
NanOlogy

NanOlogy Approach

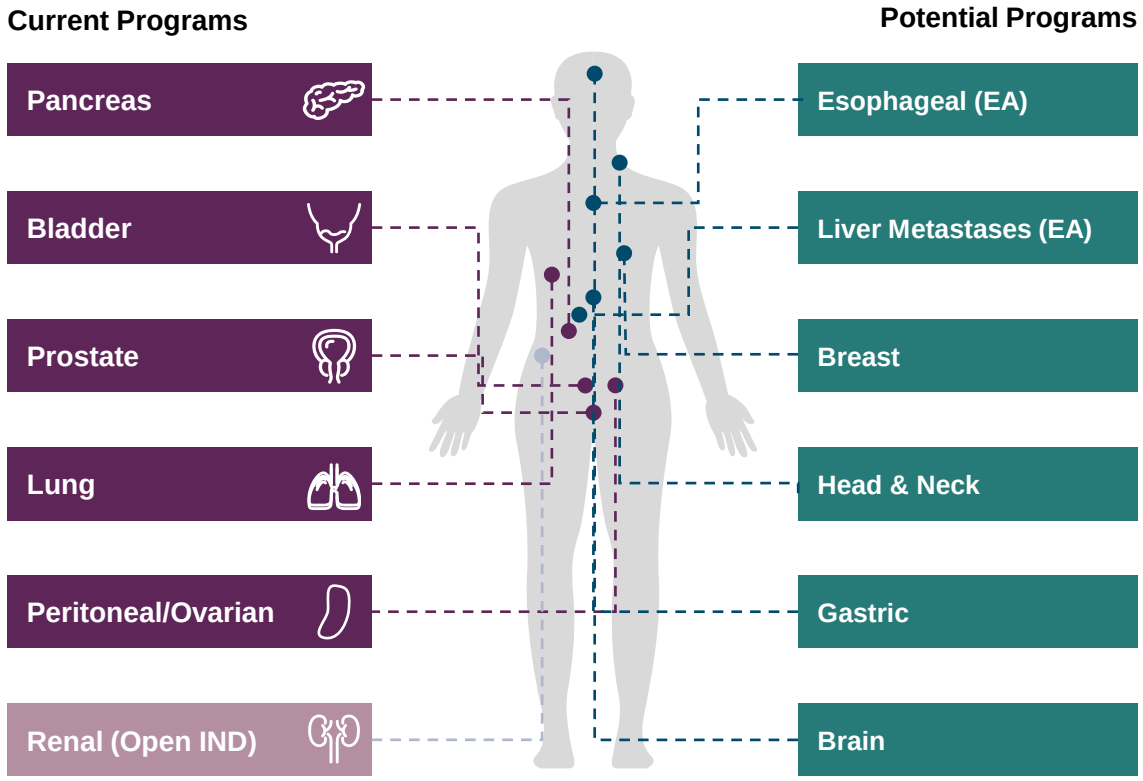
Maximize cancer drug concentration in solid tumors to improve efficacy and minimize off-target systemic toxicity

- ✓ **NanOlogy is advancing a unique particle engineering breakthrough in solid tumor treatment**
- ✓ **Our clinical research is demonstrating:**
  - **Favorable tumor response**
  - **Immunogenic effect**
  - **Minimal toxicity**
- ✓ **Experienced Team:**
  - **Particle engineering technology & scale up**
  - **Preclinical and early clinical research**
  - **Pharma startups, licensing, M&A, operations, and partnerships**

Clinical Stage Interventional Oncology Drug Company

Developing Breakthrough Tumor-Directed Drug Therapies for Solid Tumors

- Patented large surface area microparticle (LSAM) oncology drug platform engineered for solid tumors
- NanoPac® (LSAM paclitaxel) and NanoDoce® (LSAM docetaxel) in clinical development
- 7 clinical trials / 5 solid tumors / > 160 patients
- Promising efficacy data
- Clinical evidence of immune effect
- Excellent safety profile
- Tumor-directed therapy with multiple routes of local administration



Particle Engineering Technology

Super Critical Precipitation (SCP) Production Technology

Engineered Particles with Optimal Attributes for Tumor-Directed Drug Delivery

High Drug Load

- Volume of open space in the tumor is small
- SCP Technology forms particles of **100% pure drug without any excipients** for intratumoral delivery
- Other technologies require excipients significantly reducing drug load and potential for efficacy

Right Particle Size

- SCP Technology forms particles **large enough for tumor entrapment**
- The longer drug remains in the tumor releasing drug at high concentration, the **longer the direct tumor kill**
- Smaller particles formed by other technologies simply diffuse out of the tumor or are otherwise quickly eliminated

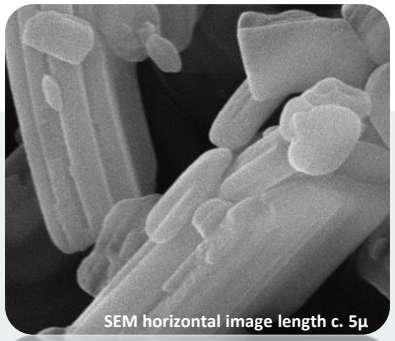
Large Surface Area

- Poorly soluble API crystals typically cannot be suspended and have insufficient surface area for drug release
- Tumor-directed delivery requires particles with a surface area sufficient for therapeutic drug release
- LSAMs act as a pure drug depot with a **large surface area for prolonged therapeutic drug release**

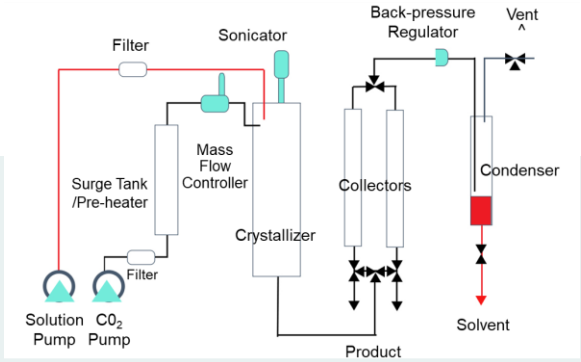
Large Surface Area Microparticles (LSAMs)

Enabled by a Proprietary SCP Particle Engineering Technology Platform

API Crystals

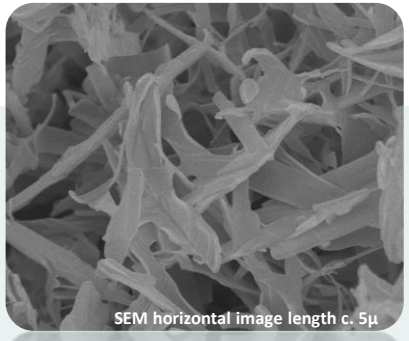


- ✓ Large and bulky crystals
- ✓ Large distribution around mean particle size
- ✓ Poor uniformity of suspensions
- ✓ Poor drug release due to small surface area
- ✓ Limited to dissolution in solvent as a solution for IV delivery



- ✓ GMP commercial scale production equipment
- ✓ API crystals dissolved in organic solvent and injected into precipitation chamber
- ✓ Dispersed by sonication into small uniform droplets
- ✓ Solvent stripped away from droplets via supercritical fluid carbon dioxide
- ✓ Stable microparticles of pure drug precipitated and collected on harvesting filters
- ✓ **Technology feasibility established in multiple drug classes (TKIs, PARPIs, cisplatin, other)**

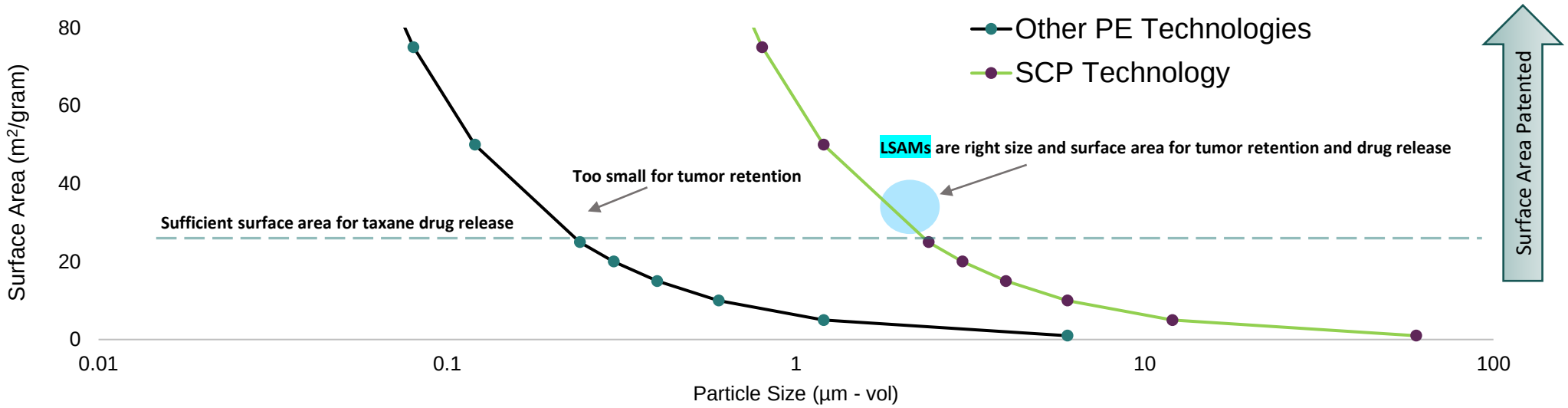
LSAMs



- ✓ Narrow mean particle size distribution
- ✓ Excellent suspension uniformity
- ✓ Microparticles each containing > 1 billion drug molecules suspended in saline-based fluid for local delivery
- ✓ Disproportionately large surface area to particle size ratio allows for:
  - ✓ Particle entrapment
  - ✓ Prolonged therapeutic drug release

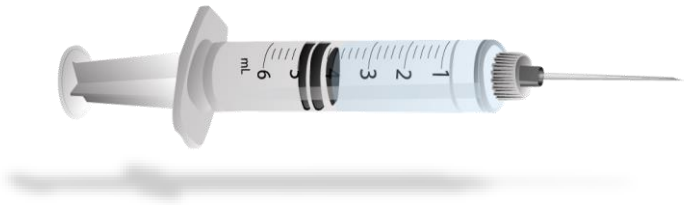
Uniqueness of the SCP Particle Engineering Technology

- The SCP technology is different from all other particle engineering (PE) technologies (CESS, RESS, spray drying, milling)
- The SCP technology has a unique ability to engineer **large particles with surface area of a much smaller particle**
- This uniquely **disproportionate surface area to particle size ratio** is optimal for tumor-directed delivery
- The larger size allows for **retention** in the tumor and large surface area for molecular drug **release**
- Taxane **particles with surface area ≥ 18 m^2/g** are protected by a **composition of matter patent** valid until June 2036

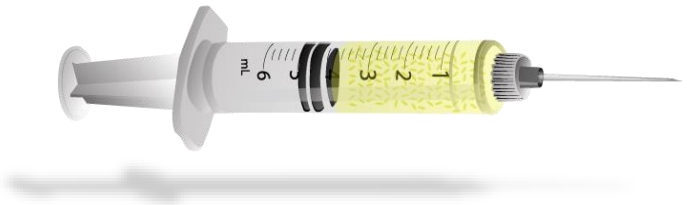


LSAMs Offer Much Longer Drug Retention in Solid Tumors

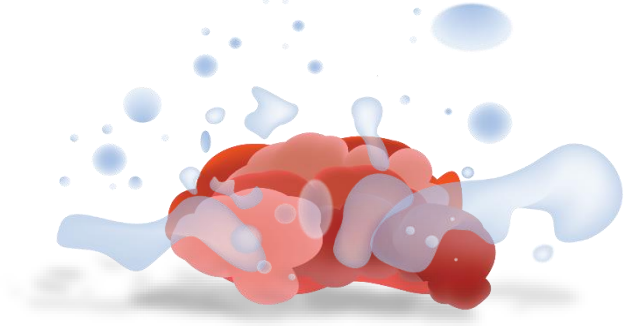
Taxane Solution for Injection



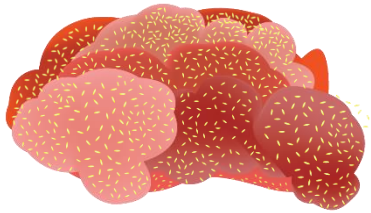
NanoPac or NanoDoce Suspension



Tumor Site

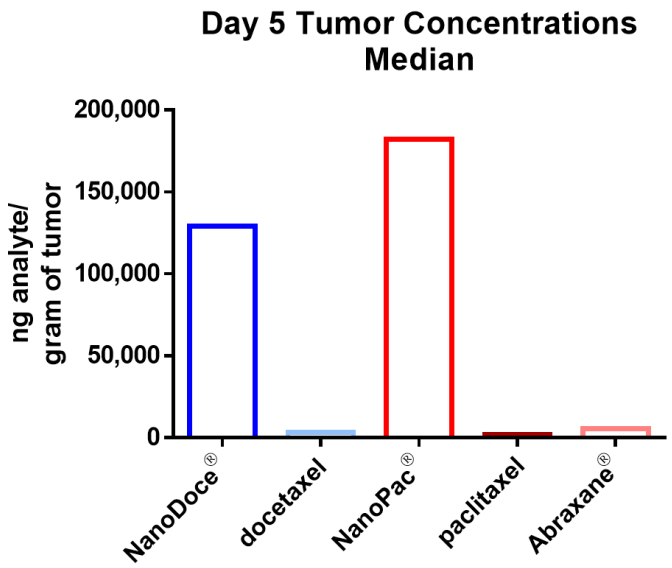


Paclitaxel or docetaxel injection are designed for IV administration and quickly diffuse out of the tumor if injected intratumorally



NanoPac and NanoDoce LSAMs are designed for local administration, and become entrapped in the tumor resulting in sustained therapeutic molecular drug release

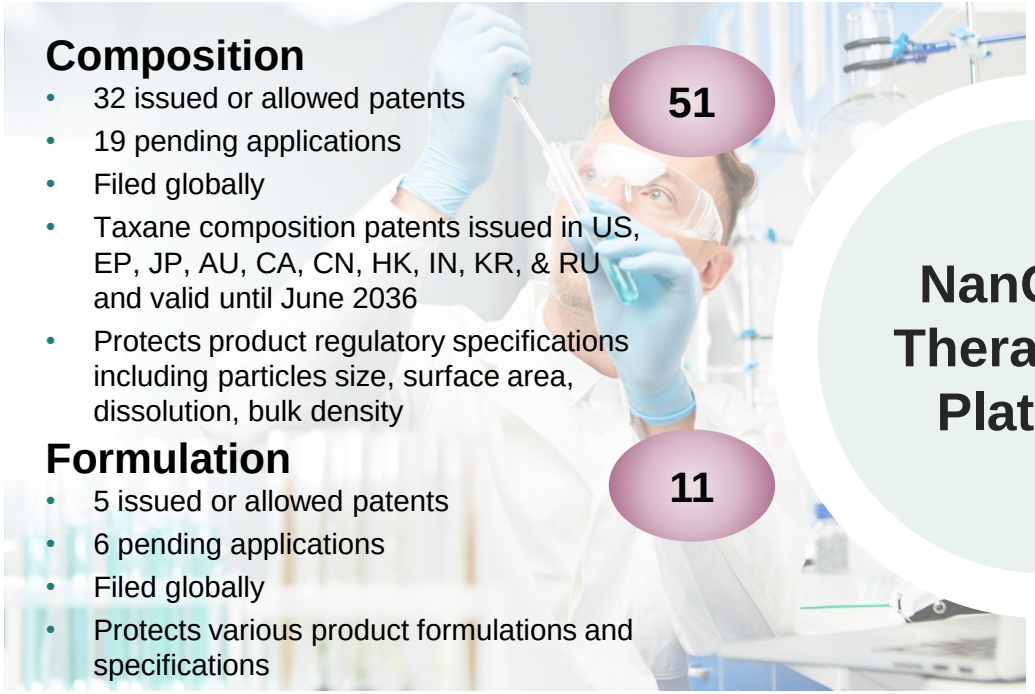
Tumor tissue concentration of NanoPac® and NanoDoce® versus comparators all given intratumorally in mice



Adapted from Verco, S., Maulhardt, H., Baltezor, M. et al. Drug Del Transl Res. (2020). ABRAXANE® is a registered trademark of Abraxis Bioscience LLC, a BMS company.

Extensive Global IP Portfolio

IP Protection Like a New Chemical Entity



Composition

51

- 32 issued or allowed patents
- 19 pending applications
- Filed globally
- Taxane composition patents issued in US, EP, JP, AU, CA, CN, HK, IN, KR, & RU and valid until June 2036
- Protects product regulatory specifications including particles size, surface area, dissolution, bulk density

Formulation

11

- 5 issued or allowed patents
- 6 pending applications
- Filed globally
- Protects various product formulations and specifications

NanOlogy Therapeutic Platform

Uses/Indications

127

- 56 issued or allowed patents
- 71 pending applications
- Filed globally
- Protects broad uses: key cancer indications, solid tumors, neoplasia
- Protects routes of administration: IT, IP, inhalation, instillation, topical

Process

76

- 64 issued or allowed patents
- 12 pending applications
- Filed globally
- Protects equipment, assembly, nozzle, methods, precipitation, collection

As of May 2022

Includes

- Combinations with IO
- TKIs, PARPs, Cisplatin
- Orphan designation (ovarian)
- Reducing & Inhibiting Metastasis
- Cancer vaccines/ adoptive cell therapy

Clinical Overview

Robust Clinical Development Pipeline

Product	Therapeutic Area	Delivery	IND	Phase 1	Phase 2	Phase 3
NanoPac® (LSAM Paclitaxel) for Sterile Suspension	Locally Advanced Pancreatic Adenocarcinoma	Intratumoral				
	Mucinous Cystic Pancreatic Neoplasms	Intracystic				
	Peritoneal Malignancies/Ovarian Cancer	Intraperitoneal				
	Prostate Cancer	Intratumoral				
	Lung Cancer	Intratumoral				
NanoDoce® (LSAM Docetaxel) for Sterile Suspension	High-Risk 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				
NanoPac® (LSAM Paclitaxel) for Inhalation	Lung Cancer	Nebulized Inhalation				
Topical Submicron Particle Paclitaxel (SOR007)	Cutaneous Metastases (CMOBC)	Topical				

NanOlogy

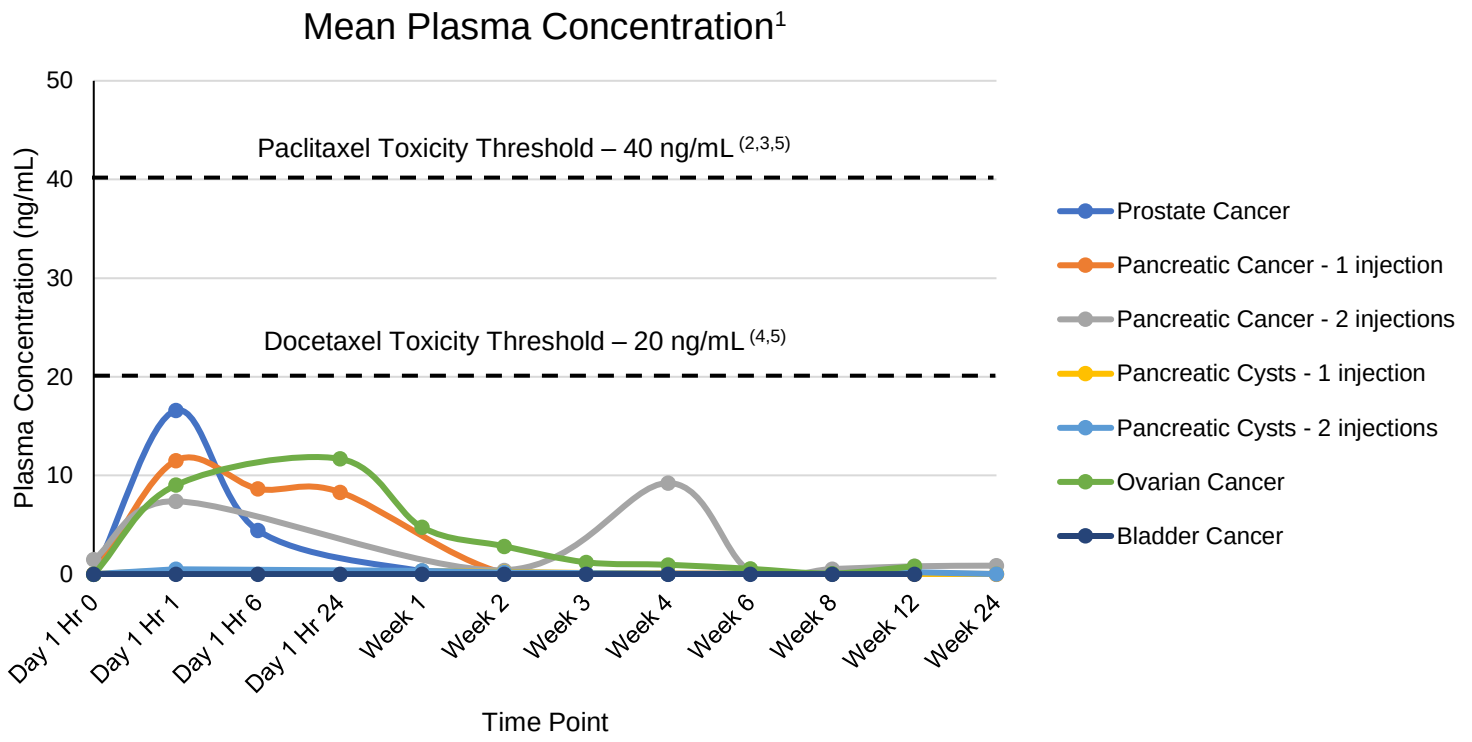
NanoPac® and NanoDoce® Safety Profile

	Clinical Trial	Subjects	Events		Systemic SAEs			Local SAEs		
			TEAE	SAE	Possibly Related	Probably Related	Definitely Related	Possibly Related	Probably Related	Definitely Related
NanoPac	Pancreatic Cancer	54	390	50	0	0	0	6	0	0
NanoPac	Pancreatic Cysts	19	99	5	0	0	0	0	1	0
NanoPac	Peritoneal Malignancies	21	332	24	1	0	0	1	0	0
NanoPac	Ovarian Cancer	10	208	13	0	0	0	7	0	0
NanoPac	Prostate Cancer	17	76	0	0	0	0	0	0	0
NanoPac	Lung Cancer	12	140	13	0	0	0	0	0	0
NanoDoce	Bladder Cancer (NMIBC)	19	144	1	0	0	0	0	0	0
NanoDoce	Bladder Cancer (MIBC)	17	74	3	0	0	0	0	0	0

As of May 2022

Plasma Levels from NanOlogy 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. NanoDoce® in bladder cancer only; NanoPac® in all other trials
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

NanOlogy Clinical Data Highlights

	Indication	Subjects	Trial Phase	Dose	Dose Range	Clinical Data Summary

NanoPac®	Locally Advanced Pancreatic Cancer NCT03077685	54	Phase 2a	**EUS-FNI**
				• 1st cohort: dose rising single intratumoral (IT) injection
				• 2nd cohort: 2 x monthly IT injections
				• 3rd cohort: 4 x monthly IT injections
					20% tumor volume (up to 5 mL)
					6, 10, and 15mg/Ml
						• Safe/well tolerated; mild/mod transient abdominal pain; no reports of pancreatitis
						• 1st cohort complete (n=10):
						  • Safety established; 15 mg/mL advanced to 2nd cohort
						• 2nd cohort complete (n=22):
						  • DCR (SD+PR+CR) at 6M = 88%; mOS: 19.7 months
						  • Neoadjuvant subset (n=14/22):
						  • 8/14 restaged (57%); 6 resected
						  • 5/6 R0 (83%); 3 x 90%+ pCR
						  • mOS: 35.2M/18.9M (resected/nonresected subjects)
						• 3rd cohort: 19 subjects enrolled: data trending positive (preliminary read 3Q2022)

	Pancreatic Cysts (MCN/IPMN) NCT03188991	19	Phase 2a	**EUS-FNI** • 1 intracystic injection • 2 intracystic injections (12 weeks apart)	Equal to volume aspirated from cyst 6, 10, and 15mg/mL	• Cyst volume reduction in 14/19 (74%) subjects at 6M • Evidence in selected subjects 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	• 6/21 (29%) subjects (salvage patients) survived > 1 year • Peritoneal fluid concentrations 450-2900 times greater than peak plasma drug concentrations/plasma concentration subtoxic at all timepoints
	Ovarian Cancer NCT03029585	10	Phase 2	**Intraperitoneal** • 1 intraperitoneal instillation at end of debulking surgery	100 – 200mg/m^2	• PFS 60% ≥ 6M • ORR 50% (CR 20%; PR 30%) • OS 70% > 1 year
	Prostate Cancer NCT03077659	16	Phase 1	**TPUS-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%
	Lung Cancer NCT04314895	15/18	Phase 2a	**EBUS-TBNI** • Up to 3 x monthly IT injections	20% tumor/node volume 15mg/mL	• Safety established in initial subjects • Preliminary evidence of tumor response (preliminary read 3Q2022)
NanoDoce®	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 9/19 (47%) (all doses) • CR > 7M 7/9 (78%) (high dose cohort)
	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 NanoDoce

As of May 2022. Preliminary data for trials in process.

DFB investigational drugs have not yet been proven as required by US FDA or any other regulatory authority to be safe and effective and are not approved for commercial distribution.
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