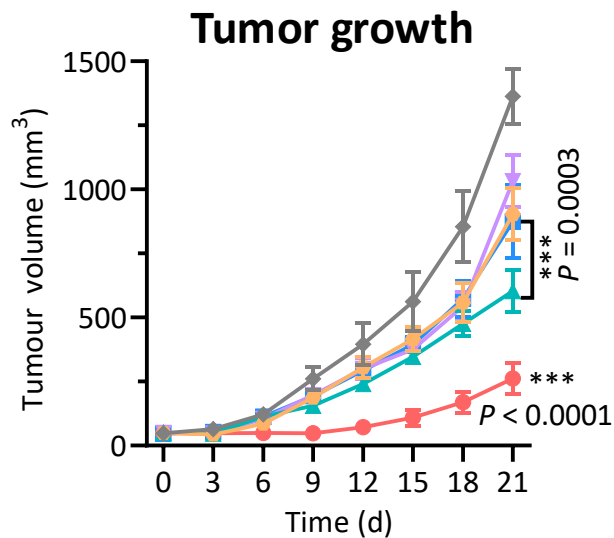
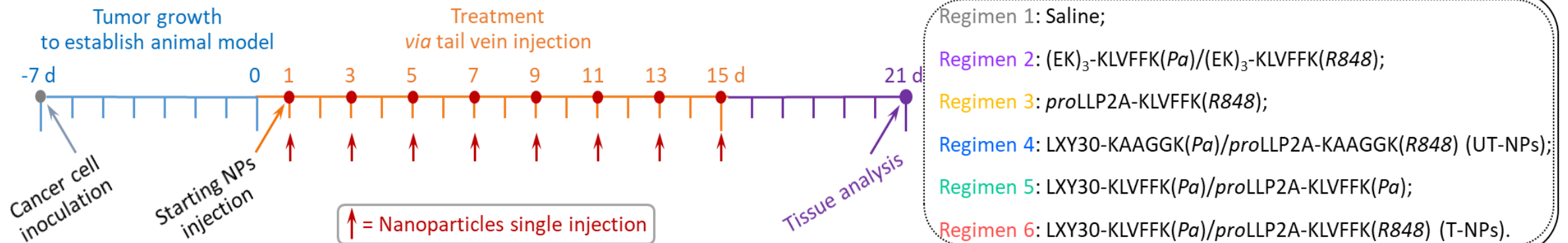
Pre-clinical results:

- **100% cure** in relevant murine mouse models of Breast and Lung Cancer in combination with anti-PD-1
- Demonstrated **durability**
- **No** observed **toxicity**
- Ability to turn immunologically “cold” tumors **“hot”**

Technology spun-off from the University of California Davis Cancer Center

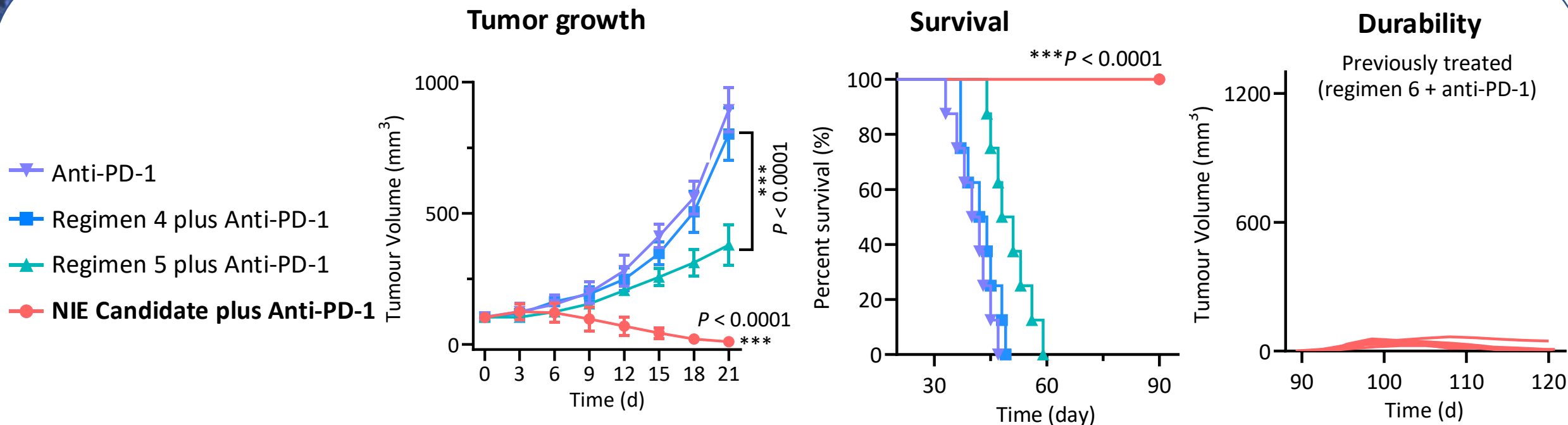
NIE: Monotherapy in 4T1 Murine Breast Cancer Model

Potential to be used for Patients not eligible for ICI's



Combination Therapy: Our NIE + anti-PD-1 in Breast Cancer Model

*We Demonstrated Memory Response and Durability in Mice;
Reinoculation of 4T1 Breast Cancer Cells on Day 90*



Regimen 4: Construct excluded KVLFFK (un-transformable negative control)

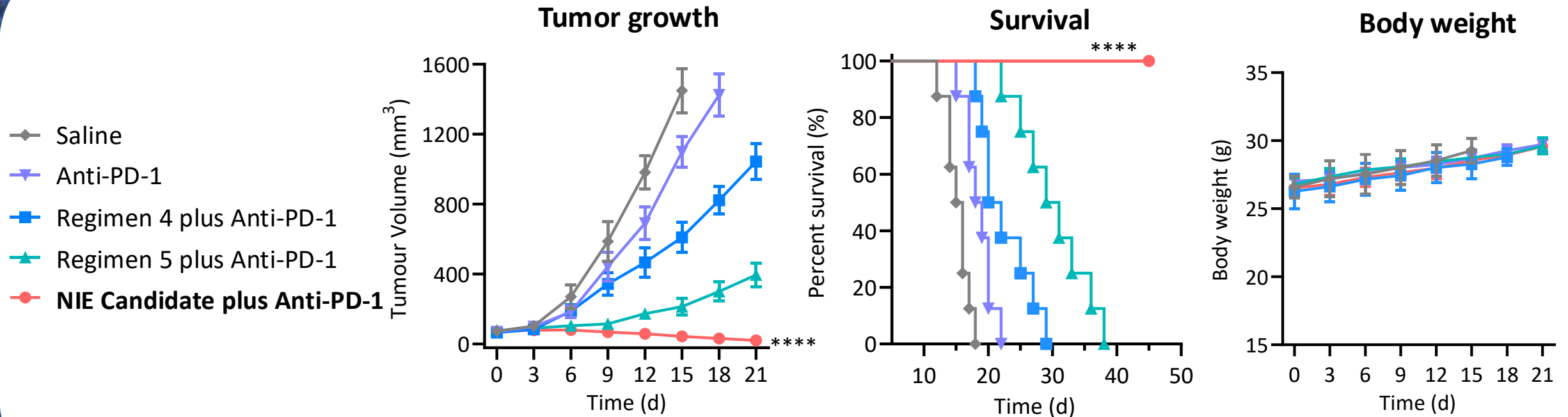
Regimen 5: Construct excluded R848 Resiquimod

4T1 Breast tumor model
N = 8 mice per regimen

Note: Lu and Lam. *Nano Letters* 22:6866-6876, 2022

Combination Therapy: Our NIE + anti-PD-1 in Lung Cancer Model

Demonstrated Tumor Inhibitory Effect with No Change in Body Weight



Regimen 4: Construct excluded KVLFFK (un-transformable negative control)

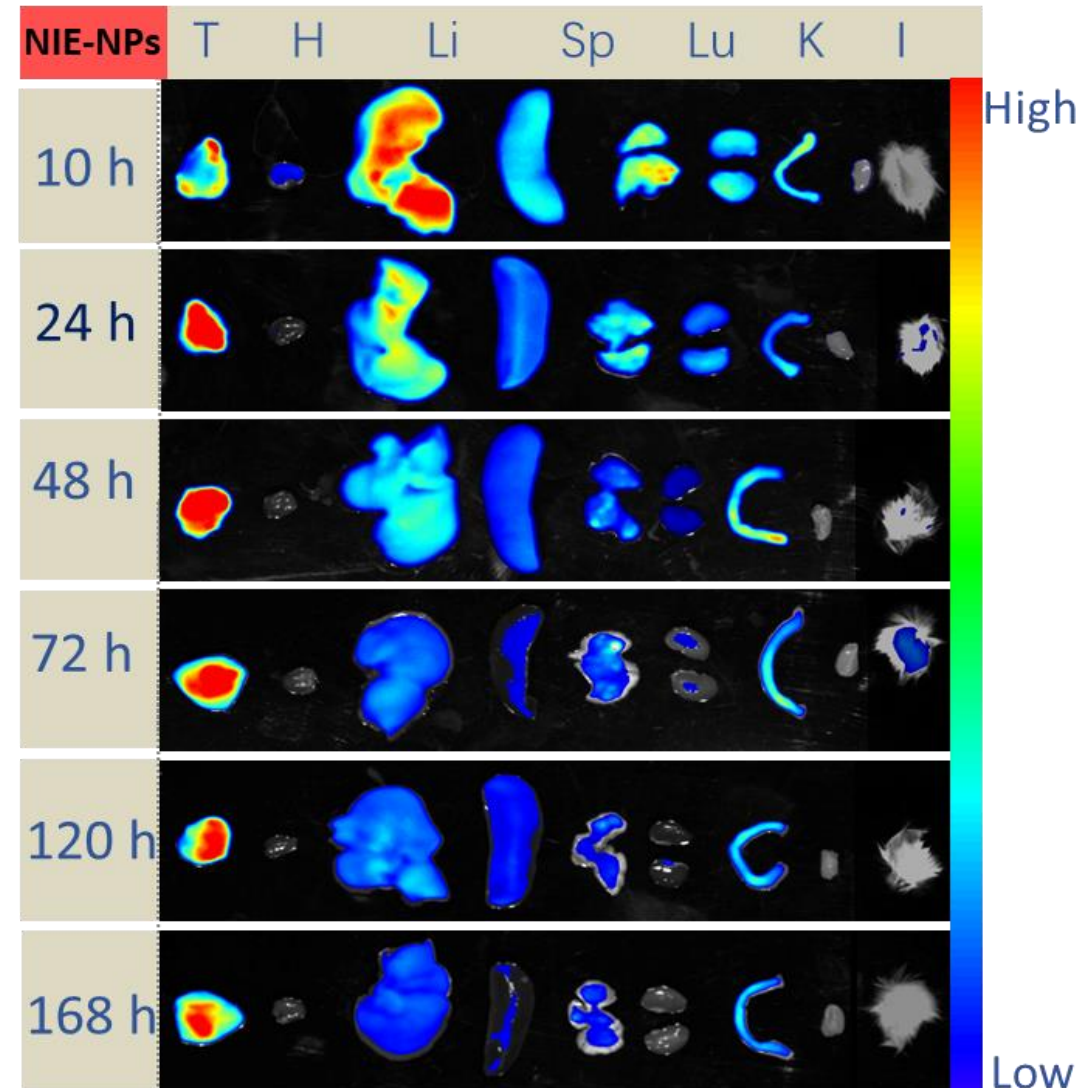
Regimen 5: Construct excluded R848 Resiquimod

Lewis Lung Cancer Model
N = 8 mice per regimen

Note: Lu and Lam. *Nano Letters* 22:6866-6876, 2022

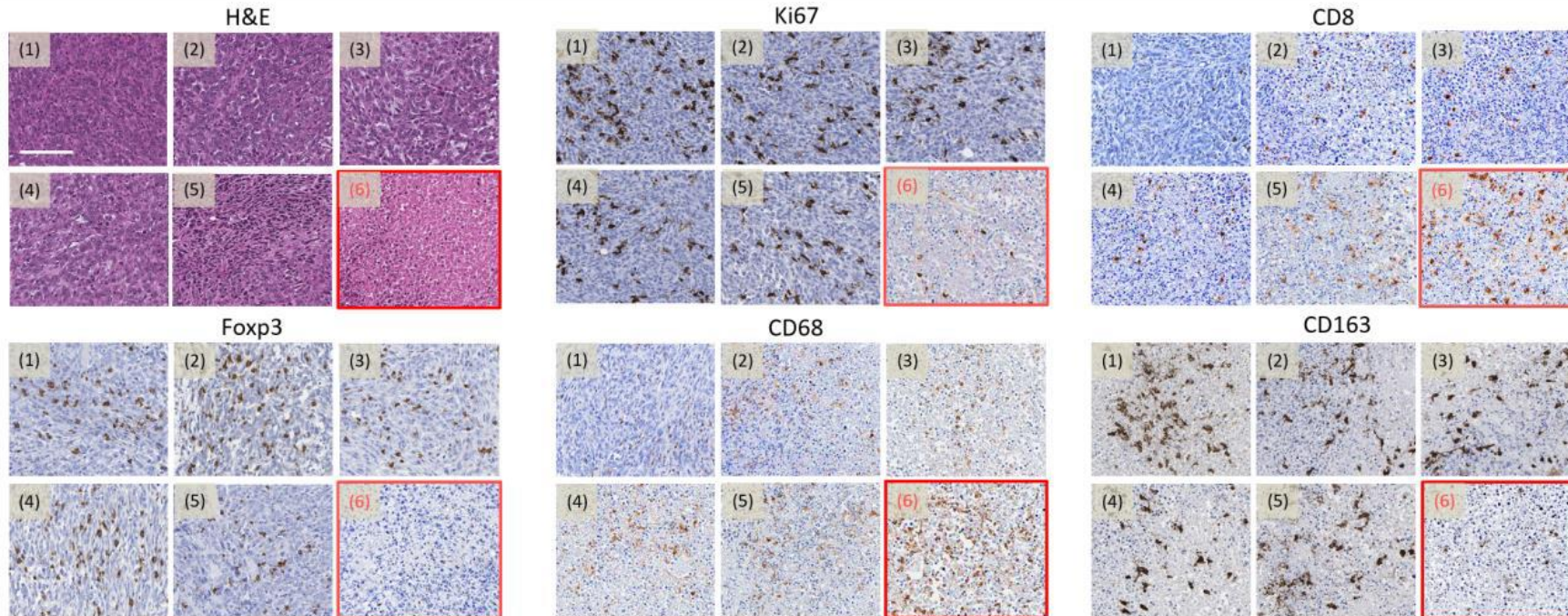
Our NIE: Durability with no Off-Target Systemic Toxicity

- Prolonged retention of the immunomodulatory agent and capturing of the immune cells at the TME
- Rapid clearance in off target organs --
 - T: Tumor H: Heart
 - Li: Liver Sp: Spleen
 - Lu: Lung K: Kidney
 - I: Intestine
- No indications of toxicity in gross histology
- Steady weight gain for all animals throughout the study



Changes in the Tumor Microenvironment Pre and Post Therapy

Recruitment of CD8, reduction of Foxp3 and conversion of CD163 to CD63
M2 to M1 macrophages



Diversity of Applications Creates a Strong Basis for Growth

Current Pipeline

- NIE ± anti-PD1 in NSCLC + other tumor types
- NIE targeting HER2+ in breast & gastric tumors

Additional delivery of agents for Oncology

- Targeted delivery of doxorubicin
 - Manuscript in preparation
- Other off-patent drugs: paclitaxel, cabazitaxel, DM1, MMAE, SN-38, RNA
- Proprietary targeted compounds in collaboration with pharma partners

Inflammatory Diseases

- Targeted delivery of dexamethasone to immune cells
- Targeted delivery of other anti-inflammatory drugs

Infectious Diseases

- Anti-viral and anti-microbial drugs
 - Patent application in process
 - Manuscript in preparation



References:

Advanced Delivery Reviews 157 (2020) 161-178

Nature Nanotechnology Vol 16 April 2021 369 -384

Our Diversified Portfolio and Clinical Approach

*Two validated preclinical lead candidates
among several platform establishing indications*

Platform	Indication	Discovery	IND-enabling	Clinical
NIE*	NSCLC, Melanoma Breast, Head and Neck Squamous Cell Carcinoma ("HNSCC")			
Other Applications	Solid Tumors			

* The Phase I/II study will include two arms; patients with NSCLC and a second arm which will be a basket study that may include patients with melanoma, breast, HNSCC and other malignancies.



Planned Clinical Trials for Development of First NIE

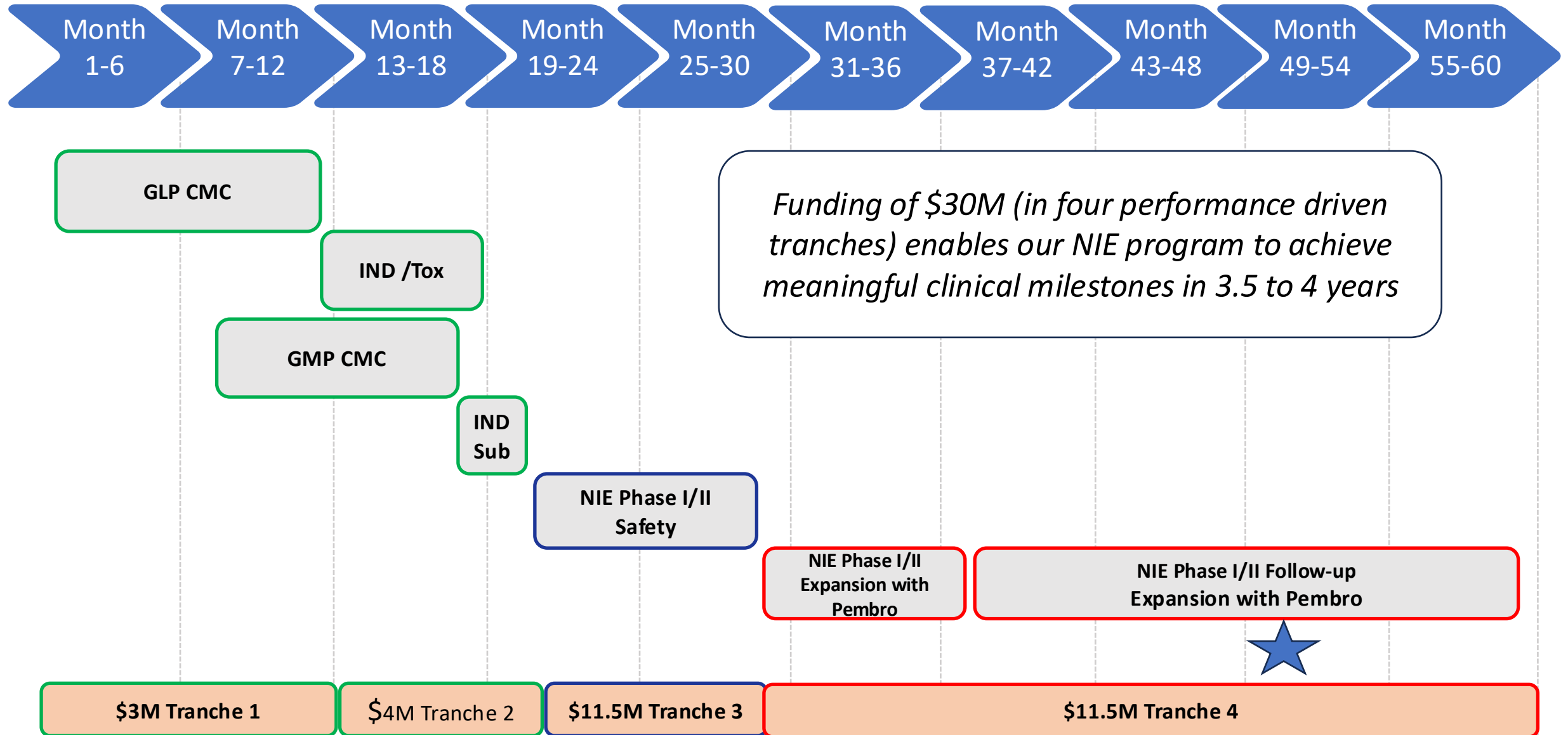
- Phase I/II Study with a potential of three arms
 - 1) lung cancer
 - 2) basket of breast, HNSCC, GBM
 - 3) perhaps a third melanoma cohort
- Dose Escalation followed by Dose Expansion; a potential for sequential biopsies
- Within four (4+) years followed by an Adaptive Phase II/III clinical trial of 300 patients
- Protocol Drafted – first study with University of California Davis Comprehensive Cancer Center under a clinical research agreement



Artificial Intelligence to Predict Patient Response

- Patient response to be characterized by strength and breadth of immune response in the tumor microenvironment
 - RNA Seq – interrogating 800 genes – pre and post clinical therapy via sequential biopsies if tissue location amenable
 - Changes in phenotypic and spatial distribution of multiple immune cells, pre and post therapy
 - Changes in cytokine expression – pre and post therapy
 - Changes in MDSCs, Tregs – pre and post therapy
- Artificial Intelligence / Machine Learning to identify biomarkers that predict response and clinical efficacy
 - In collaboration with INSERM (French NIH) led by Dr. Jerome Galon

Our Clinical Plan & Funding Needs: Reaching Value Enhancing Milestones



Committed & Experienced Leadership

Leadership Team



Anthony Maida III, PhD
Chief Executive Officer
Chairman of the Board



Robert Pierce, MD
Chief Medical Officer



Patrick Bigot, MBA
Chief Business Officer



Seymour Fine, MD
Head of Regulatory Affairs



Board of Directors



Anthony Maida III, PhD
Co-founder, CEO,
Chairman of the Board



Kit Lam, MD, PhD
Co-founder, SAB Chair
Board Member



Richard Slansky
Board Member



Bernice Welles, MD
Board Member



William Ashton
Board Member



SAB: An International Who's Who of Cancer Immunotherapy

Scientific Advisory Board



Kit Lam, MD, PhD
Chair Scientific Advisory Board
Board Member

UC DAVIS
HEALTH



Jose Lutzky, MD

Director, Cutaneous Oncology
at Sylvester Comprehensive
Cancer Center, Miami, FL



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Director of Research at INSERM
and Head of an INSERM laboratory
at the Cordeliers Research Center
in Paris, France



James Talmadge, PhD

Professor, Department of
Pathology and Microbiology,
UNMC, Omaha, NE



Primo Lara, MD

Director UC Davis NCI-Designated
Comprehensive Cancer Center, Exec
Associate Dean, Cancer Programs,
Professor, Department of Internal
Medicine, Sacramento, CA



Kim Margolin, MD

Medical Director of the Melanoma
Program at Saint John's Cancer
Institute (SJCI), Santa Monica, CA



David Gandara, MD

Professor at UC Davis NCI-
Designated Comprehensive Cancer
Center, Sacramento, CA

We are Well Positioned to Manage Technology & Execution Risks

Risk	Mitigation
<i>Competing nanoparticle peptide technology</i>	<ul style="list-style-type: none">• First-to-market mindset• Robustness of the technology enables expanded patent claims• Rapid Phase I/II execution and developed plans progress to a proposed adaptive study
<i>Manufacturing & scale-up</i>	<ul style="list-style-type: none">• Demonstrate commercial scale feasibility at the GLP stage
<i>Slow clinical trial enrollment</i>	<ul style="list-style-type: none">• Expansion of clinical sites to include the UC Cancer Consortium and NCI-designated Comprehensive Cancer Centers
<i>Limited nano immuno-engager clinical results</i>	<ul style="list-style-type: none">• Second product development of HER2+ in various indications
<i>Unknown or unanticipated risks</i>	<ul style="list-style-type: none">• Experienced broad cross functional management team & scientific/clinical advisors
<i>Macro-economic environment and difficult US capital investment market</i>	<ul style="list-style-type: none">• Non-dilutive financing options• International economic interest

----- COMPANY-SPECIFIC RISKS -----
----- INDUSTRY RISKS -----

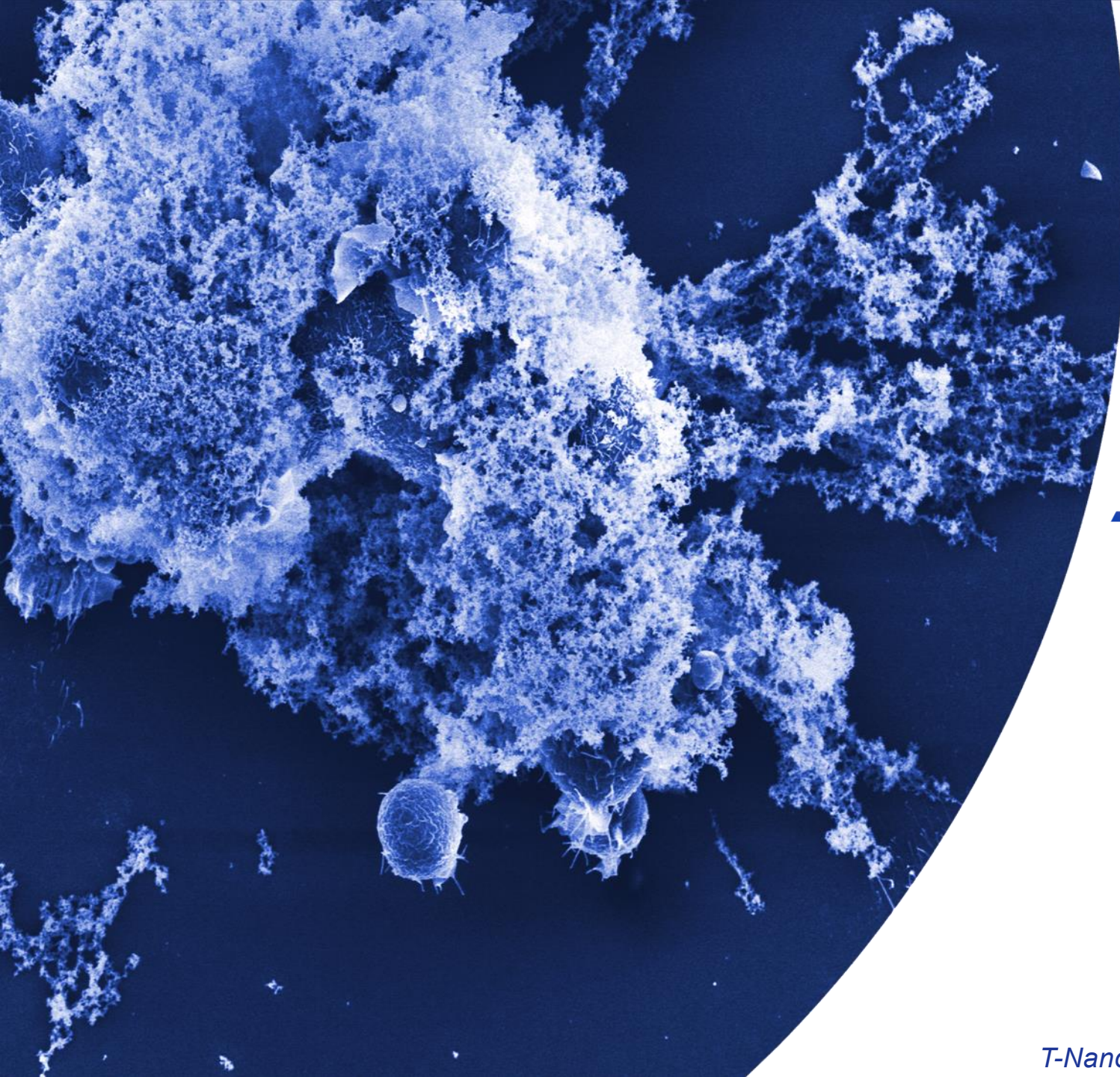


Summary: Why Invest in T-NanoBio Therapeutics?

- **Patient focus** with goal to improve patient outcomes and benefit >850K patients in the US annually and many more worldwide
- **Compelling pre-clinical data:**
 - In combination with anti-PD-1, our NIE candidate product **cured** lung and breast cancer in mice
 - Demonstrated consistent conversion of immunologically **“cold”** to **“hot”** tumors in mice
- **Differentiated profile** versus competitive programs: i) delivers potent immune stimulant resiquimod, and ii) recruits cytotoxic immune cells
- **Multiple product candidates** with platform interest by KOLs
- **Attractive clinical plan** with acceleration possibilities
- **Leadership team** of experienced scientific/clinical/business professionals

Seeking \$30M tranch

- Efficient capital resourcing to start a Phase I/II study within 20 months of funding leading to **meaningful clinical milestones** within 3-4 years



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intelligence together.*