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Aiming to improve solid tumor response without adding toxicity

Key Unmet Need in Oncology

- **Improve the treatment of solid tumors**
  - **" Despite all the advancements in IO, single agents are insufficient to treat most solid tumors, and rational systemic combination therapies will remain SOC for the foreseeable future, likely forever…"[1]**
  - **Key consequence is stacked toxicities that limit use**

- **Opportunity**
  - **Growing recognition of the:**
    - **Benefits of intratumoral therapy[2]**
    - **Value of debulking/priming the primary tumor in conjunction with systemic therapy[3,4]**
  - **Improvements in imaging technologies and procedures now allow local access to solid tumors throughout the body**
  - **Systemic combination therapies are limited by toxicity**

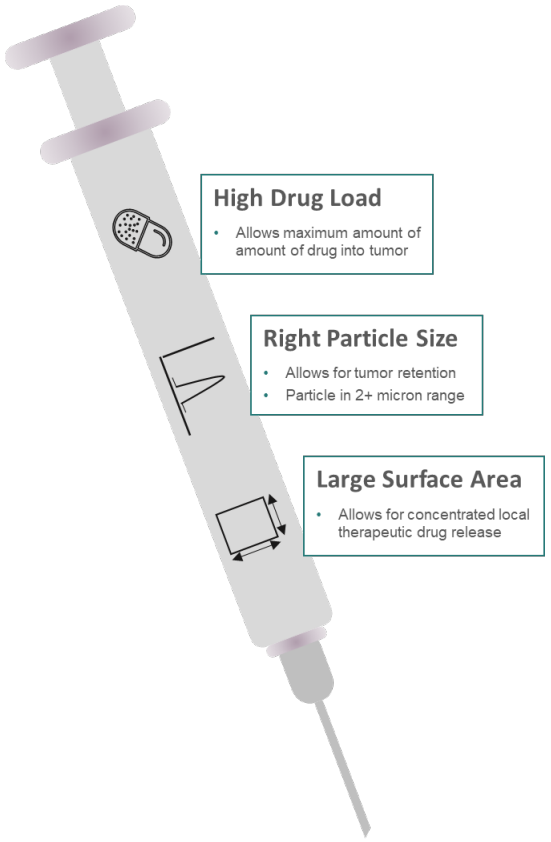
- **Nanology Solution**
  - **Proprietary Purcision™ technology platform engineers patented large surface area microparticles (LSAMs) of pure chemotoxic agents optimized for intratumoral delivery**

1. Charles Drake, MD, PhD remarks at the 10th IO 360 Conference (Feb 2024)
2. Luke et. al. SITC recommendations on IT immunotherapy clinical trials. JITC 2024
3. Oppel et. al Frontiers (2020)
4. Hishida et. al. JJCO (2021)

NanOlogy Purcision™ Particle Engineering Technology

Enables large surface area microparticles (LSAMs) of pure drug optimized for intratumoral drug delivery

Particle attributes for optimal intratumoral delivery



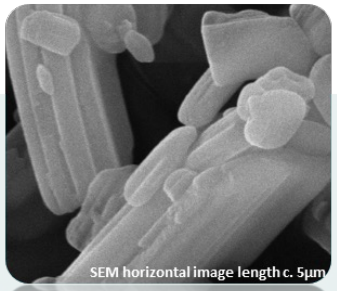
High Drug Load
- Allows maximum amount of amount of drug into tumor

Right Particle Size
- Allows for tumor retention
- Particle in 2+ micron range

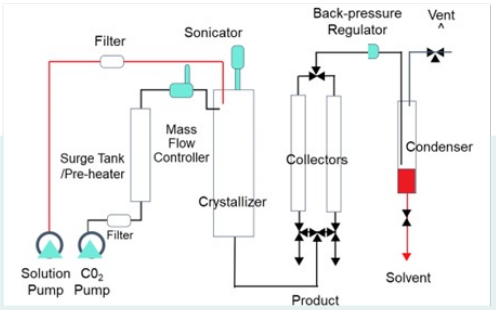
Large Surface Area
- Allows for concentrated local therapeutic drug release

Proprietary Purcision technology platform enabling LSAMs

Unprocessed Drug Substance

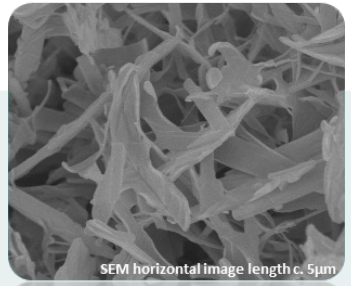


- ✓ Large and bulky crystals
- ✓ Infeasible to form pharmaceutically acceptable particle suspensions
- ✓ Limited to dissolution in solvent as a solution for IV delivery



- ✓ GMP commercial scale production suitable for clinical supplies and commercial launch
- ✓ Uniquely uses supercritical fluid carbon dioxide as antisolvent
- ✓ Platform technology for multiple drug classes (taxanes, platins, TKIs, PARPIs, others)

LSAMs



- ✓ 100% pure drug with no excipients or coating agents
- ✓ Right particle size for tumor retention
- ✓ Increased surface area for high continuous local therapeutic drug release
- ✓ Decreased bulk density for excellent suspension uniformity

Global intellectual property portfolio of more than 100 patents including:
- **Composition of matter patent on LSAMs through 2036**
- **Use of IT LSAMs with any systemic immune checkpoint inhibitor through 2038 offering potential product lifecycle extension for immune checkpoint inhibitors coming off patent**

diZerega et.al. Oncol Ther 2024

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NanOlogy Development Assets & Pipeline

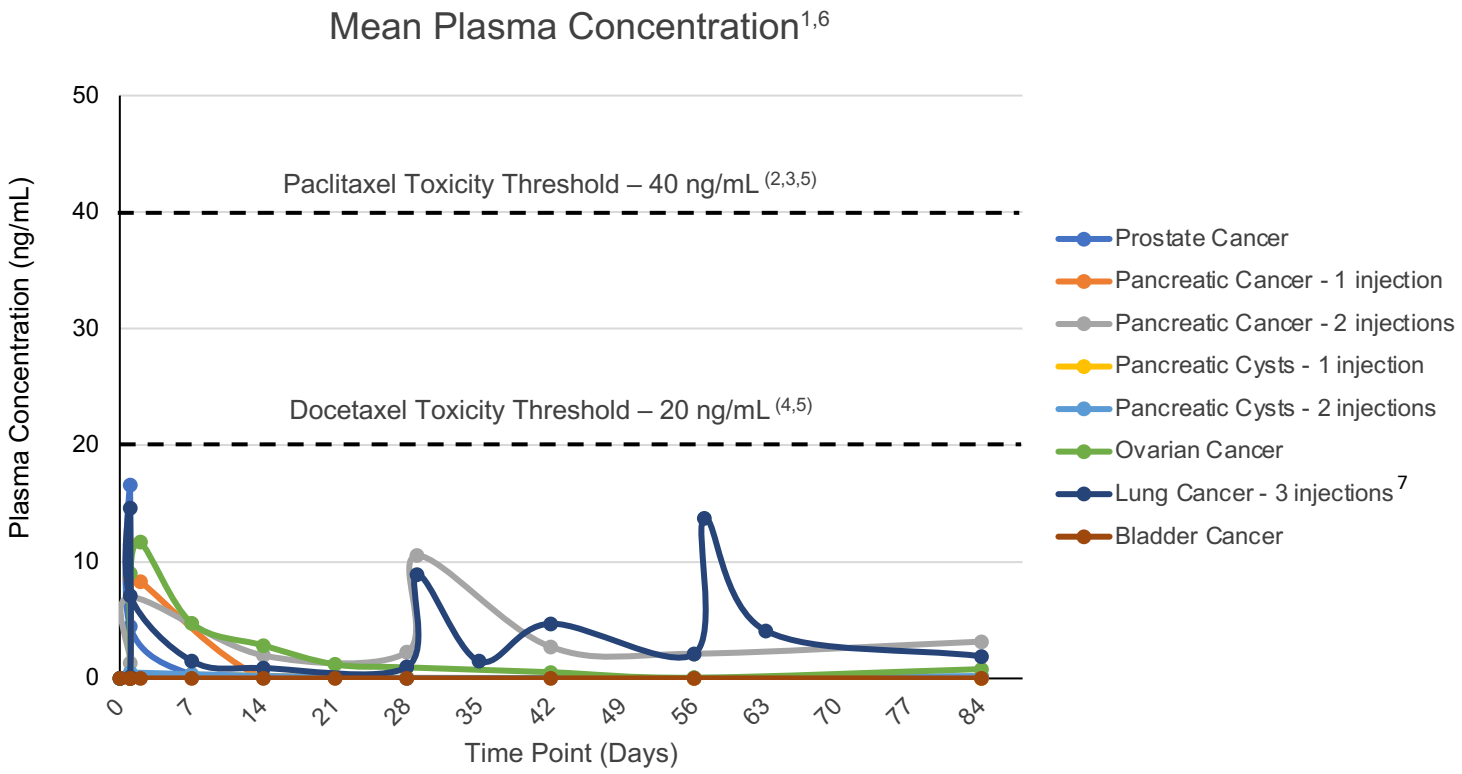
Product	Therapeutic Area	Delivery	Feasibility	IND	Phase 1	Phase 2	Phase 3
LSAM-PTX for Sterile Suspension	Non-Small Cell Lung Cancer	Intratumoral	*Lead Program*				
	Locally Advanced Pancreatic Adenocarcinoma	Intratumoral	*Lead Program*				
	Prostate Cancer	Intratumoral					
	Peritoneal Malignancies / Ovarian Cancer	Intraperitoneal					
	Mucinous Cystic Pancreatic Neoplasms	Intracystic					
LSAM-DTX for Sterile Suspension	Non-Muscle Invasive Bladder Cancer	Resection Bed Injection & Intravesical Instillations					
	Muscle Invasive Bladder Cancer	Resection Bed Injection & Intravesical Instillations					
	Renal Cell Carcinoma	Intratumoral					
	Prostate Cancer	Intratumoral					
LSAM-Cisplatin for Sterile Suspension	Brain Tumors	Intratumoral					
	Solid Tumors	Intratumoral					
LSAM-PTX for Inhalation	Non-Small Cell Lung Cancer	Nebulized Inhalation					
Submicron Particle Paclitaxel for Topical Application	Cutaneous Metastases of Breast Cancer	Topical					
LSAM-PARPs for Sterile Suspension	Solid Tumors	Intratumoral					
LSAM-TKIs for Sterile Suspension	Solid Tumors	Intratumoral					

Excellent Safety Profile Established in 175 Patients

	Clinical Trial	Subjects	Events		Systemic SAEs			Local SAEs		
			TEAE	SAE	Possibly Related	Probably Related	Definitely Related	Possibly Related	Probably Related	Definitely Related
LSAM-PTX	Pancreatic Cancer	54	435	54	0	0	0	6	0	0
LSAM-PTX	Pancreatic Cysts	19	99	5	0	0	0	0	1	0
LSAM-PTX	Peritoneal Malignancies	21	332	24	1	0	0	1	0	0
LSAM-PTX	Ovarian Cancer	10	208	13	0	0	0	7	0	0
LSAM-PTX	Prostate Cancer	17	76	0	0	0	0	0	0	0
LSAM-PTX	Lung Cancer	18	217	23	1	0	0	0	0	0
LSAM-DTX	Bladder Cancer (NMIBC)	19	144	1	0	0	0	0	0	0
LSAM-DTX	Bladder Cancer (MIBC)	17	74	3	0	0	0	0	0	0

Plasma Levels from Clinical Trials

Subtoxic plasma drug concentrations at all timepoints demonstrated by clinical PK analysis



Avoids the systemic toxicities associated with systemic cancer treatments:

- Neutropenia
- Thrombocytopenia
- Peripheral neuropathy
- Alopecia
- Nausea & vomiting
- Colitis & severe diarrhea
- Rash & pruritis
- Hepatotoxicity
- Dose reduction or discontinuation

1. LSAM-DTX in bladder cancer only; all others LSAM-PTX
2. Clin Cancer Res 1999;5:767-774
3. S07-GM-01-2017
4. British Journal of Cancer (2007) 97, 290 – 296
5. LLOQ paclitaxel = 25 pg/mL; LLOQ docetaxel = 10 ng/mL
6. diZerega et.al. Oncol Ther 2024
7. NSCLC excludes 2 outlier subjects receiving ~ 5x mean dose for all subjects in the trial.

Non-Small Cell Lung Cancer Clinical Trial

Phase 2a Trial of Intratumoral LSAM-PTX + SOC in NSCLC (n=18)

Design Overview

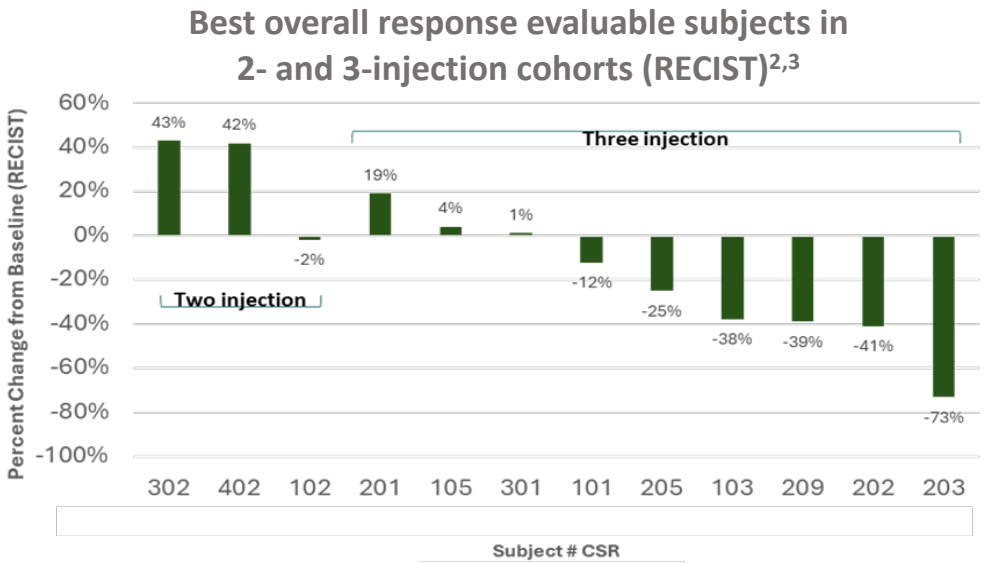
- Single arm dose rising/expansion trial
- Primary or recurrent nonoperable stage 3/4 NSCLC
- Endobronchial ultrasound-guided transbronchial needle injection
- Up to 3 x IT and/or intranodal injections q 4 weeks + SOC
- Evaluated safety; PK; OS; DCR; tumor response; immune response

Principal Investigators

- **Hiren Mehta, MD** University of Florida
- **Jason Akulian, MD** University of North Carolina Health
- **Christine Argento, MD** Johns Hopkins Medicine
- **Abhishek Biswas, MD** Parkview Cancer Institute

Clinical Highlights[1]

- Safe/well tolerated; only 11% TEAEs possibly related to drug; no confirmed drug-related TEAEs or SAEs
- DCR evaluable subjects at 3M/6M: 80% (8/10) / 86% (6/7)
- OS 3M/6M/12M (2 or 3-inj)[2,3]: 73% (11/15) / 53% (8/15) / 36% (5/14)[4]
- Evidence of peripheral anti-tumor immunomodulation



Best overall response all evaluable subjects (n=12)

- PR 4/12 (33%); SD 6/12 (50%); PD 2/12 (17%)

Best overall response by dose

- 2 injection (n=3): SD 1/3 (33%); PD 2/3 (67%)
- 3 injection (n=9): PR 4/9 (44%); SD 5/9 (56%)

Signal of a dose-response relationship

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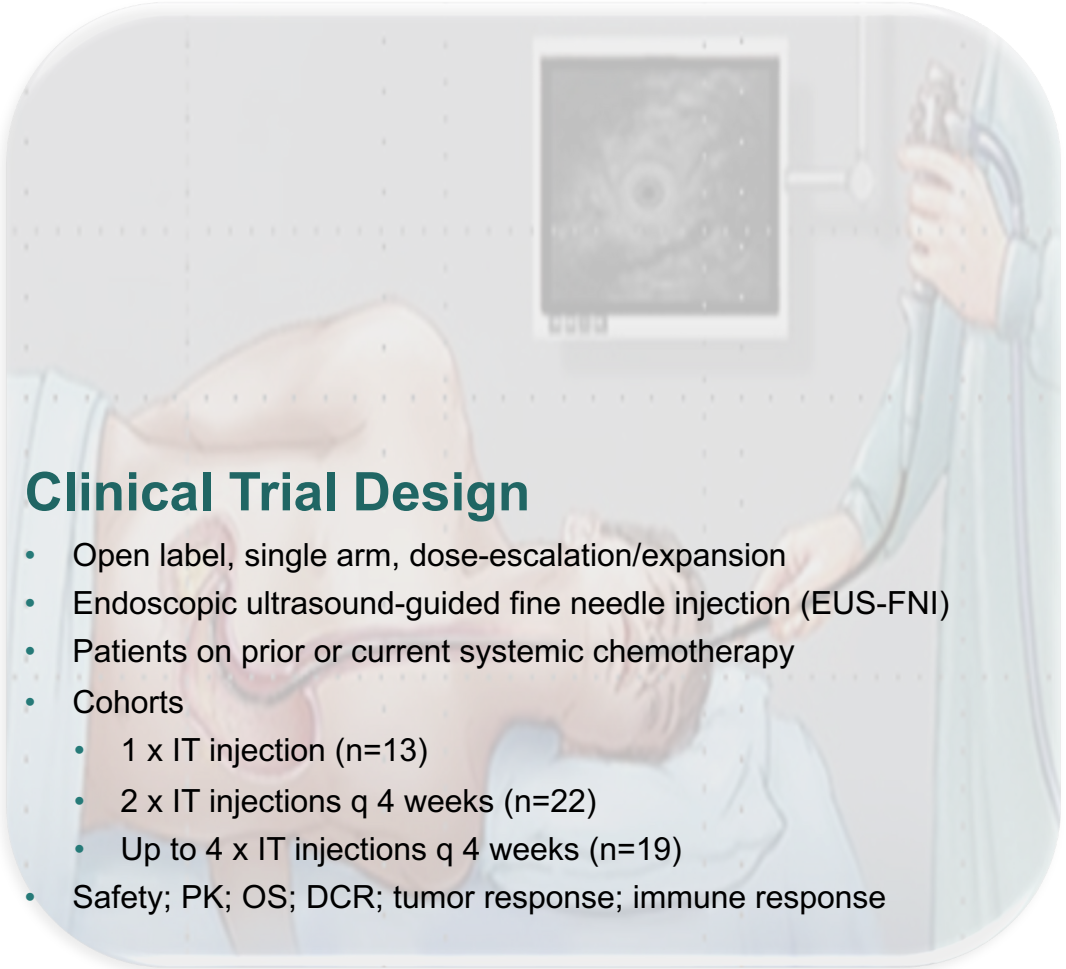
1. Mehta et. al. *NACLC* abstract/poster Dec 2023
2. 1-inj (n=2); 2-inj (n=5); 3-inj (n=10)
3. CSR NANOPAC 2020-01 2024; IND #147012; NCT04314895
4. 1 subject lost to follow up

Pancreas Cancer Clinical Trial

Phase 2a Trial of Intratumoral LSAM-PTX + SOC in Locally Advanced Pancreatic Cancer (n=54)



Clinical Trial Design

- Open label, single arm, dose-escalation/expansion
- Endoscopic ultrasound-guided fine needle injection (EUS-FNI)
- Patients on prior or current systemic chemotherapy
- Cohorts
  - 1 x IT injection (n=13)
  - 2 x IT injections q 4 weeks (n=22)
  - Up to 4 x IT injections q 4 weeks (n=19)
- Safety; PK; OS; DCR; tumor response; immune response

Clinical Highlights[1,2,3,4]

- Safe/well tolerated; mild/mod transient abdominal pain; no confirmed drug-related TEAEs/SAEs; no reports of pancreatitis
- 12/39 (31%) evaluable subjects receiving 2, 3, or 4 monthly IT injections of LSAM-PTX were downstaged from nonresectable to resectable
- Median OS resected/nonresected subjects: 35.2M/18.9M
- Evidence of tissue/peripheral immunomodulation

Principal Investigators

- **Neil Sharma, MD** Parkview Health (MD Anderson Network)
- **Simon Lo, MD** Cedars-Sinai Medical Center
- **Mohamed Othman, MD** Baylor College of Medicine
- **Antonio Mendoza-Ladd, MD** Texas Tech HSC El Paso

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1. Sharma et. al. *Pancreas* Mar 2023
2. Hendifar et. al. *AACR pancreatic cancer conf* Sep 2023
3. Gopakumar et. al. *AACR pancreatic cancer conf* Sep 2023
4. NCT03077685; FDA IND#132692; NanoPac-2016-05

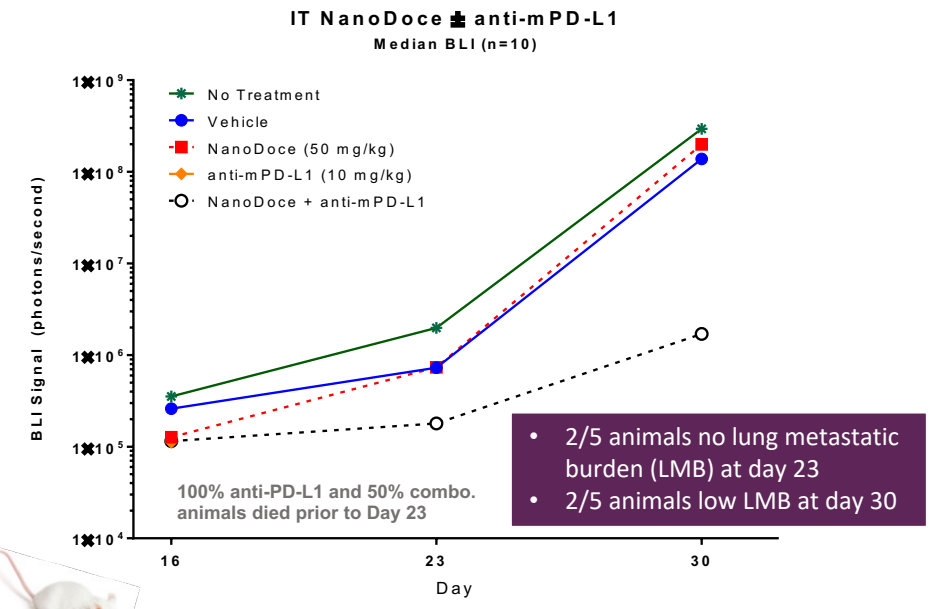
Clinical Data Highlights from

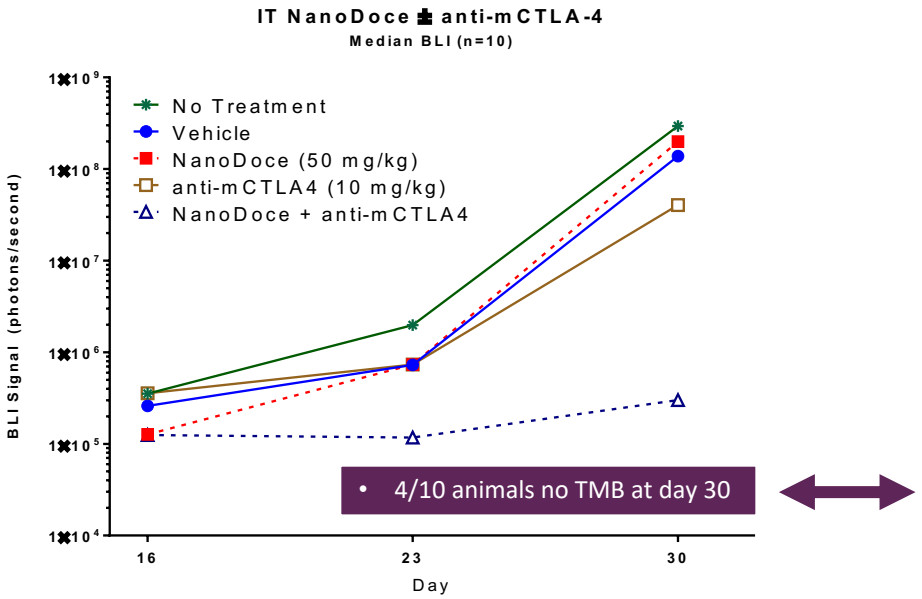
	Indication	Subjects	Trial Phase	Dose	Dose Range	Clinical Data Summary
LSAM-PTX	Pancreatic Cysts (MCN/IPMN) NCT03188991	19	Phase 2a	**EUS-FNI** • 1 intracystic injection • 2 intracystic injections (0,3M)	Equal to volume aspirated from cyst 6, 10, and 15mg/mL	• Safe/well tolerated • Cyst volume reduction in 14/19 (74%) subjects • Evidence of epithelial lining necrosis (-DNA or endomicroscopy) • PK analysis of cyst fluid at 3M > 250ng/mL (ULOQ) paclitaxel
	Peritoneal Malignancies NCT00666991	21	Phase 1	**Intraperitoneal** • 1 to 6 intraperitoneal infusions	50 – 275mg/m^2	• Safe/well tolerated • 6/21 (29%) subjects (salvage patients) survived > 1 year • Sustained peritoneal fluid concentrations 450-2900 times greater than plasma drug concentrations, which are subtoxic at all timepoints
	Ovarian Cancer NCT03029585	10	Phase 2	**Intraperitoneal** • 1 intraperitoneal instillation at end of debulking surgery	100 – 200mg/m^2	• Safe/well tolerated • PFS 60% ≥ 6M • ORR 50% (CR 20%; PR 30%) • OS 70% > 1 year
	Prostate Cancer NCT03077659	16	Phase 1	**TRUS-guided-FNI** • 1 intralobular injection • 28 days before prostatectomy	20% lobe volume (up to 5 mL) 6, 10, and 15mg/mL	• Safe/well tolerated; no reports of prostatitis • Mean tumor volume reduction 46% • Mean PSA-density decrease 35% • Evidence of tumor infiltrating lymphocytes in prostate histology • Drug in lymph nodes/ejaculate
LSAM-DTX	hrNMIBC NCT03636256	19	Phase 1/2	**Cystoscope-guided-IMI & IVT** • Intramural (IMI) post TURBT • Intravesical Therapy (IVT) x 10	3-15mg 50-75mg	• CR 4M 15/19 (79%) (all doses) • CR >7M 7/9 (78%) (high dose cohort) • **Evidence of tissue immunomodulation**
	MIBC NCT03636256	17	Phase 1/2	• IMI/IVT post TURBT x 1	3-15mg 50-75mg	• CR 45 days 9/17 (53%) • Series of 5 subjects with long-term CR following TURBT + IMI/IVT LSAM-DTX

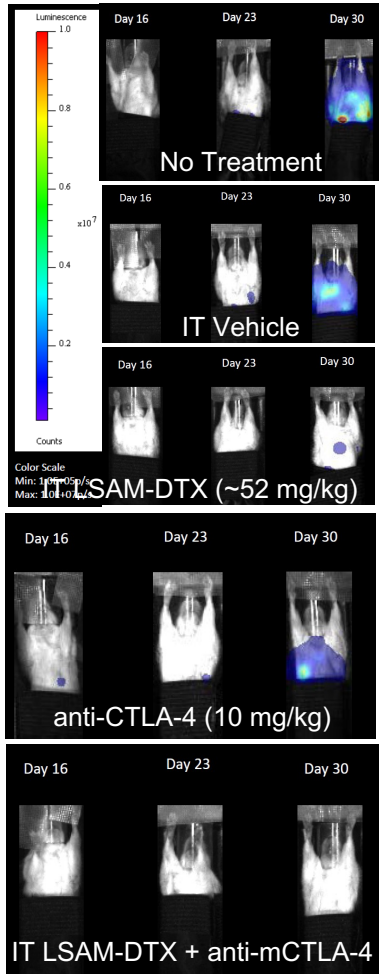
Immune Checkpoint Inhibitor Synergy with LSAM-DTX

Preclinical Combinatorial Study in 4T1 (luc) Metastatic Breast Cancer Orthotopic Model

- Anti-CTLA-4 + IT LSAM-DTX (NanoDoce) – Confirmed synergy
  - 4/10 animals had no thoracic metastatic burden (TMB) on Day 30
- Anti-PD-L1 + IT LSAM-DTX – Apparent synergy
  - 2/5 animals had no TMB detected on Day 23 and 2/5 had minimal TMB on Day 30
  - 100% of animals in PD-L1 and 50% in combination arm died early in study preventing confirmation
- Anti-PD-1 not active in this model







Med Oncol. 2021 Jul 31;38(9):106. doi: 10.1007/s12032-021-01555-1

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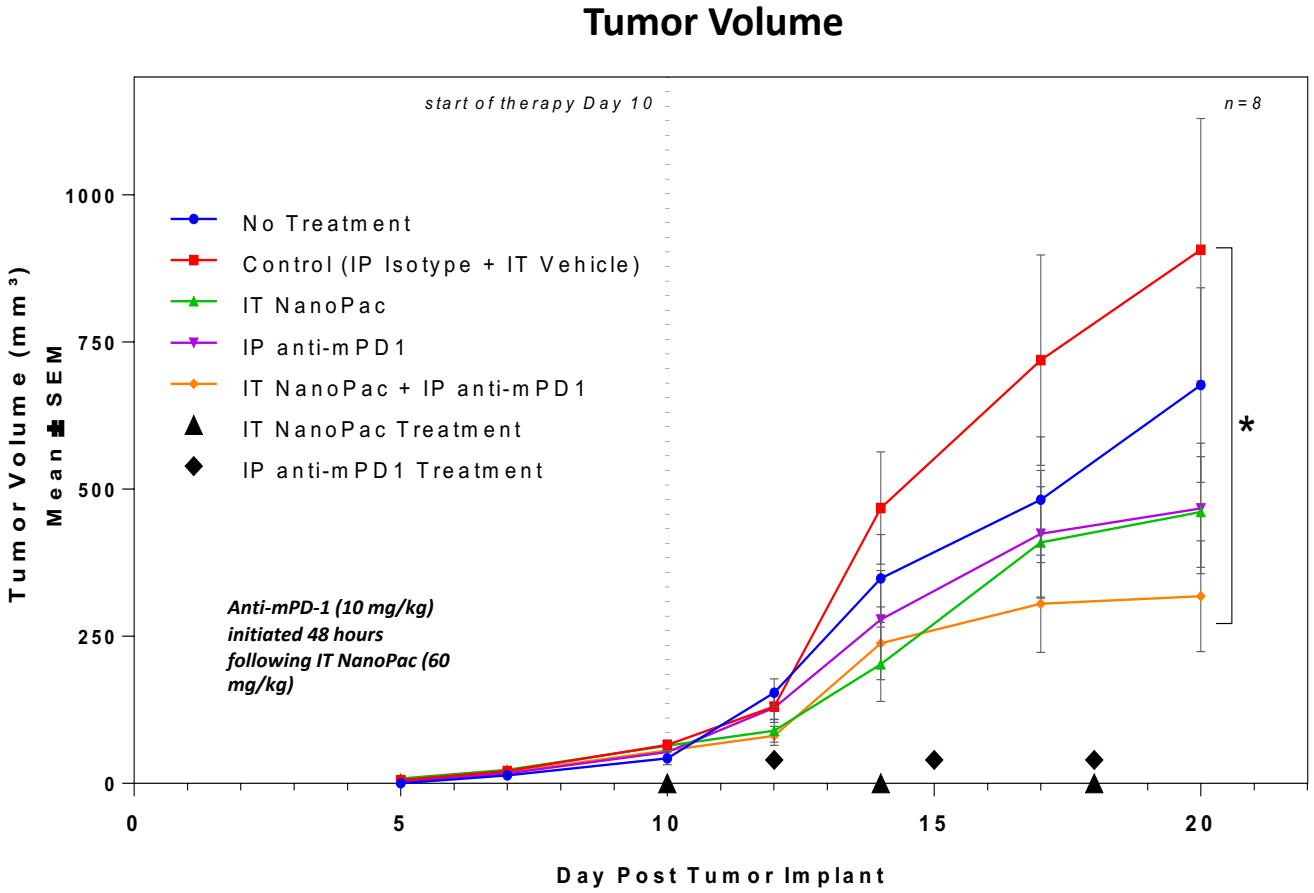
Immune Checkpoint Inhibitor Synergy with LSAM-PTX

Preclinical Combinatorial Study in Syngeneic Melanoma (Clone M3) Model

- Combination IT LSAM-PTX (NanoPac) + anti-PD-1 results in significant tumor volume reduction
- Combination is well tolerated with no weight loss or early termination
- In the melanoma model, statistically significant immune changes seen in combination treatment include:
  - Increases in granulocytes in tumor and blood (*)
  - Increases in NK cells in lymph nodes (*)
  - Decreases in MDSC in tumor (*)



*Tumor volume: * = $p < 0.05$ via one-way ANOVA with Dunn's test; animals terminated early due to reaching tumor volume trigger are assigned a Day 20 tumor volume = 1800 mm^3.*

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Internal report: P-PM-01-2021

diZerega et.al. Oncol Ther 2024