



**NASDAQ: CLSN**

***Rodman & Renshaw 17<sup>th</sup> Annual Global Investment Conference***

*St. Regis Hotel, New York*

*September 9, 2015*



# 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
- 1<sup>st</sup> Line Therapies
- Oncology Focused

### **Strong cash position following EGEN acquisition**

# 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**

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
<b>Primary Liver</b>	ThermoDox - OPTIMA Study			Phase III enrolling
<b>RCW Breast</b>	ThermoDox - Euro-DIGNITY			Phase II initiating
<b>Ovarian</b>	GEN-1 - 1 <sup>st</sup> line OVATION		Phase I enrolling	
<b>Glioblastoma</b>	GEN-1 - Pre-Clinical		Efficacy/Safety/Toxicology	

## Near-Term Clinical Milestones:

- GEN-1 Translational Data from Phase 1 Ovarian Cancer Trial
- GEN-1 First Patient Phase 1b OVATION Neo-Adjuvant Ovarian Cancer Trial
- GEN-1 Preclinical Data and IND for GBM Brain Cancer
- OPTIMA trial agreement CFDA
- First Patient in EU-Dignity
- Phase II DIGNITY Study at San Antonio Breast Cancer Conference

# Hepatocellular Carcinoma

## Large and Deadly Global Cancer

### ● 5<sup>th</sup> 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

### ● 4<sup>th</sup> highest mortality

- 5-year survival rate less than 10%
- Median survival from time of diagnosis is less than 40 months
- 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”**



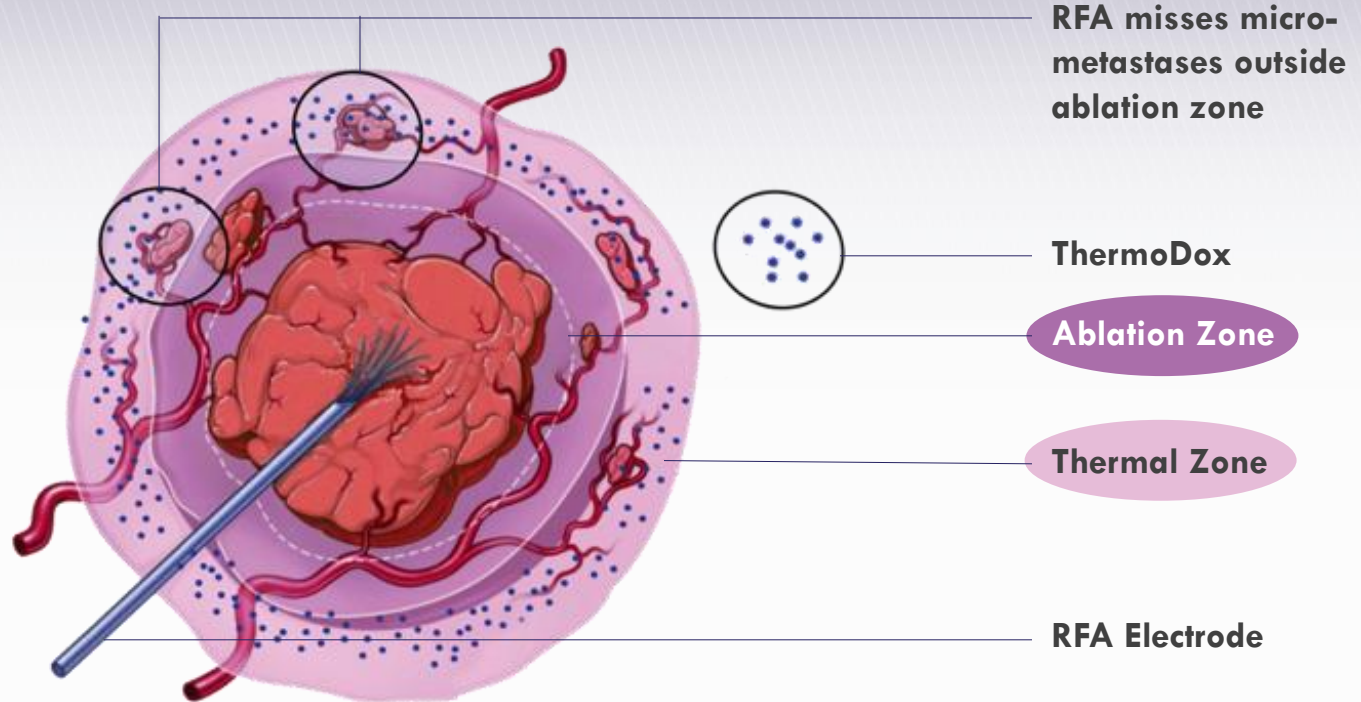
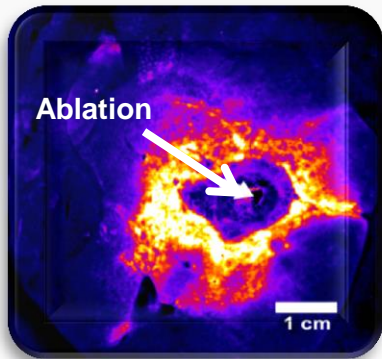
# RF Liver Ablation + ThermoDox®

## Expanding the Treatment Zone Addresses RFA Limitations

ThermoDox

+

sRFA 45



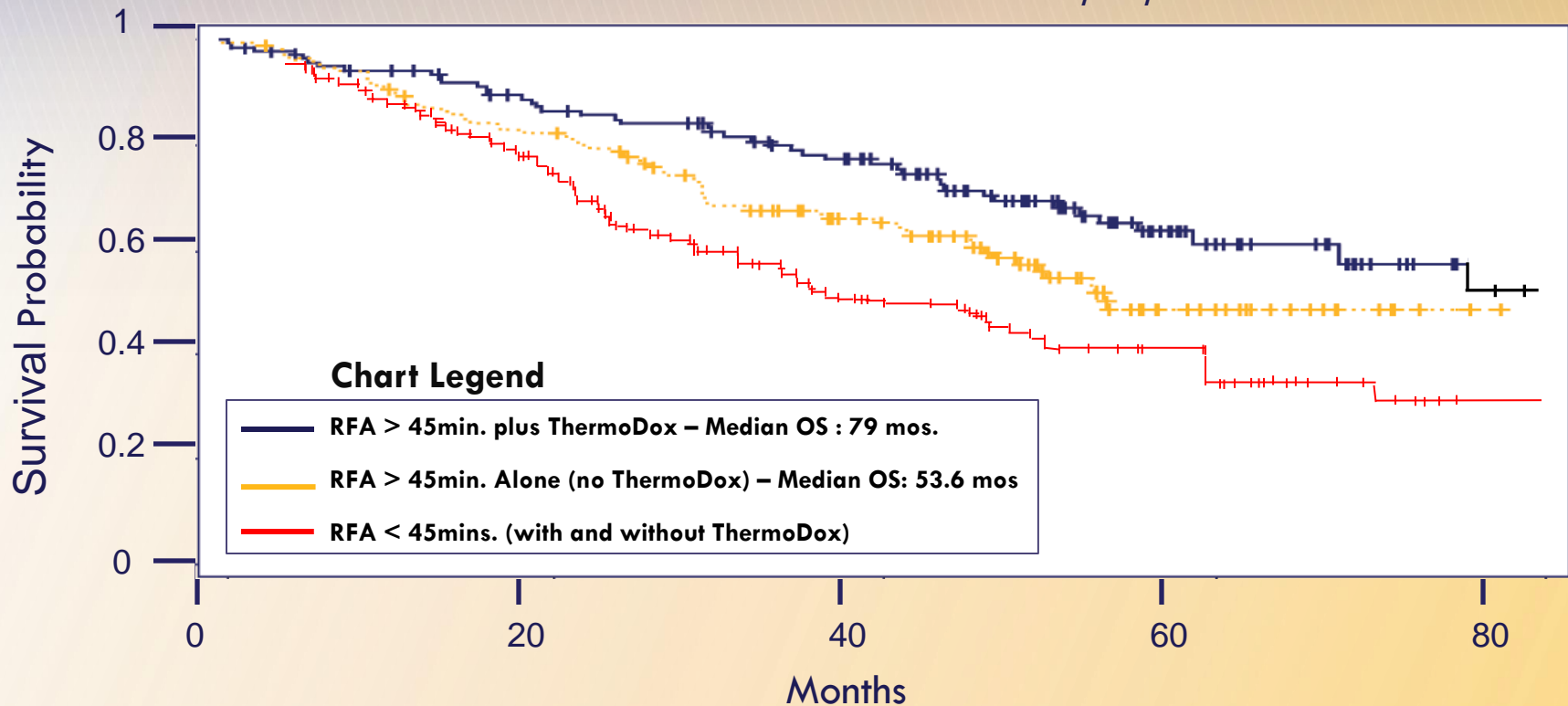
- ThermoDox infused IV ~15 minutes prior to sRFA
- ThermoDox concentrates in the “Thermal Zone” over a 45 minute period
- Doxorubicin is released in the “Thermal Zone” expanding treatment area

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

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

167 Patients RFA < 45 minutes

## OVERALL SURVIVAL as of 7/15/2015



**OS sRFA > 45mins. +/- ThermoDox**

**HR=0.63 (95% CI 0.43 - 0.93) P Value=0.0198**

sRFA **45** Standardized RFA > 45 mins.

**Celsion**



# Phase 3 OPTIMA Study Design

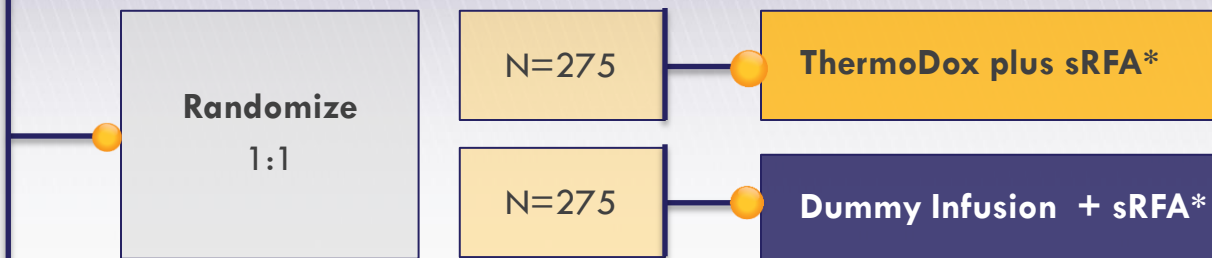
## ThermoDox Plus RFA <sup>45</sup>

### 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



### Primary Endpoint

Overall Survival (OS)

### Secondary Endpoints

Progression Free Survival; Safety

### Interim Efficacy Analysis

118 OS Events /  $HR < 0.61$

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

\*Standardized Radiofrequency Ablation > 45 minutes

# Phase 2 RCW Breast Cancer Study

## ThermoDox + Hyperthermia

### Phase 2 DIGNITY Study

#### Primary Objectives

- Evaluated local-regional breast tumor response. 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
- Established pharmacokinetic bioequivalence between ThermoDox manufactured at two different manufacturing sites.

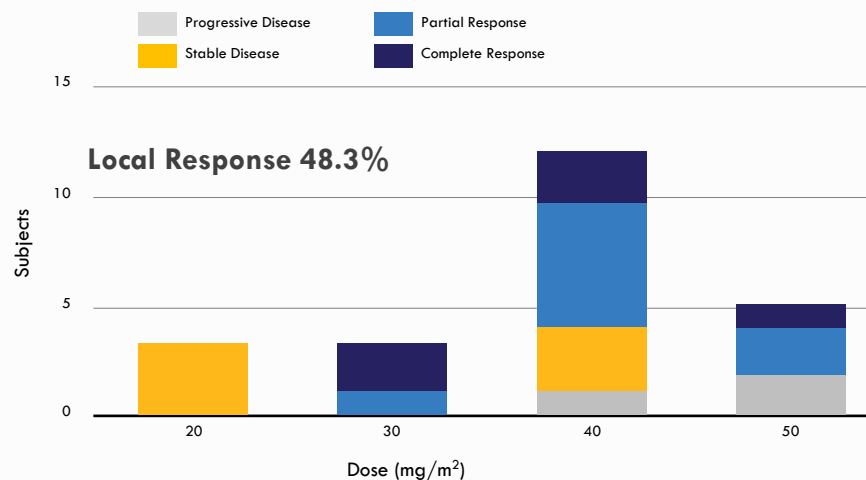
Limited Treatment Options



Complete Response



Combined Phase 1 Data (n = 29)



# Euro-DIGNITY Study

## ThermoDox + Hyperthermia + Radiation

### Primary Objective


- Evaluate loco-regional breast tumor control in patients undergoing Tri-Modal Therapy

**70 patients to be enrolled**

### Open Label Design

### Study Timelines

- Site Activation: Q4 2015
- Recruitment Period: 2016 – 2017
- LP/LV through Follow-Up: 2018



### A. ALBA ON 4000

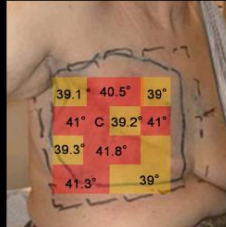
THERMODOX OPTIMAL HT DEVICE MAIN REQUIREMENTS



#### 2. POWER-TEMPERATURE AUTHOMATIC CONTROL FOR HOMOGENEUS TEMPERATURE DISTRIBUTION

39.5° C      42° C

THERMODOX INACTIVATION	THERMODOX ACTIVATION	THERMODOX INACTIVATION
------------------------	----------------------	------------------------



Temperature map data (°C):

39.1°	40.5°	39°
41°	39.2°	41°
39.3°	41.8°	
41.3°		39°

# Early Access Program in Europe

## ThermoDox for RCW and HCC Patients

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

- License/Distribution Agreement signed with myTomorrows in 2015
- EAP in Europe is over \$6B per year

### **EAP Requirements**

- Product must be in Phase 2 trials or later; have shown evidence of efficacy
- May be provided to patient with serious disease and no alternative therapy exists
- Awareness and physician training are used to educate the medical community

### **EAP Pricing/Market**

- HCC and RCW breast cancer ~40K incidence
- 23 EU countries + Israel.
- Product pricing determined by the Sponsor

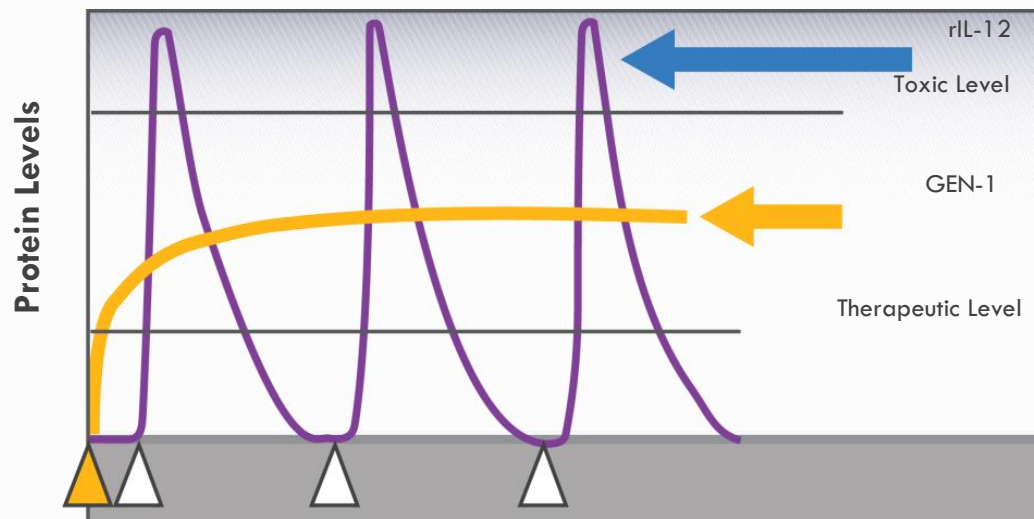
# GEN-1

## Novel PPC Nanoparticle + Plasmid Coded for IL-12

### Rationale for Local Therapy with DNA Nanoparticles

- Local production of potent cytokine IL-12
- IL-12 recruits immune system with multiple mechanisms of action
- NK Cell Activation, T Cell Activation, Anti-angiogenesis, and T-Reg Suppression
- Avoids serious toxicities and poor pK of recombinant IL-12

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



## Local Immunotherapy Addresses Limitations of Chemotherapy

The diagram illustrates a patient's torso with a peritoneal dialysis catheter inserted into the peritoneal cavity. A blue tube connects the catheter to a dialyzer. Labels include 'Peritoneal cavity' pointing to the abdominal area and 'Peritoneal Mets' pointing to yellow starburst shapes representing metastases. The dialyzer is shown as a blue rectangular unit with two ports.

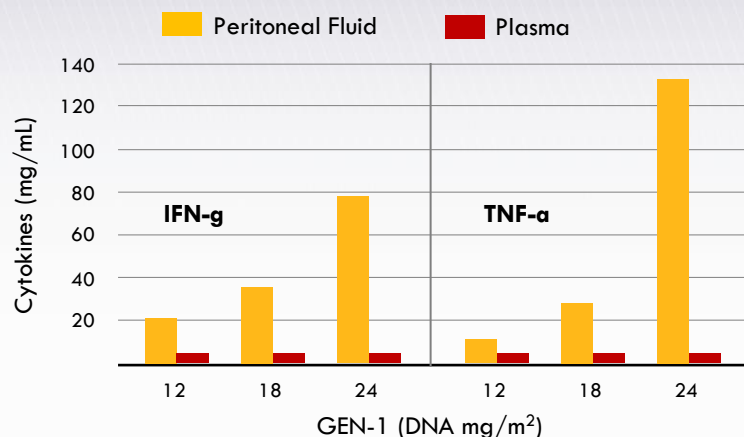


- IL-12 Plasmid

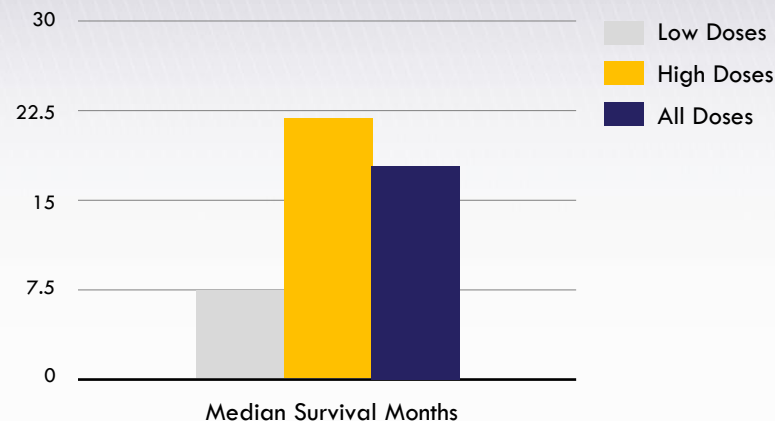
- GEN-1 causes the production of IL-12 at cancer site
- IL-12 addresses cancer cells that are chemo-resistant by recruiting the immune system, inducing powerful anti-cancer mechanisms
- Clinical experience strongly supports development in combination with first line treatment



### 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



# Phase IB Study

## Platinum Resistant Ovarian Cancer conducted by GOG

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

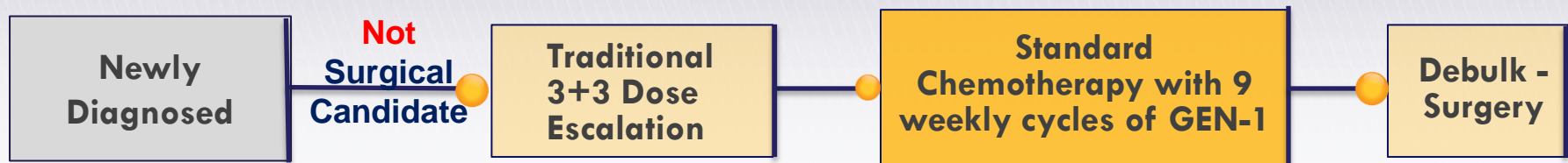
Traditional 3+3 Escalation Design (n=16; enrollment completed)

Dose Level	GEN-1 (mg/m <sup>2</sup> )	Doxil (mg/m <sup>2</sup> )	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<sup>2</sup> dose
  - Clinical Response Rate (SD+PR+CR) (all doses): > **50%**
  - Clinical Response Rate (SD+PR+CR) at 36 mg/m<sup>2</sup> dose: **86%**
- Compares favorably to current SoC in Platinum Resistant Ovarian Cancer
  - Single Agent Doxil in four (4) previous studies: Overall Clinical Response Rate (SD+PR+CR) of < **50%**

# 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)

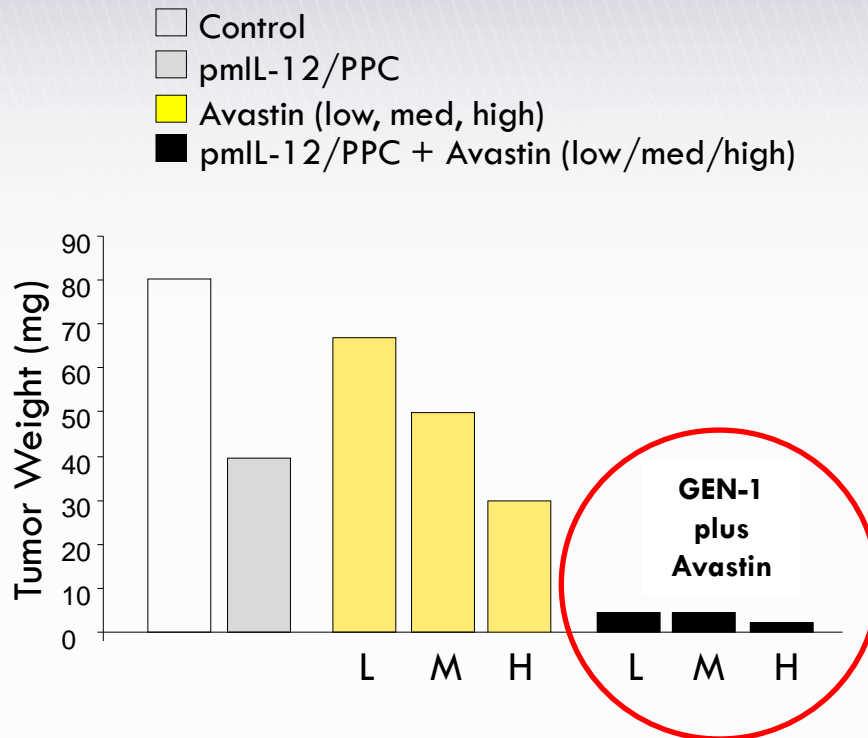
### Secondary Endpoints

pCR, PFS,  $\uparrow$ IFN $\gamma$ ,  $\uparrow$ IL-12,  $\downarrow$ VEGF

# GEN-1 + Avastin in Disseminated Ovarian Cancer

## Pre-Clinical Study

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



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

Human ovarian cancer cells were implanted IP.

- Avastin treatment at 5 mg/kg, 10 mg/kg \and 20 mg/kg was initiated 9 days after tumor implantation
- pmlL-12/PPC was given weekly for 4 weeks; 14 days after tumor implantation

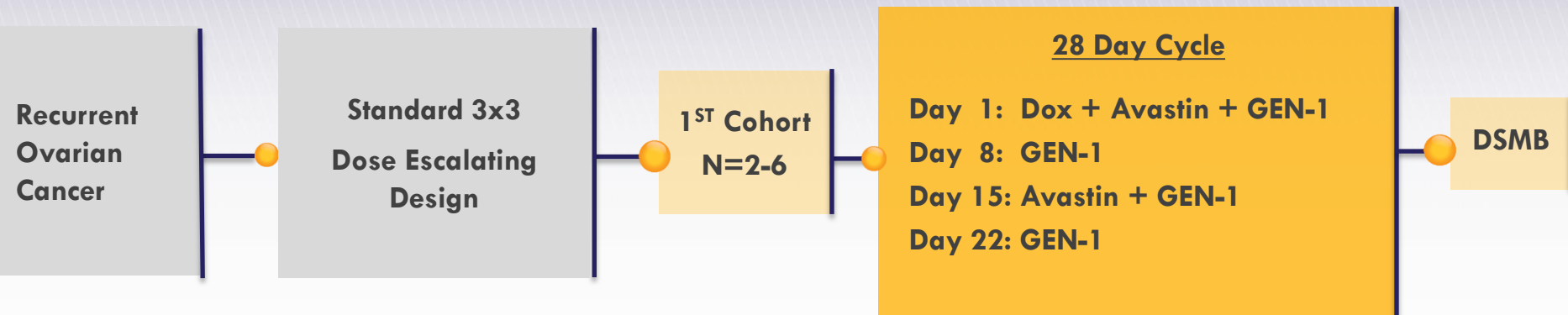
# Phase I/II in Platinum Resistant Ovarian Cancer

## GEN-1 in Combination with Avastin + Doxil

- Inhibition of VEGF by IL-12 through the interferon-gamma pathway helps explain 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. Now completing pre-clinical safety study with Doxil + Avastin
- Phase 1 design to optimize GEN-1 and Avastin dosing to enhance safety profile and establish efficacy for Phase 2
- IND this year; Initiate trial in early 2016

# GEN-1 with Avastin<sup>®</sup> and Doxil

## Platinum – Resistant Recurrent Ovarian Cancer



**Primary Endpoint**

Optimal Safe Dose

**Secondary Endpoint**

Clinical Objective Tumor Response

**Secondary Endpoint  
(Biological/Immunological)**

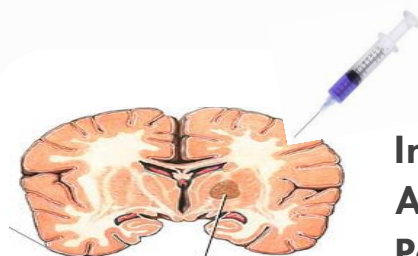
IL-12, IFN- $\gamma$ , TNF- $\alpha$ , IL-10, TGF- $\beta$ , and VEGF concentrations in the blood and peritoneal fluid

# Glioblastoma Multiform

Phase I in 2016

## Preclinical Experience

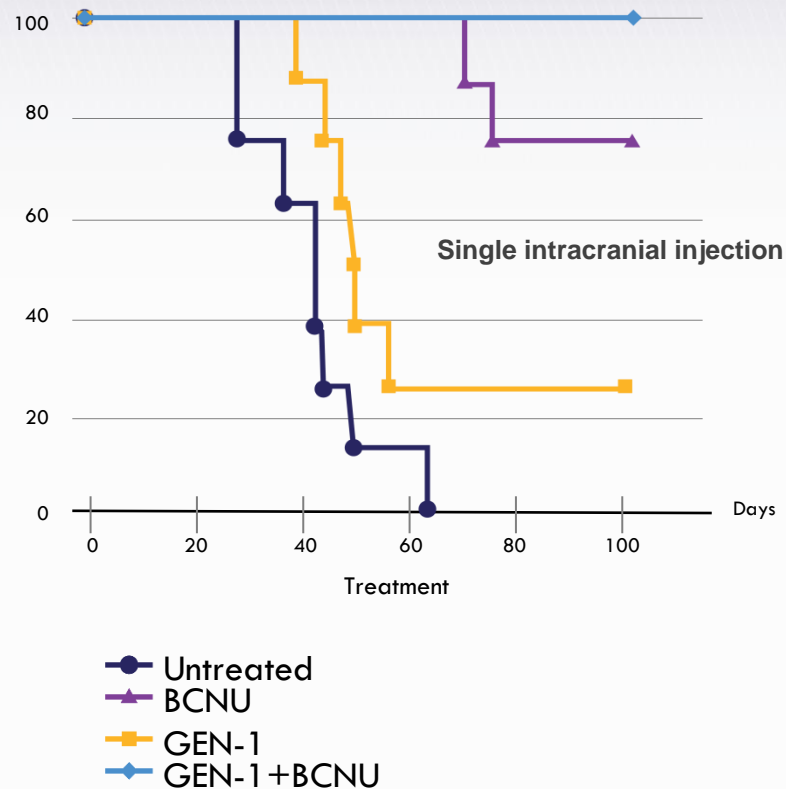
- IL-12 expression for one month in normal brain tissue
- Mechanism for local administration
- Bio-distribution studies
- Safety established



Brain tumor

**Intra-Cranial  
Administration  
Post-Resection**

## Survival Benefits in Glioma Model



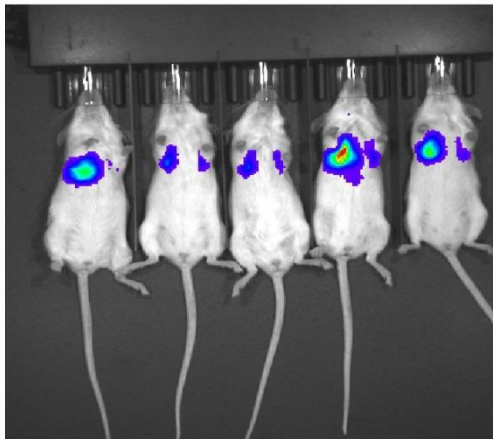
# TheraSilence

## Systemic RNA Delivery to the Lung

### Staramine and Polymeric Systems

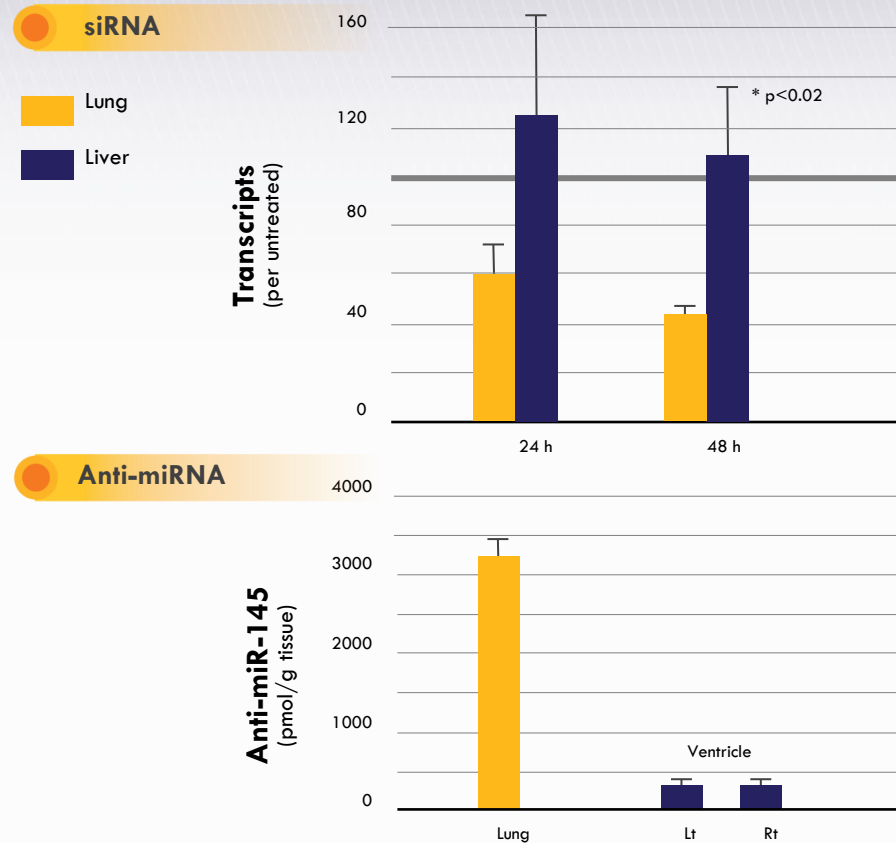
- mRNA pre-clinical program in NHP and murine models
- siRNA pre-clinical PAH and other pulmonary diseases
- miRNA in Lung Cancer

### Intravenous Delivery of Luciferase mRNA



Celsion Nano-Particle

### Unique Lung Delivery - Independent of RNA Type

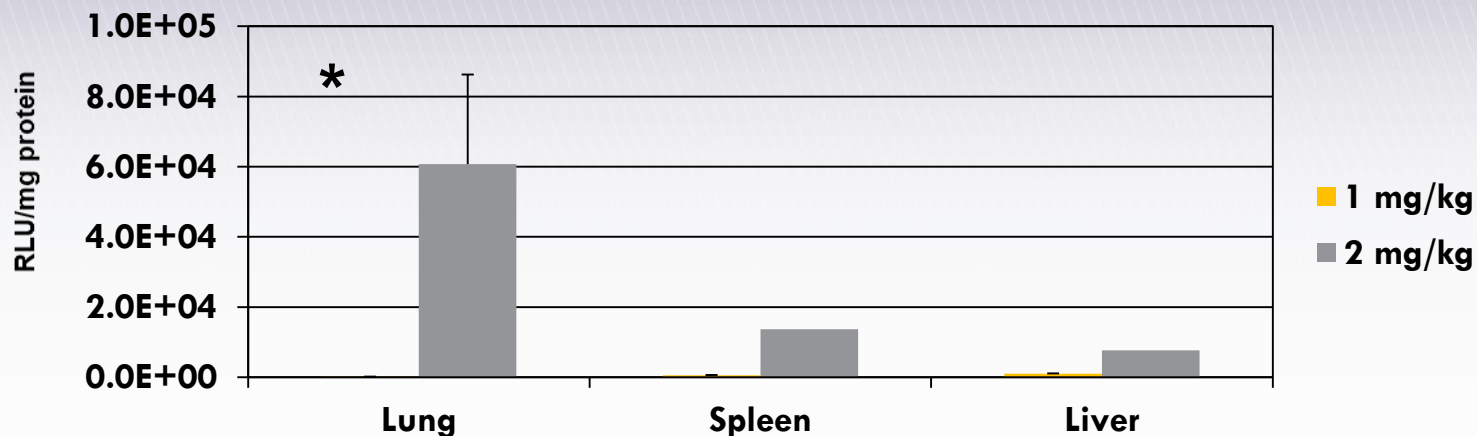




# mRNA Tissue Luciferase Expression Levels

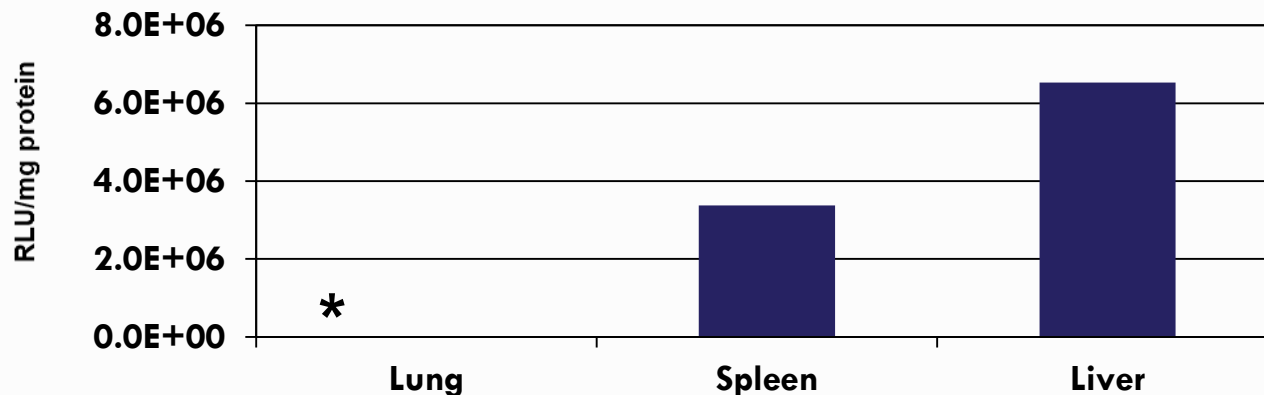
## Non-Human Primate Study

### TheraSilence - BD15



\*Average of 4 samples

### LDF Control



# 2015 Goals

## First Half

- ThermoDox Early Access Program in Europe for RCW Breast Cancer ✓
- GEN-1 Development Overview & FDA Acceptance of Neoadjuvant Ovarian Study ✓
- OS Sweep for HEAT Study as of 1/15/2015 – Subgroup HR = 0.629; Pvalue= 0.02 ✓
- TheraSilence (GEN-2) Non-Human Primate Data ✓
- Interim Data on US DIGNITY Phase II Study ✓
- Final Clinical Data from GEN-1 Phase 1b GOG Ovarian Study (ASCO) ✓

## Second Half

- OS Sweep for HEAT Study as of 7/15/15 – Subgroup HR = 0.63;  $P_{\text{value}} = 0.0198$  ✓
- ThermoDox Early Access Program Expanded for Primary Liver Cancer (HCC) ✓
- Initiate Patient Enrollment: GEN-1 Neo-adjuvant Ovarian Study
- Translational Data from Phase 1b GOG Ovarian Study (GEN-1 + Doxil)
- **1<sup>st</sup> Patient in the ThermoDox EAP in Europe**
- GEN-1: Pre-Clinical Efficacy Data in Ovarian Cancer and GBM
- **Collaboration Agreement(s) for TheraSilence RNA Delivery**
- IND Submission for Phase I Study of GEN-1 + Doxil + Avastin Ovarian Study
- Final Clinical Data from ThermoDox Phase 2 DIGNITY Study (San Antonio Breast)
- Initiate Patient Enrollment: ThermoDox Euro-DIGNITY Study

# Financial Overview

<b>Cash &amp; Investments (6/30/15)</b>	<b>\$31 million</b>
<b>Estimated cash usage per month</b>	<b>~\$1.4 million</b>
<b>Market Capitalization</b>	<b>\$50 million</b>
<b>Common shares outstanding</b>	<b>23 million</b>
<b>Fully diluted shares outstanding</b>	<b>31 million</b>
<b>Avg Daily Trading Volume</b>	<b>~ 275,000</b>



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