

# Corporate Presentation May 2017



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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.

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# Offering Summary

Issuer Celsion Corporation

Symbol / Exchange CLSN / NASDAQ CM

Type of Offering S-1 Follow-On

Offering Type Common Stock and Warrants (100% Primary)

Offering Size \$15 million

Marketing Weeks of May 30th – June 5th

Expected Pricing June 14th

Use of Proceeds

Continue funding development of the OPTIMA Study and

the OVATION Study and for general corporate purposes,

including research and development activities, capital

expenditures and working capital

Sole Underwriter Oppenheimer & Co.



# **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 1st 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**



Lysolipid Thermally
Sensitive Liposomes
Known Chemotherapeutics

# ThermoDox<sup>®</sup>

### Targeted Doxorubicin Delivery

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



Synthetic Non-viral Vector DNA Plasmids coded for Therapeutic Proteins

#### GEN-1

### Localized IL-12 Immunotherapy

Neoadjuvant Study in 1st 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				
Pre-Clinical	Ovarian Cancer	GEN-1/OVATION Study		Phase I enrolling			
	MI Bladder Cancer	ThermoDox	Efficacy/Safety/ToxicologyComplete				
	Glioblastoma	GEN-1	Efficacy/Safet	y/Safety/Toxicology			



# **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"

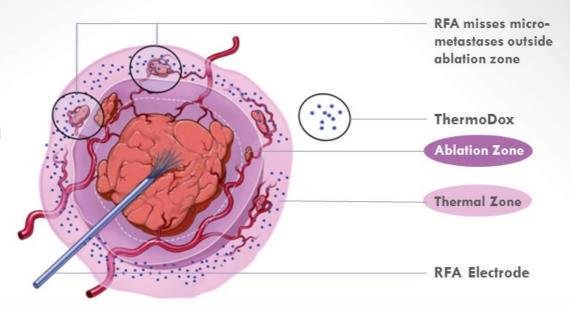
Market Opportunity >200K Patients

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

# ThermoDox + RFAblation

# 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

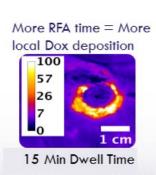


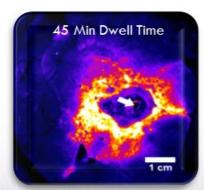


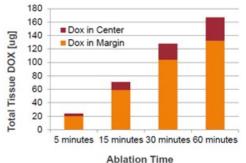
# The Optima Study

#### 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:







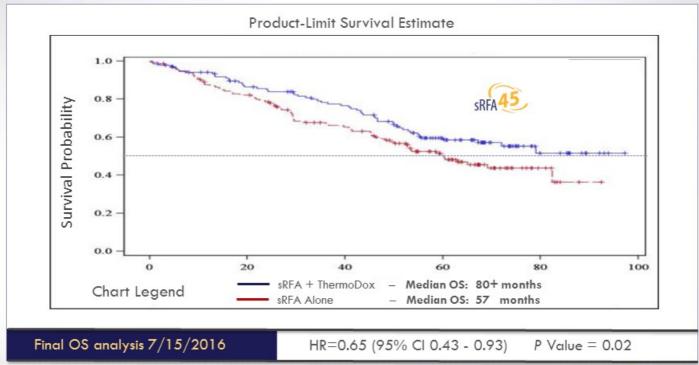
Multivariate analysis
points to RFA dwell time
with ThermoDox as the
factor correlating to
significant improvement in
survival

# 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)

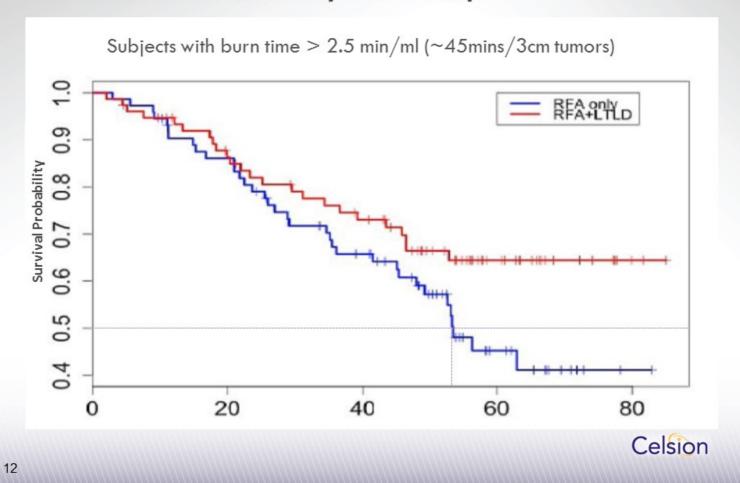


For all single lesion RFA-only patients:

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



# **NIH Confirms HEAT Study Sub-Group**



# ThermoDox + RFA vs TACE

# Intermediate HCC

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

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DEB TACE - Doxorubicin Eluding Beads

# 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

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

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

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

Cancer September 15, 2014

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

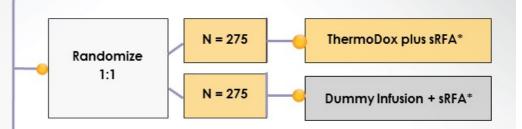
# **Phase III OPTIMA Study Design**

#### **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 Secondary Endpoints	Overall Survival (OS)  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



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Standardized Radiofrequency Ablation > 45 minutes



# 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

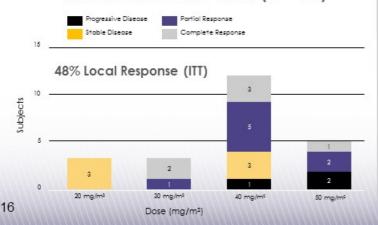
#### **Limited Treatment Options**



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





### ThermoDox for Bladder Cancer

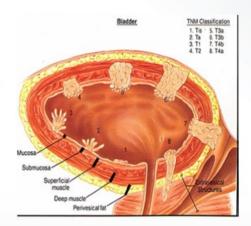
### Preclinical Studies at Duke University and the NIH

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

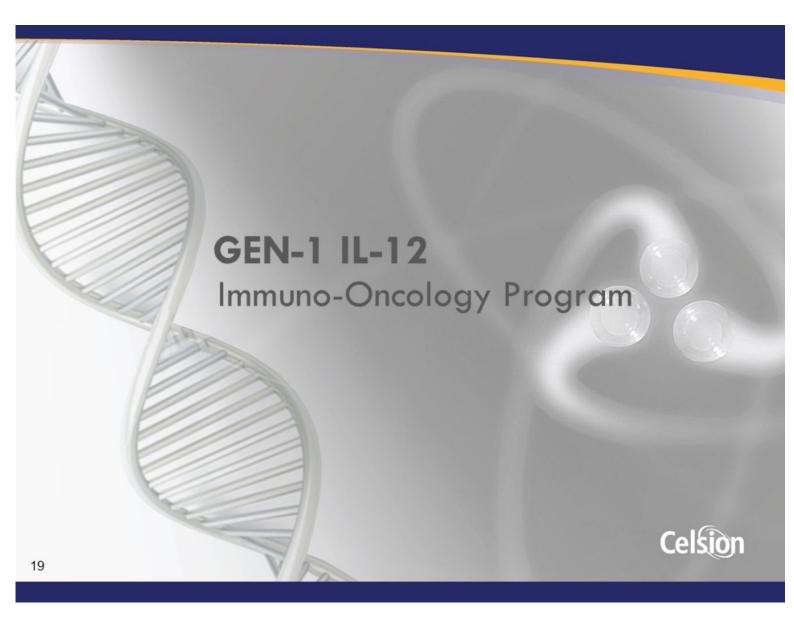
- 70% of new cases are non-muscle invasive
- Incomplete response of bladder tumors to intravesical drugs. like doxorubicin, has been attributed to inadequate drug delivery

### 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





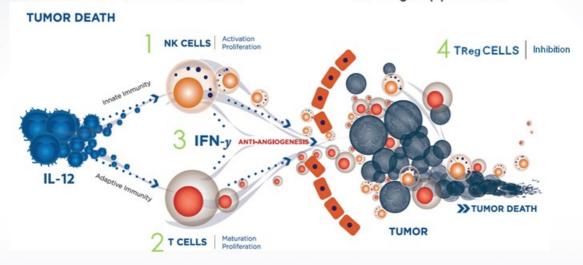


# IL-12

# A Powerful Immune Modulating Agent; Multiple Mechanisms

# Mechanisms of Action

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





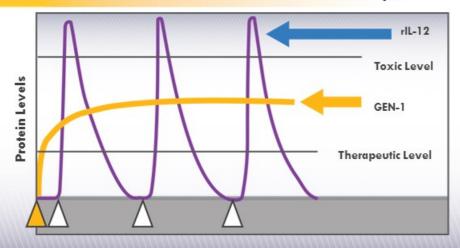
### GEN-1

### 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

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### **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 intraperitoneal administered therapy
  - GEN-1 administered IP; ideal adjuvant to SoC therapy

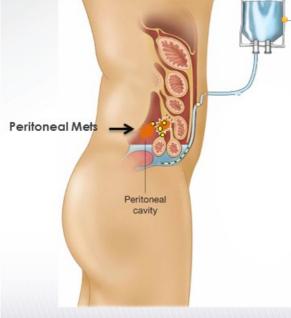


Sources: Cancer Statistics, American Cancer Society; Globocan; SEER database



Local Immunotherapy





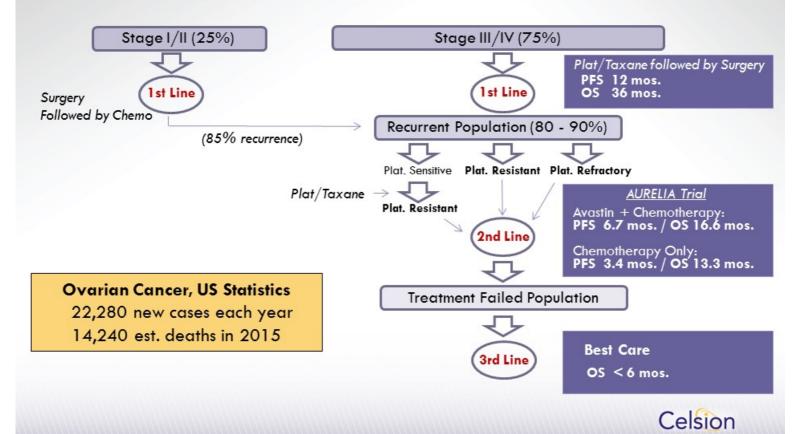


- GEN-1 causes the controlled local production of IL-12 at the cancer site
- IL-12 addresses cancer cells by recruiting the immune system, inducing powerful anti-cancer mechanisms for an immune attack

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### **Ovarian Cancer Treatment Path**

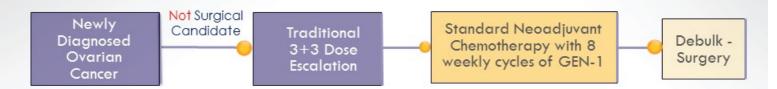


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# **GEN-1Phase I Study**

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, ↑IFNγ, ↑IL-12, ↓VEGF and Tumor-specific T-cell response CD4+,CD8+

# **OVATION Study**

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

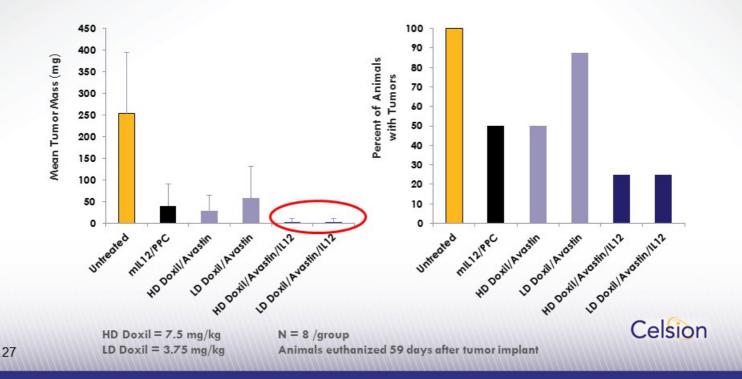
- 1st 12 patients dosed, there has been a
  - 100% disease control rate (DCR)
  - 75% objective response rate (ORR)
- Of the 11 surgically resected patients:
  - All patients had successful resections of their tumors
  - One patient demonstrated a complete pathological response (PCR)
  - 55% of patients had a RO (margin negative) resection
- Of the 5 treated (so far) at the highest doses, all were RO
- All patients show a greater than 90% drop in their CA-125 protein levels 2
- 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)</p>
  - 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



### GEN-1 + Doxil Phase 1b Trial

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

GEN-1 (mg/m²)	Doxil (mg/m²)				
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%</li>

#### **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

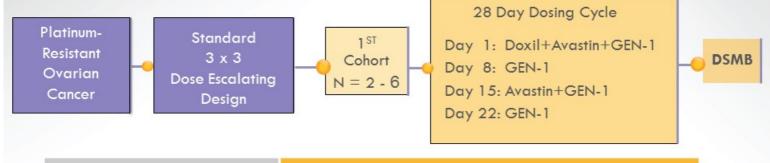
Significant increase in key downstream mediators of IL-12

- IFN- $\gamma$  and TNF- $\alpha$ : ~5-fold increase observed in peritoneal fluid above pretreatment level with the highest increase observed at 77-fold
- Very low to non-detectable levels of IFNγ and TNF-α 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-γ, TNF-α, VEGF
Treatment period	28 day cycles continue until GEN-1 or Avastin treatment is no longer tolerated



# Milestone Events (2016 - 2018)

	2016			2017			2018				
	Q1 Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
ThermoDox											
	Initiate	HEAT Study	NIH						OPTIMA		1st Interim
OPTIMA	Enrollment i		resentation at	OPTIMA	,				Enrollment		Efficacy
STUDY	China 7	√ (China cohorf) √	RSNA √	50% Complete	V				Complete		Endpoint
									1st Efficacy		
Euro-DIGNITY							Initiate		Assessment		Enrollment
STUDY							Enrollment		(24 pts)		Complete
GEN-1											
		Translational									
	Efficac y Dat	a Research Data	Efficacy Data	Efficacy Data	Final Efficacy &						
OVATION	from	, from ,	from	from	TR Data from						
STUDY	Cohorts 1 &	2√Cohorts 1 & 2√	Cohort 3	Cohort 4√	Cohorts 1-4						
	TR Data from	1.44		2							Efficacy & TR
Avastin+Doxil	Phase 1b Pre-Clin Data	at					Submit IND for	Initiate			data from
Study	Ovarian Study AACR	$\sqrt{}$					Ph 1/2 Study	Enrollment			Phase 1
RNA											
Delivery								v.			
	Pre-Clin Dat										
	(Collaboration	on				Potential Co-					
	w/RNA					Development					
Lung Cancer	company					Collaboration					

√ Achieved to-date

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# **Financial Overview**

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

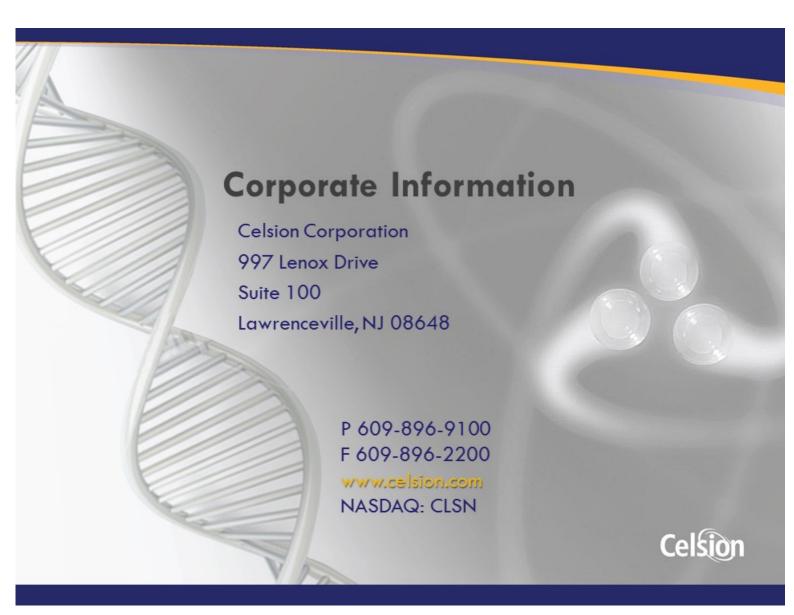
Estimated cash usage per month ~\$1.33 million

Market Capitalization \$13 million

Common shares outstanding 4 million

Fully diluted shares outstanding 6.1 million

Avg Pre-Split Daily Trading Volume > 2 million



Celsion has filed a registration statement (including a prospectus) with the SEC for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement and the other documents Celsion has filed with the SEC for more complete information about Celsion and this offering. You may get these documents for free by visiting EDGAR on the SEC's web site at www.sec.gov. Alternatively, Celsion, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by contacting Oppenheimer & Co. Inc., 300 Madison Avenue, New York, New York 10017.