
# NASDAQ: CLSN

*July 2015*

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# Safe Harbor Statement

Except for historical information, the statements made in this presentation are forward-looking statements involving significant risks and uncertainties.

These risks and uncertainties, including those related to the future financial position and business strategy of the Company, are detailed in the Company's filings with the Securities and Exchange Commission.

# A Fully Integrated Oncology Company

## Deep Pipeline and Multiple Technology Platforms

**Chemotherapy, Immunotherapy and RNA Therapy Platforms**

**Multiple near term opportunities for value creation**

- Phase 3 in Primary Liver Cancer (HCC)
- Phase 2 in RCW Breast Cancer
- Phase 1 in Ovarian Cancer
- Pre-Clinical/Phase 1 in GBM Brain Cancer
- Pre-Clinical Research for RNA Lung Specific Delivery

**Discovery assets complement proven development capabilities**

- Nanoparticle Technology
- 1st Line Therapies
- Oncology Focused

**Strong cash position following EGEN acquisition**

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# Three Platforms to Drive Growth

## LTSL

**Lysolipid Thermally Sensitive Liposomes**

**ThermoDox:**
Liposomal Doxorubicin

Phase 3 Study in HCC
Phase 2 Study in RCW

## TheraPlas

**DNA-based Non-viral Immunotherapy**

**GEN-1:**
IL-12 Immunotherapy

Phase 1 in Ovarian Cancer
Pre-Clinical/Phase 1 in GBM

## TheraSilence

**RNA-based Non-viral Carriers, Lung Specific**

**GEN-2:**
Delivery of siRNA, mRNA,

Pre-Clinical Delivery Cancer
Pre-Clinical Delivery PAH, ++

# Pipeline of Targeted Therapeutic Agents

| INDICATION | PRODUCT CANDIDATE | PRE-CLINICAL | PHASE 1-2 | PHASE 3 |
|---|---|---|---|---|
| Primary Liver | ThermoDox®/OPTIMA Study | | | Phase III enrolling |
| RCW Breast | ThermoDox/US & Euro-DIGNITY | | Phase II enrolling | |
| Ovarian | GEN-1/Multiple Studies | | Phase I enrolling | |
| Glioblastoma | GEN-1 | Pre-Clin. Efficacy/Safety/Toxicology | | |
| Lung Disease | GEN-2/TheraSilence | Efficacy/Safety/Tox | | |

**Key Near-Term Milestones:**

- ASCO abstract from GOG (GEN-1+Doxil) Ovarian Cancer Trial
- Translational Data from GOG (GEN-1+Doxil) Ovarian Cancer Trial
- Initiation of GEN-1 Phase 1b Neo-Adjuvant Ovarian Cancer Trial
- Updated OS Data from HEAT Study
- PoC Preclinical Data for GEN-1+SoC in GBM Brain Cancer

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LTSL Platform
ThermoDox®
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# Hepatocellular Carcinoma

## Large and Deadly Global Cancer

- **5th most prevalent**
  - 800,000 annual incidence worldwide; growing 5% per year
  - By 2020, expected to be the #1 cancer, surpassing lung cancer
  - China has 50% of new cases; 75% in Asia
- **4th highest mortality**
  - 5-year survival rate less than 10%
  - Median survival from time of diagnosis is less than 3 years
  - Cure, usually through surgery, is possible in less than 20% of patients
- **Local therapies include:**
  - RFA, TACE and radiation
  - RFA is the dominant treatment average local recurrence rate of 50% for lesions > 3 cm
  - ThermoDox + RFA addresses limitations of current standard of care by **"Expanding the Treatment Zone"**

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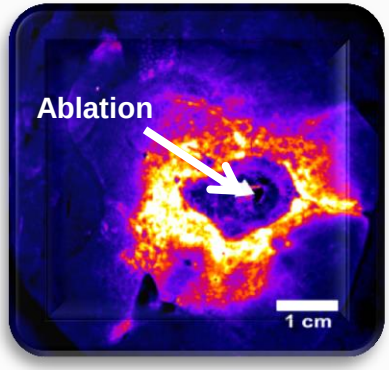
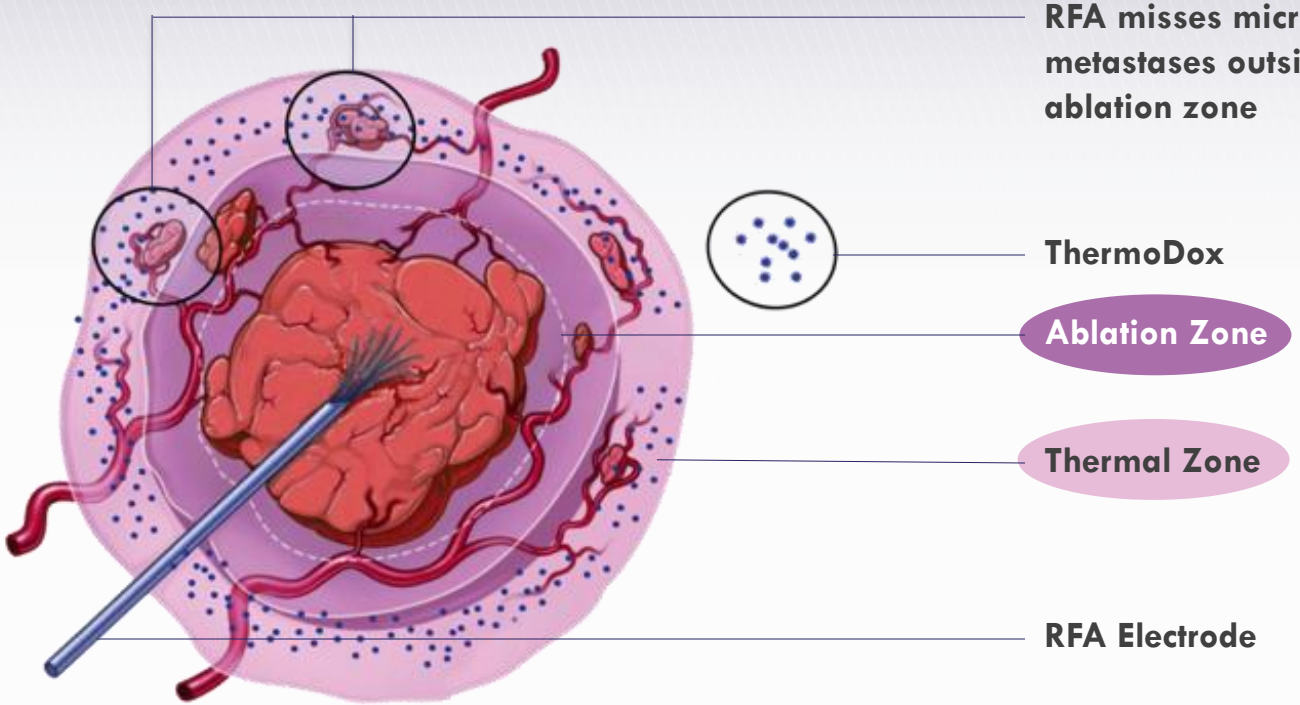
# RF Liver Ablation + ThermoDox

## Expanding the Treatment Zone Addresses RFA Limitations

**ThermoDox**
**+**
**sRFA 45**




- ThermoDox infused IV ~15 minutes prior to sRFA
- ThermoDox concentrates in the "Thermal Zone" over a 45 minute period
- Doxorubicin is released in the "Thermal Zone" expanding treatment area

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# Learnings from HEAT Study

## Advanced Understanding of RFA and HCC Treatment

### Data from 285 Patient Subgroup Reviewed at Multiple International Medical Conferences

- RFA must be used within its engineered design limitations
  - 3 cm or greater lesions require multiple overlapping ablations
  - Longer RFA time (> 45 minutes) result in better outcomes
- Heating duration directly affects clinical outcome by allowing for high local perfusion of drug at the tumor site
  - High tissue concentration of ThermoDox prevents recurrence
  - Supported by Multivariate Cox Regression Analysis
- PFS is not a reliable endpoint in HCC trials

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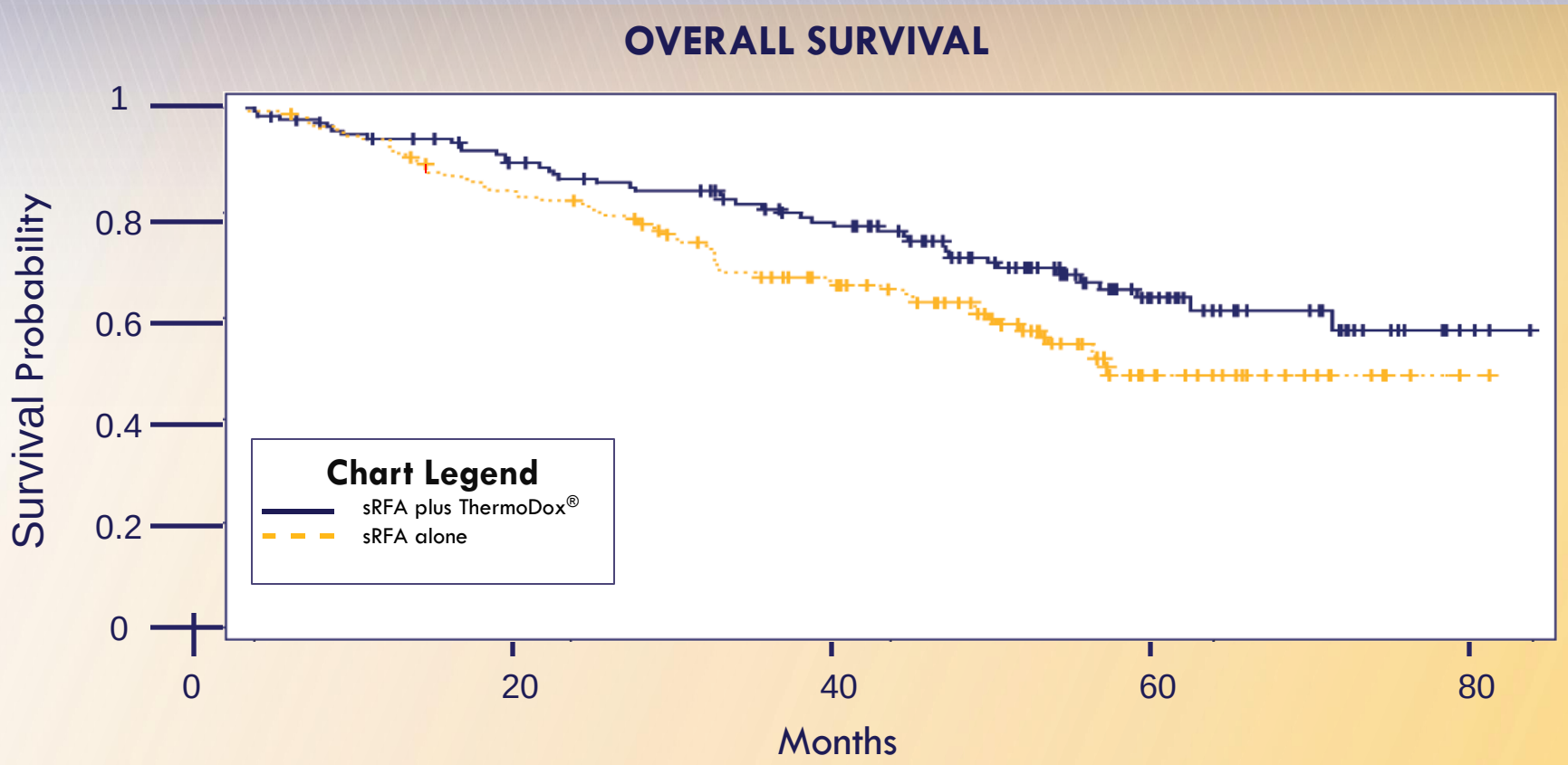
# Sub-Group Analysis of HEAT Study Data

285 Patients with Standardized RFA (>45 minutes)




| Overall Survival as of 1/15/2015 | HR=0.628 (95% CI 0.420 - 0.939) *P* Value = 0.02 |
|---|---|

sRFA45 Standardized RFA > 45 mins.

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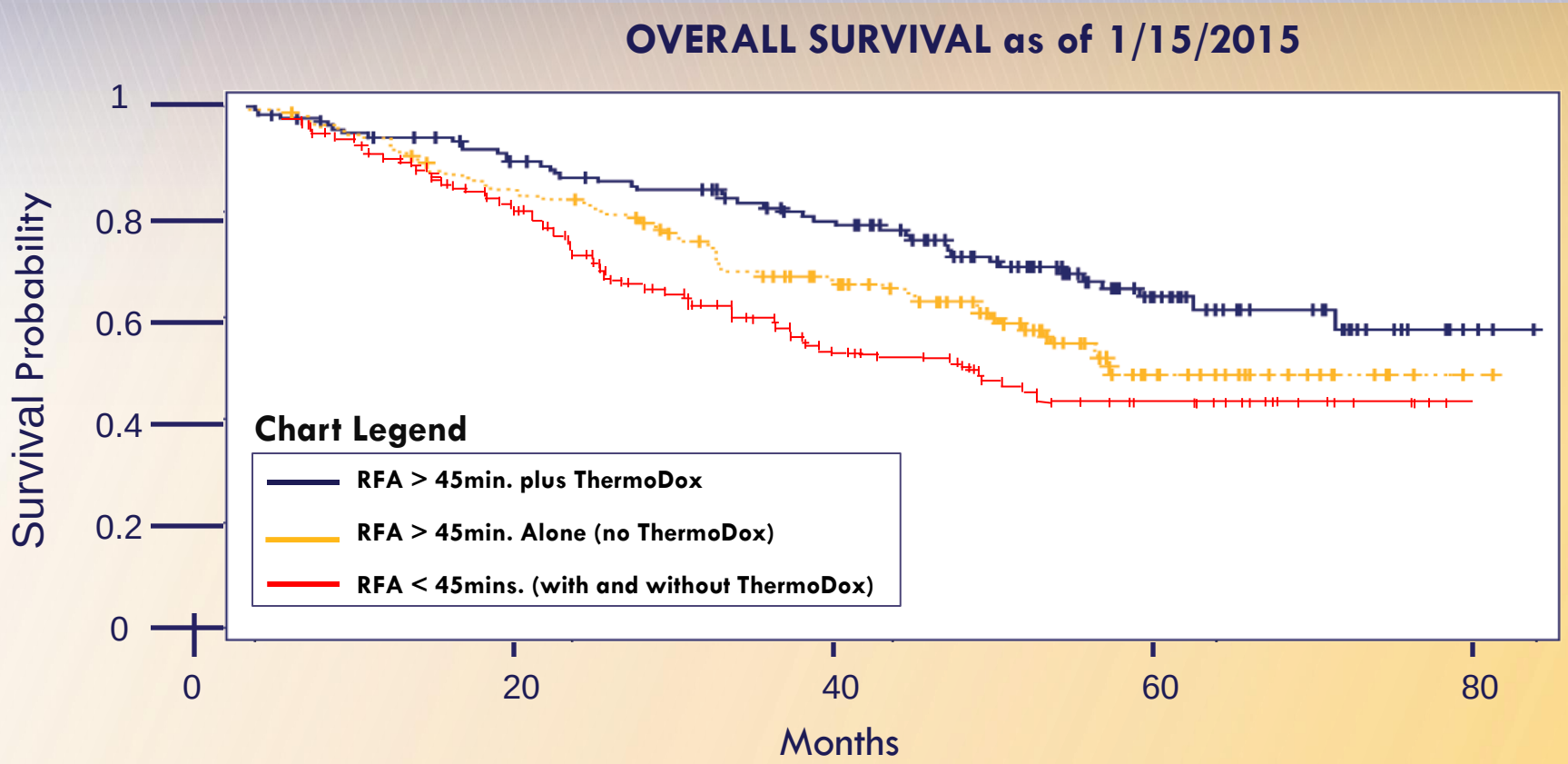
# Sub-Group Analysis (Single Lesion) of HEAT Study

285 Patients Standardized RFA >45 minutes +/- ThermoDox vs
167 Patients RFA < 45 minutes




| OS sRFA > 45mins. +/- ThermoDox | HR=0.628 (95% CI 0.420 - 0.939) *P* Value=0.02 |
|---|---|

sRFA45 Standardized RFA > 45 mins.

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# Phase 3 OPTIMA Study Design

## ThermoDox Plus sRFA*

**General Eligibility**
- Non-resectable HCC
- Single lesions
- Lesion > 3 cm but not > 7 cm
- Treatment naïve
- Child-Pugh A

**Stratification**
- Lesion size: 3-5 cm / 5-7 cm
- Geography

**Randomize**
1:1

N=275 — **ThermoDox plus sRFA***

N=275 — **Dummy Infusion + sRFA***

| | |
|---|---|
| **Primary Endpoint** | Overall Survival (OS) |
| **Secondary Endpoints** | Progression Free Survival; Safety |
| **Interim Efficacy Analysis** | 118 OS Events / HR < 0.61<br>158 OS Events / HR < 0.70 |
| **Final Efficacy** | 197 OS Events / HR < 0.75 |

First Patient Enrolled Q3 – 2014

~75 Clinical Sites in 13 Countries

*sRFA45 Standardized Radiofrequency Ablation > 45 minutes

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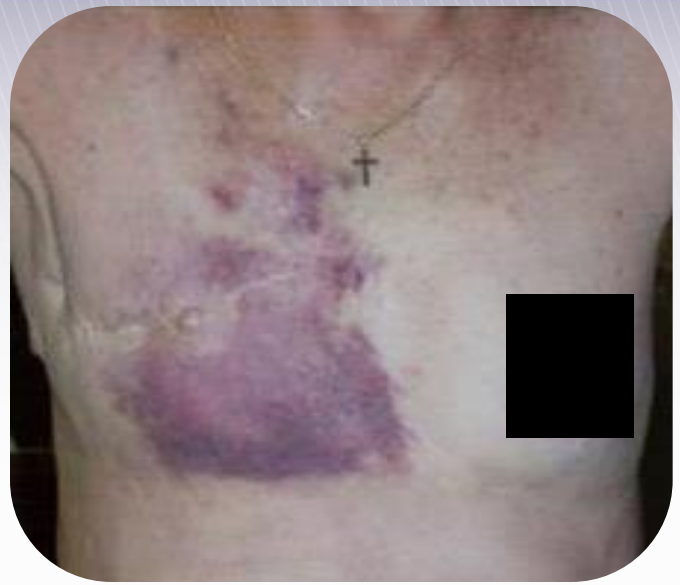
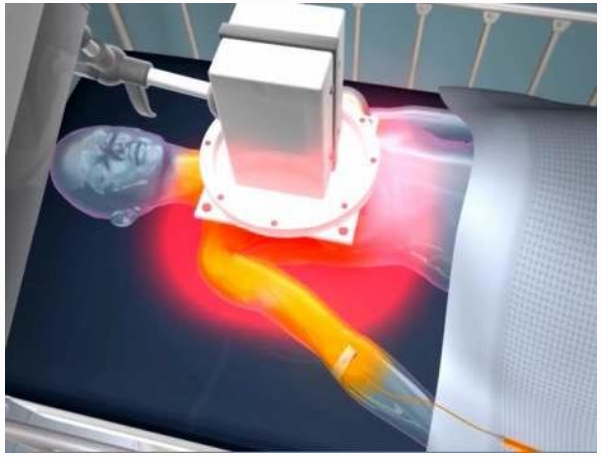
# Recurrent Chest Wall Breast Cancer

## Very Difficult with Severe Complications

- Breast cancer recurring in the chest wall affects ~35,000 post-mastectomy patients in the US and Europe annually
- Up to 40% of women undergoing a mastectomy as primary treatment will experience local recurrence
- Reappearance of cancer in the ipsilateral breast or the chest wall





- Patients have ulceration, bleeding and pain, highly debilitating and visible cancer
- Local tumor control is a primary objective in treating these patients

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# Phase 2 RCW Breast Cancer Study

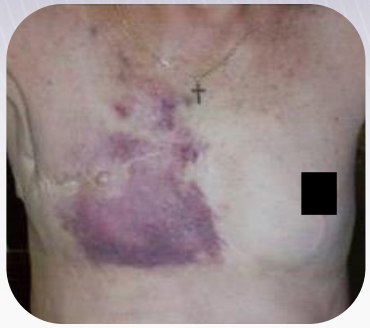
## ThermoDox + Hyperthermia

### Phase 2 DIGNITY Study

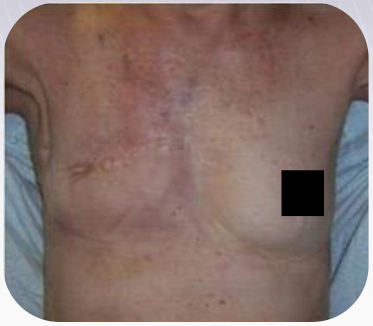
Primary Objectives

- Evaluate local-regional breast tumor response in patients undergoing ThermoDox + hyperthermia; 17 patients enrolled & treated, 13 evaluable for efficacy
  - All patients experienced stabilization of disease
  - 70% of patients in evaluable population observed local responses - 5 CRs & 4 PRs
- Establish pharmacokinetic bioequivalence between ThermoDox manufactured at two different manufacturing sites

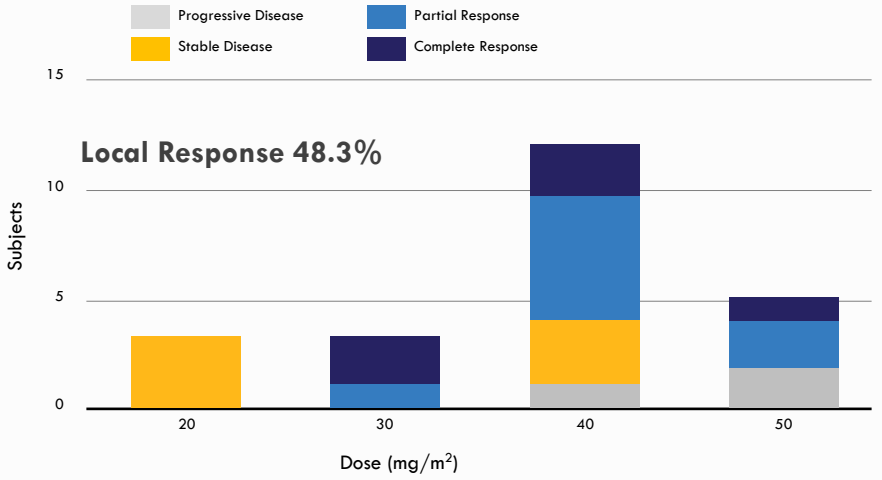
**Limited Treatment Options**



**Complete Response**



**Combined Phase 1 Data (n = 29)**



# Euro-DIGNITY Study

## ThermoDox + Hyperthermia + Radiation

### Primary Objectives

- Evaluate complete and partial response after 3 cycles of ThermoDox + Hyperthermia & Radiation Treatment (Tri-Modal Therapy)
- Evaluate loco-regional breast tumor control in patients undergoing Tri-Modal Therapy

### 100 patients to be enrolled

### Open Label Design

### Study Timelines

- Site Activation: Q3 2015
- Recruitment Period: Q3 2015 – 2017
- LP/LV through Follow-Up: 2018

# Early Access Program (EAP) in Europe

## ThermoDox for RCW Breast Cancer Patients

**EAP offers patients access to innovative non-registered pharmaceuticals**

- EAP (Specials Market) in Europe is over $6B per year
- License/Distribution Agreement signed with myTomorrows in Jan 2015
- May be provided to patient with a life threatening or debilitating disease and no alternative therapy exists

**EAP Requirements**

- Product must be in Phase 2 trials or later; have shown evidence of efficacy and in an active program for registration
- Awareness and physician training are used to educate the medical community

**EAP Pricing/Market**

- Product pricing determined by the Sponsor; Equivalent to registered products
- Partnered with myTomorrows
- RCW breast cancer in EU is ~25,000 patients annually
- 35 to 40 Centers of Excellence in EU that treat patients with RCW breast cancer using Thermal Therapy

# TheraPlas Platform

## GEN-1

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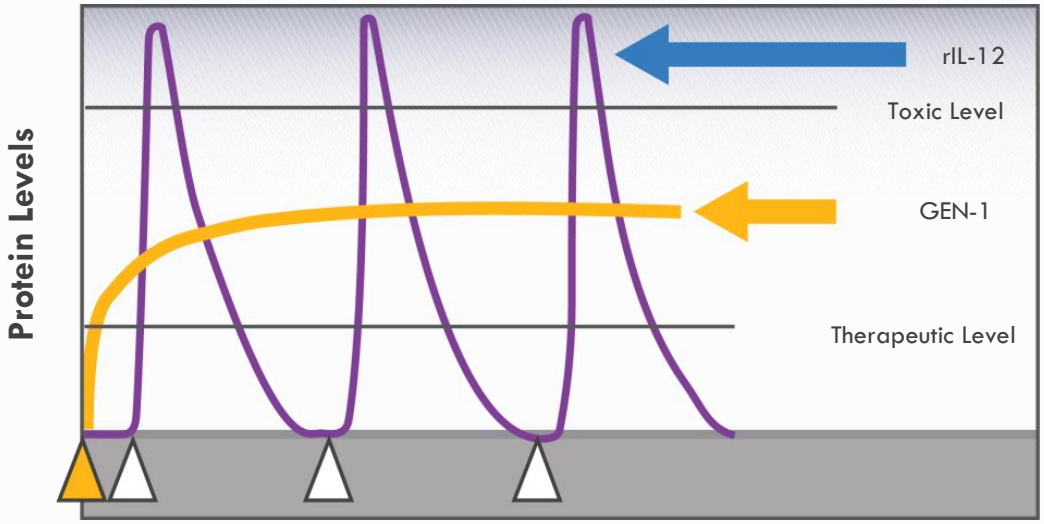
# GEN-1

## Novel PPC Plasmid DNA Nanoparticle

### Rationale for Local Therapy with DNA Nanoparticles

- Local production of potent cytokine IL-12
- Recruits immune system, multiple mechanisms, effective in multiple cancer types
- Avoids serious toxicities and poor pK of recombinant IL-12

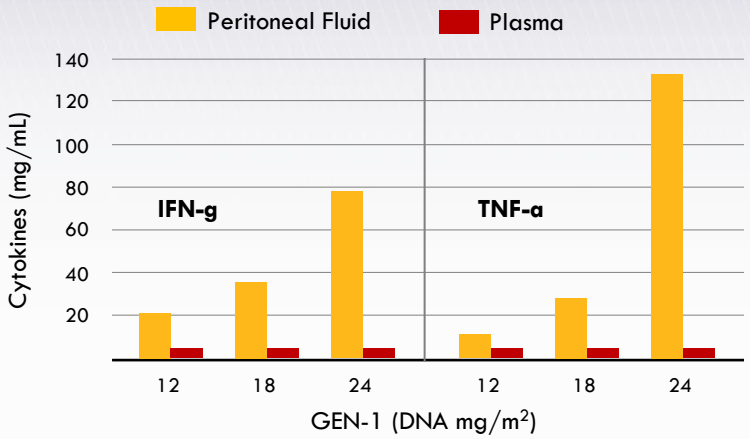
### GEN-1 an Alternative to rIL-12 Poor pK



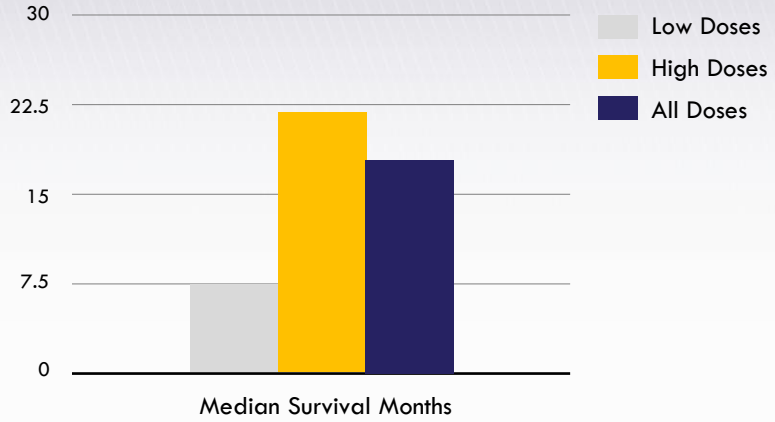
# GEN-1

## Clinical Experience To-Date

### 1 Convincing Evidence of Biological Activity




### 2 Single Agent Benefit




### 3 Lack of Overlapping Toxicities Allows for Combination Therapies

**GEN-1 (IP)**

- Gastrointestinal
- Low Grade Fever
- Chills
- Catheter Site Pain/Redness
- Abdominal Discomfort

**Chemotherapy (IP)**

- Cardiovascular, Hematological
- Metabolic, Neurologic
- Fever, Infection
- Urinary Problems , Gastrointestinal
- Hepatic, Fatigue, Metabolic, Pain

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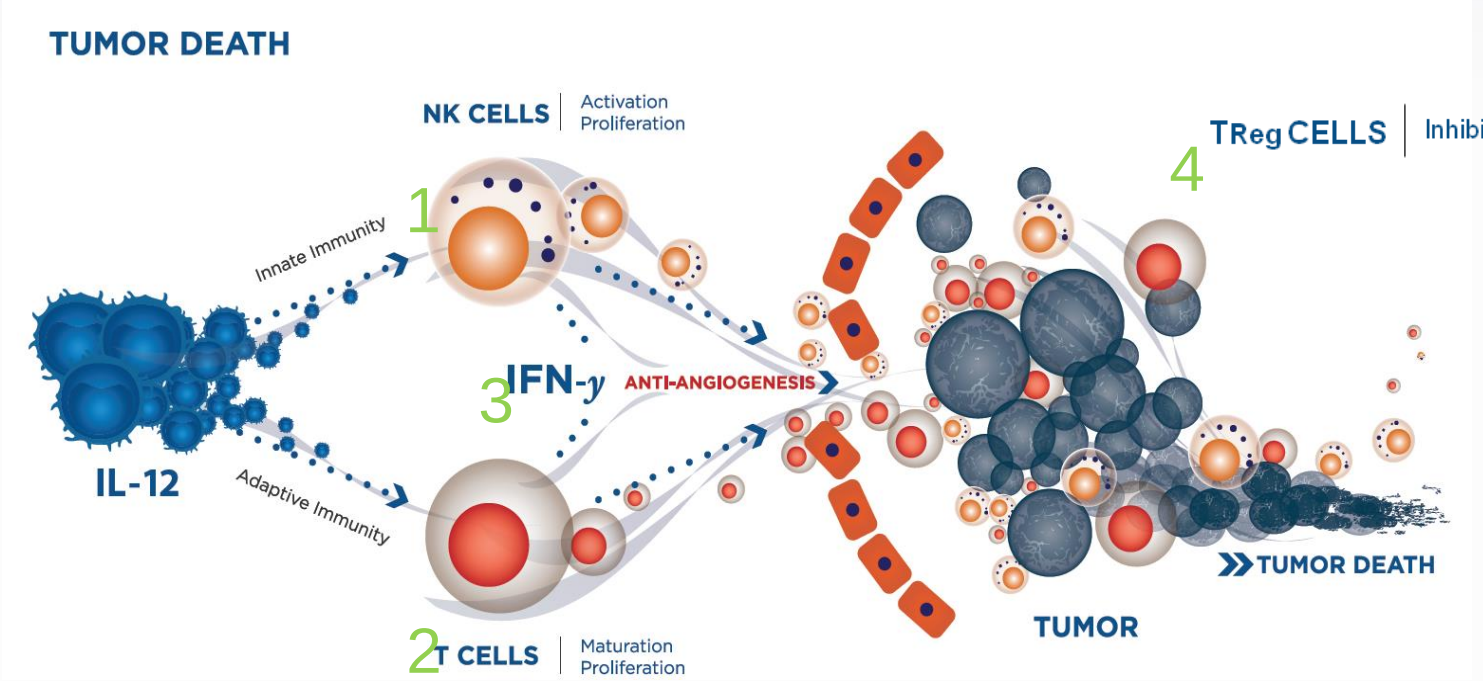
# **IL-12:** A Powerful Immune Modulating Agent with Multiple Mechanisms of Action

## Mechanisms of Action

1. NK Cell Activation
2. T Cell Activation
3. Anti-angiogenesis
4. T Reg suppression



# Ovarian Cancer

## Large and Deadly Global Cancer

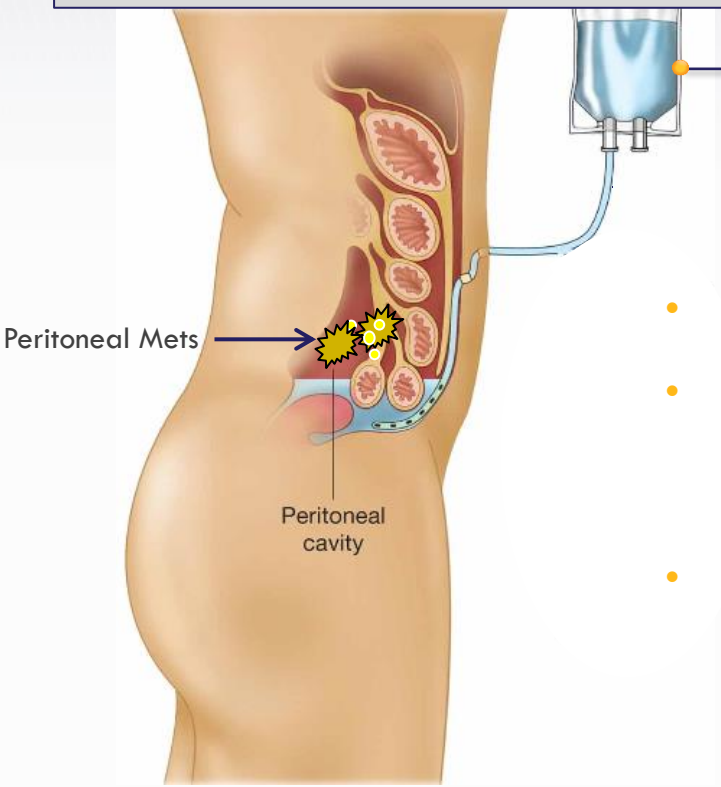
- **8th most diagnosed cancer among women**
  - 225,000 annual incidence worldwide
  - 22,000 in US and 100,000 in developed countries
- **5th highest mortality among women**
  - 5-year survival rate for all stages is 45%; Survival rate reduces dramatically if not localized cancer
  - 15% diagnosed with localized cancer, eligible for potentially curative surgery
- **Local therapies for ovarian cancer**
  - Ovarian cancer is not diagnosed early - spreads to regional/mets requiring combo regimens
  - Most common site of recurrence in abdomen– importance of intra-peritoneal administered therapy
  - GEN-1 administered IP; ideal adjuvant to SoC therapy

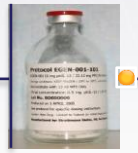
Sources: Cancer Statistics, American Cancer Society; Globocan; SEER database

# GEN-1 for Ovarian Cancer

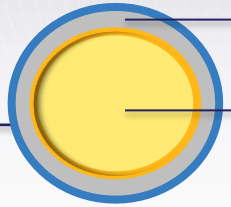
## Local Immunotherapy Addresses Limitations of Chemotherapy

**Persistent Local Delivery of an Immune Agent with a Single Administration**



GEN-1




**Stable Nanoparticles for Local Delivery**

- GEN-1causes the production of IL-12 at cancer site
- IL-12 addresses cancer cells that are chemo-resistant by recruiting the immune system, inducing powerful anti-cancer mechanisms
- Clinical experience strongly supports development in combination with first line treatment

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# Phase Ib Trial: GEN-1 + Doxil

## Platinum Resistant Ovarian Cancer

**Safety, Biological Activity & Efficacy of Combination Therapy**

Traditional 3+3 Escalation Design (n=16; enrollment completed)

| Dose Level | GEN-1 (mg/m$^2$) | Doxil (mg/m$^2$) | Status |
|---|---|---|---|
| 1 | 24 | 40 | Completed |
| 2 | 36 | 40 | Completed |
| 3 | 36 | 50 | Completed |

- All doses well tolerated; no DLTs
- Better clinical responses at 36 mg/m$^2$ dose
  - Clinical Response Rate (SD+PR+CR) (all doses): > **50%**
  - Clinical Response Rate (SD+PR+CR) at 36 mg/m$^2$ dose: **86%**
- Compares favorably to current SoC in Platinum Resistant Ovarian Cancer
  - Single Agent Doxil in four (4) previous studies: **45-50%** Overall CRR

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# GEN-1 as a First Line Treatment in Ovarian Cancer

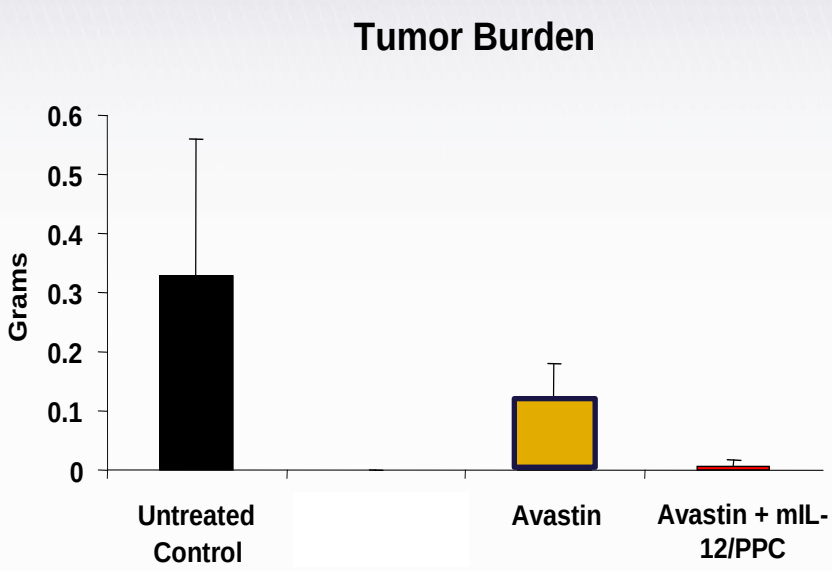
## Phase I Study

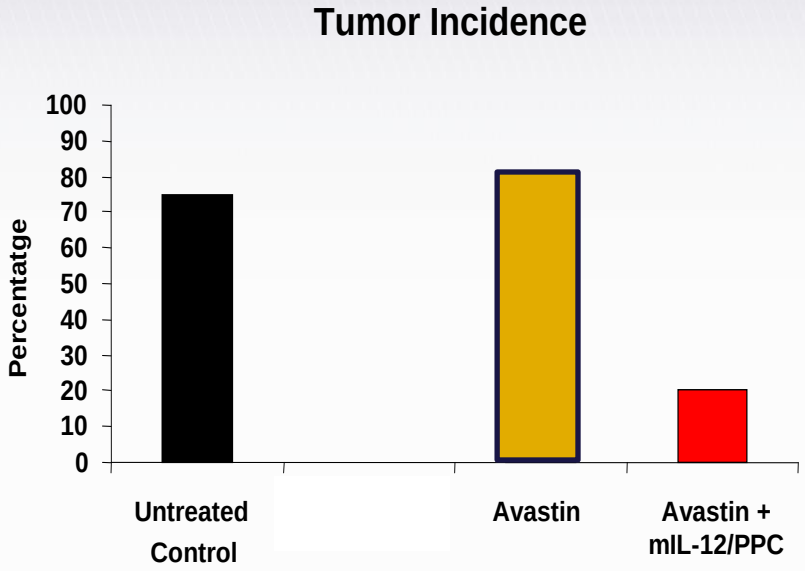

| | |
|---|---|
| **Neoadjuvant Study in Newly Diagnosed Ovarian Cancer Patients** | To determine safety, dose, and feasibility in target patient population |
| **Primary Endpoint** | Optimal Dose (Max or MTD) |
| **Secondary Endpoints** | pCR, PFS, ↑IFNγ, ↑IL-12, ↓VEGF |

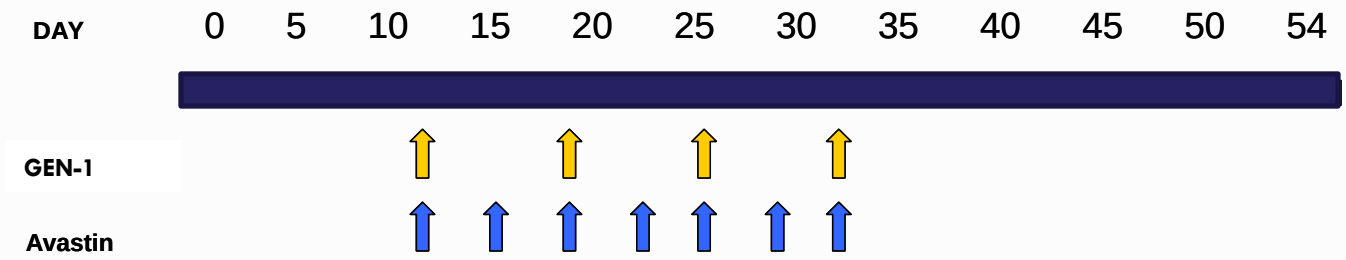
# GEN-1 + Avastin in Disseminated Ovarian Cancer

## Pre-Clinical Study

**Dramatic Improvement in Avastin Activity in Combination with pmIL-12/PPC (GEN-1) (Study 1)**



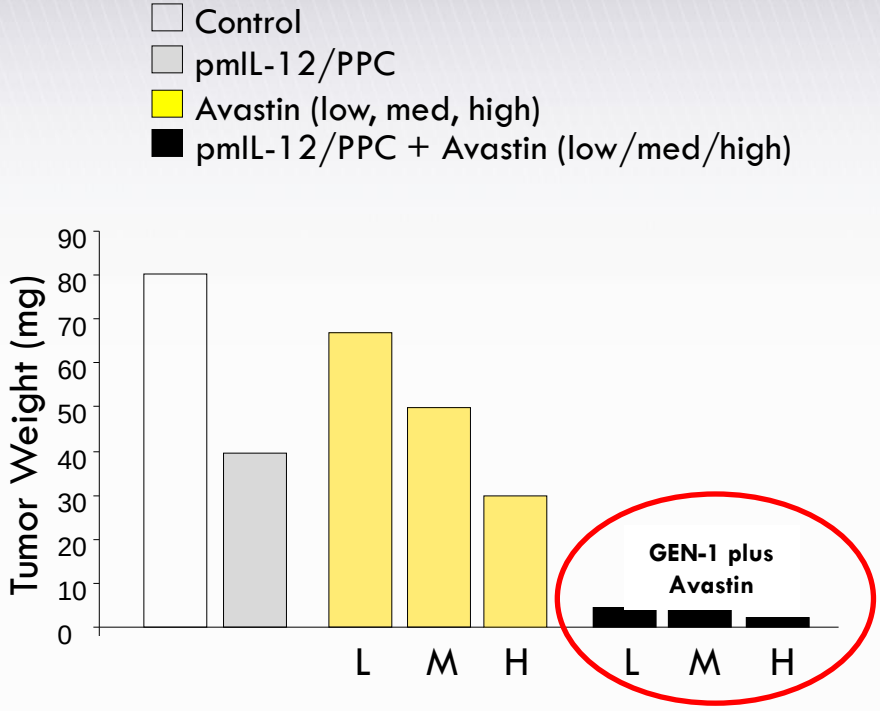



# GEN-1 + Avastin in Disseminated Ovarian Cancer

## Second Pre-Clinical Study

### Dramatic Improvement in Avastin Activity in Combination with pmIL-12/PPC (GEN-1)




| Comparison | # | Mean Tumor Burden | Two-Tailed P-Value |
|---|---|---|---|
| Avastin +GEN-1 vs. Control | 18<br>5 | 3.45 mg<br>80.1 mg | 0.035 |
| Avastin+GEN-1 vs. Avastin | 18<br>18 | 3.45 mg<br>48.9 mg | 0.025 |
| Avastin+GEN-1 vs. GEN-1 | 18<br>6 | 3.45 mg<br>41.6 mg | 0.012 |

Human ovarian cancer cells were implanted IP.

- Avastin treatment at 5 mg/kg (low), 10 mg/kg (medium) and 20 mg/kg (high) was initiated 9 days after tumor implantation
- pmIL-12/PPC was given weekly for 4 weeks; 14 days after tumor implantation

# Proposed Phase I/II in Platinum Resistant Ovarian Cancer

## GEN-1 with Avastin + Doxil, the SoC

- Inhibition of VEGF synthesis by IL-12 through the interferon-gamma (IFN-gamma) pathway helps explain the remarkable synergy between GEN-1 and Avastin
- Potentially addresses the VEGF escape mechanism described in resistance to Avastin therapy
- Previous clinical studies have shown excellent safety of GEN-1 with Doxil in this patient population
- Phase 1 design to optimize GEN-1 and Avastin dosing to enhance safety profile and establish efficacy
- Initiate trial in late 2015/early 2016

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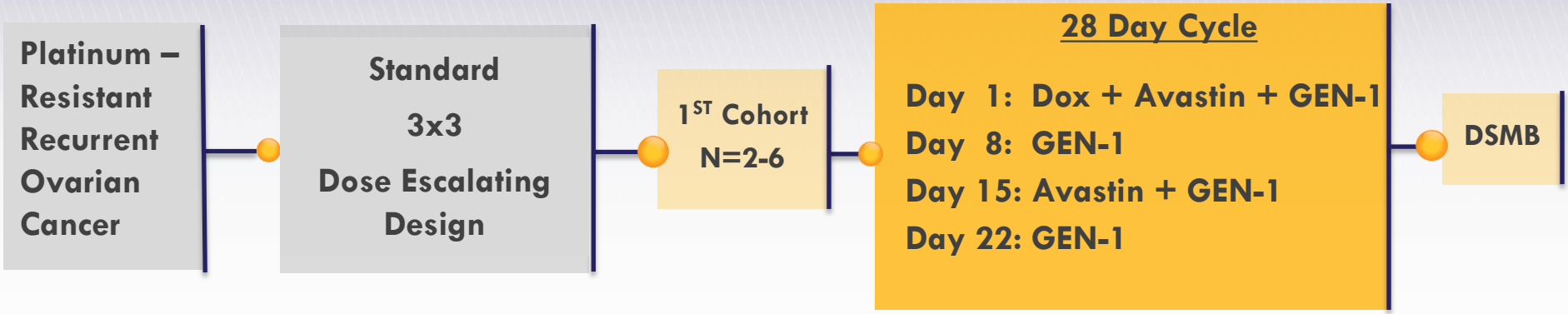
# GEN-1 with Avastin® and Doxil

## Platinum – Resistant Recurrent Ovarian Cancer




| | |
|---|---|
| **Primary Endpoint** | Optimal Safe Dose (Max or MTD) |
| **Secondary Endpoint** | Clinical Objective Tumor Response (RECIST) |
| **Secondary Endpoint (Biological/Immunological)** | IL-12, IFN-γ, TNF-α, IL-10, TGF-β, and VEGF concentrations in the blood and peritoneal fluid |

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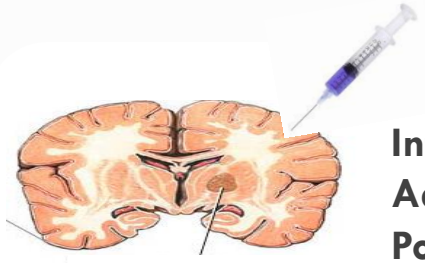
# Glioblastoma Multiform

## Planned Phase 1 in 2nd Half of 2015

### Preclinical Experience

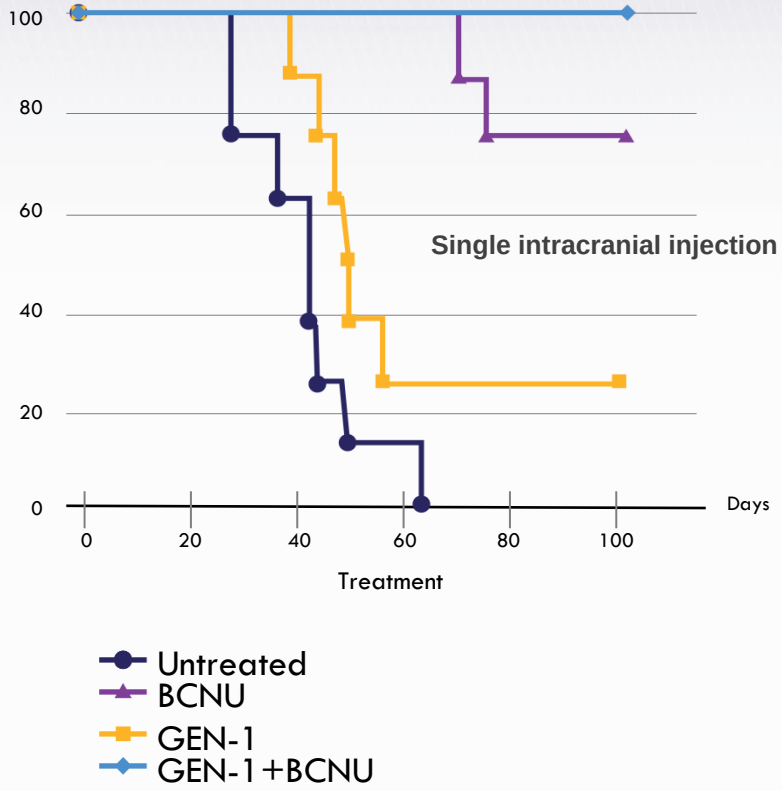
- IL-12 expression for one month in normal brain tissue
- Mechanism for local administration
- Bio-distribution studies
- Safety established



Brain tumor

**Intra-Cranial Administration Post-Resection**

### Survival Benefits in Glioma Model

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TheraSilence™ Platform
Lung-Specific Delivery of
RNA Therapeutics
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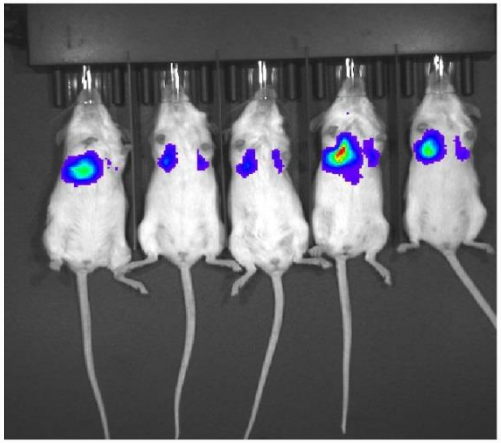
# TheraSilence

## Systemic RNA Delivery to the Lung

### Staramine and Polymeric Systems

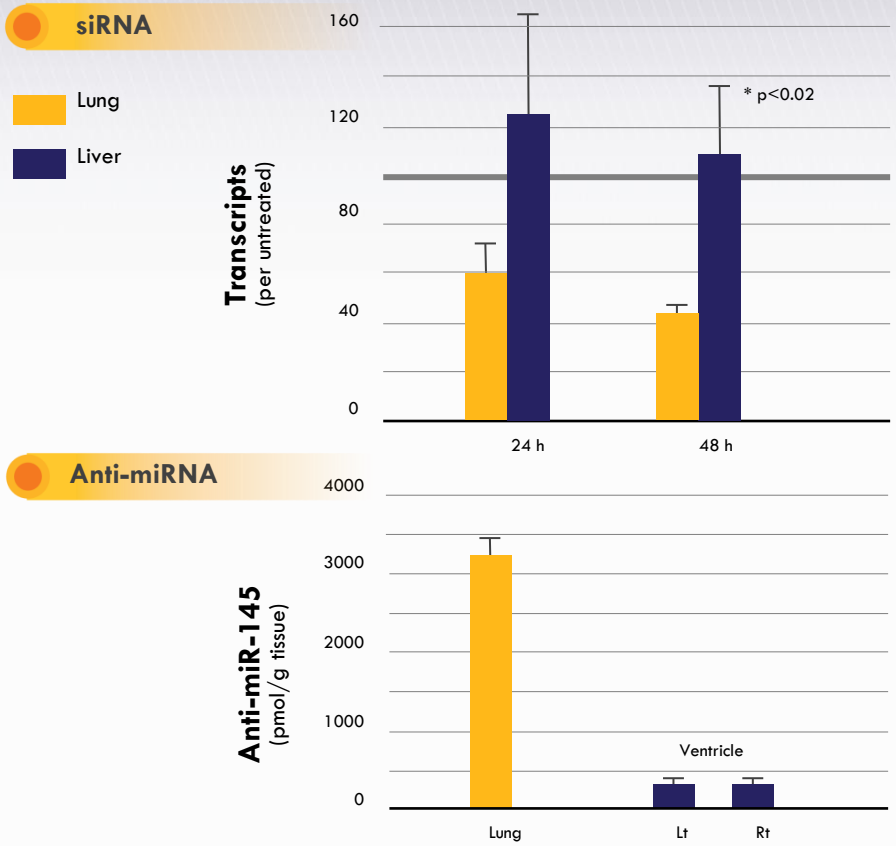
- mRNA pre-clinical program in NHP and murine models
- siRNA pre-clinical PAH and other pulminary diseases

### Intra-Venous Delivery of Luciferase mRNA



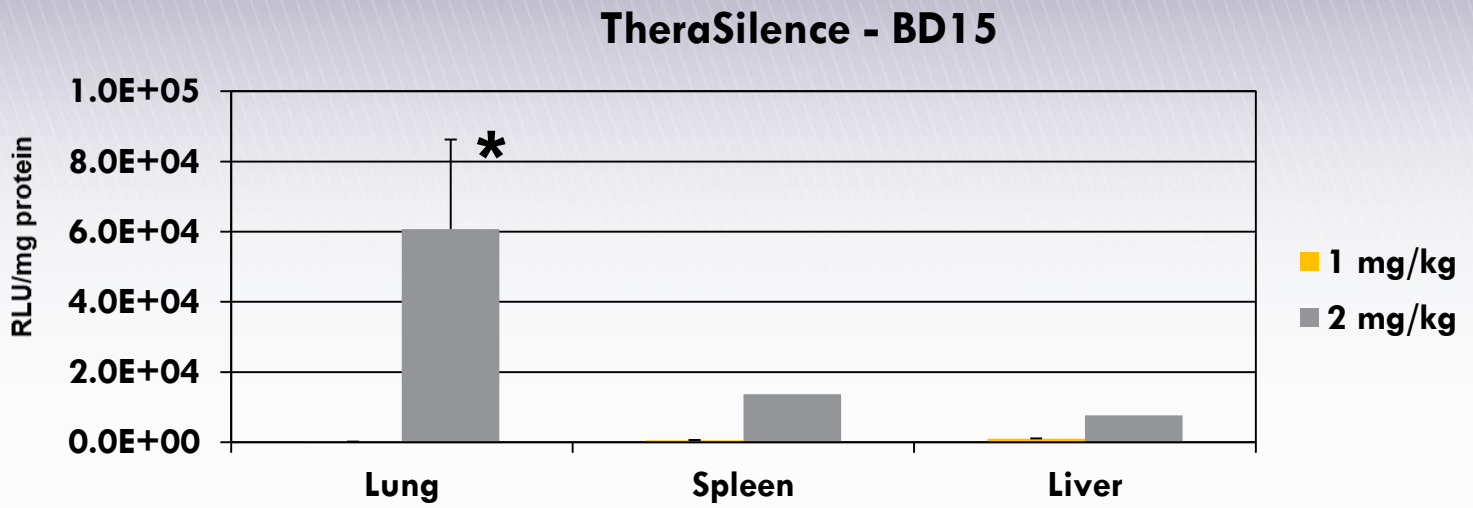
Celsion BD15k Nano-Particle

### Unique Lung Delivery - Independent of RNA Type



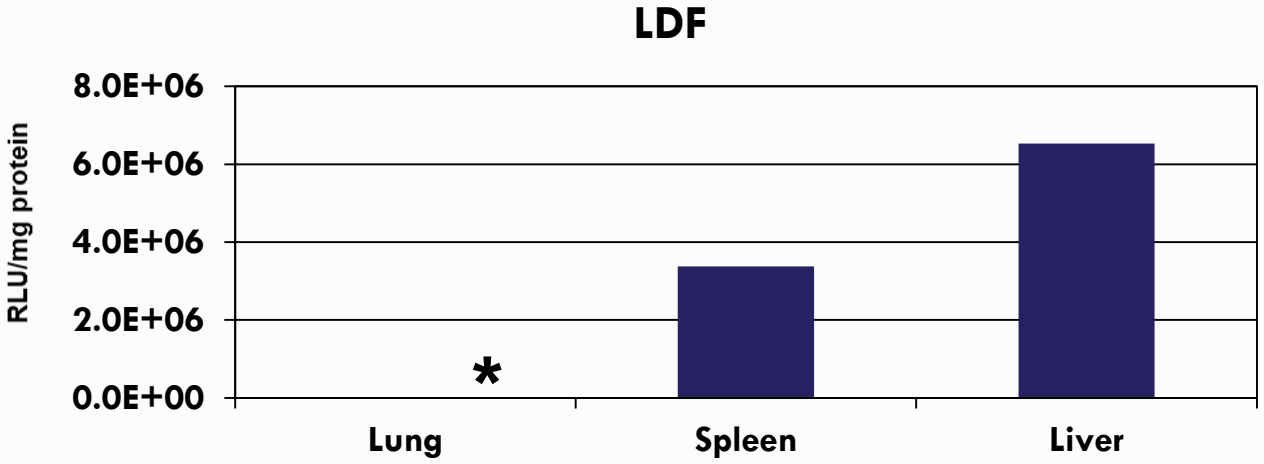
# Tissue Luciferase Expression Levels

## Non-Human Primate Study




*Average of 4 samples

PRIMARILY LUNG EXPRESSION




PRIMARILY LIVER/SPLEEN EXPRESSION

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# Strong Patent and Regulatory Protection

## Chemotherapy Delivery

### LTSL Platform

**CoM Patent (2021)**
**Method Patent (2026)**
Orphan Drug Designation for HCC

- U.S. 7 year exclusivity
- Europe 10 year exclusivity

Eligible for 5 year Hatch-Waxman (2031)

## DNA Delivery

### TheraPlas

**CoM Patent (2027)**
Eligible for Orphan Designation for Ovarian and GBM

- U.S. 7 year exclusivity

## RNA Delivery

### TheraSilence

**CoM Patent (2031)**
Delivery of RNAi, siRNA and miRNA

### Cell derived RNA + Delivery

**CoM Patent (2030)**
Proprietary RNA + Delivery System

# 2015 Goals

## First Half

- ThermoDox Early Access Program in Europe for RCW Breast Cancer √
- GEN-1 Development Overview & FDA Acceptance of Neoadjuvant Ovarian Study √
- Latest OS Sweep for HEAT Study – Subgroup HR = 0.629; Pvalue= 0.02 √
- TheraSilence Non-Human Primate Data √
- Final Clinical Data from GEN-1 Phase 1b GOG Ovarian Study (ASCO) √
- Translational Data from Phase 1b Ovarian Study (GEN-1 + Doxil)

## Second Half

- Initiate Patient Enrollment: ThermoDox Euro-DIGNITY Study
- GEN-1 Pre-Clinical Efficacy Data in GBM
- Initiate Patient Enrollment: GEN-1 Neoadjuvant Ovarian Study
- Collaboration Agreement(s) for TheraSilence RNA Delivery
- Initiate Patient Enrollment: GEN-1 + SOC Phase 1/2 GBM Study
- Initiate Patient Enrollment: GEN-1 + Doxil + Avastin Ovarian Study
- Final Clinical Data from ThermoDox Phase 2 US DIGNITY Study (San Antonio Breast)
- ~25% of Patients Enrolled in Phase III OPTIMA Study for HCC

# Financial Overview

| | |
|---|---|
| **Cash & Investments (3/31/15)** | $30.1 million |
| **At-The-Market RD Offering (5/2015)** | $8.0 million |
| **Estimated cash usage per month** | ~$1.6 million |
| **Market Capitalization** | $60 million |
| **Common shares outstanding** | 23 million |
| **Fully diluted shares outstanding** | 31 million |
| **Avg Daily Trading Volume** | ~ 275,000 |

Celsion

# Corporate Information

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