Breakthrough Therapeutics
Targeted NanoSpheres (TNS)

Timothy Enns, CEO

Biotech Showcase Digital

January, 2021

NanoValent Pharmaceuticals, Inc (NVP)

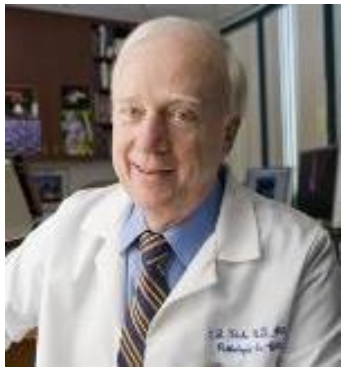
Cofounders Jon Nagy and Tim Triche came together in 2006 to create a breakthrough therapeutic for a rare childhood cancer Ewing Sarcoma and developed a platform that we are advancing for several indications. NVP management has raised over $5 million to date and retains 88% equity.

- **Jon Nagy, PhD, Chief Scientific Officer**

  Dr. Nagy received his PhD in synthetic organic chemistry from Iowa State University in 1983, and completed doctoral training at UC Berkeley. In 1990, Dr. Nagy joined Lawrence Berkeley National Laboratory where he generated seven issued patents and 15 scientific publications, including a paper in *Science* related to polymer films and nanoparticles. In 1999, Dr. Nagy joined LigoCyte Pharmaceuticals as Director of Chemistry and Nanoparticle research.

- **Timothy Triche MD, PhD, Chief Medical Officer**

  Dr. Triche is board certified in pathology and is Head of Precision Medicine at Children's Hospital Los Angeles and a professor at the University of Southern California. His expertise centers on pediatric and adult cancer genomics. He has received over $100M grant funding since leaving the NCI, where he held a tenured faculty position. Dr. Triche has been a principle and founder in several publicly traded companies that have raised over $200M in public markets. He was co-founder of OncorMed and GenomeDx.



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The Problem

- How can you treat a patient's tumor without killing the patient?

The Answer

- Target the cancer cells directly with a potent, proven, effective systemic therapy.

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The Cancer Opportunity

- Chemotherapeutics (cytotoxics) remain pivotal to cancer therapy.
- Cytotoxics have improved survival, but toxicity limits efficacy and causes both short-term and longer-term serious complications.
- Approved untargeted “encapsulated” cytotoxics like Doxil®, Onivyde® and Abraxane® have changed toxicity with minor efficacy advantages.
- Antibody, immunotherapy, signal based and ADC based therapeutics have emerged. However, despite significant efficacy improvement in many challenging cancers, toxicities and extreme economic challenges remain for many large groups of patients.
- Targeted therapeutics can improve efficacy and reduce toxicities.

An innovative platform generating novel and truly targeted products from known cytotoxics or emerging therapeutics, improving efficacy and reducing toxicities, should create significant value.

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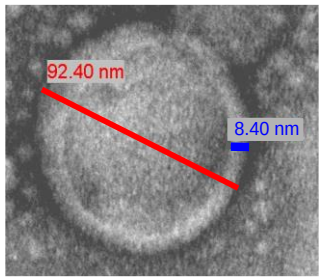
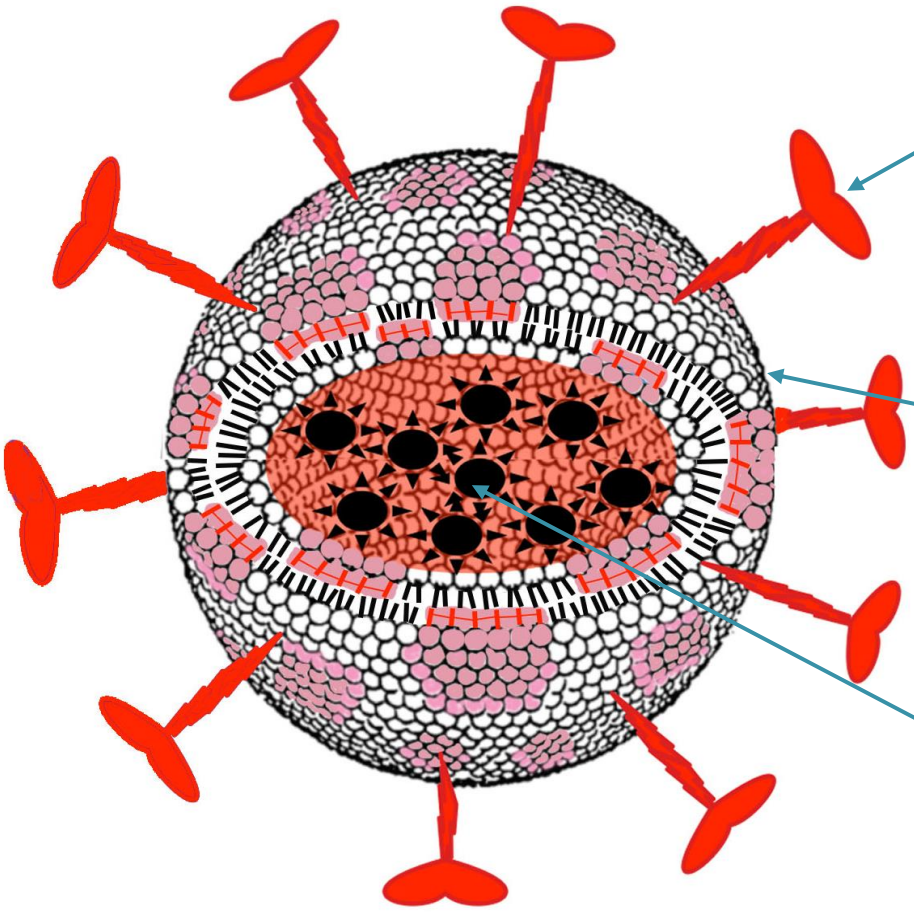
NV103 TNS

Targeted NanoSphere





1. Anti CD99 Targeting Antibody
    1. Ewing's sarcoma
    2. Hepatocellular carcinoma
    3. Glioblastoma
2. Patented Lipid Shell
    1. Polymerizable lipids
    2. Phospholipids
    3. Cholesterol
    4. Polyethylene glycol
3. Known Therapeutic Payload
    1. Irinotecan

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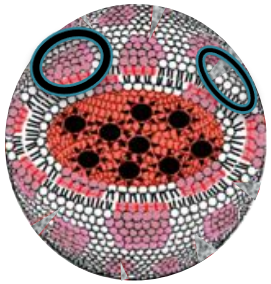
TNS Intellectual Property

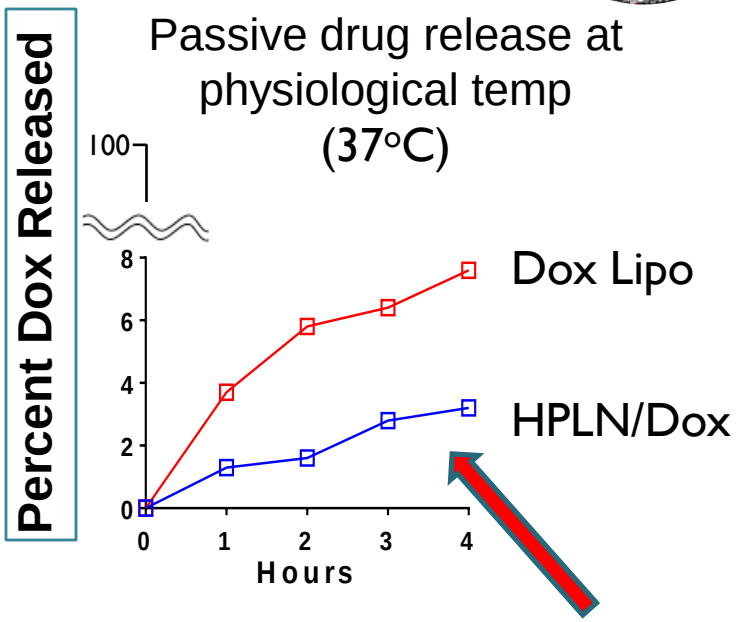
Hybrid Polymerized Lipid Nanosphere (HPLN)
Improve Stability & Bioavailability

Novel Polymer Regions



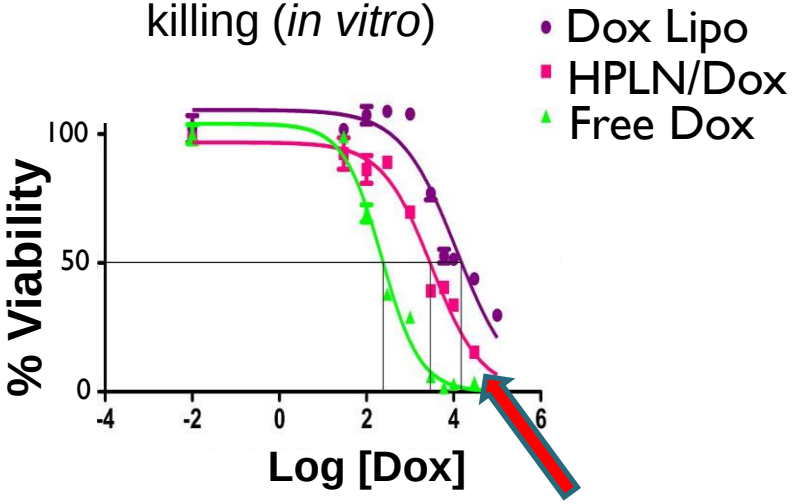
Lipid Membrane Region

Passive drug release at physiological temp (37°C)



*Superior drug **retention** under physiological conditions*

Drug release leading to tumor cell killing (*in vitro*)



*Superior drug **release** in tumor cells leading to more efficacious killing*

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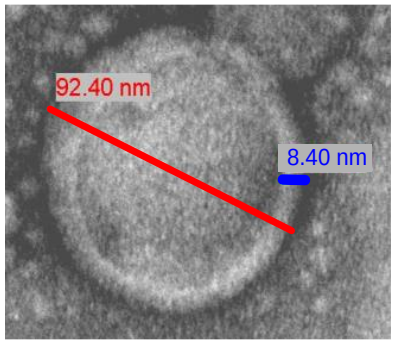
NV103: Target Market CD99 Cancers

CD99 (MIC2) is a cell surface protein and is frequently overexpressed in many types of tumors:

Ewing sarcoma or Ewing Family Tumors / PNET:

- ✓ 100% CD99 Positive
- ✓ Largely pediatric / juvenile
- ✓ US/EU 5y prevalence 3k
- ✓ 5 year survival 15 to 30% (Metastatic)

- **Hepatocellular Carcinoma (HCC)**
  - ✓ 100% CD99 Positive
  - ✓ US/EU 5y prevalence 200k, WW incidence 800k
  - ✓ Median survival 6 to 20 months, 5 year survival 10%
- **Acute lymphoblastic lymphoma (ALL)**
  - ✓ 100% CD99 Positive
  - ✓ US/EU 5y prevalence 50k
- **Other:**
  - ✓ Glioblastoma (GBM) (50%+) (US/EU 5y prevalence 25k)
  - Over 40 other different tumors or cancer subtypes are CD99 positive



References:

- International Journal of Molecular Science 2019, 20, 1137 CD99 Expression in GBM Subtypes and Role in Migration and Invasion
- Journal of Cell Communication and Signalling (2018) 12:55-68 CD99 at the Crossroads of Physiology and Pathology

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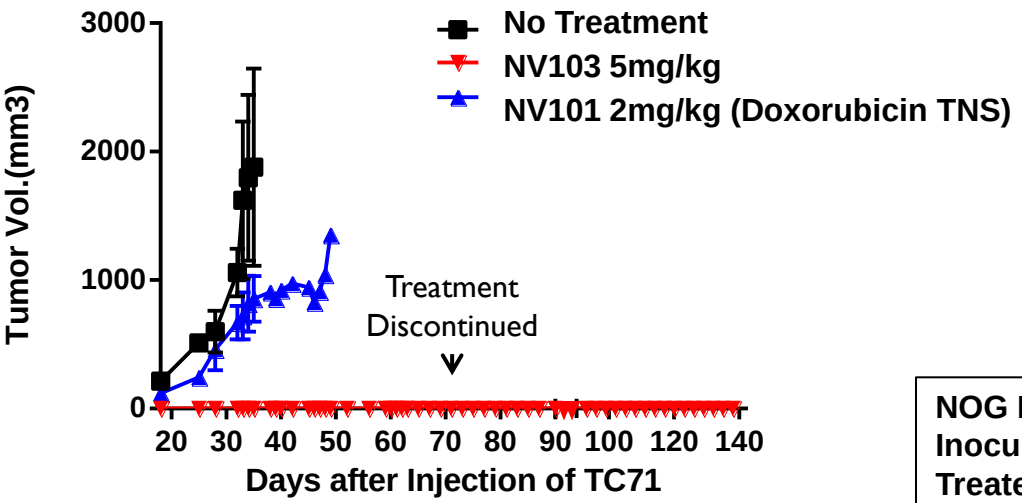
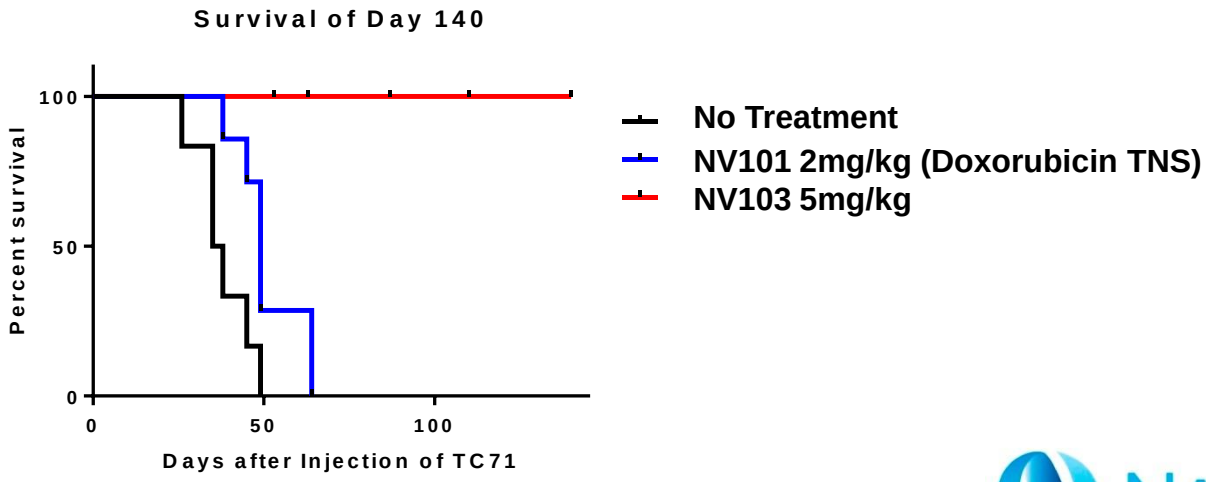
NV103 (CD99/Irinotecan) First Efficacy Ewing Sarcoma (ES)



NOG Mice
Inoculated with TC71 ES
Treated twice/wk



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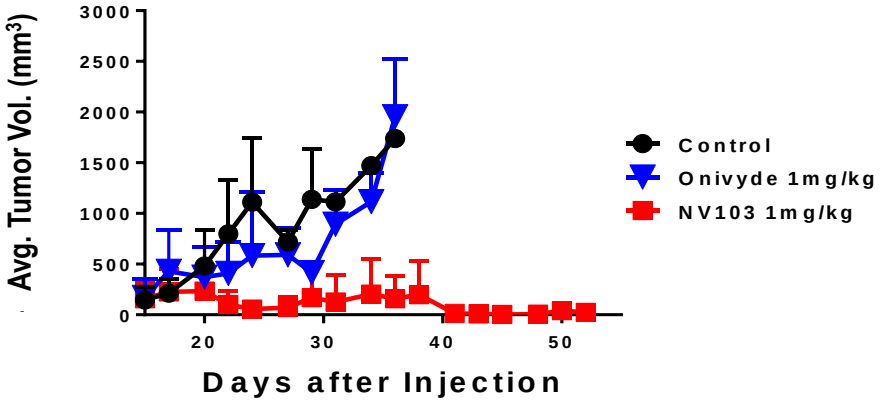
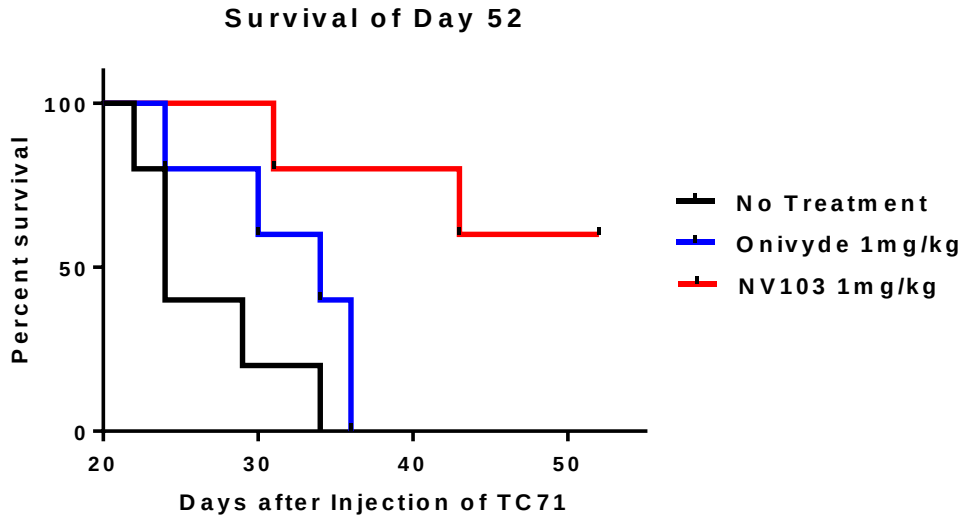
NV103 vs Liposomal Irinotecan TC71 Ewing Sarcoma



NV103 at **1mg/kg** improves tumor control and survival versus Onivyde (liposomal irinotecan) and control



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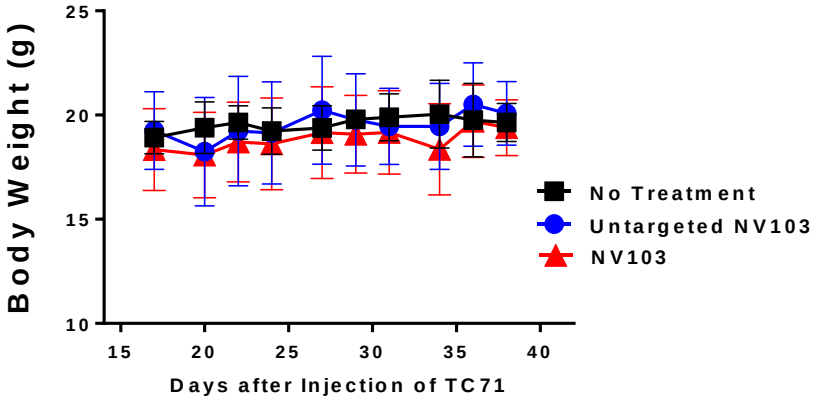
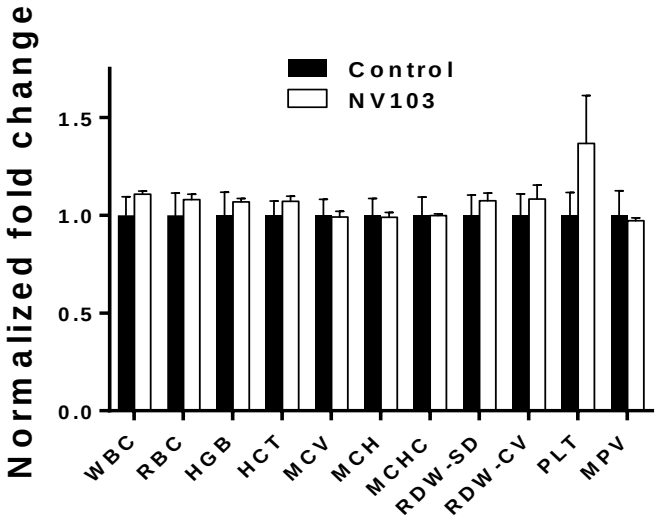
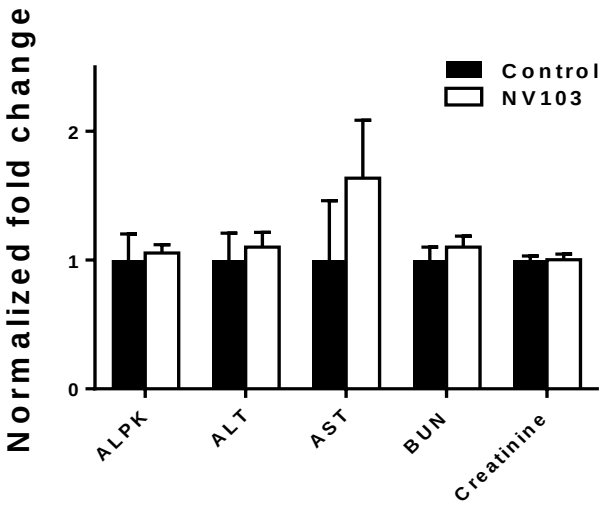
NV103 Off-Target Toxicity



NV103 **10mg/kg** treated mice showed almost no toxicity compared to untreated controls in body weight, organ toxicity or chemistry panel values





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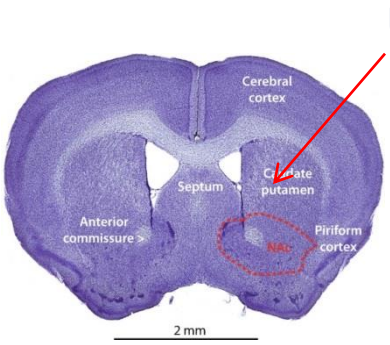
NV103 and anti-B7H3-HPLN/Irinotecan TNS Treatment of GBM (U251-Luc)



- 20 NOG Mice, 6-8 weeks old
- Randomize to treatment groups following tumor implant verification
- IV injections twice per week
- Treatments:
  - Control
  - Irinotecan, 10mg/kg
  - NV103, 10mg/kg
  - anti-B7H3 HPLN/Ir, 10mg/kg
- Weekly Xenogen Imaging

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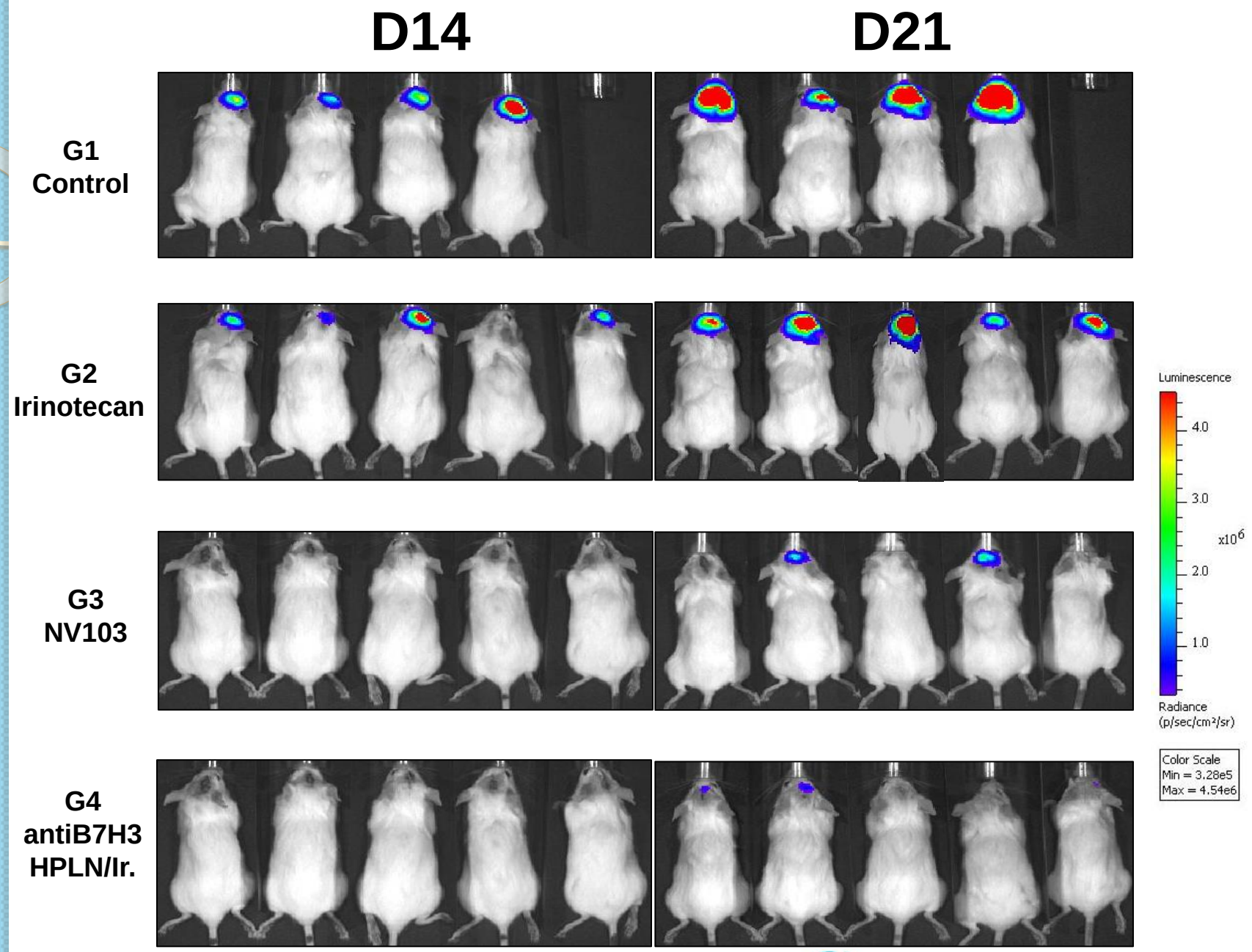

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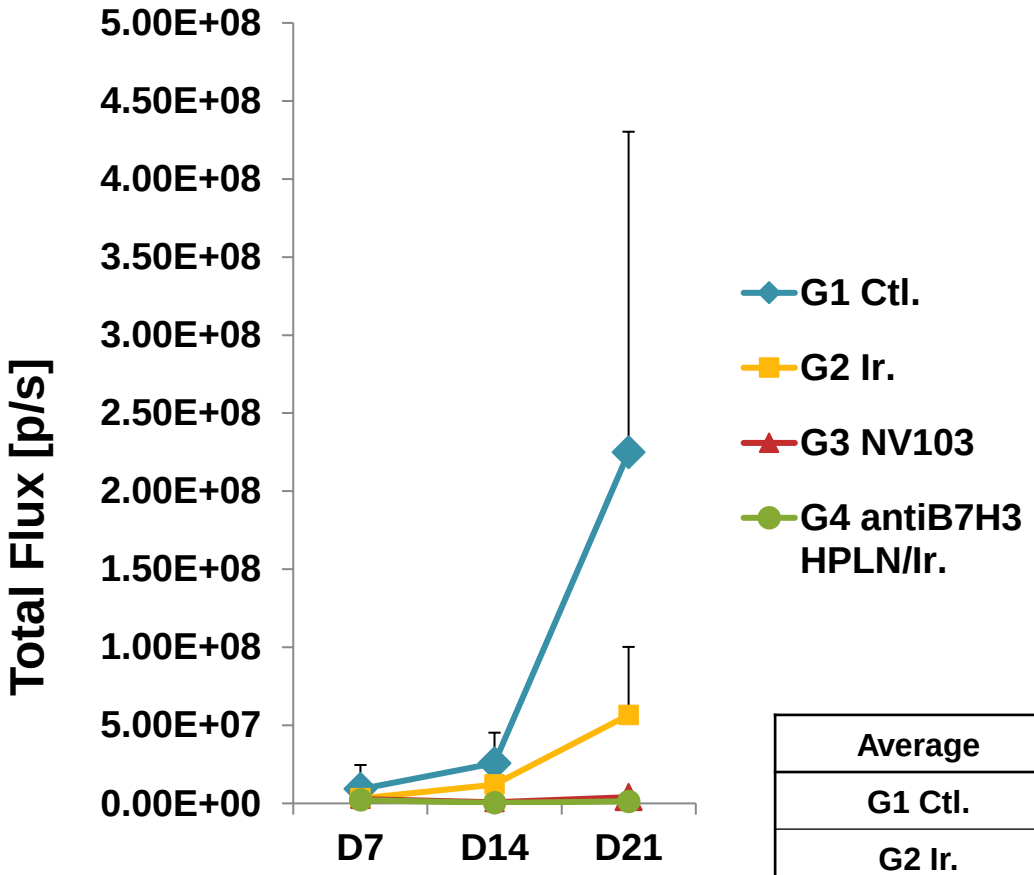
Average Xenogen Tumor Image Signal



Average	D7	D14	D21
G1 Ctl.	9.10E+06	2.56E+07	2.25E+08
G2 Ir.	3.10E+06	1.20E+07	5.66E+07
G3 NV103	2.73E+06	7.10E+05	3.92E+06
G4 antiB7H3 HPLN/Ir.	2.11E+06	3.10E+05	1.25E+06

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Ongoing NV103 Pre-BLA Activities

- GLP / GMP SOP and scale up with CMO suppliers
  - Austin Chemical – Ardena: HPLN, loading and final API
  - LakePharma: Antibody production
- Dose, scheduling and intensity evaluation
- Toxicity and tumor kinetics data
- MOA and efficacy predictability
- Efficacy in other tumors (HCC, GBM & ALL)
- Peer reviewed publications
- Partnering development

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- **NV201 Adhesion Program**
- **with Boston University**

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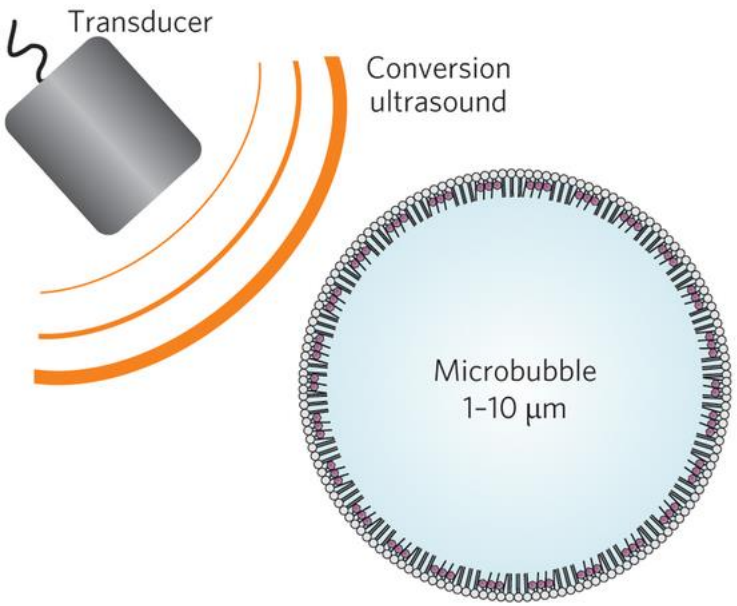
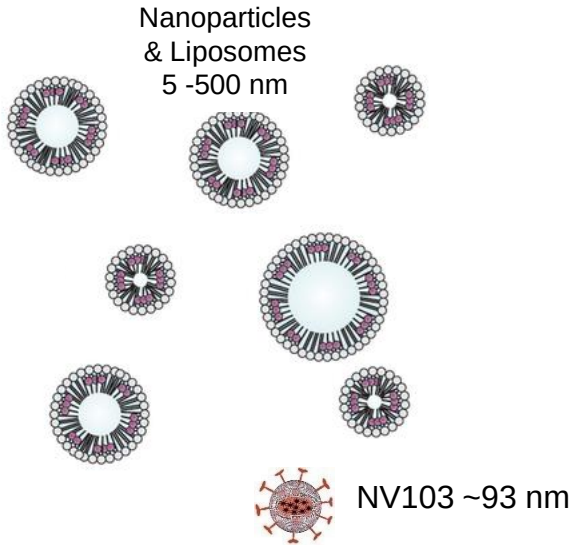
Ultrasound Contrast Microbubbles



Relative Size ~10-20X



- Microbubbles are gas filled lipid shells used as ultrasound contrast agents (UCA)
- Microbubble based UCAs are approved by the FDA for echocardiography
- Approved IV administered microbubbles have less than 10 minute utility
- US Patent application 13/699,298 11/20/2012

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NV201: Targeted MicroSphere (TMS) Microbubble

- TMSs
  - TMS microbubbles are stabilized by polymerized lipids for longer physiological half life than FDA approved microbubbles
  - CREKA, a pentapeptide (amino acids; Cys-Arg-Glu-Lys-Ala), is the targeting moiety that actively binds to fibrin and not fibrinogen
  - Therapeutic Mono-dispersed TMSs: Sized 1.5µm to 2.5µm with nitrogen
  - Patent claims include both diagnostic and therapeutic applications

1. Park et al., ACS Appl. Mater. Interfaces 2016, 8, 31541−31549
2. Park et al., Langmuir. 2012 February 28; 28(8): 3766–3772
3. Gormley et al., Langmuir. 2019 Feb 8 /acs.langmuir.8b03692.

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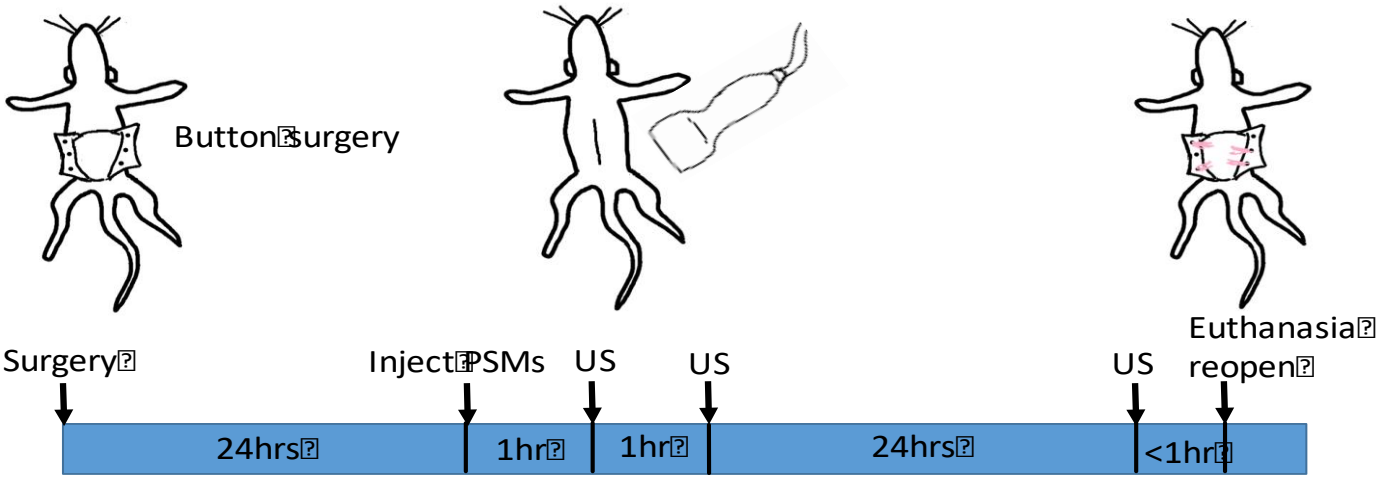
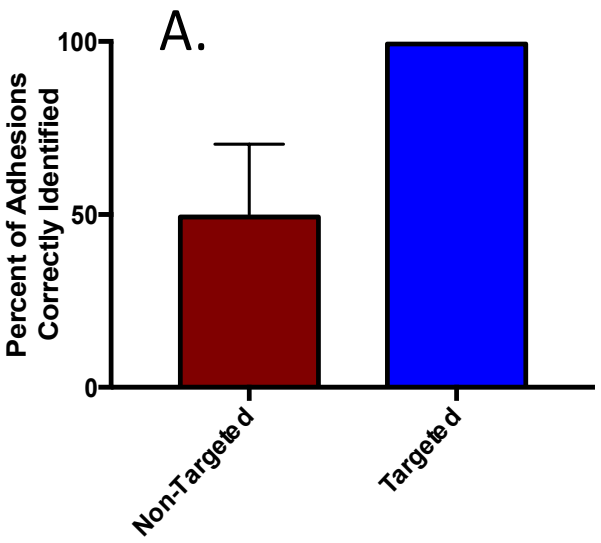
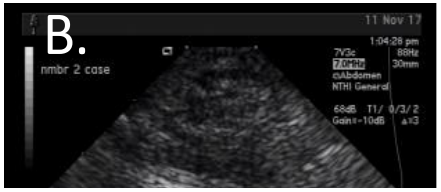
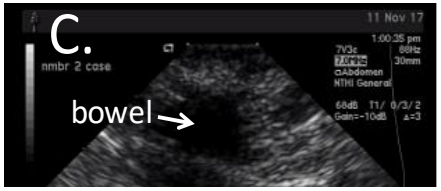
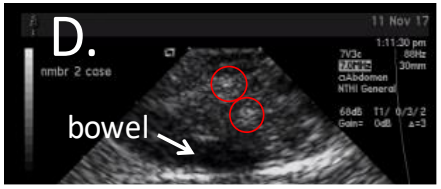
Adhesion Rat Model











Poly-dispersed TMSs

TMS Sham Surgery
TMS seen, no adhesion

Non targeted TMS -
no adhesions identified

TMS strong signal,
adhesions confirmed

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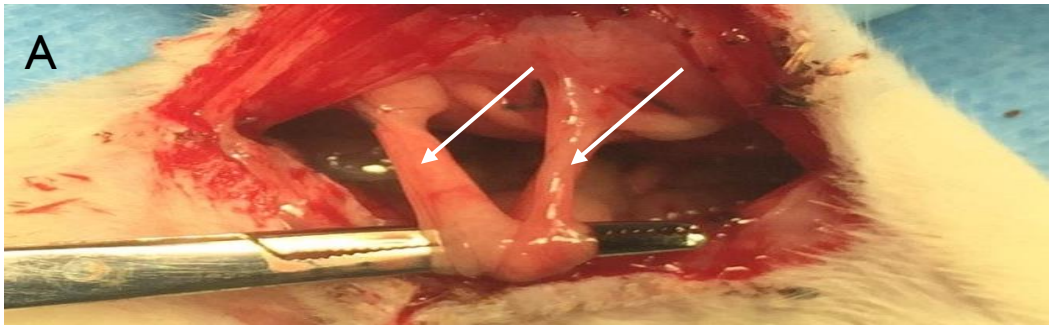
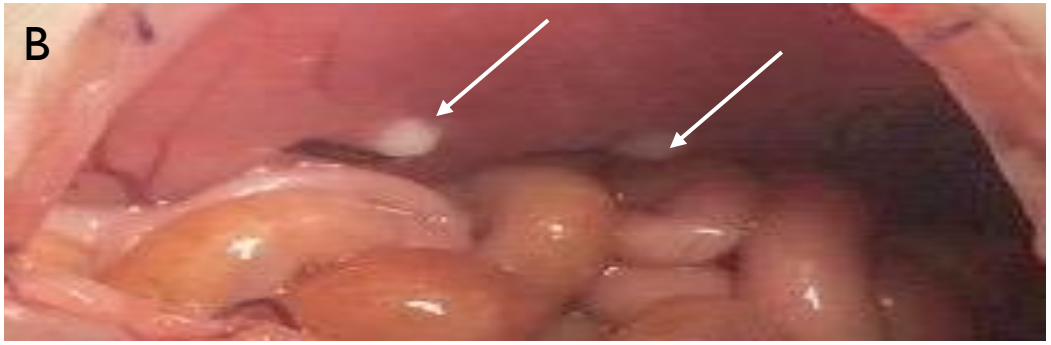
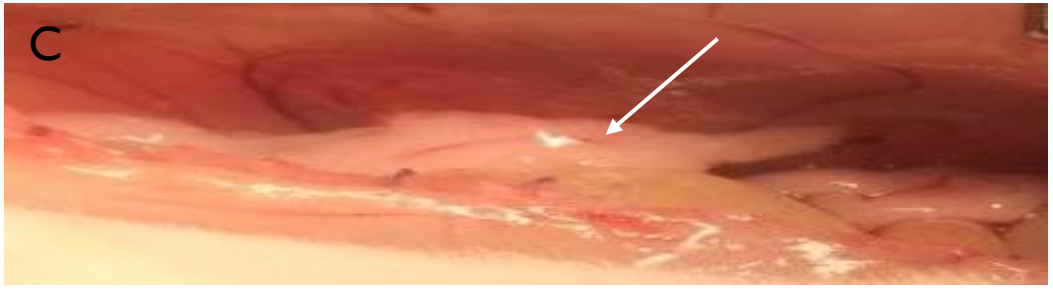
TMS (Mono-dispersed)



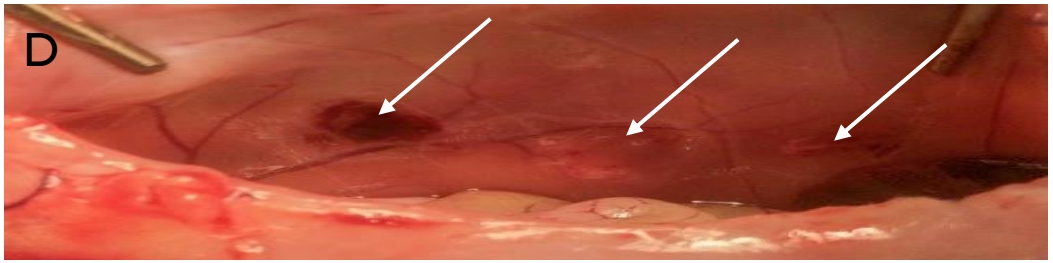
A. Untreated control with 2 button induced adhesions



B. TMS: Button sites appear inflamed with no adhesions



C. Non-targeted TMS: Large adhesion spanning all 3 ablation sites



D. TMS: Ablation sites are visible with no adhesions (Positive control)

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Surgical Adhesions

- Adhesions are bands of fibrous scar tissue that form rapidly following surgery
- Post surgical adhesions occur in almost 100% of abdominal surgery patients
- Most adhesions are asymptomatic, yet 1/3 of patients, undergoing invasive surgeries, are readmitted, an average of two times, due to complications Arung et al. 2011
- Post-surgical morbidity from adhesion formation can include chronic abdominal or pelvic pain, infertility in women, and potentially fatal intestinal obstructions
- Laparoscopic procedures can potentially reduce adhesive small bowel disease, yet the incidence of post-surgical intraperitoneal adhesions has not declined over the last 20 years Ward and Panitch 2011
- Post surgical adhesive small bowel disease is the primary diagnosis for 12-16% of all surgical admissions Maung et al. 2012
- A 2010 survey found that over 7 million abdominal and pelvic surgical procedures of all types were performed
- The total annual cost of surgeries to relieve surgically-related small bowel obstructions, surgical adhesion-related infertility, and other surgical adhesion-related complications was estimated to be as high as $5 billion in the US alone in 2008 Wiseman 2008

Key Development Activities 2020-22

	2020	2021	2022
NVP	← HPLN production / precursor development (NV103 and NV201) for CHLA / Boston →		
CHLA	SBIR NV103 project – in vitro/rodent →		
	TNS R & D →		
Lake-pharma	Scale up of commercial anti C99 antibody GLP/GMP →		NCI Phase 2B Matching Grants
Ardena	HPLN/Ir formulation + CD99 coupling + analytical methods	GLP scale up + analytics + stability	→
		GMP scale up + stability to trial materials	
TD2	PK studies / Project work up	Toxicology, CMC and IND Regulatory Filings	Clinical studies NV103
Boston	SBIR Adhesions program phase 2		NCI Phase 2B Matching Grants

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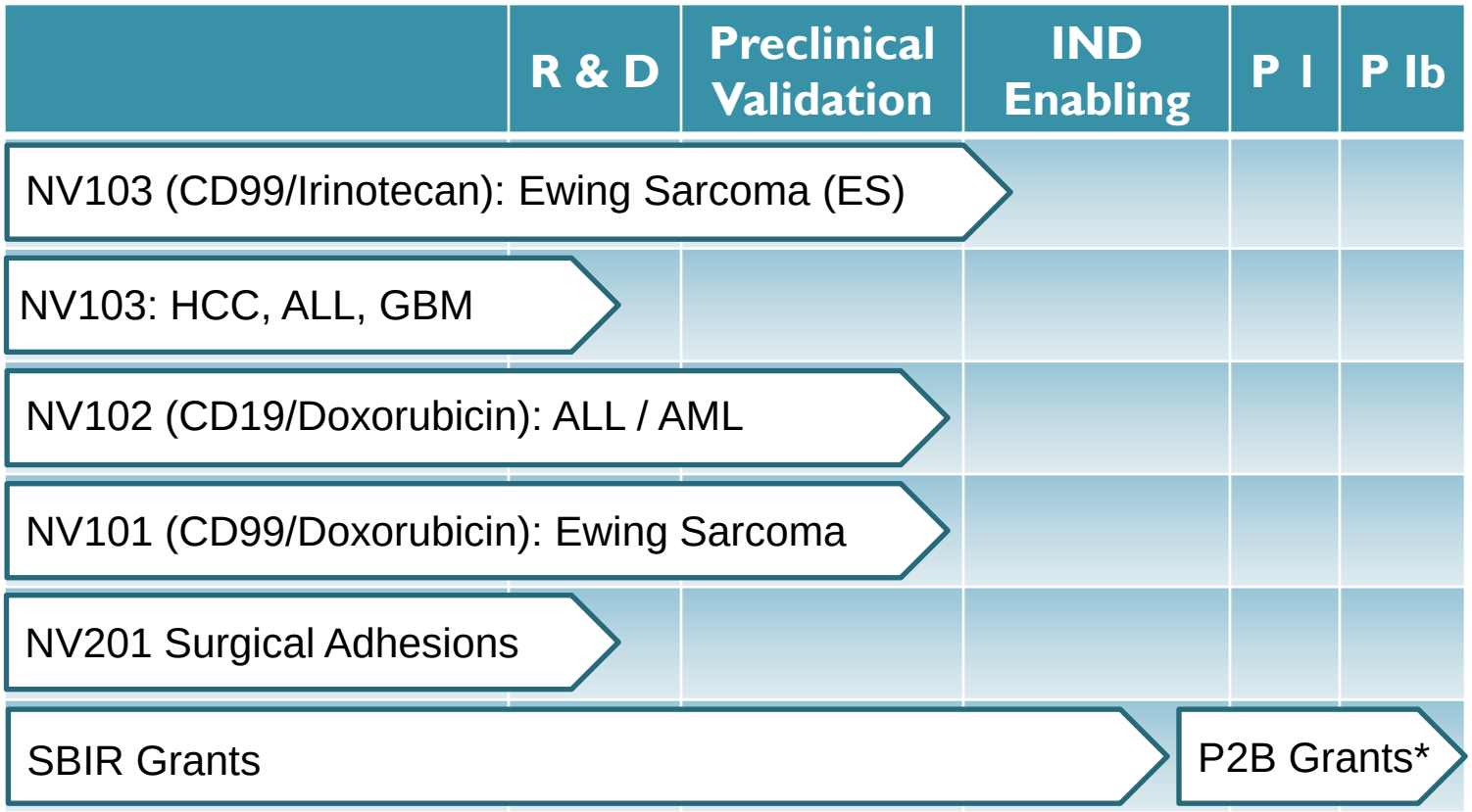
Product & Project Pipeline



* File for $8 M in matching grants

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Funding Raised to Date

NSF SBIR	Targeted Nanoparticle Delivery Agent for Treatment of Adult Leukemia	01/01/12	$149,848
NSF SBIR	Targeted Nanoparticle Delivery Agent for Treatment of Adult Leukemia	10/01/13	$500,000
NIH STTR	Targeted Polymerized Shell Microbubbles to Image Surgical Adhesions	02/01/16	$238,728
NIH STTR	Nanoparticle Delivery System for Ewing Sarcoma Treatment	04/15/16	$240,750
Montana	Montana SBIR/STTR Matching Funds Program – Phase 1	10/01/16	$30,000
Management+	Primary Equity Capitalization	02/14/17	$127,044
Angel Investors	Convertible Notes	07/01/17	$265,000
Montana	Montana SBIR/STTR Matching Funds Program – Phase 2	07/01/18	$30,000
NIH SBIR	Targeted PS Microbubbles to Image and Treat Surgical Adhesions	09/01/18	$1,597,000
NIH SBIR	NV103: Antibody Conjugated Nanoparticle for ES Targeted Therapy	09/14/18	$2,381,000
Funds Raised to Date			**$5,559,370**
		Equity	$127,044
		Notes	$265,000
		Grants	$5,167,326

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Current SBIR Grant Funding ~$4 Million

(in thousands)

	Q4 18	Q1 19	Q2 19	Q3 19	Q4 19	Q1 20	Q2 20	Q3 20	Q4 20	Q1 21	Total
NanoValent											
NV103 FastTrack	$83	$83	$176	$176	$176	$176	$168	$168	$168	$168	$1,543
NV201 Phase 2	$114	$114	$114	$114	$105	$105	$105	$105	$0	$0	$874
Total NV	$197	$197	$290	$290	$281	$281	$272	$272	$168	$168	$2,417
CHLA	$37	$37	$94	$94	$94	$94	$97	$97	$97	$97	$838
Boston University	$94	$94	$94	$94	$87	$87	$87	$87	$0	$0	$723
	$328	$328	$478	$478	$462	$462	$456	$456	$265	$265	$3,978

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Unique Opportunity

- Cohesive small international team working collaboratively in a virtual structure since 2016
- Preclinical therapeutics that
  - Target with antibodies or peptides
  - Shield the body with lipid nanoparticles
  - Destroy target cells without traditional toxicity
- Potential one and done financing
  - $8 Million in an equity raise
  - $8 Million in matching NCI Phase2B Grants
  - NV103 to Phase 2a data
  - NV201 to IND/BLA

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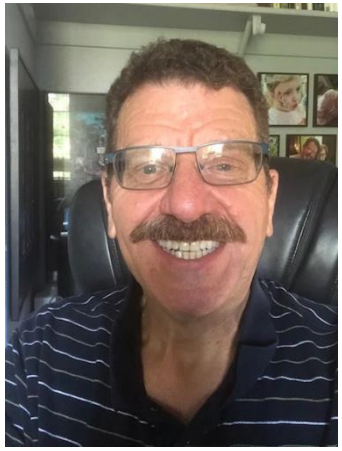
Pre COVID-19

Sheltered in Place



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