



Corporate Presentation

May 2017

Celsion

# Safe Harbor Statement

This presentation and any statements made for and during any presentation or meeting contain forward-looking statements related to Celsion Corporation ("Celsion") under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995 and are subject to risks and uncertainties that could cause actual results to differ materially from those projected.

These statements may be identified by the use of forward-looking words such as "anticipate," "planned," "believe," "forecast," "estimated," "expected," and "intend," among others. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. Such factors include, among other things, unforeseen changes in the course of research and development activities and in clinical trials; possible changes in cost, timing and progress of development, preclinical studies, clinical trials and regulatory submissions; Celsion's ability to obtain and maintain regulatory approval of any of its product candidates; possible changes in capital structure, financial condition, future working capital needs and other financial items; changes in approaches to medical treatment; introduction of new products by others; success or failure of our current or future collaboration arrangements, risks and uncertainties associated with possible acquisitions of other technologies, assets or businesses; the ability to obtain additional funds for operations; the ability to obtain and maintain intellectual property protection for technologies and product candidates and the ability to operate the business without infringing the intellectual property rights of others; the reliance on third parties to conduct preclinical studies or clinical trials; the rate and degree of market acceptance of any approved product candidates; possible actions by customers, suppliers, strategic partners, potential strategic partners, competitors and regulatory authorities; compliance with listing standards of The NASDAQ Capital Market; and those risks listed under "Risk Factors" as set forth in Celsion's most recent periodic reports filed with the Securities and Exchange Commission, including Celsion's Form 10-K for the year ended December 31, 2016.

While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Celsion does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances except as required by law.



# Oncology Company

Capital Efficient Drug Development

Nanoparticle-Based Technology Platforms Driving Growth

## Targeting Chemotherapy

Phase III Study in Primary Liver Cancer (The OPTIMA Study)

Phase II Study in RCW Breast Cancer (The Euro-DIGNITY Study)

## Gene Mediated Immuno-Oncology

Phase I Neoadjuvant Therapy in 1<sup>st</sup> Line Ovarian Cancer (The OVATION Study)

Phase I/II Combination Therapy with Avastin 2<sup>nd</sup> line Ovarian Cancer

# Our Two Clinical Stage Platforms

## **LTSL**

Lysolipid Thermally  
Sensitive Liposomes  
Known Chemotherapeutics

## **TheraPlas™**

Synthetic Non-viral Vector  
DNA Plasmids coded for  
Therapeutic Proteins

## **ThermoDox®**

### Targeted Doxorubicin Delivery

- Phase III Study Enrolling in HCC
- Phase II Study in RCW Breast Cancer

## **GEN-1**

### Localized IL-12 Immunotherapy

- Neoadjuvant Study in 1<sup>st</sup> Line Ovarian

# Pipeline of Targeting Therapeutics

	INDICATION	PRODUCT CANDIDATE	PRE-CLINICAL	PHASE 1-2	PHASE 3
Clinical	Primary Liver Cancer	ThermoDox/OPTIMA Study	Phase III enrolling		
	RCW Breast Cancer	ThermoDox /Euro-DIGNITY	Phase II initiating		
	Ovarian Cancer	GEN-1 /OVATION Study	Phase I enrolling		
Pre-Clinical	MI Bladder Cancer	ThermoDox	Efficacy/Safety/Toxicology Complete		
	Glioblastoma	GEN-1	Efficacy/Safety/Toxicology		



Chemotherapy

ThermoDox<sup>®</sup>

Celsion



# Hepatocellular Carcinoma

## Large and Deadly Global Cancer

### ● 5<sup>th</sup> most prevalent

- 800,000 global incidence growing 5% annually
- By 2030, expected to be the #3 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 3 years<sup>1</sup>
- Curative surgery is approx. 20% of patients

### ● Local therapies include:

- RFA, TACE and radiation
- RFA is the dominant treatment with local recurrence rates >50% for lesions >3 cm
- ThermoDox + RFA addresses limitations of current standard of care by **“Expanding the Treatment Zone”**

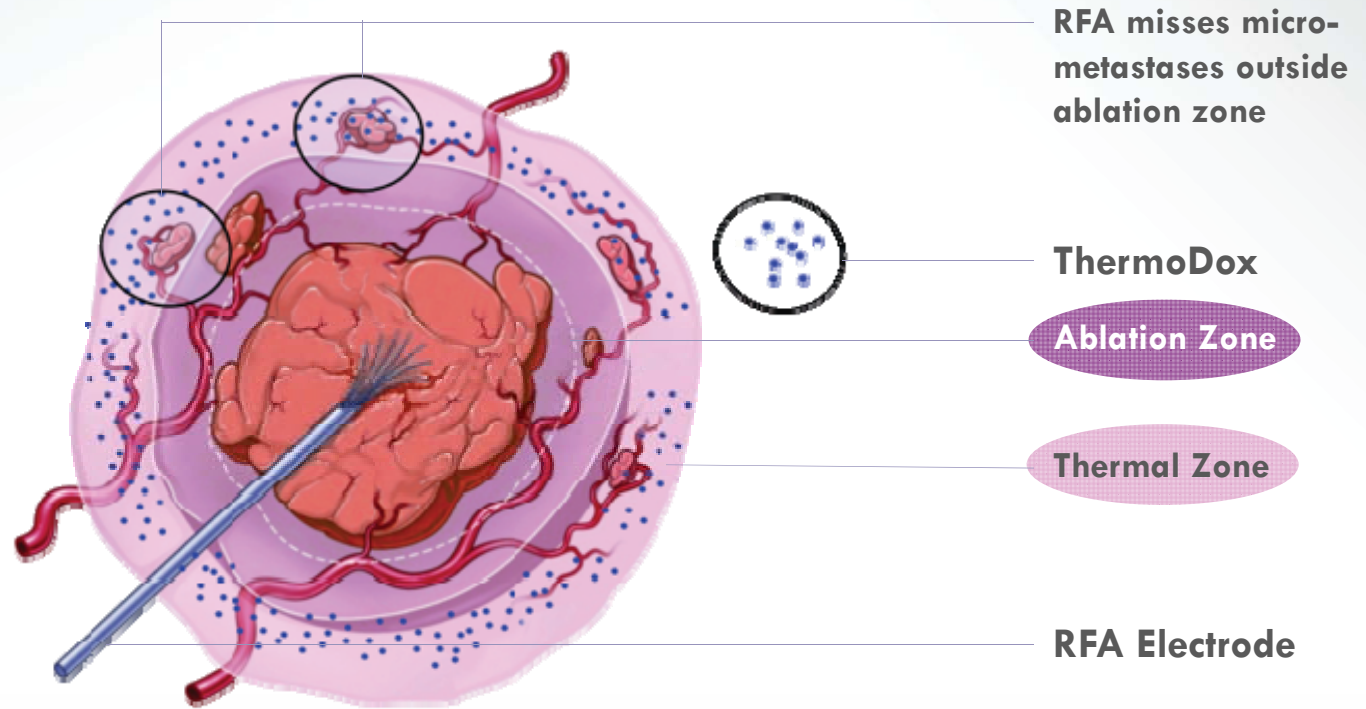
**Market Opportunity >200K Patients**

<sup>1</sup> Journal of Hepatology 2012 vol. 56 | 908-943

# ThermoDox + RF Ablation

## Expanding the Treatment Zone to Address RFA's Limitations

- ThermoDox infused IV ~15 minutes prior to sRFA
- RFA ablates tumor and creates a "Thermal Zone" in margin surrounding the tumor
- Doxorubicin is released in the "Thermal Zone" expanding treatment area and killing the metastases outside the ablation zone



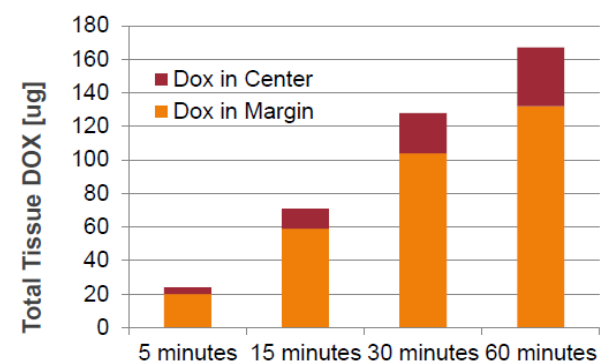
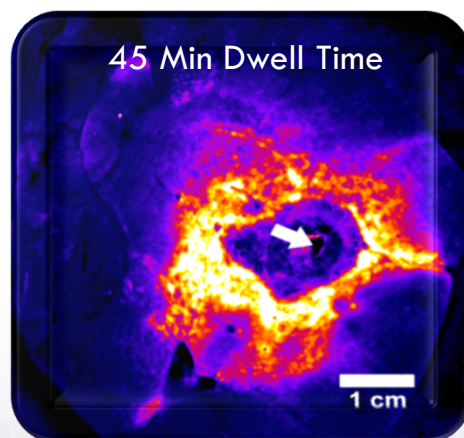
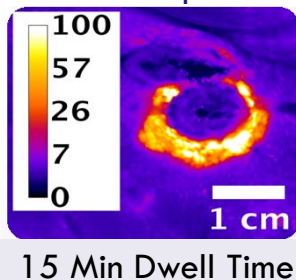


# The Optima Study

## Learnings from the 700 patient *HEAT Study*: RFA Dwell Time Matters

- Pre-specified analysis of HEAT Study data showed that patients with smaller lesions (3-5 cm) appeared to do better with ThermoDox
- When standardized for dwell time and lesion number, ThermoDox patients demonstrated clear difference in Overall Survival
- The hypothesis that dwell time increases local doxorubicin concentration was demonstrated in a computational model
- The hypothesis was further tested and demonstrated in an in-vivo pig model:

More RFA time = More local Dox deposition



Ablation Time

- Multivariate analysis points to RFA dwell time with ThermoDox as the factor correlating to significant improvement in survival

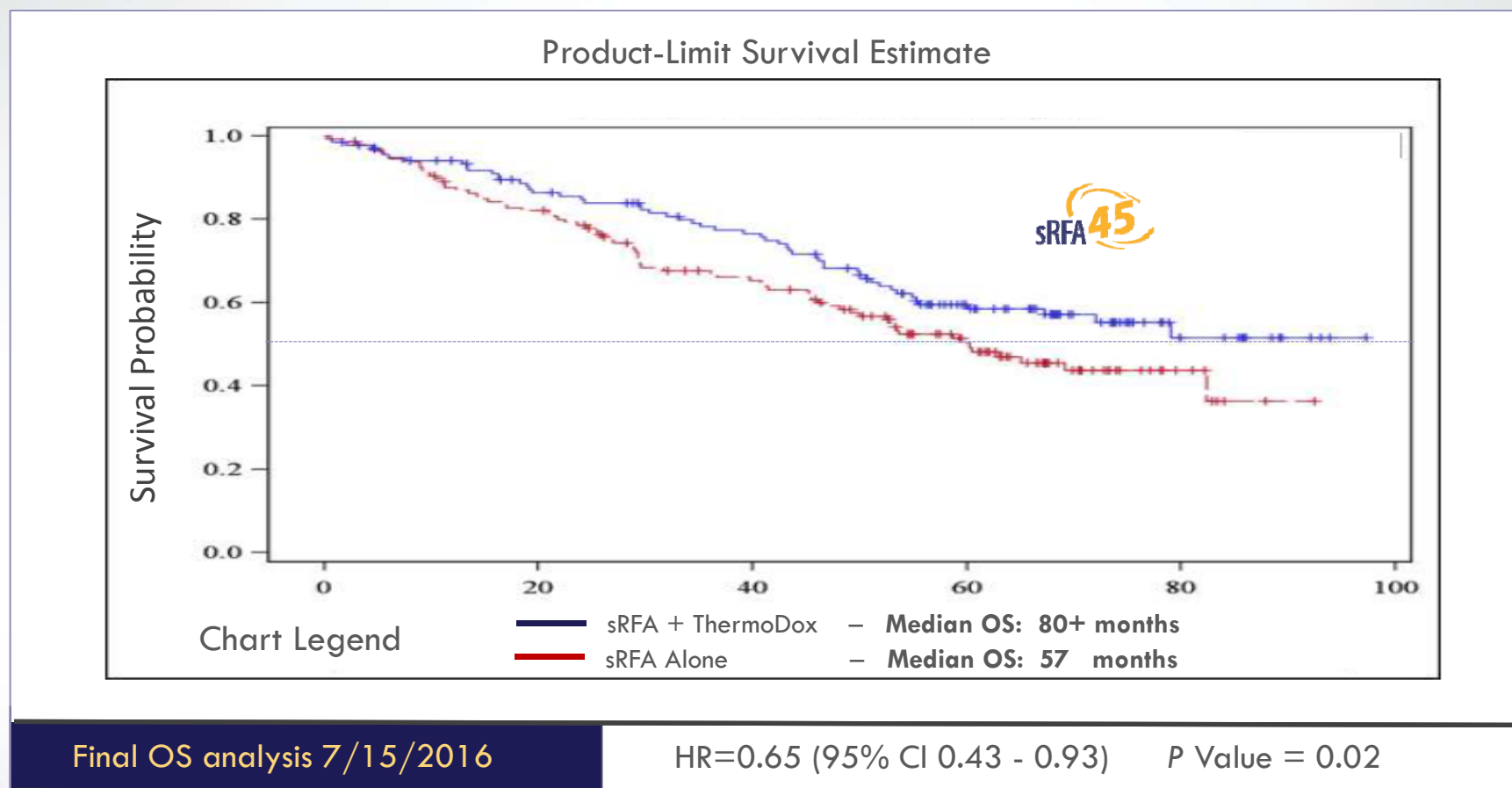
Celsion

# ThermoDox: HCC

## Sub-Group Analysis of HEAT Study Data

### More than Two Years Overall Survival Benefit

285 Patients with Standardized RFA > 45 minutes (sRFA)



# RFA Dwell Time Matters

## Independent Confirmation from NIH Analysis of HEAT Study Data

**Evaluated RFA burn time per tumor volume (min/ml) for correlation with clinical outcome**

- **Overall Findings**

Increase in *burn time* per tumor volume improves OS in ThermoDox + RFA patients compared to RFA only patients, n=437

- **For all single lesion RFA + ThermoDox patients:**

One unit increase in RFA duration per tumor volume improved OS by 20% (p=0.017, n=227)

- More dramatic differences in subgroup of patients with RFA burn times per tumor volume > 2.5 minutes/ml
- Cox multiple covariate analysis showed OS to be significant (p=0.038, HR=0.85)



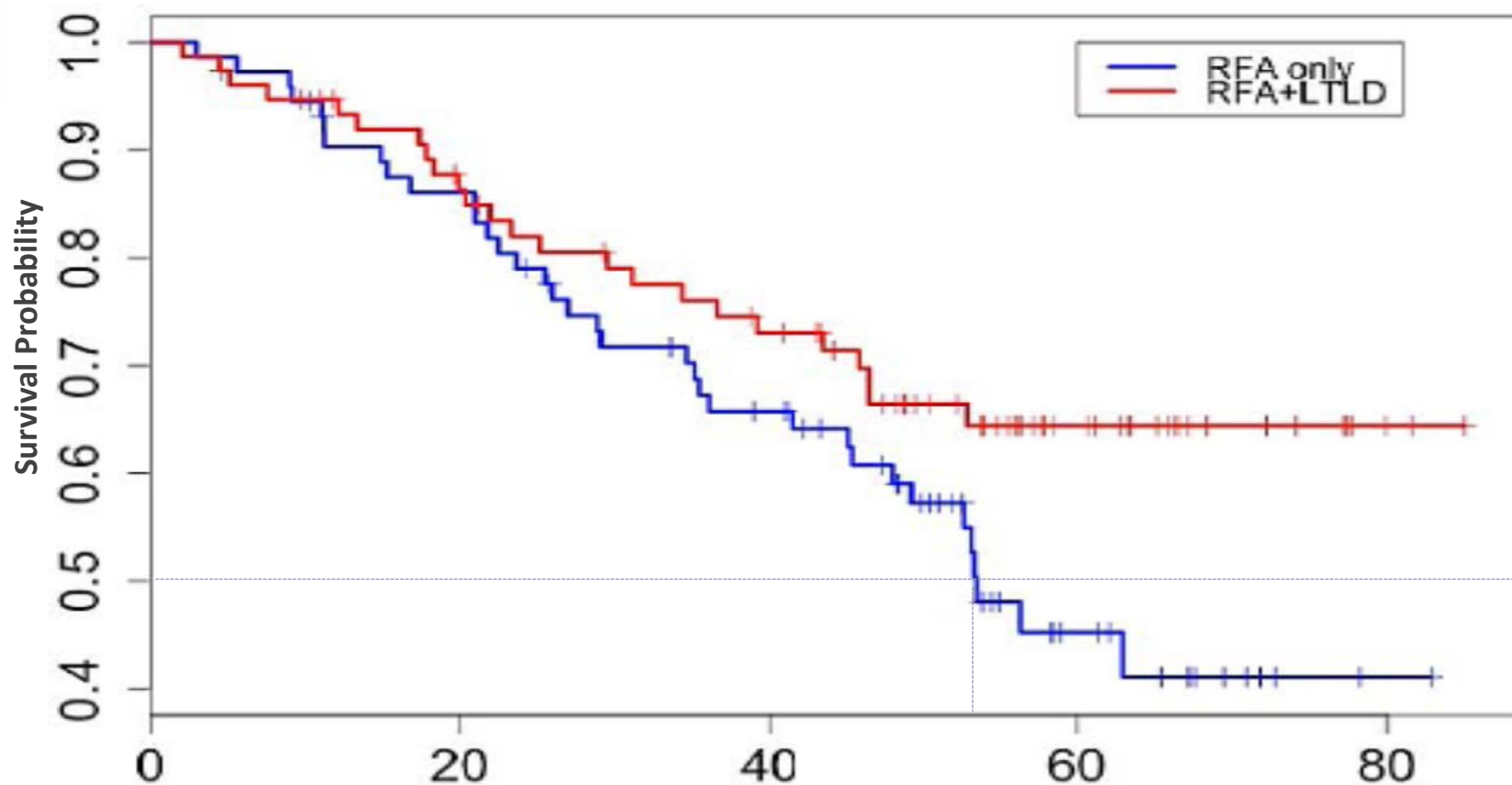
- **For all single lesion RFA-only patients:**

Burn time per tumor volume did not have a significant effect (p=0.57, n=210)

Celsion

# NIH Confirms HEAT Study Sub-Group

Subjects with burn time  $> 2.5$  min/ml ( $\sim 45$ mins/3cm tumors)



# ThermoDox + RFA vs TACE

## Intermediate HCC

		Study	Lesion size	N	Median OS (mos.)	Year 1 (%)	Year 2 (%)	Year 3 (%)
		HEAT Study ITT Population	Overall: 2.7 - 7.5 cm Mean: 4.2 cm Median: 4 cm	701	53 mos.	85%	76%	64%
HEAT Study Subgroup		<b>ThermoDox + RFA ≥ 45 min.</b>	<b>Overall: 2.7 - 6.9 cm Mean: 4.3 cm Median: 4.2 cm</b>	<b>138</b>	<b>80+ mos.</b>	<b>94%</b>	<b>85%</b>	<b>77%</b>
		RFA alone time ≥ 45 min.	Overall: 3 - 6.9 cm Mean: 4.2 cm Median: 3.9 cm	147	57 mos.	88%	79%	69%
		Ikeda et al (TACE) 2013	Median: 3.9; range 1-11 > 3.0	99 64	37 mos. NR	90% NR	75% 66%	NR NR
		Burrel (DEB TACE) 2012	BCLC A BCLC B	41 63	54 mos. 48 mos.	90% 88%	NR NR	68% 64%

Celsion



# The Clinical Management of Hepatocellular Carcinoma in the United States, Europe, and Asia

A Comprehensive and Evidence-Based Comparison and Review

Zhi Ven Fong, MD; and Kenneth K. Tanabe, MD

Hepatocellular carcinoma (HCC), the most common primary malignancy of the liver, represents 1 of the leading causes of cancer deaths in the world with an estimated 21,670 deaths in the United States in 2013. In contrast to other malignancies, there is an array of treatment options for HCC involving several specialties in the multidisciplinary care of the patient. Consequently, vast heterogeneity in management tendencies has been observed. The objective of this report was to review and compare guidelines on the management of HCC from the United States (National Comprehensive Cancer Network), Europe (European Association for the Study of the

Cancer September 15, 2014

**TABLE 5.** Survival Outcomes 3 Years After Surgical Resection and Radiofrequency Ablation of Hepatocellular Carcinoma Based Dichotomized Based on Tumor Size

Tumor Size, cm	3-Year OS Rate, %			3-Year DFS Rate, %		
	Resection	RFA	P	Resection	RFA	P
≤3	79	50	NS	67	34	NS
>3	59	24	.007	43	12	.003

Abbreviations: DFS, disease-free survival; NS, nonsignificant; OS, overall survival; RFA, radiofrequency ablation.

HEAT Study showed 3-Year OS Rate of 77% (July 2015)

Celsion



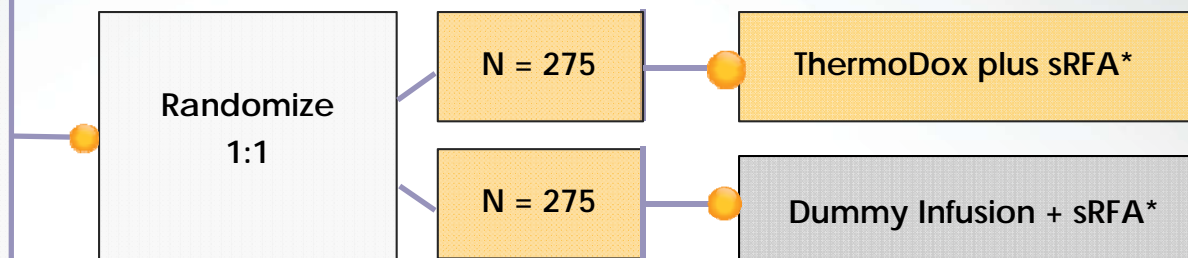
# Phase III OPTIMA Study Design

## 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
- RFA Technique (Percutaneous, Laparoscopy, or Surgical)



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

~ 65 Clinical Sites in  
14 Countries

# ThermoDox for RCW Breast Cancer

## Difficult to Treat with Severe Complications

- Breast cancer recurring in the chest wall affects ~35,000 post-mastectomy patients in the US and Europe annually<sup>1</sup>
- Up to 40% of women undergoing a mastectomy as primary treatment will experience local recurrence
- Local tumor control is a primary objective in treating these patients

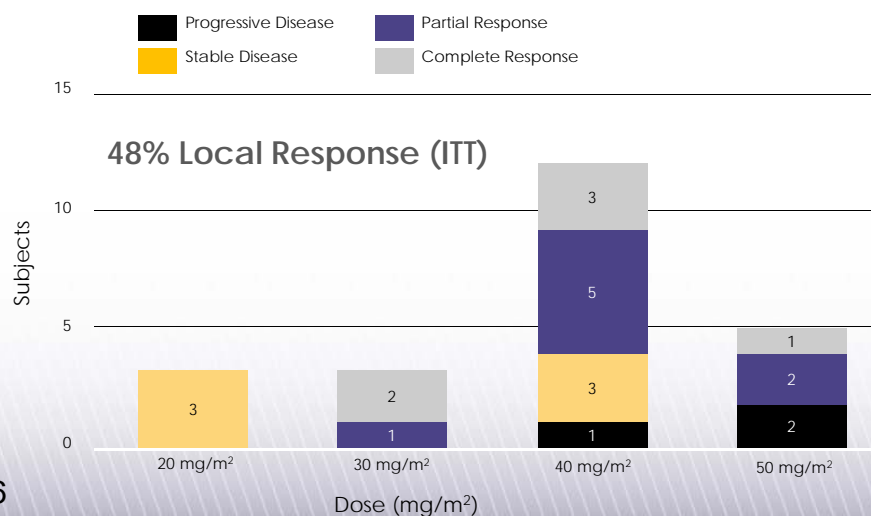
Limited Treatment Options



Complete Response



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



### Phase 2 US DIGNITY Study

Evaluate local-regional breast tumor response.  
17 patients enrolled; 12 evaluable for efficacy

- All evaluable patients experienced stabilization of disease; 67% of patients in evaluable population observed local responses - 5 CRs & 3 PRs
- 47% Local Response (ITT)

<sup>1</sup> Agency for Healthcare Research and Quality 2009; Bian et al. 2008; Clemons et al. 2001

# ThermoDox: Euro-DIGNITY Study

## ThermoDox + Hyperthermia + Radiation

### Primary Objectives

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

**70 patients to be enrolled**

### Open Label Design

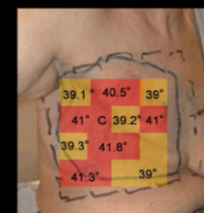
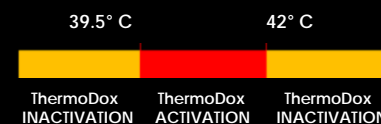
### Study Timelines

- Site Activation: Pending
- Expected Recruitment Period: H2-2017 through 2018

### OPTIMAL HT DEVICE



Automated Temperature Control provides homogeneous, local temperature distribution



Celsion

# ThermoDox for Bladder Cancer

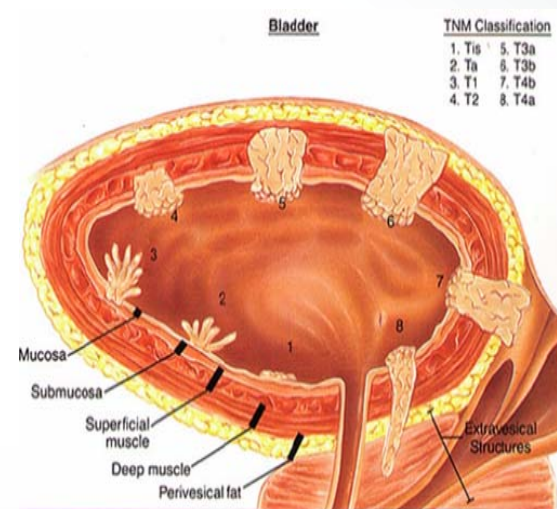
## Preclinical Studies at Duke University and the NIH

**79,000 new cases and 16,800 deaths in the U.S. (2015)**

- 70% of new cases are non-muscle invasive
- Incomplete response of bladder tumors to intravesical drugs. like doxorubicin, has been attributed to inadequate drug delivery

## Two independent preclinical studies conducted by Duke University and National Institutes of Health

- ThermoDox delivers doxorubicin at 10x that of free dox and at levels well above required therapeutic effects
- Minimizes unwanted drug delivery to other organs
- Heat-targeted drug delivery has the potential to make systemic chemotherapy more effective while improving safety







# **GEN-1 IL-12**

## **Immuno-Oncology Program**

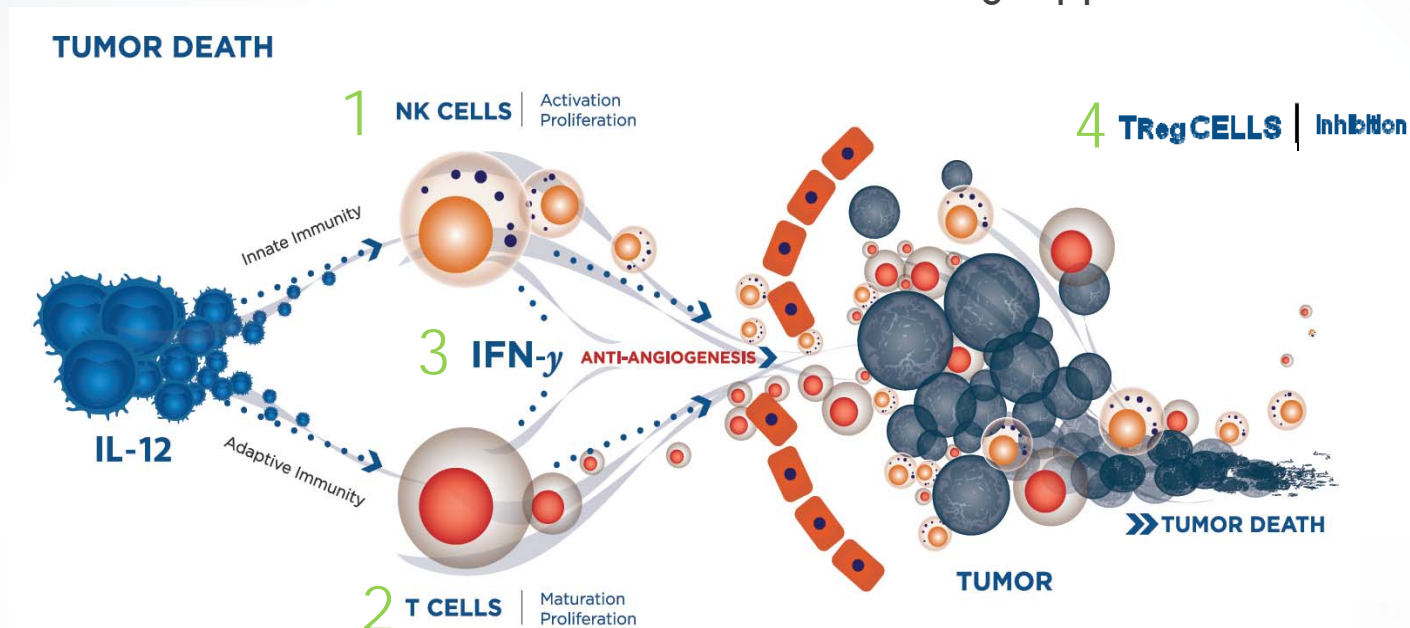
**Celsion**

# IL-12

A Powerful Immune Modulating Agent; Multiple Mechanisms

## Mechanisms of Action

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





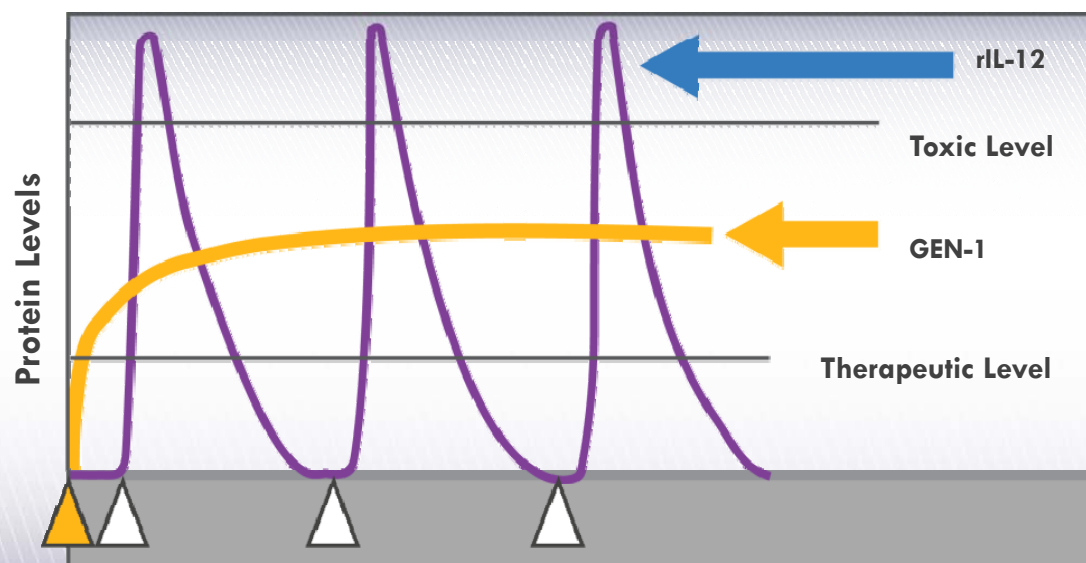
# GEN-1

## Novel Polymer-Plasmid DNA Nanoparticle

### ● Rationale for Local Therapy with GEN-1 DNA Nanoparticles

- Loco-regional production of potent cytokine IL-12 avoid toxicities and poor pK associated with systemic recombinant IL-12
- Persistent local delivery of IL-12 lasts up to one week and dosing can be repeated
- Ideal for long-term maintenance therapy

### ● GEN-1 is an Effective Alternative to rIL-12 Poor pK



100 nm

Celsion

# Ovarian Cancer

## Large and Deadly Global Cancer

### ● 8<sup>th</sup> most diagnosed cancer among women

- 225,000 annual incidence worldwide
- 22,280 in US and 100,000 in developed countries
- 14,240 deaths in 2015

### ● 5<sup>th</sup> highest mortality among women

- 5-year survival rate for all stages is >50%
- Survival rate reduces dramatically if not localized cancer
- 15% diagnosed with localized cancer, eligible for potentially curative surgery

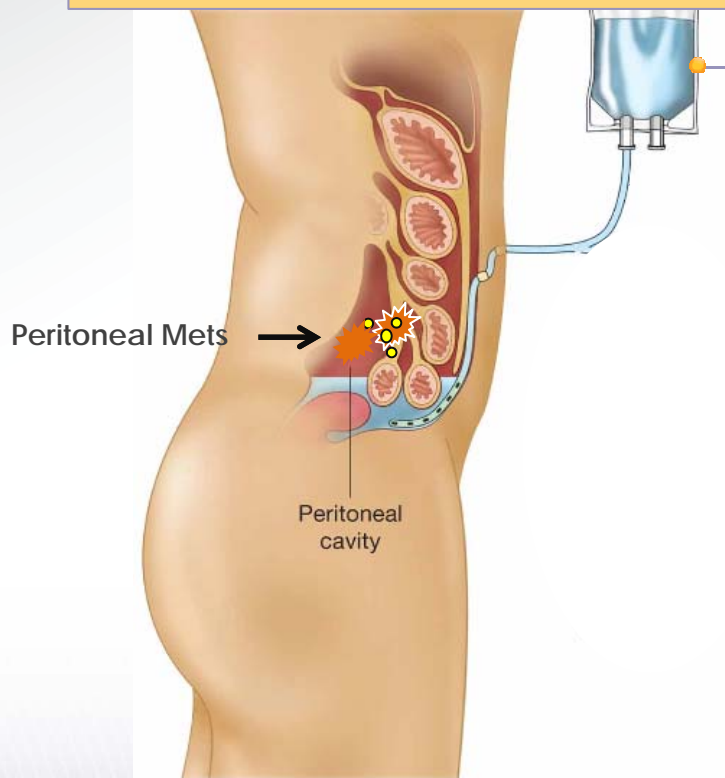
### ● Local therapies for ovarian cancer

- 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

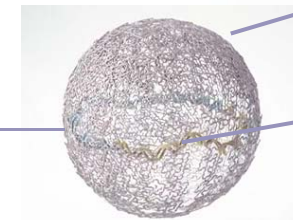
# GEN-1 for Ovarian Cancer

## Local Immunotherapy

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



**GEN-1**



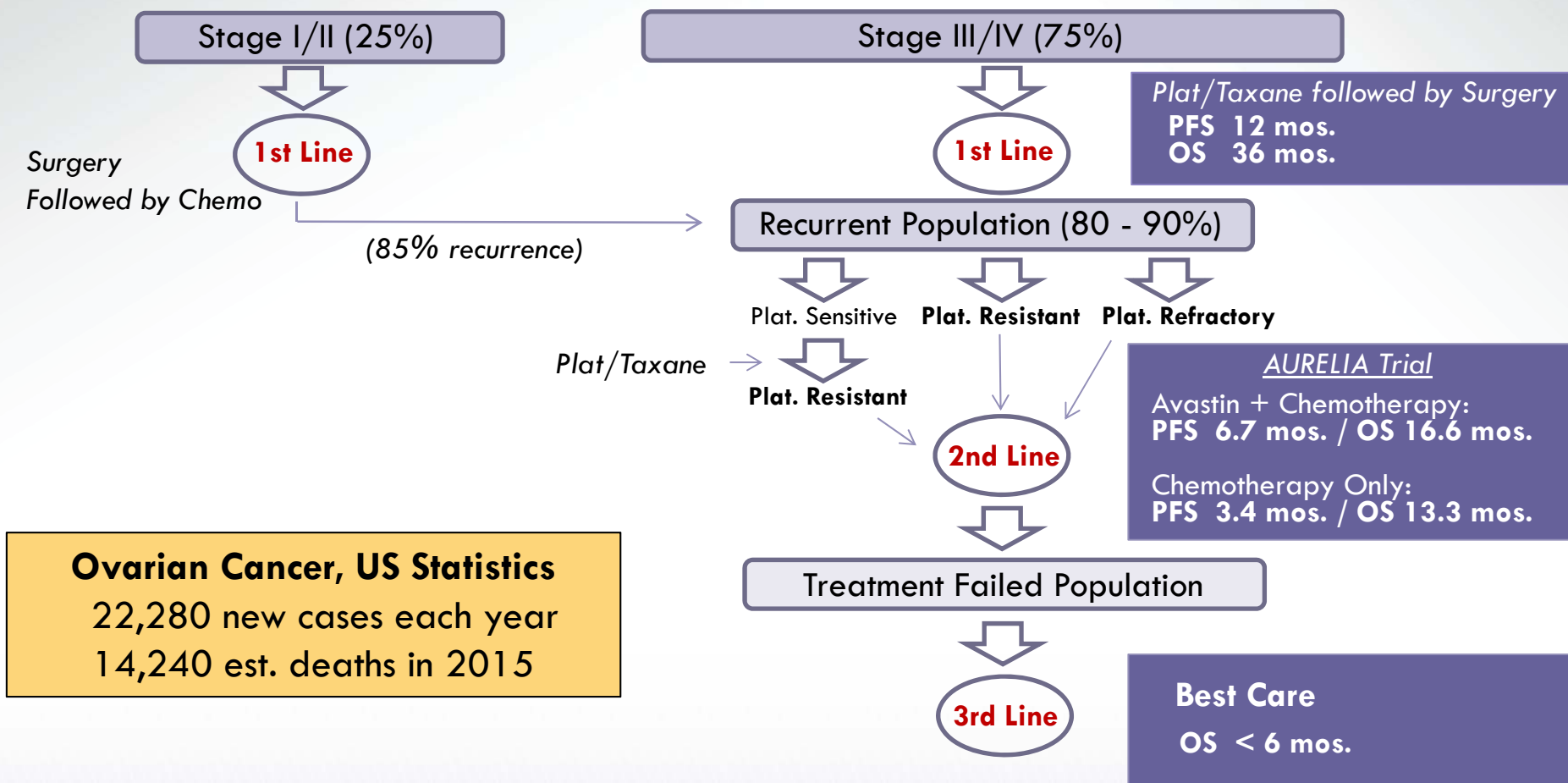
**PPC Delivery System  
(PEG-PEI-Chol)**

**IL-12 Plasmid**

**Stable Nanoparticles  
for Local Delivery**

- GEN-1 causes the controlled local production of IL-12 at the cancer site
- IL-12 addresses cancer cells by recruiting the immune system, inducing powerful anti-cancer mechanisms for an immune attack

# Ovarian Cancer Treatment Path



**Ovarian Cancer, US Statistics**  
22,280 new cases each year  
14,240 est. deaths in 2015

# GEN-1 Phase I Study

1<sup>st</sup> Line in Ovarian Cancer

## The OVATION Study



Neoadjuvant Study in Newly Diagnosed Ovarian Cancer Patients

To determine safety, dose, and feasibility in target patient population

Primary Endpoint

Optimal Therapeutic Dose

Secondary Endpoints

pCR, PFS,  $\uparrow$ IFN $\gamma$ ,  $\uparrow$ IL-12,  $\downarrow$ VEGF and Tumor-specific T-cell response CD4+, CD8+

Celsion



# OVATION Study

## Totality of Results in the First Four Patient Cohorts, n=12

- 1<sup>st</sup> 12 patients dosed, there has been a
  - 100% disease control rate (DCR)
  - 75% objective response rate (ORR)
- Of the 11 surgically resected patients:
  - All patients had successful resections of their tumors
  - One patient demonstrated a complete pathological response (PCR) <sup>1</sup>
  - 55% of patients had a R0 (margin – negative) resection
- Of the 5 treated (so far) at the highest doses, all were R0
- All patients show a greater than 90% drop in their CA-125 protein levels <sup>2</sup>
- Ratio of CD8+/FoxP3+ cells was increased in all four evaluable patients demonstrating a potential shift in tumor environment to favoring immune stimulation following NACT + GEN-1 therapy

1 In a 332 patient GOG Study, cPR's were seen in < 6.5% of patients; Strong correlation with improvement in Overall Survival (median OS of 72 mos.) which is a 3 year improvement over patients having a microPR or macroPR (Pvalue = 0.018)

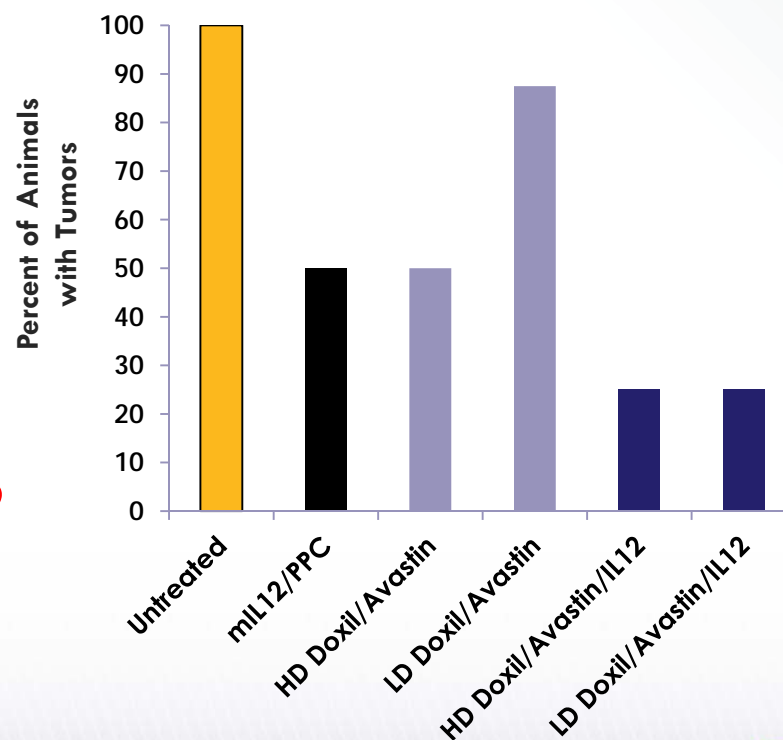
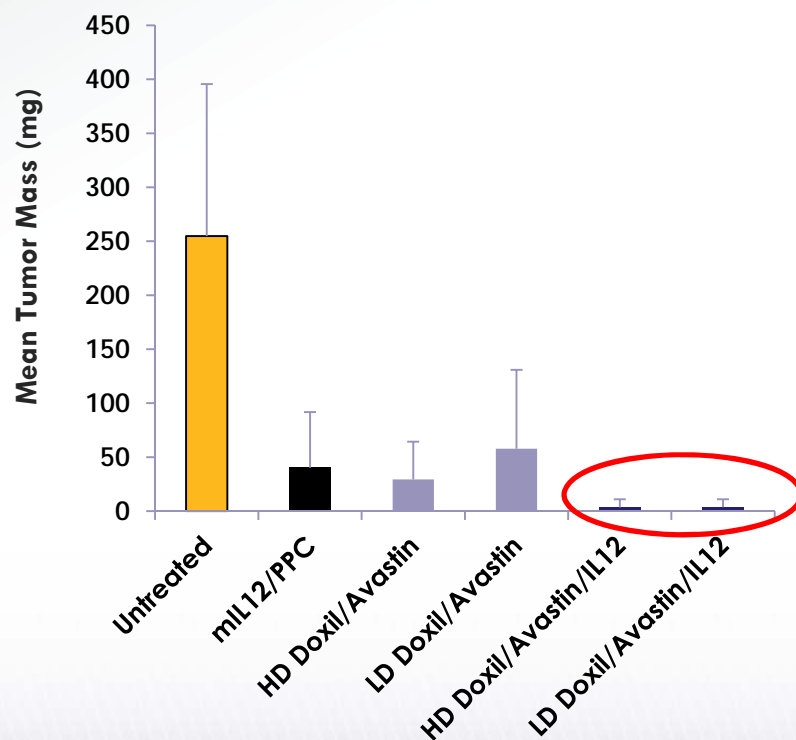
2 50% reduction in CA-125 levels from baseline that is maintained for > 2 weeks is considered a CA-125 Responder



# GEN-1: Preclinical Studies

## GEN-1 + Doxil + Avastin

- Doxil + Avastin is 2<sup>nd</sup> line SoC for platinum-resistant ovarian cancer.
- Adding Avastin Results in a > 98% Reduction in Tumor Burden



HD Doxil = 7.5 mg/kg  
LD Doxil = 3.75 mg/kg

N = 8 /group  
Animals euthanized 59 days after tumor implant

# GEN-1 + Doxil Phase 1b Trial

## 2<sup>nd</sup> Line

GEN-1 (mg/m <sup>2</sup> )	Doxil (mg/m <sup>2</sup> )
24	40
36	40
36	50

### Clinical Observations

- All doses well tolerated with no DLTs
- Clinical response rate:
  - All doses: > **50%**
  - Highest dose: **86%**
- Single agent Doxil comparison 4 previous studies:
  - Clinical RR < **50%**

### Translational Data Findings

Significant increase in immunologically active IL-12 levels in peritoneal fluid

- Detectable for at least one week after GEN-1 dosing
- Not detectable or very low in plasma

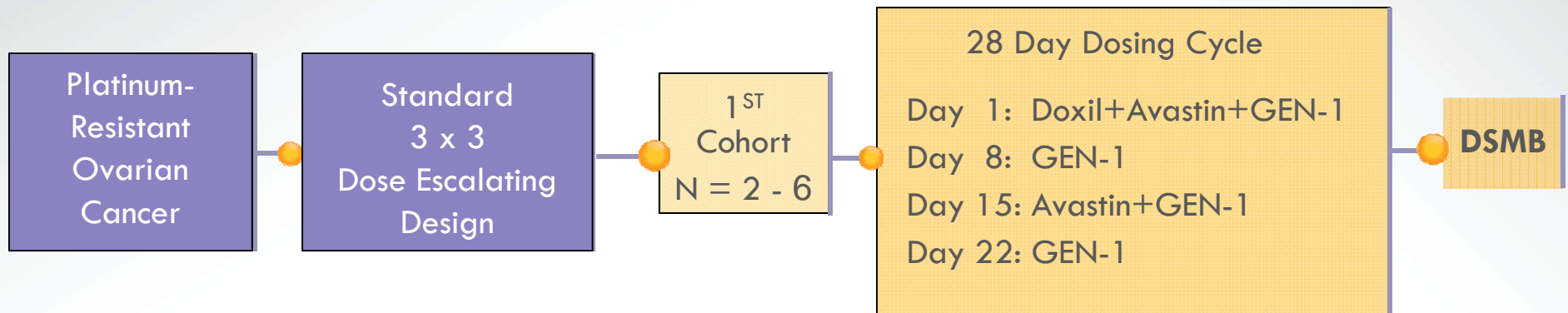
Significant increase in key downstream mediators of IL-12

- IFN- $\gamma$  and TNF- $\alpha$ : ~5-fold increase observed in peritoneal fluid above pre-treatment level with the highest increase observed at 77-fold
- Very low to non-detectable levels of IFN $\gamma$  and TNF- $\alpha$  in plasma



# GEN-1 + Avastin and Doxil Trial Design

## 2nd Line



Primary Endpoint Phase I Primary Endpoint Phase II	Optimal Safe Dose (Max or MTD) Clinical Objective Tumor Response (RECIST)
Secondary Endpoint	IL-12, IFN- $\gamma$ , TNF- $\alpha$ , VEGF
Treatment period	28 day cycles continue until GEN-1 or Avastin treatment is no longer tolerated



# **Milestones & Financials**

**Celsion**

# Milestone Events (2016 - 2018)

	2016				2017				2018			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
ThermoDox												
OPTIMA STUDY		Initiate Enrollment in China ✓	HEAT Study OS Data (China cohort) ✓	NIH Presentation at RSNA ✓	OPTIMA 50% Complete ✓					OPTIMA Enrollment Complete		1st Interim Efficacy Endpoint
Euro-DIGNITY STUDY								Initiate Enrollment		1st Efficacy Assessment (24 pts)		Enrollment Complete
GEN-1												
OVATION STUDY		Efficacy Data from Cohorts 1 & 2 ✓	Translational Research Data from Cohorts 1 & 2 ✓	Efficacy Data from Cohort 3 ✓	Efficacy Data from Cohort 4 ✓	Final Efficacy & TR Data from Cohorts 1-4						
Avastin+Doxil Study	TR Data from Phase 1b Ovarian Study ✓	Pre-Clin Data at AACR ✓						Submit IND for Ph 1/2 Study		Initiate Enrollment		Efficacy & TR data from Phase 1
RNA Delivery												
Lung Cancer		Pre-Clin Data (Collaboration w/ RNA company) ✓					Potential Co-Development Collaboration					

✓ Achieved to-date

# Financial Overview

Cash & Investments (3/31/17)	\$4.5 million
------------------------------	---------------

Estimated cash usage per month	~\$1.33 million
--------------------------------	-----------------

Market Capitalization	\$13 million
-----------------------	--------------

Common shares outstanding	4 million
---------------------------	-----------

Fully diluted shares outstanding	6.1 million
----------------------------------	-------------

Avg Daily Trading Volume	> 2 million
--------------------------	-------------





# Corporate Information

Celsion Corporation  
997 Lenox Drive  
Suite 100  
Lawrenceville, NJ 08648

P 609-896-9100  
F 609-896-2200  
[www.celsion.com](http://www.celsion.com)  
NASDAQ: CLSN

**Celsion**