



2018 Disruptive Growth and Healthcare Conference  
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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, 2017.

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# Clinical-Stage Oncology Company

Two Nanoparticle-Based Technology Platforms Driving Growth

## **LTSL**

Lysolipid Thermally  
Sensitive Liposomes (LTSL)  
Known Chemotherapeutics



### **ThermoDox®**

Targeted Doxorubicin Delivery

- Phase III Study Enrolling in Liver Cancer
- Phase II Study in Recurrent Chest Wall Breast Cancer

## **TheraPlas**

Synthetic Non-viral Vector  
DNA Plasmids Coded for  
Therapeutic Proteins



### **GEN-1**

Localized Interleukin-12 (IL-12) Immunotherapy

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

# Celsion Proprietary Therapeutic Pipeline

## Capital-Efficient Drug Development

|              | INDICATION                                | PRODUCT CANDIDATE       | PRE-CLINICAL                         | PHASE 1-2 | PHASE 3 |
|--------------|---|-------------------------|--------------------------------------|-----------|---------|
| Clinical     | <b>Primary Liver Cancer</b>               | ThermoDox/OPTIMA Study  | Enrolling Phase III<br>~85% Complete |           |         |
|              | <b>Ovarian Cancer</b>                     | GEN-1 /OVATION II Study | Initiating Phase I/II                |           |         |
| Pre-Clinical | <b>Non Muscle Invasive Bladder Cancer</b> | ThermoDox               | Efficacy/Safety/Toxicology Complete  |           |         |
|              | <b>Glioblastoma</b>                       | GEN-1                   | Efficacy/Safety/Toxicology Complete  |           |         |



Chemotherapy

ThermoDox<sup>®</sup>

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# Hepatocellular Carcinoma (HCC)

## High Global Incidence and Mortality

### ● 5<sup>th</sup> most prevalent

- 850,000 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 possible in less than 20% of patients<sup>1</sup>

### ● Current local therapies include:

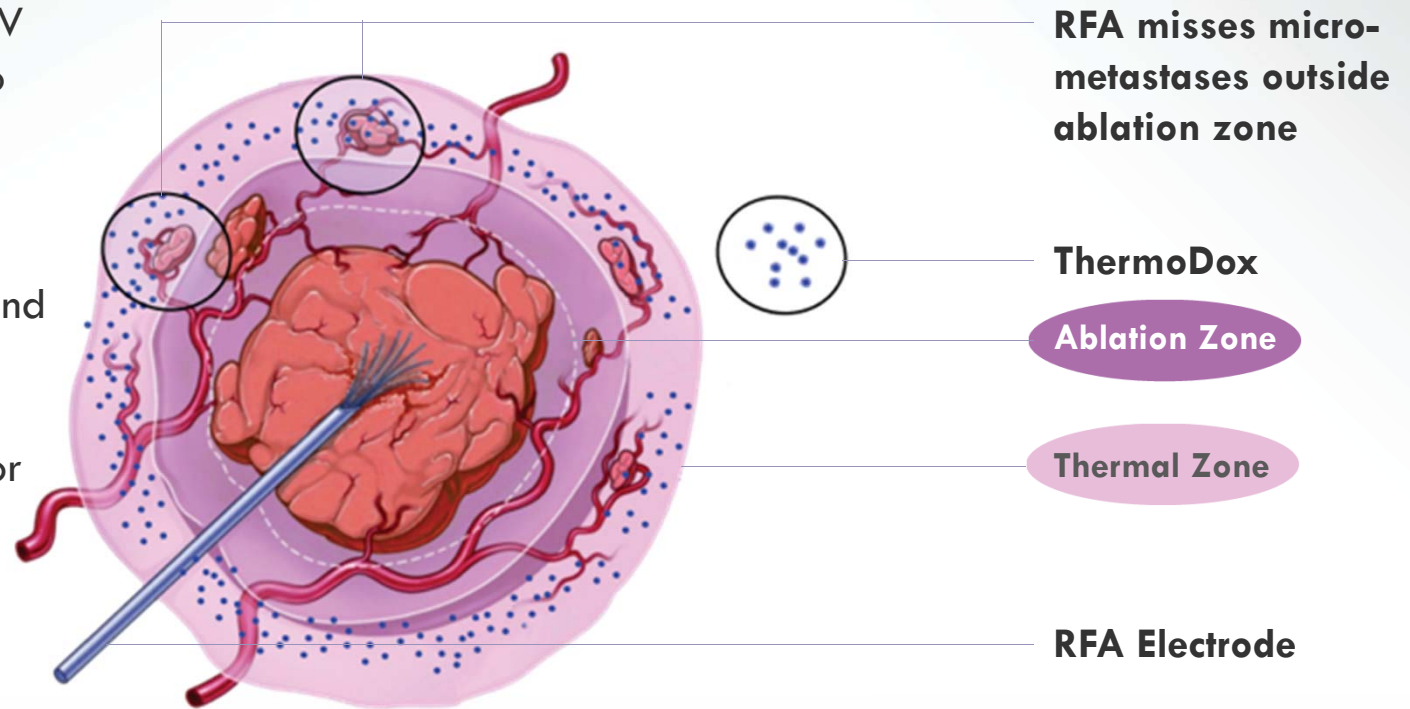
- Radiofrequency Ablation (RFA), transarterial chemoembolization (TACE) and radiation
- RFA is the dominant treatment with local recurrence rates >50% for lesions >3 cm

***Addressable Market Opportunity >200K Patients***

# ThermoDox + Radiofrequency Ablation

Designed to Address RFA Limitations by Expanding Treatment Zone

- ThermoDox infused IV ~15 minutes prior to radiofrequency ablation
- 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



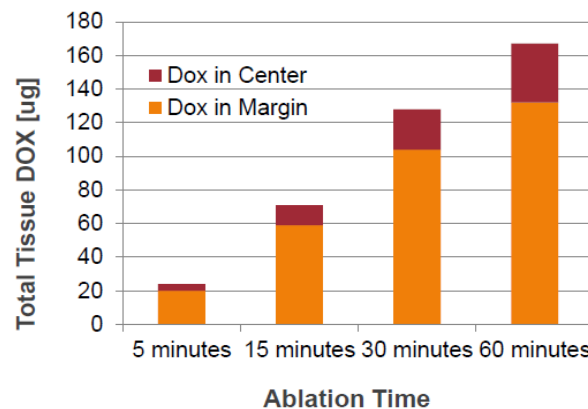
# HEAT Study: RFA Dwell Time Matters

## 701-Patient HEAT Study Results Inform ThermoDox+ RFA Clinical Plan

- Pre-specified analysis of completed HEAT Study data showed that patients with smaller HCC lesions (3-5 cm) appeared to have better outcomes with ThermoDox
- Dwell time effect on increasing local doxorubicin demonstrated in a computational model and an *in-vivo* porcine model.\*

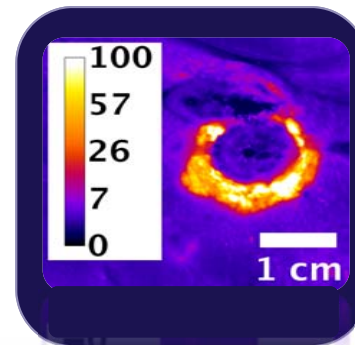
### Computational Model

Doxorubicin Concentrations

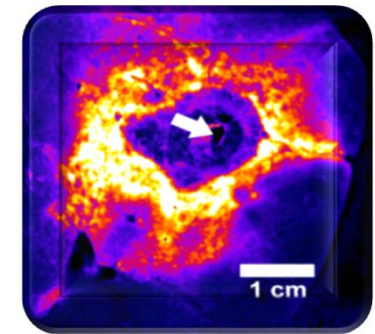


### Porcine Model

More RFA time = More local Dox deposition



15 Min Dwell Time



45 Min Dwell Time

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

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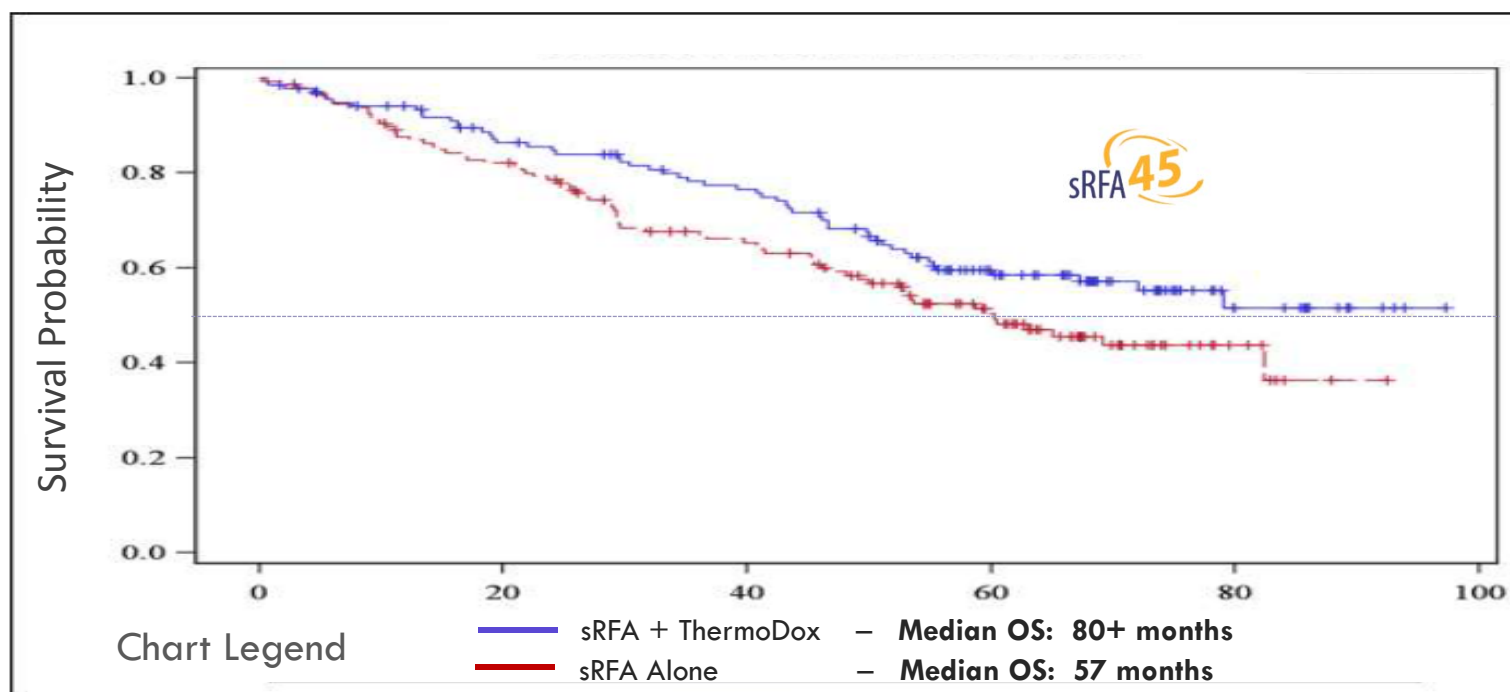
\* Gasselhuber, et al, Int J. Hyperthermia 2010 & Swensen, et al, Plos One, 10/15



# HEAT Study Sub-Group Analysis

When standardized for dwell time and number of lesions, patients given ThermoDox + RFA demonstrated a two-year improvement in overall survival\*

285 Patients With Standardized RFA >45 Minutes (sRFA)



Final OS Analysis as of 7/15/2016:

HR = 0.65 (95% CI 0.43 - 0.93) P Value = 0.02

\* Tak, et al CCR 10/10/17

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# RFA Dwell Time Matters

## Independent NIH Analysis Supports Conclusions from HEAT Study

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

- **Overall Findings**

Increase in *burn time* per tumor volume improved Overall Survival (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%, 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)

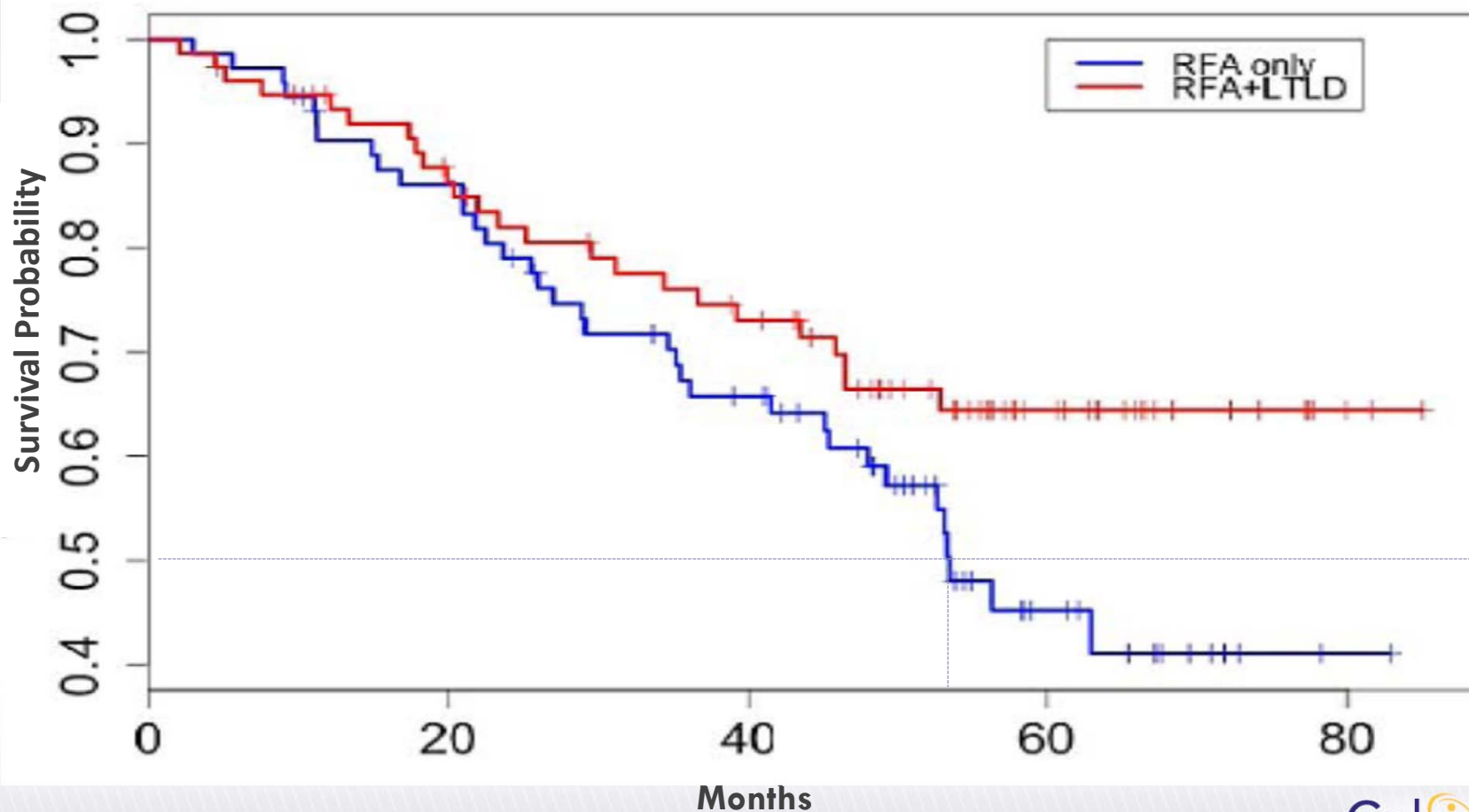


- **For all single lesion RFA-only patients:**

- Burn time per tumor volume did not have a significant effect, n=210

## NIH Analysis Supports HEAT Study Sub-Group

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



# ThermoDox + RFA HEAT Study Analysis

Relative to TACE – Intermediate HCC Patient Population

|                     |  | Study                             | Lesion size  | N          | Median OS (mos.)   | Year 1 (%) | Year 2 (%) | Year 3 (%) |
|---------------------|--|-----------------------------------|--|------------|--------------------|------------|------------|------------|
|                     |  | HEAT Study ITT Population         | Overall: 2.7 - 7.5 cm<br>Mean: 4.2 cm<br>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<br/>Mean: 4.3 cm<br/>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<br>Mean: 4.2 cm<br>Median: 3.9 cm            | 147        | 57 mos.            | 88%        | 79%        | 69%        |
|                     |  | Ikeda et al (TACE) 2013           | Median: 3.9; range 1-11<br>> 3.0                                 | 99<br>64   | 37 mos.<br>NR      | 90%<br>NR  | 75%<br>66% | NR<br>NR   |
|                     |  | Burrel (DEB TACE) 2012            | BCLC A<br>BCLC B   | 41<br>63   | 54 mos.<br>48 mos. | 90%<br>88% | NR<br>NR   | 68%<br>64% |

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# 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

| 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)

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# Phase III OPTIMA Study Design

## Applying Learnings From HEAT Study to OPTIMA

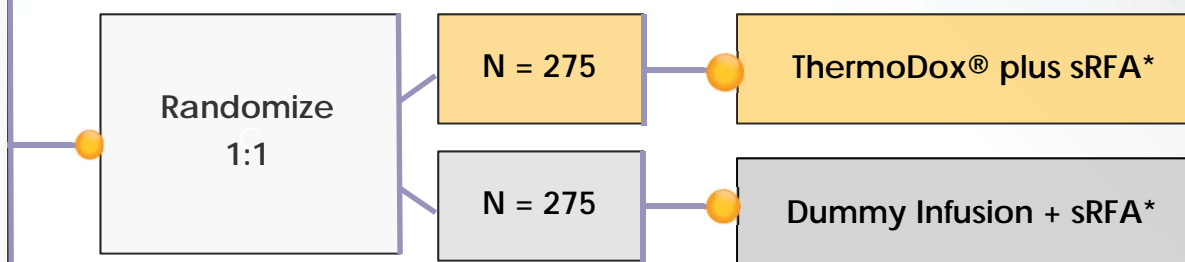
### General Eligibility

- 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)

- ~ 85% Enrolled
- Completed 2<sup>nd</sup> half 2018



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

~ 65 Clinical Sites in  
14 Countries

1<sup>st</sup> Interim: Q1-2019

2<sup>nd</sup> Interim: Q4-2019



# **GEN-1 IL-12**

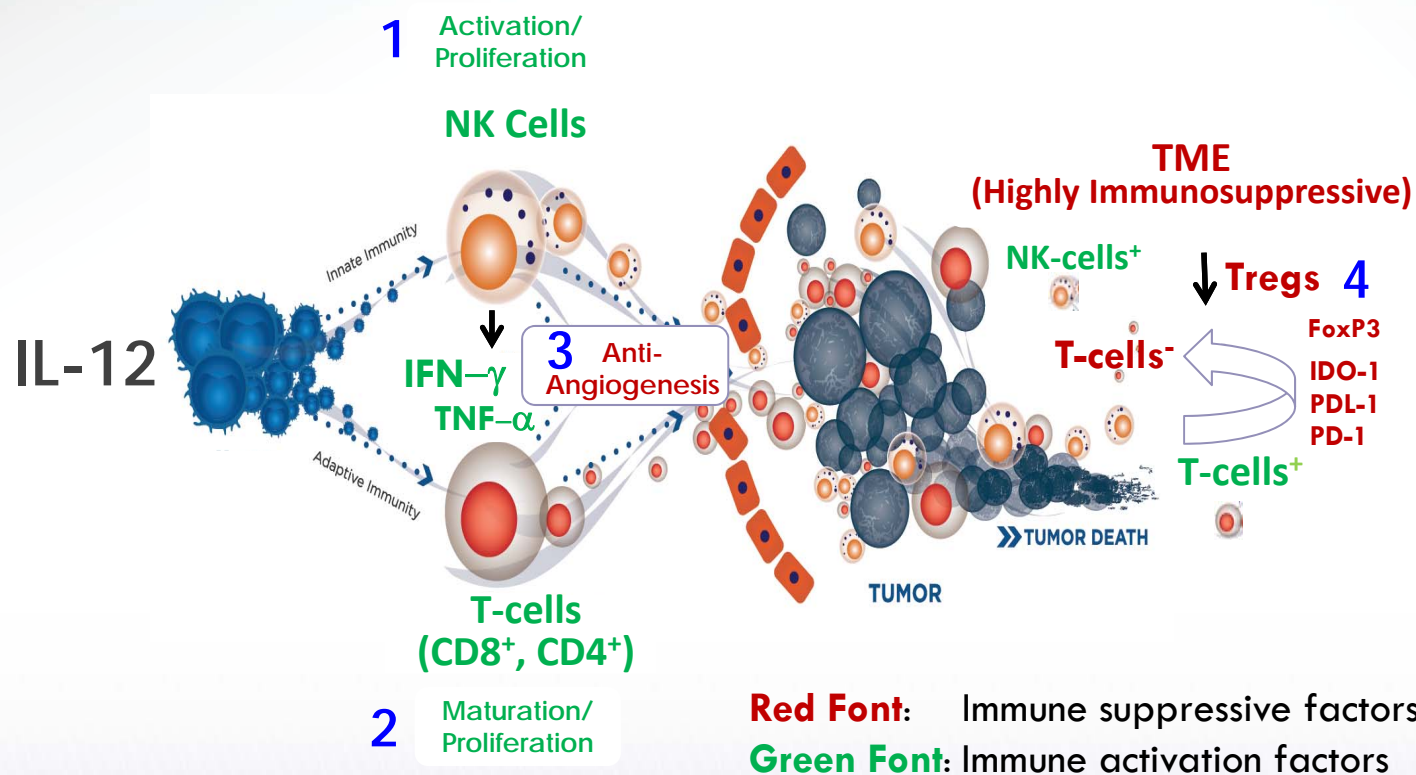
## Immuno-Oncology Program

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# Interleukin-12

## A Powerful Immune-Modulating Agent; Multiple Mechanisms

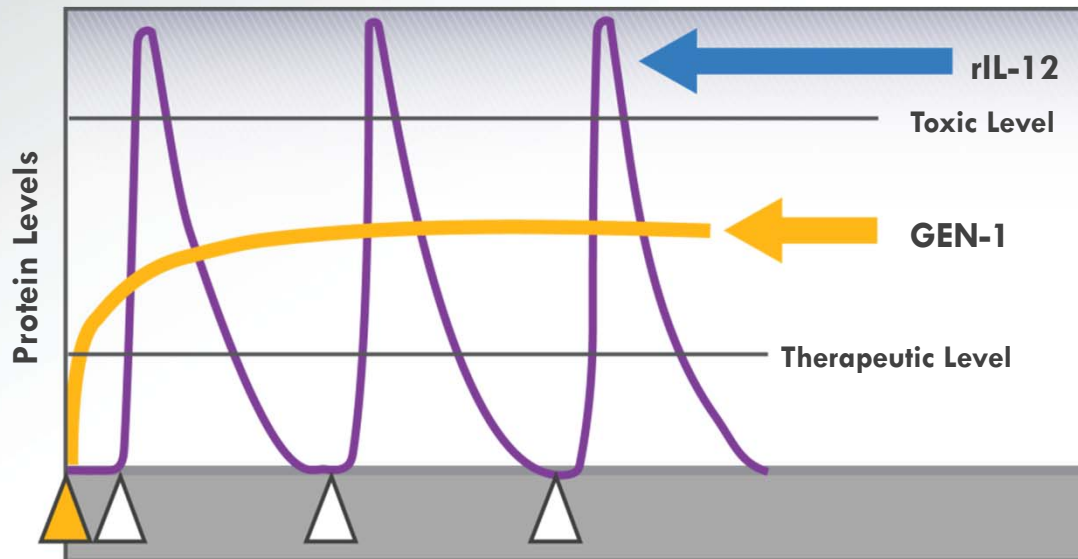
### Four Distinct Mechanisms of Immune Modulation by IL-12





# GEN-1: Designed to Address IL-12 Toxicity

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



Poor kinetics requires frequent and high doses of rIL-12

GEN-1 provides persistent local therapy

## GEN-1 addresses rIL-12 Poor Pharmacokinetics (pK)

- Loco-regional production of IL-12 avoids toxicities and poor pK of systemic rIL-12
- Persistent local delivery of IL-12 lasts up to one week and
- Dosing can be repeated
- Potential utility for long-term maintenance therapy

## Local Immunotherapy

Peritoneal cavity

Peritoneal Mets

The diagram illustrates a patient's torso with a peritoneal dialysis catheter inserted into the peritoneal cavity. A dialysis bag is connected to the catheter. The peritoneal cavity is shown with several organs, including the liver, stomach, and intestines. A label 'Peritoneal cavity' points to the space. Another label 'Peritoneal Mets' with an arrow points to a cluster of yellow and orange dots representing metastases near the liver.



### IL-12 Plasmid

- Celsion

# Ovarian Cancer

## High Global Incidence and Mortality<sup>1</sup>

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

- 225,000 annual incidence worldwide
- 22,280 in U.S. and 100,000 in developed countries
- 14,240 deaths from ovarian cancer in the U.S. (2015)

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

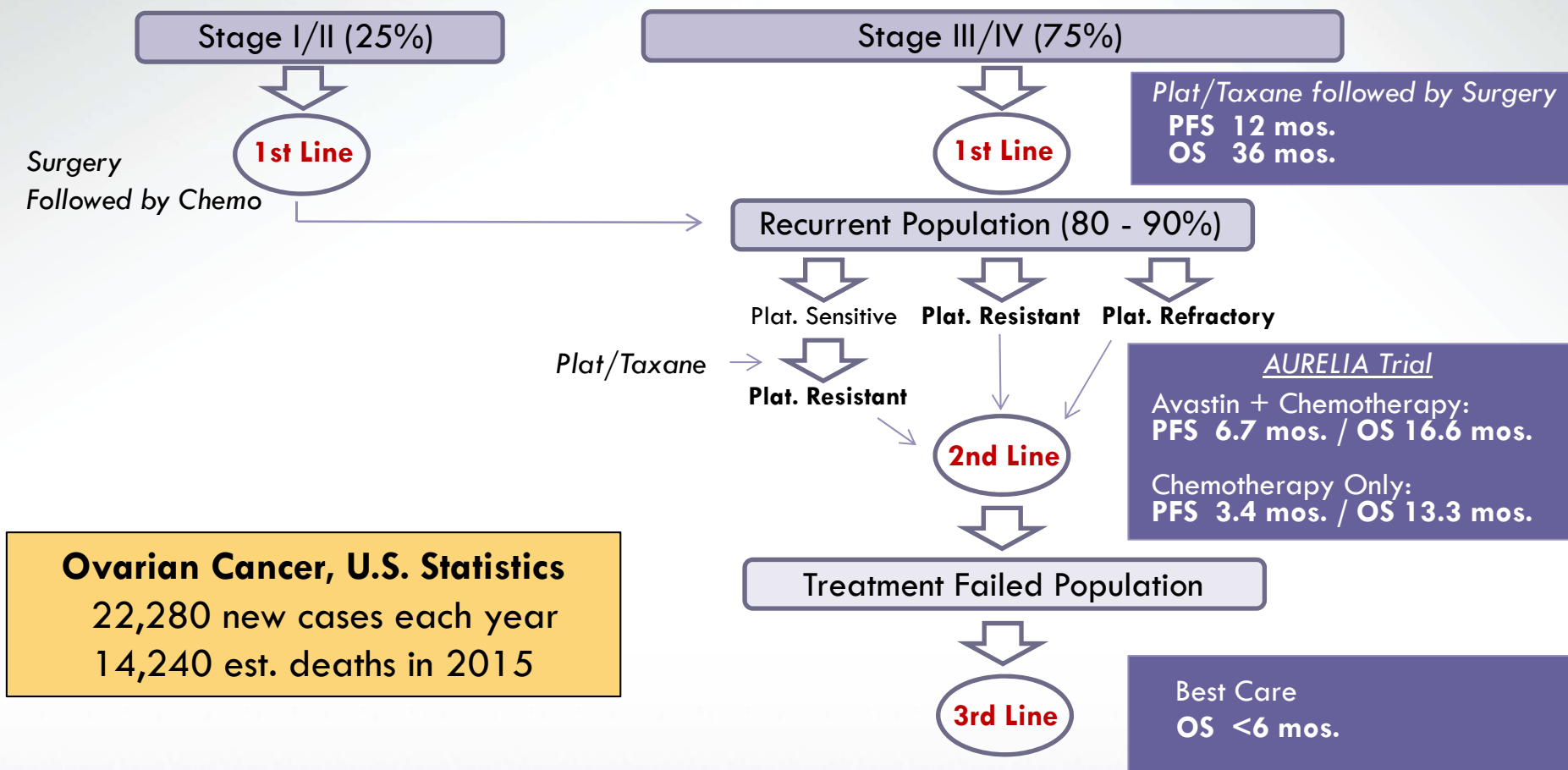
- 5-year survival rate for all stages is >50%
- Survival rate dramatically reduced if not localized cancer
- 15% diagnosed with localized cancer, eligible for potentially curative surgery

### ● Local therapies for ovarian cancer

- Ovarian cancer is not diagnosed early – over 60% of women diagnosed with Stage III/IV
- Most common site of recurrence in abdomen—importance of intra-peritoneal-administered therapy

***Addressable Market Opportunity > 100K Patients***

# Ovarian Cancer Treatment Path



## Ovarian Cancer, U.S. Statistics

22,280 new cases each year  
14,240 est. deaths in 2015



## Clinical Experience With GEN-1 in Ovarian Cancer

- Multiple trials completed, 75 patients treated
- Shown to be well-tolerated
- Clear evidence of biological activity & clinical benefit have been demonstrated
- Maximum Tolerated Dose has not been reached

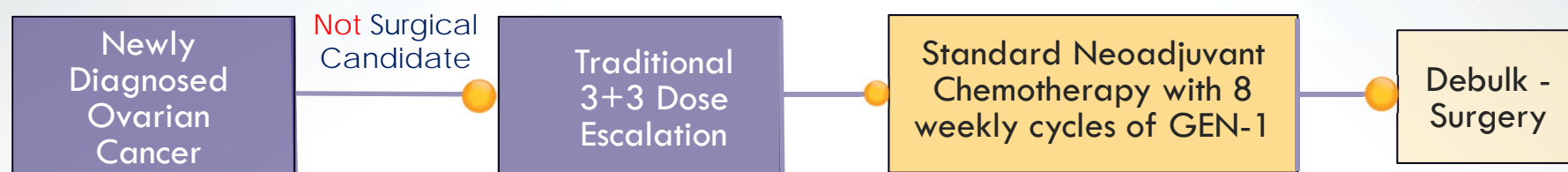
| Study     | Mono/Combo              | Study Phase | Disease            | N  |
|-----------|-------------------------|-------------|--------------------|----|
| GEN-1-101 | Monotherapy             | I           | Platinum-resistant | 13 |
| GOG-170Q* | Monotherapy             | II          | Platinum-resistant | 20 |
| GEN-1-201 | + Carboplatin/Docetaxel | I           | Platinum-sensitive | 13 |
| GOG-9928* | + Doxil                 | Ib          | Platinum-resistant | 14 |
| OVATION   | + Carboplatin/Taxol     | I           | Newly diagnosed    | 15 |

\* Studies conducted by NCI-NRG (Gynecologic Oncology Group - GOG)

# GEN-1 Phase I Study

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

## OVATION I 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+

# OVATION I Study

## Final Efficacy Results

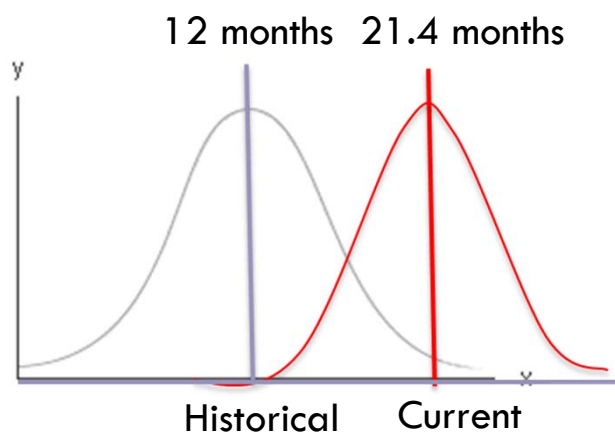
|                                  | 36 mg/m <sup>2</sup> | 47 mg/m <sup>2</sup> | 61 mg/m <sup>2</sup> | 79 mg/m <sup>2</sup> |                 |
|----------------------------------|----------------------|----------------------|----------------------|----------------------|-----------------|
| <i>RECIST Response</i>           | Cohort 1<br>(n=3)    | Cohort 2<br>(n=3)    | Cohort 3<br>(n=3)    | Cohort 4<br>(n=5)    | Total<br>(n=14) |
| Complete Response                | 1, 33.3%             | 0, 0%                | 0, 0%                | 1, 20%               | 2, 14%          |
| Partial Response                 | 0, 0%                | 3, 100%              | 3, 100%              | 4, 80%               | 10, 72%         |
| Stable Disease                   | 2, 66.6%             | 0, 0%                | 0, 0%                | 0, 0%                | 2, 14%          |
| <i>Interval Debulking Status</i> | Cohort 1<br>(n=3)    | Cohort 2<br>(n=3)    | Cohort 3<br>(n=3)    | Cohort 4<br>(n=5)    | Total<br>(n=14) |
| R0                               | 2, 66.6%             | 0, 0%                | 2, 66.6%             | 5, 100%              | 9, 64.3%        |
| R1                               | 1, 33.3%             | 2, 66.6%             | 0, 0%                | 0, 0%                | 3, 21.4%        |
| R2                               | 0, 0%                | 1, 33.3%             | 1, 33.3%             | 0, 0%                | 2, 14.3%        |
| <i>Pathological Response</i>     | Cohort 1<br>(n=3)    | Cohort 2<br>(n=3)    | Cohort 3<br>(n=3)    | Cohort 4<br>(n=5)    | Total<br>(n=14) |
| cPR                              | 1, 33.3%             | 0, 0%                | 0, 0%                | 0, 0%                | 1, 7%           |
| microPR                          | 1, 33.3%             | 2, 66.6%             | 1, 33.3%             | 3, 60%               | 7, 50%          |
| macroPR                          | 1, 33.3%             | 1, 33.3%             | 2, 66.6%             | 2, 40%               | 6, 43%          |

- All patients showed a > 90% drop in their CA-125 protein levels
- 50% reduction in CA-125 levels maintained for > 2 weeks is considered a CA-125 Responder

# OVATION Study

## Progression Free Survival Estimates

Current Estimated Median PFS ----- 21.4 months  
Historical Estimated PFS ----- 12.0 months



| Cohort (mg/m <sup>2</sup> ) | PFS   | Progression |
|-----------------------------|-------|-------------|
| 36                          | 19.25 | 3/3         |
| 47                          | 22.6+ | 0/3         |
| 61                          | 18.7+ | 1/3         |
| 79                          | 16.2+ | 2/5*        |

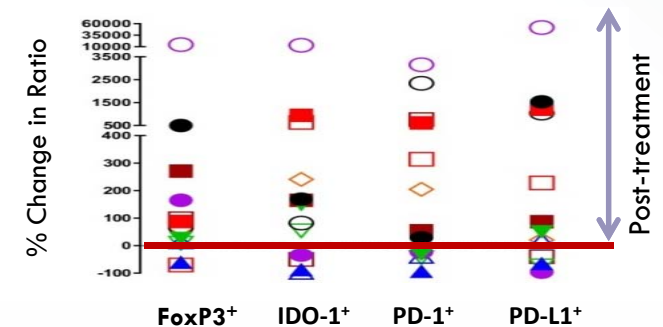
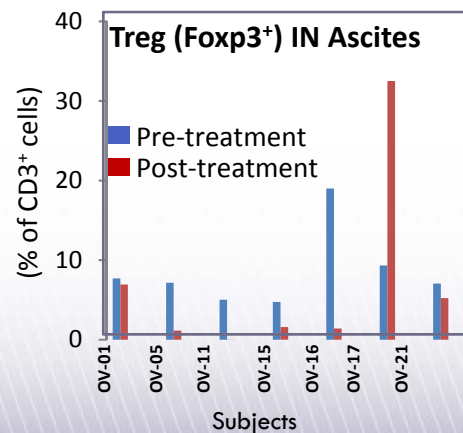
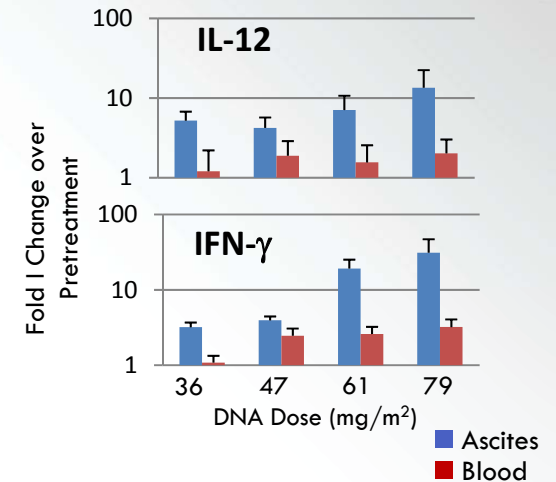
\* One patient dropped out after 2 treatments and progressed

+ Data not mature



# Shift in TME: Favoring Immune Stimulation Over Suppression Following GEN-1 + NACT

- Dose dependent local increase in immune cytokines, IL-12 and IFN- $\gamma$ , at the tumor site (ascites) but not as much in blood
- Increase in the ratio of immunostimulatory T-cells (CD8<sup>+</sup>) to immunosuppressive T-cell signals (FoxP3<sup>+</sup>, IDO-1<sup>+</sup>, PD-1<sup>+</sup>, PDL-1<sup>+</sup>) in approximately 70% of patients
- Decrease in immuno-suppressive cells population in ascites in a majority of patients



# GEN-1 Phase I/II Study

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

## OVATION II Study



Neoadjuvant Study in Newly Diagnosed Advanced Stage Ovarian Cancer Patients (FIGO IIIC & IV)

To determine early efficacy, biological activity and safety with NAC in advanced ovarian cancer

Primary Endpoint

Progression Free Survival

Secondary Endpoints

Objective Clinical Response, Pathological Complete Response, Surgical Response, Safety, Biological Activity, and Serum CA-125 Concentrations

# GEN-1 Phase I/II Study

## OVATION II Study Design

| Arm                | Treatment   | Before IDS |      |       |      |      |       |      |      |       | Interval<br>Debulking<br>Surgery | After IDS |      |       |      |      |       |      |      |       |
|--------------------|-------------|------------|------|-------|------|------|-------|------|------|-------|----------------------------------|-----------|------|-------|------|------|-------|------|------|-------|
|                    |             | C1D1       | C1D8 | C1D15 | C2D1 | C2D8 | C2D15 | C3D1 | C3D8 | C3D15 |                                  | C4D1      | C4D8 | C4D15 | C5D1 | C5D8 | C5D15 | C6D1 | C6D8 | C6D15 |
| Arm 1              | Carboplatin | X          |      |       | X    |      |       | X    |      |       | X                                | X         |      |       | X    |      |       | X    |      |       |
|                    | Paclitaxel  | X          |      |       | X    |      |       | X    |      |       |                                  | X         |      |       | X    |      |       | X    |      |       |
|                    | GEN-1       |            | X    | X     | X    | X    | X     | X    | X    | X     |                                  | X         | X    | X     | X    | X    | X     | X    | X    | X     |
| Arm 2<br>(control) | Carboplatin | X          |      |       | X    |      |       | X    |      |       | X                                | X         |      |       | X    |      |       | X    |      |       |
|                    | Paclitaxel  | X          |      |       | X    |      |       | X    |      |       |                                  | X         |      |       | X    |      |       | X    |      |       |
|                    | Placebo     |            |      |       |      |      |       |      |      |       |                                  |           |      |       |      |      |       |      |      |       |

- 130 patients
- Primary Endpoint = PFS
- Subjects randomized 1:1 on standard neoadjuvant chemotherapy (NAC) vs. standard NAC + GEN-1



# **Milestones & Financials**

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# Major Milestone Events & Over 2 years of Cash

|   | 2018                                    |                                       |   |   | 2019                                    |                 |                 |   | 2020 |                 |                                      |    |
|---|---|---------------------------------------|---|---|---|-----------------|-----------------|---|------|-----------------|--------------------------------------|----|
|   | Q1                                      | Q2                                    | Q3                                      | Q4  | Q1                                      | Q2              | Q3              | Q4                                      | Q1   | Q2              | Q3                                   | Q4 |
| <b>ThermoDox</b>  |   |                                       |   |   |   |                 |                 |   |      |                 |                                      |    |
| <b>OPTIMA Study<br/>Phase III Trial</b>                 |   | DMC Review<br>After 75%<br>Enrollment | Enrollment<br>Complete                  |   | 1st Interim<br>Efficacy<br>(118 events) |                 |                 | 2nd Interim<br>Efficacy<br>(158 events) |      |                 | Final OS<br>Endpoint<br>(197 events) |    |
| <b>GEN-1</b>  |   |                                       |   |   |   |                 |                 |   |      |                 |                                      |    |
| <b>OVATION I<br/>Phase IB Dose<br/>Escalating Trial</b> | Interim PFS<br>Data from<br>Cohorts 1-4 |                                       | Final PFS<br>Data from<br>Cohorts 1-4   |   |   |                 |                 |   |      |                 |                                      |    |
| <b>OVATION II<br/>Phase I/II Trial</b>                  | Final IND<br>Submission                 | Initiate<br>Enrollment<br>Phase I     | *<br>Dose Escalating<br>Phase I Portion | Data from<br>Dose Escalating<br>Phase I Portion | Initiate<br>Enrollment<br>Phase II      | *<br>Enrollment | *<br>Enrollment | Complete<br>Enrollment<br>130 pts       |      | *<br>Enrollment | Final PFS<br>Data from<br>Phase II   |    |

\* Open Label Design Will Allow For Periodic Reporting of Results

\$25.5M  
in cash

→ Q3 2019

\$10M NOL Sale → Q2 2020

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## Financial Overview

|                                  |                 |
|----------------------------------|-----------------|
| Cash & Investments as of 1/10/18 | \$25.5 million  |
| Estimated cash usage per month   | ~\$1.33 million |
| Market Capitalization            | \$42 million    |
| Common shares outstanding        | 17.7 million    |
| Fully diluted shares outstanding | 21.5 million    |
| Avg. Daily Trading Volume        | ~ 350,000       |



# Corporate Information

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