ICaPath

First-in-class systemic delivery of IL-12 within PLGA nanoparticles to promote non-target immune stimulation for metastatic cancers

Non-Confidential Deck

About ICaPath

Capturing Biotech Licensing Dollars with PLGA Nano-Delivered Low Dose Cytokines

COMPANY

Headquarters: Johns Hopkins Tech Ventures, Baltimore, MD

Employees: 5

Founded: 2021

Capital Utilized: $8.5M

TECHNOLOGY

First In Class

- PLGA Nano Immuno-therapeutics *
  - Nanoparticles lower doses by "logs"
  - PLGA ensures efficacy by a delayed sustainable therapeutic release
  - Lead Asset "LD IL-12" – ICP-001™
- PLGA Nanoparticle Drug Delivery
  - Agnostic platform across biologics
- Companion Diagnostic
  - Immuno-Surveillance in "real time"

LICENSABLE ASSETS

Immunotherapy Solutions

- Low Dose IL-12 – ("LD IL-12")
- Portfolio of Metastatic Cancers:
  1 - Melanoma
  2 - Renal Cell Carcinoma
  3 - Soft Tissue Sarcoma
  4 - Pediatric Osteosarcoma
  (potential "Orphan Drug Voucher")
- Nanoparticle Drug Delivery Platform
  - "Systemic" Immuno-therapy delivery

* U.S. Patent No. 12,214,046

Foundational Key Patent *

IP supports Multiple Ground-breaking Assets and Robust Commercialization Goals

- **"Composition of Matter" patent** for proteins loaded with PLGA nanoparticles
- Covers the formulation of IL-12 and methods of creating nanospheres for use with other active moieties
- Coverage includes the US, Europe, China, India, Brazil, Japan, Korea, Australia, Canada, Hong Kong, Israel, and Mexico
- Patent is supported by our comprehensive claims, among others:
  - Precise **particle size control** (100-1000 nm) for targeted delivery.
  - **Unique composition** for improved tissue penetration.
  - **Advanced encapsulation** methods for enhanced efficiency.
  - **Controlled release** customization for optimized therapy.
  - **Stability-enhancing** formulation components.
- **Market Impact:** Strong IP creates high entry barriers, enables licensing opportunities, and positions ICaPath as a leader in immunotherapy delivery.

WILSON SONSINI GOODRICH & ROSATI

Business Strategy

$5.0M funds IND manufactured and FDA validated; Licensing dollars fund Clinical Trials

Year 1 → **Year 2** → **Years 3-5**

GMP VALIDATION and LICENSING

- Manufacture IL-12 Protein & Nanoparticle Platform (**Q2-Q4**)
- License Agreement for LD IL-12 **(Q4)**

PHASE 1 BASKET TRIAL

- Basket Trial in Immunotherapy for cancers: Melanoma, Renal, Soft tissue Sarcoma (**Q3**)
- Nano-Drug Delivery License Agreement (**Q4**)

LICENSING CASH, IPO and M&As

- Multiple Licensing Revenues from 4 NDAs
- Extend Pipeline in Therapeutic Assets
- IPO; M&A for Novel Assets

Immunotherapy has Toxicity-related Shortcomings

Figure 1

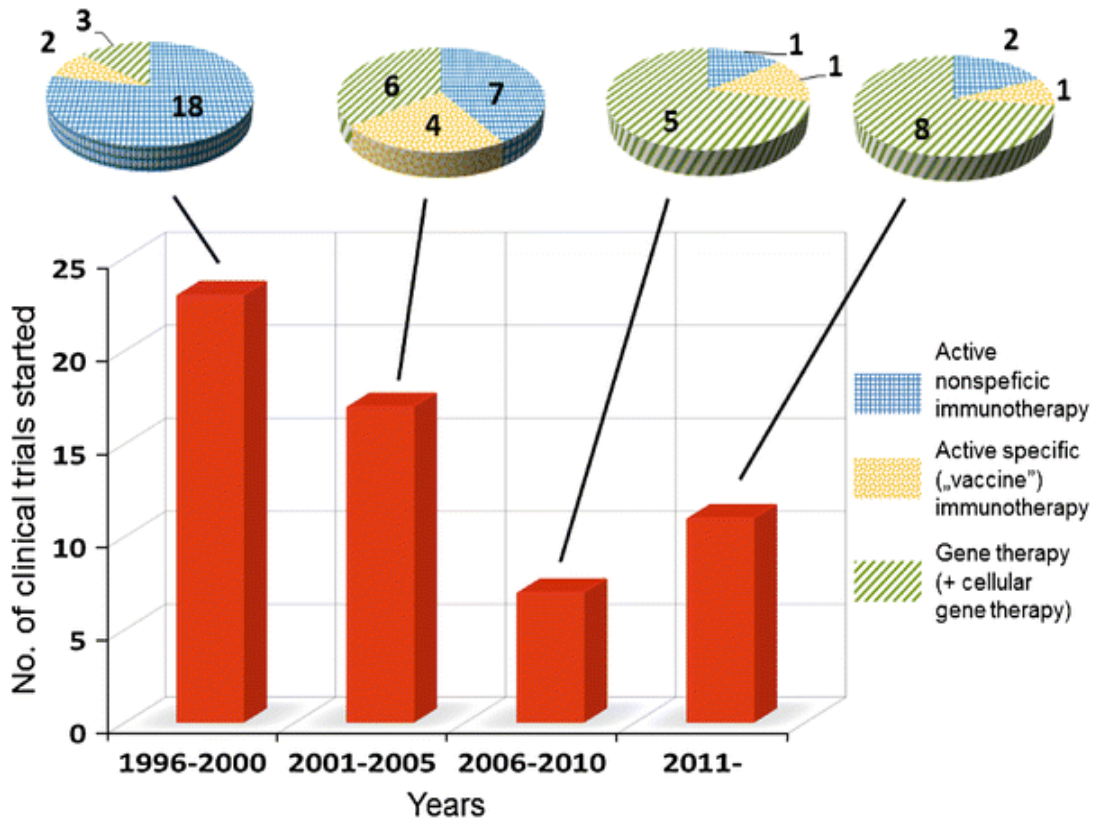


Figure 1: **Interleukin 12 (IL-12) based clinical trials in the field of solid tumor immunotherapy have had over 30 years of failed trials due to inappropriate delivery systems (ClinicalTrials.gov)**

Figure 2

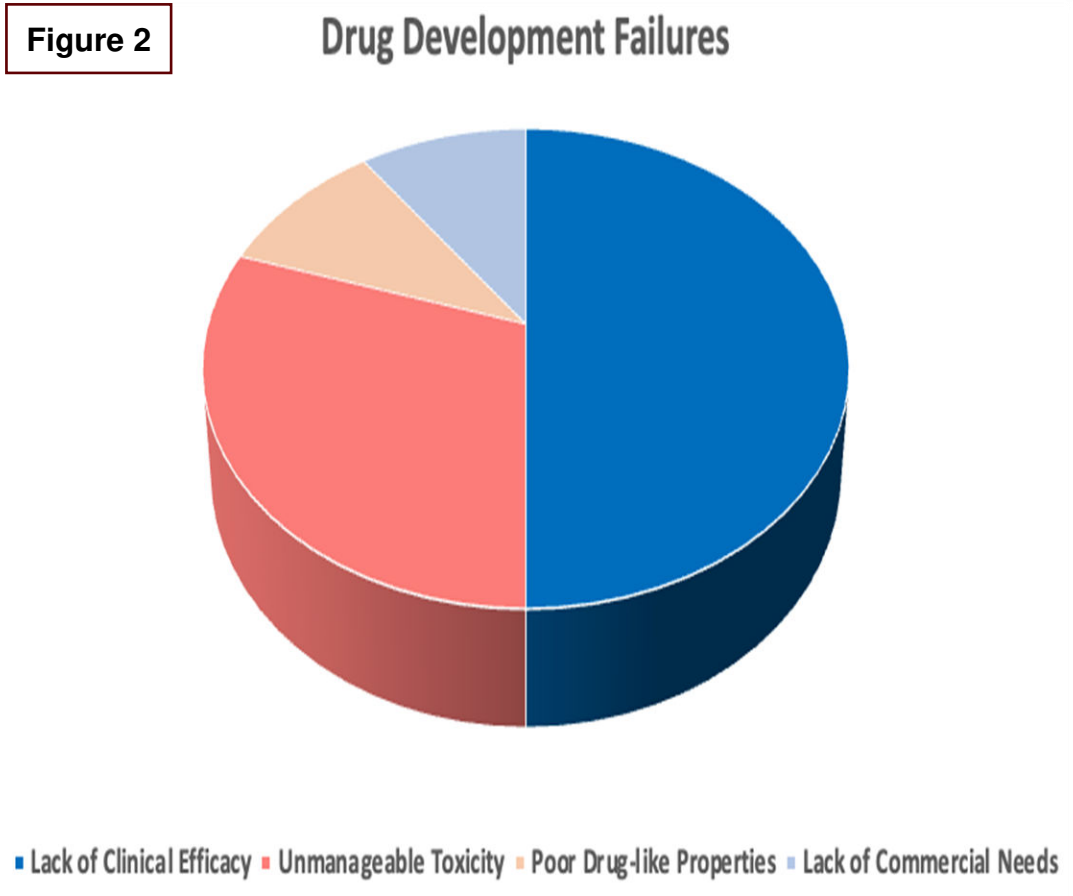


Figure 2: **Toxicity and lack of efficacy account for a large majority of drug development failures not just in oncology.**

1. Alsaab, H., et al. 6 December 2022. Pharmaceutics 2022, 14(12), 2728; DOI: 10.3390/pharmaceutics14122728
2. Jia, Z., et al. 20 September 2022. *Front. Immunol.,* Sec. Cancer Immunity and Immunotherapy. Volume 13 - 2022. DOI: 10.3389/fimmu.2022.952231
3. Lasek, W., et al. 11 February 2014; *Cancer Immunology, Immunotherapy*. DOI: 10.1007/s00262-014-1523-1
4. Nguyen, K., et al. 15 October 2020. *Front. Immunol.,* Sec. Cancer Immunity and Immunotherapy. Volume 11 - 2022. DOI: 10.3389/fimmu.2020.575597

How does ICaPath overcome the “Toxicity Hurdle”

The Basic Problem

- The use of IL-12 as the leading immunostimulation compound for cancer immunotherapy has remained unavailable for systemic delivery in clinical applications due to excessive toxicity

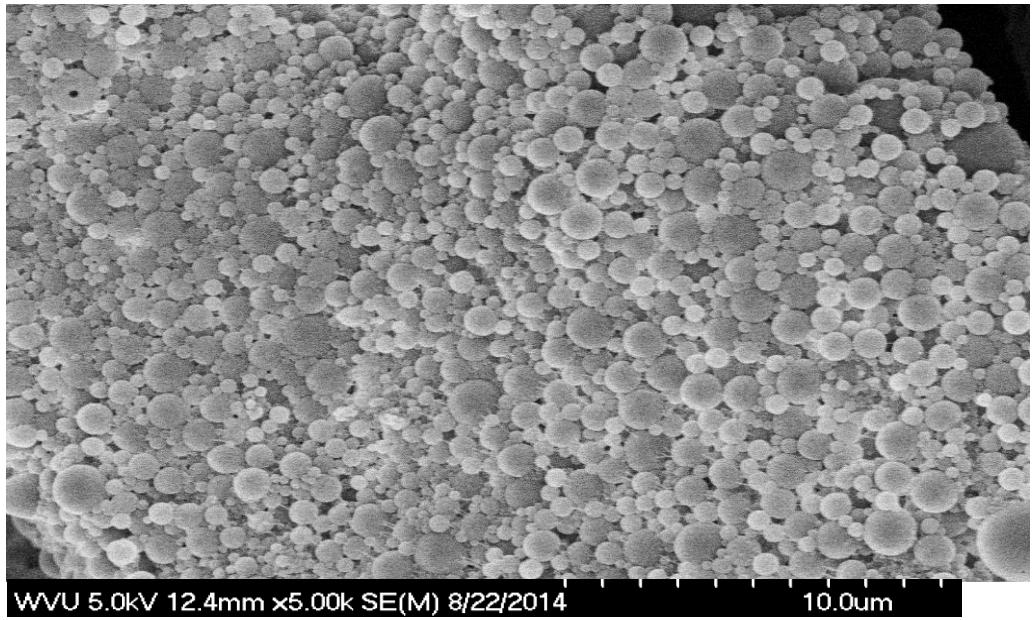
The ICaPath Solution

- ICaPaths’s PLGA/nanoparticles delivery vehicle for IL-12 is a best-in-class platform for the systemic infusion of cytokines
- Pre-clinical experiments[1,2,3] have revealed the following:
  - **toxicity issues can be eliminated**
  - nanoparticle delivery vehicle of IL-12 **positively affects bioavailability and pharmacokinetics**

1. Lacinski RA, **Lindsey** BA et al. Journal of Orthop Res. 2023 Jul;41(7):1565-1581
2. Alsaab, H., et al. 6 December 2022. *Pharmaceutics* 2022, *14*(12), 2728; DOI: 10.3390/pharmaceutics14122728
3. Lacinski RA, **Lindsey** BA et al. J Immunol Res. 2022 Apr 14;2022:6993187

Revolutionizing Systemic IL-12 Delivery: Perfecting Nanoparticle Composition

Over a decade of systematic investigation led ICaPath to identify the key parameters that maximize the pharmacokinetic and physical properties of our patented nanoparticle to safely and effectively deliver IL-12

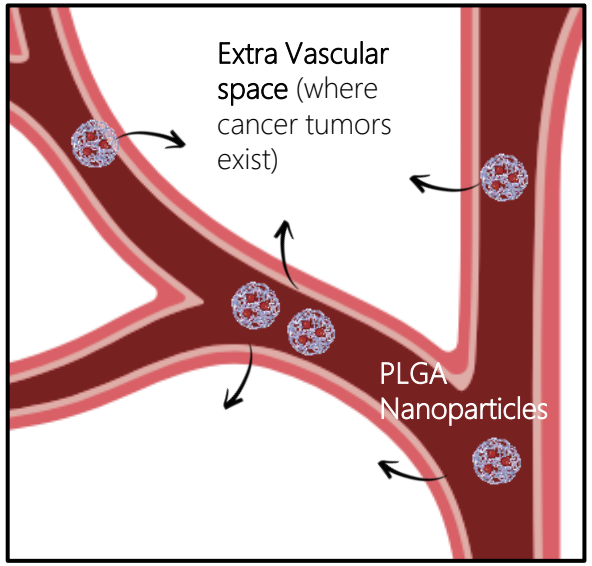


1. Best in Class Capability to load the PLGA nanoparticles
2. Best in Class Release of active Drug
3. Best in Class retention of Drug Function
4. Capable of scaling up GMP manufacturing to commercial production levels.

Nanoparticles ensure safe systemic delivery complemented by the PLGA-mediated delayed release within the interstitial space

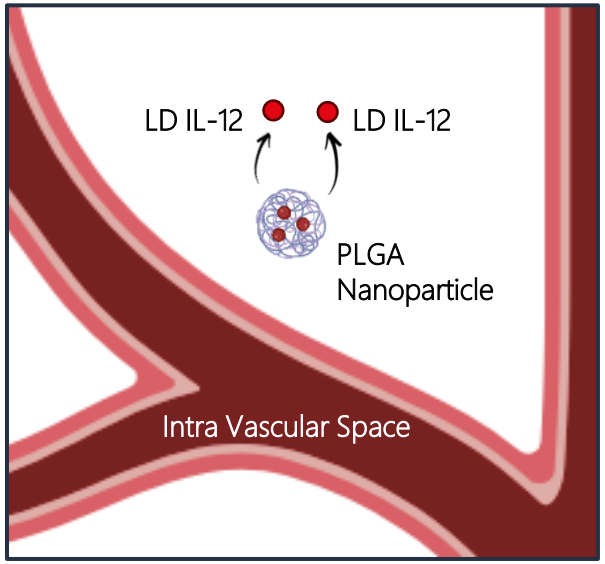
Low Dose (LD) IL-12 encapsulation with nanoparticles allow for its successful delivery within the interstitial space

LD IL-12 encapsulation with PLGA allows for a delayed release ensuring an ideal immune response



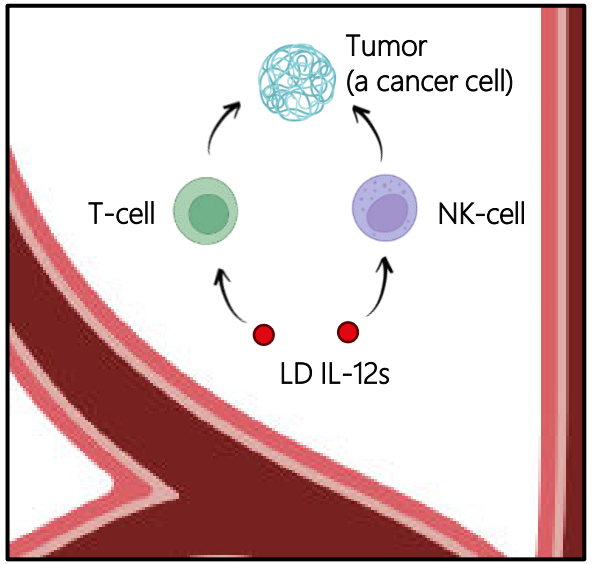
Step 1

Nanoparticles allow for moving an encapsulated IL-12 from intra to extra vascular (EV) space



Step 2

PLGA nanoparticle releases log lower doses of IL-12 ("LD IL-12") into EV space



Step 3

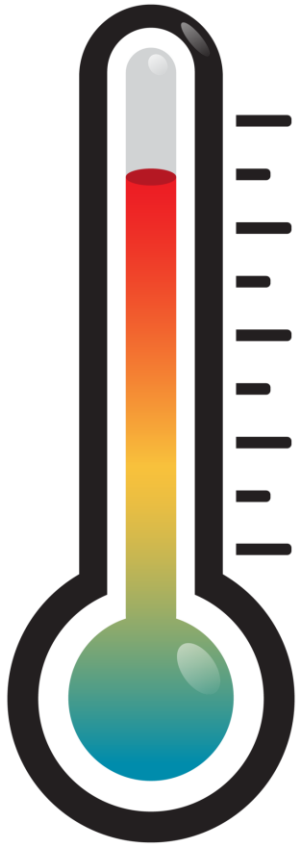
LD IL-12 seeks and activates T-cells* and NK-cells* to properly recognize and destroy tumors

ICaPath

* NK cells (Natural killer cells) are white blood cells that destroy infected and diseased cells, like cancer cells.
* T cells are white blood cells that play a central role in the body's adaptive immune response.

Nano-Encapsulation allows for Log Lower Doses

Logarithmic reductions in dosing maintains immune stimulation and efficacy with minimal toxicity



IL-12 Dose	Significance
7.5 ug/kg	HNSTD in Non-Human Primates
500 ng/kg	Maximum Tolerable Dose in Humans
1 ng/kg – 1000ng	Clinical trial doses
0.67 ng/kg	Calculated Optimal Biological Dose
0.0067 ng/kg	Dose Level 1

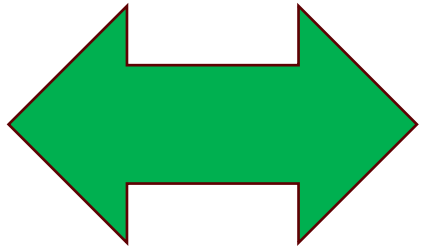
Log lower doses of IL-12 ("LD IL-12")

NHP: Non-human primate, OBD: optimal biologic Dose, HNSTD: highest non-severely toxic dose, MTD: Maximum tolerable dose

ICP-001 Yields 75% Cure Rates and No Toxicity

PLGA/Nanoparticle Delivery tested in the classic K7M2 Immunocompetent rodent model for Metastatic Osteosarcoma has yielded an unprecedented <u>75% dose specific cure rate</u> and 50% overall response.

Dose of rmIL-12ns	Metastatic Recurrence Rate (%)	Cure Rate (%)
Historic Control	85%	< 5%
0.1 mg	25%	75%
1 mg	50% (75%)	50% (25%)
10 mg	75% (100%)	25% (0%)

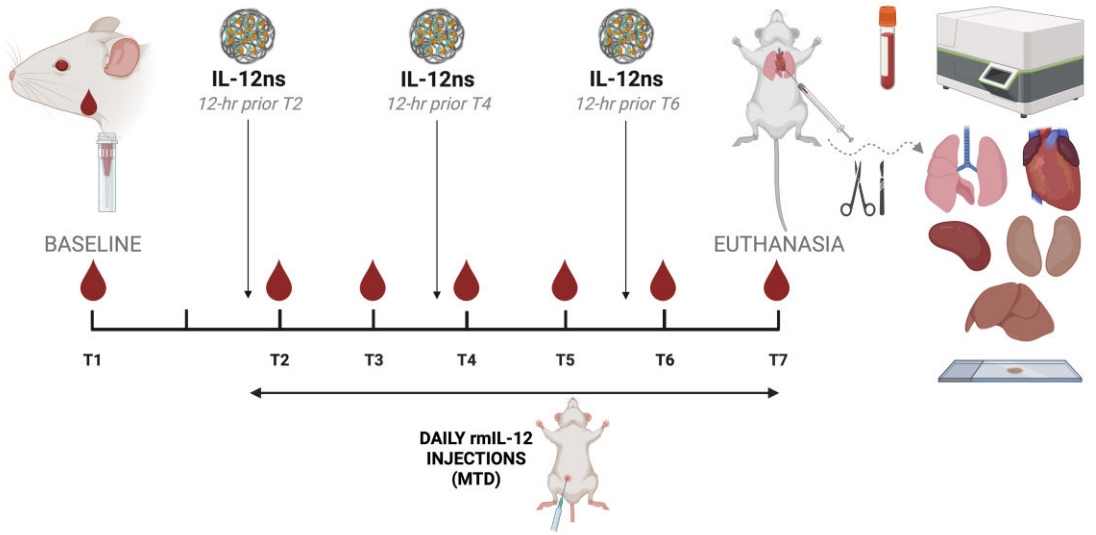


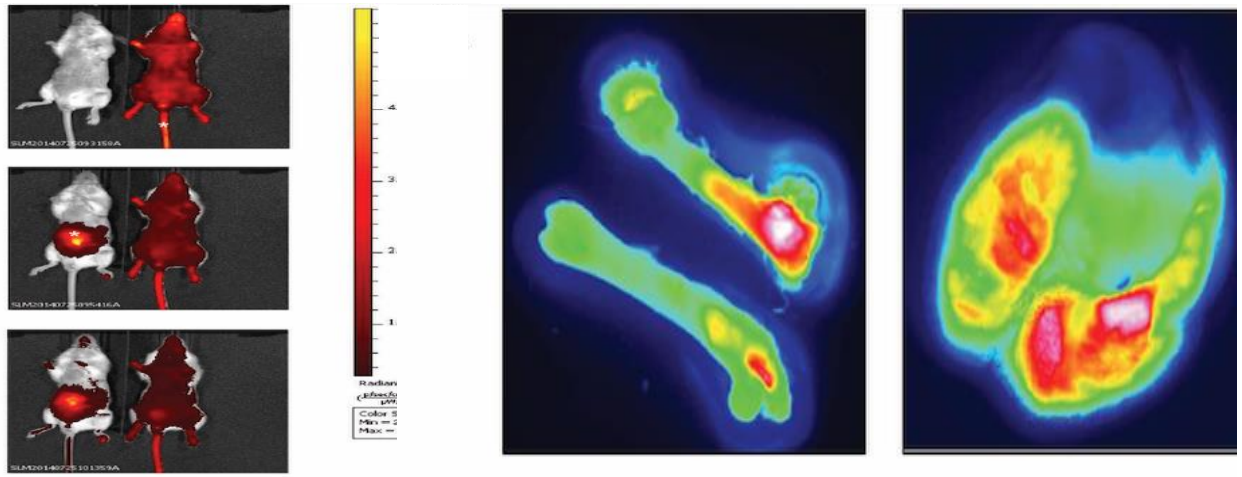
Pharm/tox studies have shown *<u>no</u>* signs of end organ damage or *<u>toxicity</u>* at all doses. The FDA has accepted to review this data for the initial FIH applications

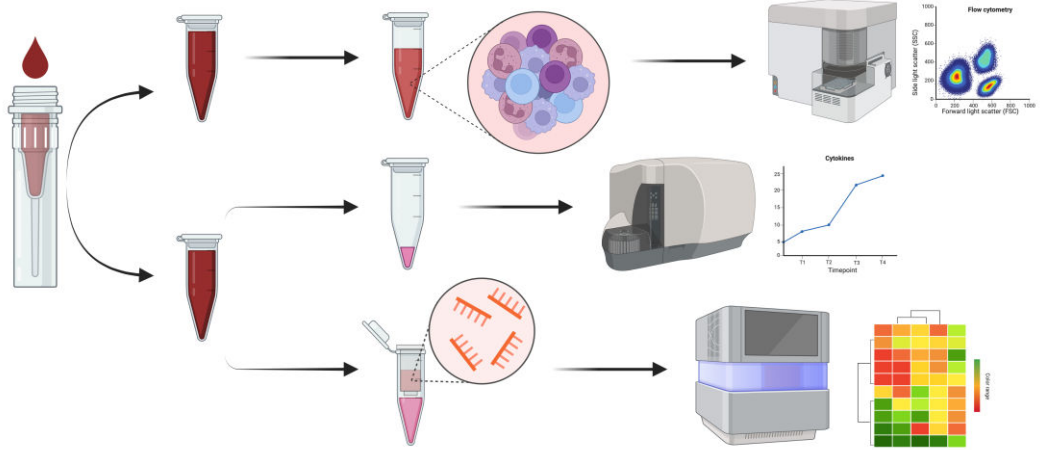
This data has been considered sufficient pre-clinical evidence by the FDA to move this therapeutic application into clinical trials in adults once the CMC has been fully optimized.

Proof-of-concept studies with 212 mice over 6 Years Investigation

- Model Development
- Biodistribution
- Developing a First in Class Blood test for tracking disease and therapeutic treatment effect
- Treatment studies showing reproducible efficacy without toxicity leading to immune response to cancer







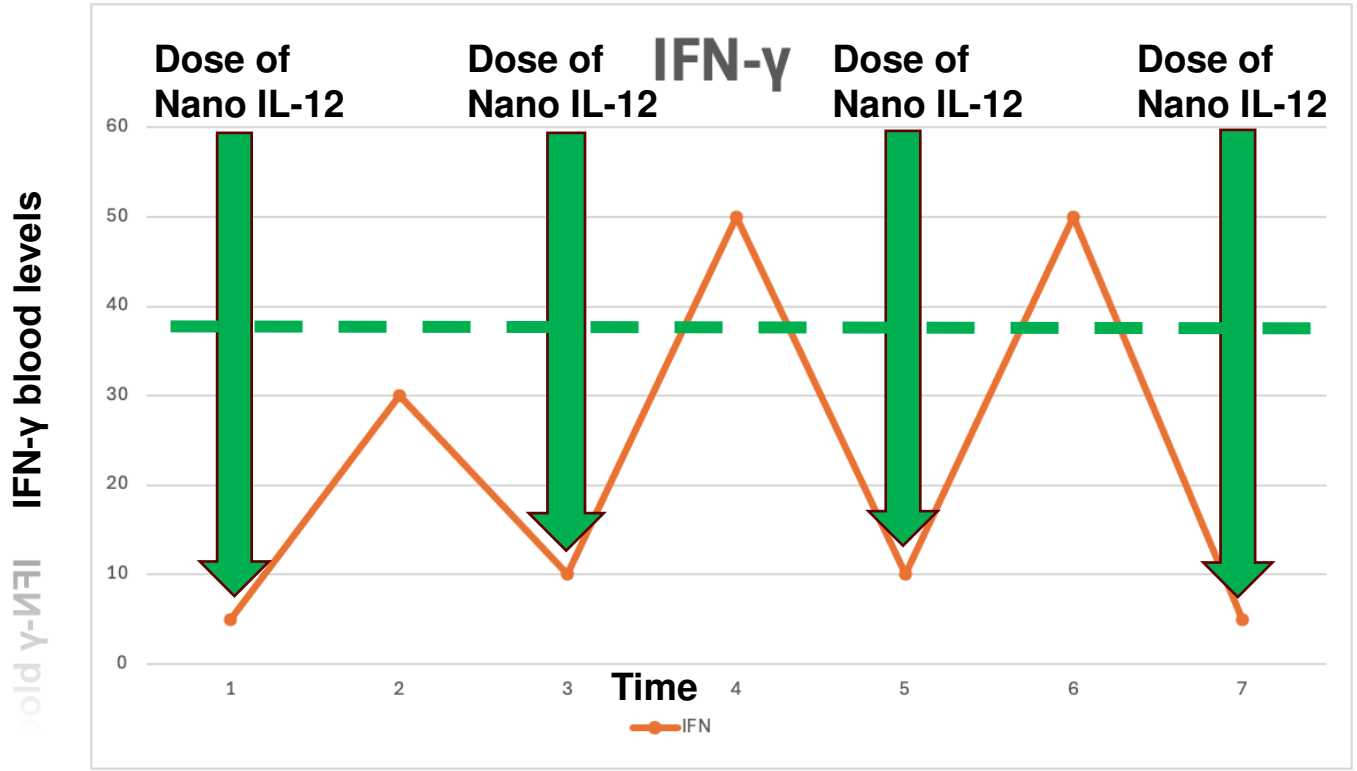
What we have learned from Historical IL-12 Clinical Trials

If you can Maintain IFN-γ levels over repeated doses of IL-12 it is associated with a Positive Clinical Response *

* Atkins, M. B., Robertson, M. J., Gordon, M., Lotze, M. T., DeCoste, M., DuBois, J. S., ... & Sherman, M. L. (1997). Phase I evaluation of intravenous recombinant human interleukin 12 in patients with advanced malignancies. *Clinical Cancer Research*, *3*(3), 409-417.

ICaPath *Can* Maintain IFN-γ Response

Through our Patented Technology we can Reproducibly maintain a systemic IFN-γ response over multiple doses and time

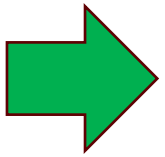


Maintenance of IFN-γ leading to clinical response

ICaPath has received a positive FDA review for the intended clinical applications of IL-12 in metastatic cancer immunotherapy

The Basic Problem

- **No IL-12 based therapeutic has been FDA approval**



The ICaPath Solution

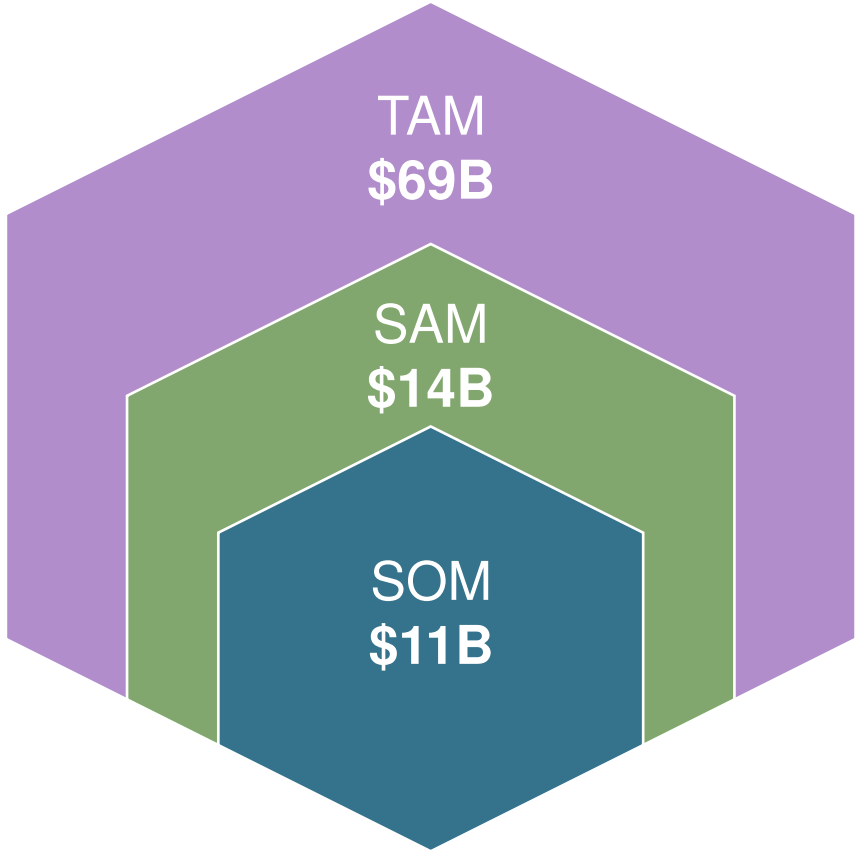
- PLGA is an **FDA-approved polymer,** which can speed up subsequent approval
- Our formulation of nano IL-12 with logarithmically lower doses has a very positive acceptance from the FDA
- Tremendous amounts of data to support the program approval with the FDA

PLGA Nanoparticle Delivery Platform: Pharmacological Advantages

Key Patent-Supported Features

- **Precise Particle Size (100–1000 nm):** Enables targeted drug delivery, improving tissue specificity and reducing off-target effects.
- **Unique Composition:** Enhances tissue penetration, facilitating deeper and more effective delivery of biologics and gene therapies.
- **Advanced Encapsulation Methods:** Improves loading efficiency for a broad range of therapeutic agents, including small molecules, peptides, proteins, and genetic constructs.
- **Controlled Release Customization:** Allows fine-tuning of drug release kinetics, optimizing treatment efficacy and minimizing dosing frequency.
- **Stability-Enhancing Formulation Components:** Maintains integrity and biological activity of sensitive therapeutics under various storage and physiological conditions.

Addressable Therapeutic Markets (USA)



Metastatic Cancers	TAM ($M)	SAM ($M)	SOM ($M)
Osteosarcoma	$356	$71	$58
Soft Tissue Sarcoma	$4,696	$939	$770
Renal Cell Carcinoma	$28,480	$5,696	$4,671
Melanoma	$35,522	$7,104	$5,826
TOTAL	$69,053	$13,811	$11,325

TAM – Total Addressable Market

SAM – Strategic Addressable Market

SOM – Strategic Obtainable Market

CliftonLarsonAllen

Sources: 1) Community Oncology Alliance, LINK; 2) Pew Research Center, LINK

Unique in the IL-12 Therapy Landscape

Biotech Company	IL-12 Therapy	Delivery Method	Clinical Trial(s)	Toxicities	Limitations
ICaPath	Low Dose IL12	• Intravenous • Local infusions	• Preclinical stage	• No systemic toxicity in pre-clinical findings	• None noted because PLGA nanoparticle delivery has no target limitation, and dosing is repeatable and consistent, maintaining continued efficacy
Roche	Recombinant human IL-12 (rhIL-12)	• Intravenous • Subcutaneous • Intraperitoneal	• Melanoma • Renal cell carcinoma • Ovarian cancer	• Systemic inflammatory response syndrome (SIRS) • T cell exhaustion	• Dose-limiting toxicities • Limited efficacy due to high loading doses for adequate tissue biodistribution
Dragonfly	Monovalent IL-12 immunoglobulin Fc fusion protein	• Intravenous	• Solid tumors	• Dose dependent awaiting trials	• Dropped by BMS because of: 1. Prolonged half life of IL-12 in circulation from modification 2. Lack of tissue penetration dosing issue
PDS Biotechnology	Tumor-targeted IL-12 therapy	• Fused ADC IL-12 (PDS01ADC) given subcutaneously	• Solid tumors	• Fatigue • Transaminase elevation • Hematologic • Dose-limiting at higher doses	• Unfavorable PK • Narrow therapeutic indexes • Tumors can develop resistance to this route • Delivery challenges in some locations • Short half-life limits doses • Limited clinical approval
xilio THERAPEUTICS / Werewolf THERAPEUTICS	Tumor-activated IL-12	• Tumor-specific activation	• Preclinical stage/clinical	• Reduced systemic toxicity	• Difficult dosing strategy because of unknown volume of activation and unknown timing
MURAL ONCOLOGY	Engineered IL-12	• Modified to reduce binding to IL-18BP	• Preclinical stage	• Expected better safety profile	• Still in development, no clinical data yet
Institute of Biophysics Chinese Academy of Sciences	Pro-IL-12	• Tumor restriction	• Preclinical stage	• Low toxicity • tumor restriction	• Still in development, no clinical data yet

Projected Milestones

Milestones (dependent on funding)	Activity	Year 1				Year 2				Year 3				Year 4				Year 5			
		Q2	Q3	Q4		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Series A	**$5M**																				
Process Development IL-12 cell line	Upstream & downstream developments																				
Validation of Immunodiagnostic platform	Setting up lab and hiring technician																				
Process/Analytical Development - CDMOs to GMP	LD IL-12 and PLGA engineering runs																				
IND Approval - GMP production	Scale-up to full GMP production																				
Non-Dilutive Capital	**SBIR/Licensing**																				
ICP-001 Phase 1	***STS, Melanoma, RCC***																				
ICP-001 Phase 2	***Pediatric Osteosarcoma***																				
ICP-001 Phase 3	***STS, Melanoma, RCC, Pediatric***																				

BLA REGULATORY

Executive Team

John W. Kennedy
Chief Financial Officer
Former CFO of SeqLL Inc. and Intercontinental Telecom Corp.

Steve Willard
Chief Executive Officer
Board Director
Former CEO of Flamel Technologies
Former CEO of Cellphire, Inc.

Phil Farabaugh
Chief Operations Officer
Former COO of VirTech Bio

Paulo Fontes, MD
Co-Founder, Director
SAB Member

Scientific Advisory Board (SAB)

James S. Allan, MD, MBA
Associate Professor of Surgery, HMS
Thoracic Surgeon, MGH
Founder and CEO, Orcadia Ventures

Charles A. Knirsch, MD, MPH
Former Vice President, Pfizer Inc. – Oncology and immuno-therapeutics
Board Expertise: Wolbitos (Chair)

Brock Lindsey, MD
Founder, Chairman of Board
SAB Member

Investment Highlights

Ask: $5.0 million at a $10 million pre-money

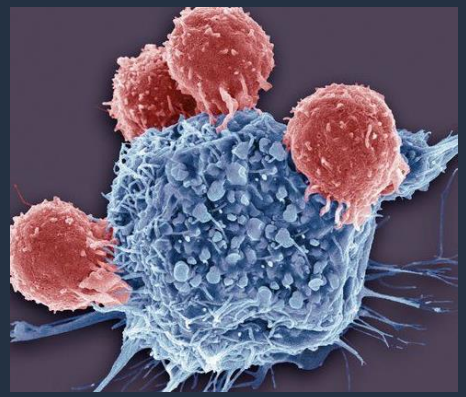
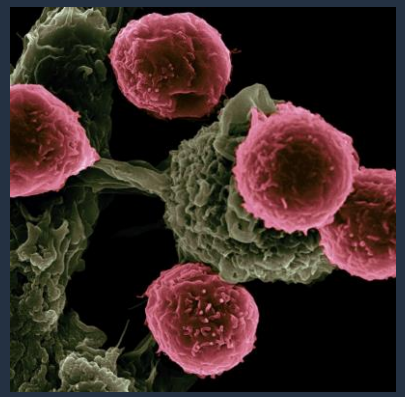
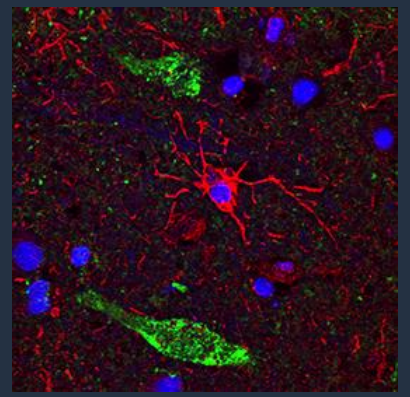
Multiple Paths to Success

- Potential market leading cancer therapeutic assets
  - Low Dose Interleukin-12 (LD IL-12)
  - Potential million $ valuations per LD-12 assets
  - Melanoma, Renal cell Carcinoma, Soft Tissue Sarcoma and Osteosarcoma
- Patent on Core Assets to be leveraged in Partnerships
  - Multiple LD IL-12 assets could bring universal breakthroughs in biologics and immuno-therapy
  - PLGA nanoparticle delivery platform could bring a breakthrough across the market for drug delivery
  - Portfolio of LD IL-12 assets could generate significant cash in a wide variety of licensing deals

Environment for Execution

- Licensing novel biotech assets is a focus by Pharma
  - Upfront cash and Milestone payments in millions of dollars over years
- Basket trial at Johns Hopkins for cost-effective launch:
  - LD IL-12 immuno-oncology for: Melanoma, Renal Cell Carcinoma, Soft Tissue Sarcoma and Osteosarcoma
  - First-in-Class Nanoparticle Drug Delivery Platform
- Executive Management with deep expertise in biotech:
  - CEO with significant background in licensing deals
  - Leadership in drug development and clinical trials

Thank You

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