Cantor Fitzgerald
Annual Healthcare Conference

July 13, 2016

Celsion

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.

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Oncology Company

Capital Efficient Drug Development

Three Nano-Particle Based Technology Platforms to Drive Growth

- **Targeted 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
  - Phase I/II Combination Therapy with Avastin 2nd line Ovarian Cancer
- **Lung Directed RNA Therapy**
  - Preclinical NHP mRNA
  - Preclinical murine miRNA

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Pipeline of Clinical and Preclinical Studies

Phase III, Phase II, and Phase I

INDICATION	CANDIDATE /Study	PRE-CLINICAL	PHASE 1-2	PHASE 3
Primary Liver	ThermoDox/OPTIMA Study			Phase III enrolling
RCW Breast	ThermoDox /Euro-DIGNITY			Phase II initiate Q4, 2016
Ovarian 1st Line	GEN-1/OVATION Study			Phase I enrolling 3rd cohort
Ovarian 2nd Line	GEN-1 + Avastin + Doxil		Phase I/II initiate Q1, 2017	
Glioblastoma	GEN-1 preclinical		Efficacy/Safety/Tox	
Lung Cancer	miRNA preclinical	Efficacy/Safety/Tox		

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Focus on Our Two Clinical Stage Platforms

LTSL

Lysolipid Thermally
Sensitive Liposomes
Known Chemotherapeutics

ThermoDox

Targeted Doxorubicin Delivery

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

TheraPlas

Synthetic Non-viral Vector
DNA-based Plasmids
Therapeutic Proteins

GEN-1

Localized IL-12 Immunotherapy

- Neoadjuvant Study in 1st Line Ovarian
- Combination Study with Avastin and Doxil in 2nd Line Ovarian Cancer

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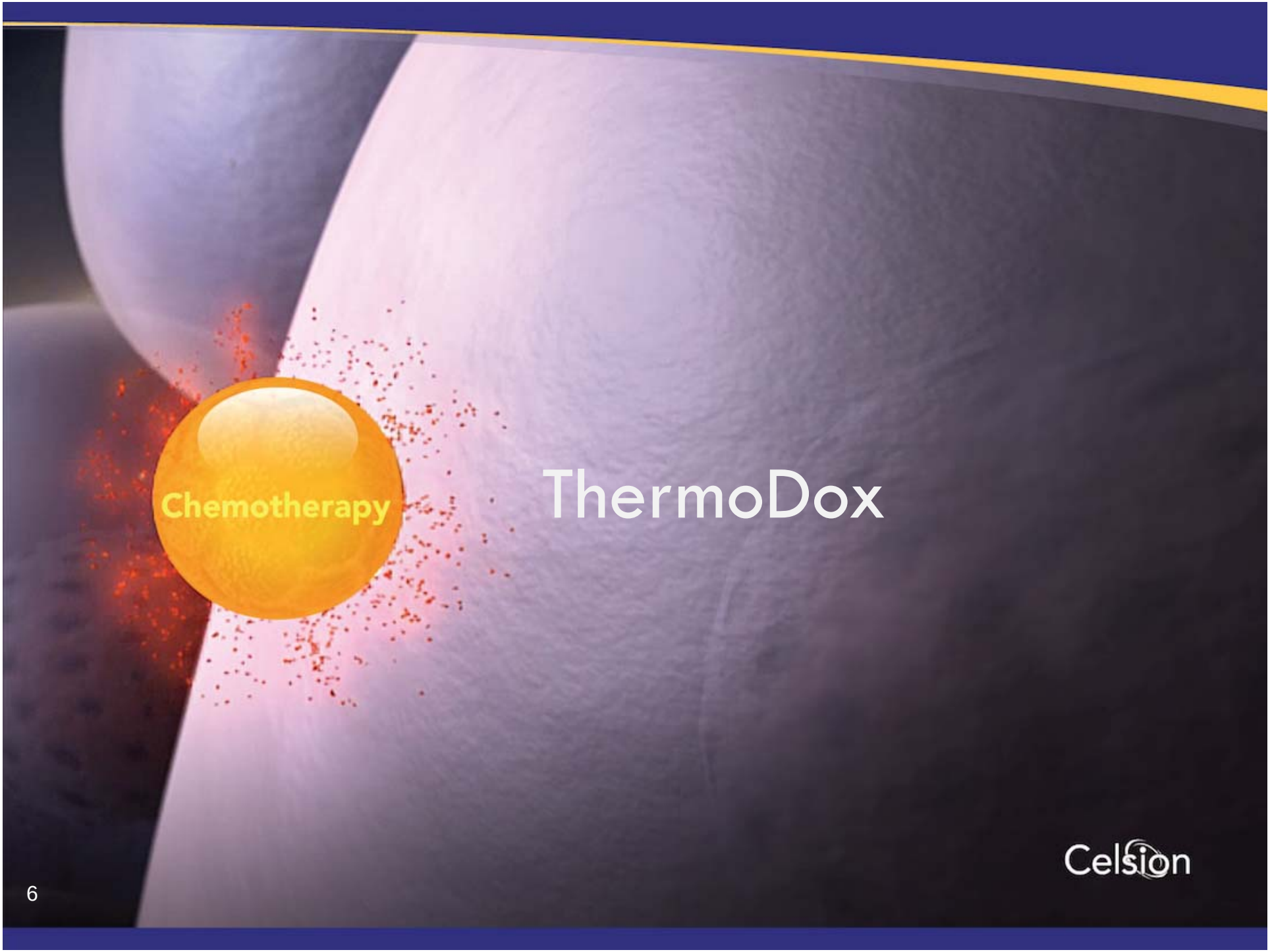
Chemotherapy
ThermoDox
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Hepatocellular Carcinoma

Large and Deadly Global Cancer

- **5th most prevalent**
  - 800,000 global incidence growing 5% annually
  - By 2020, expected to be the #1 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
  - Curative surgery is possible in less than 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
Multi-Billion Dollar Revenue Potential

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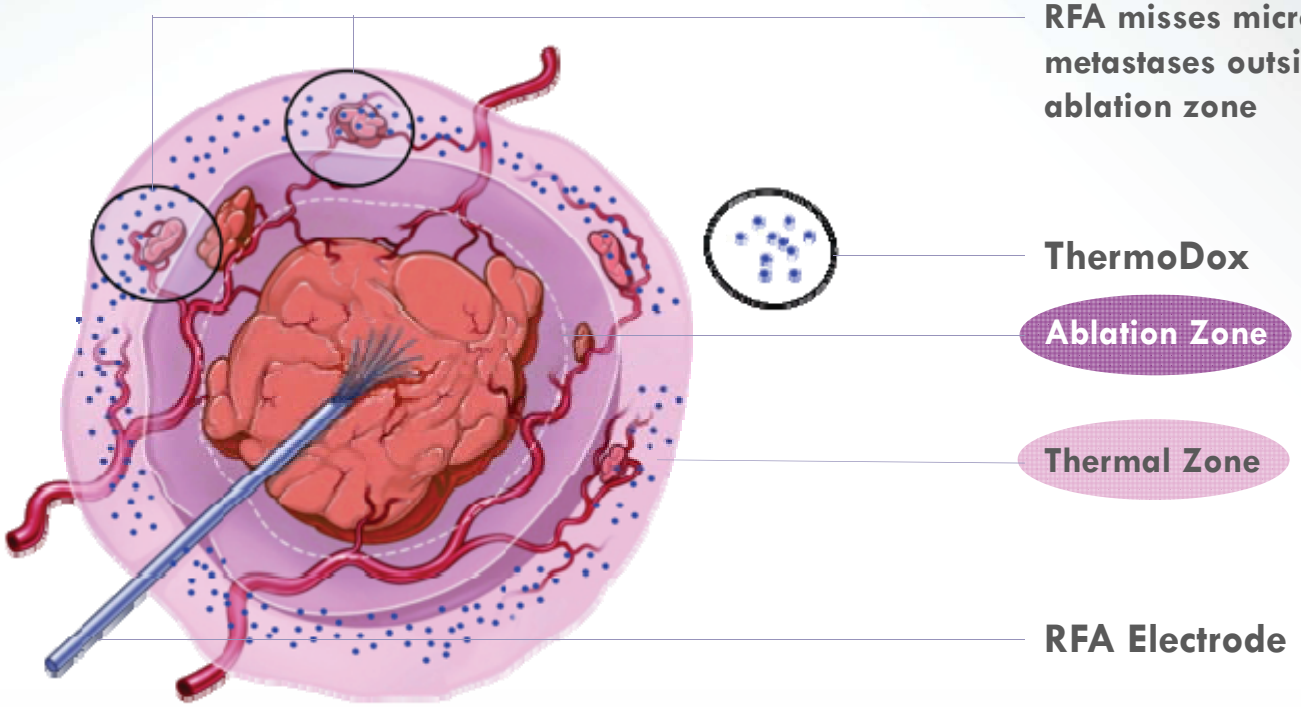
ThermoDox + RF Liver Ablation

Expanding the Treatment Zone Addresses RFA 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



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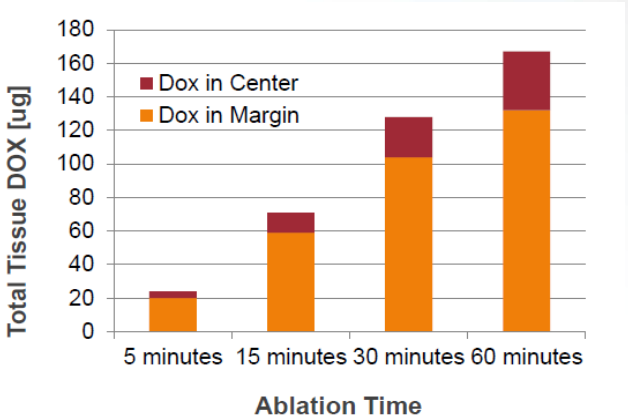
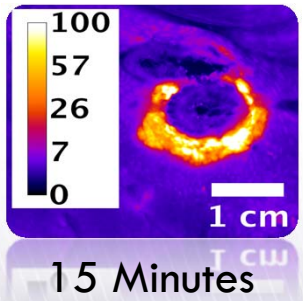
RFA Dwell Time Matters!

Learnings from the 700 patient HEAT Study

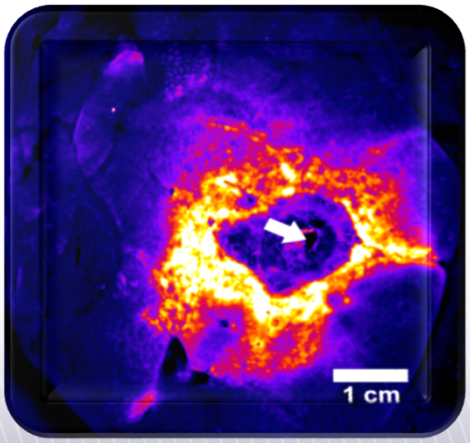
- Pre-specified analysis of HEAT Study data showed that patients with smaller lesions appeared to do better with ThermoDox.
- When standardized for dwell time and lesion number then the ThermoDox patients demonstrated difference in OS.
- The hypothesis that dwell time increases local doxorubicin concentration was then tested and demonstrated in computer simulation study.
- The hypothesis was further tested and demonstrated in an in vivo porcine model.



Gasselhuber et al, *Int J Hyperthermia*, 2012



15 Minutes



45 Minutes

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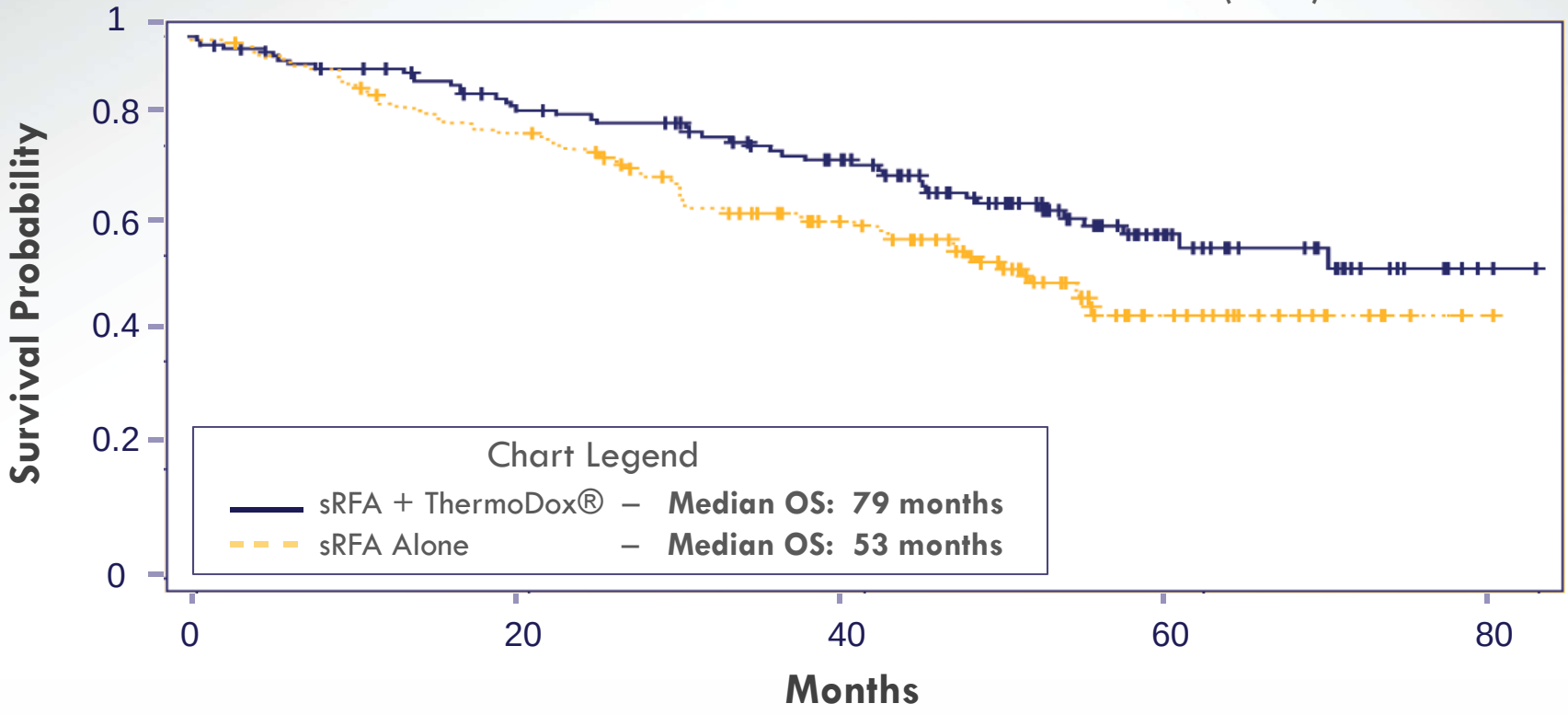
ThermoDox: HCC

Sub-Group Analysis of HEAT Study Data

Greater than Two Years Overall Survival Benefit

285 Patients with Standardized RFA > 45 minutes (sRFA)



Overall Survival as of 7/15/2015	HR=0.63 (95% CI 0.43 - 0.93) *P* Value = 0.0198

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ThermoDox + RFA vs TACE

Intermediate HCC

	HEAT Study	Lesion size	N	Median OS (mos)	Year 1 (%)	Year 2 (%)	Year 3 (%)
	ITT Population	Overall: 2.7 - 7.5 cm Mean: 4.2 cm Median: 4 cm	223	48	85	76	64
		3 cm – 5 cm	183	NE	87	80	66
		5 cm – 7 cm	40	45	75	58	54
HEAT Study Subgroup	**ThermoDox + RFA ≥ 45 min.**	**Overall: 2.7 - 6.9 cm Mean: 4.3 cm Median: 4.2 cm**	**138**	**79**	**94**	**85**	**77**
HEAT Study Subgroup	RFA alone time ≥ 45 min.	Overall: 3 - 6.9 cm Mean: 4.2 cm Median: 3.9 cm	147	54	88	79	69
	Ikeda et al (TACE) 2013	Median: 3.9; range 1-11	99	37	90	75	NR
		> 3.0	64	NR	NR	66	NR
	Burrel (DEB TACE) 2012	BCLC A	41	54	89.7	NR	67.8
		BCLC B	63	48	88.2	NR	64.4

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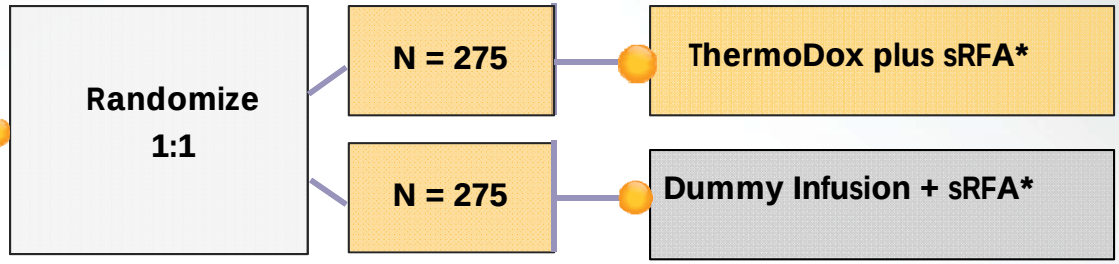
DEB TACE – Doxorubicin Eluding Beads

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

~80 Clinical Sites in
14 Countries

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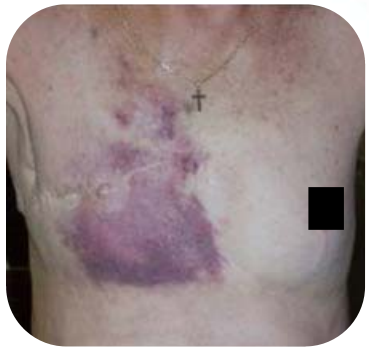
sRFA45 Standardized Radiofrequency Ablation > 45 minutes

ThermoDox: RCW Breast Cancer

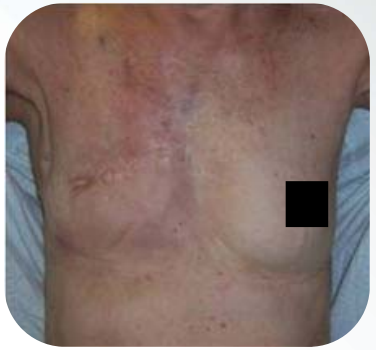
Difficult to Treat with Severe Complications

- Breast cancer recurring in the chest wall affects ~35,000 post-mastectomy patients in the US and Europe annually
- 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

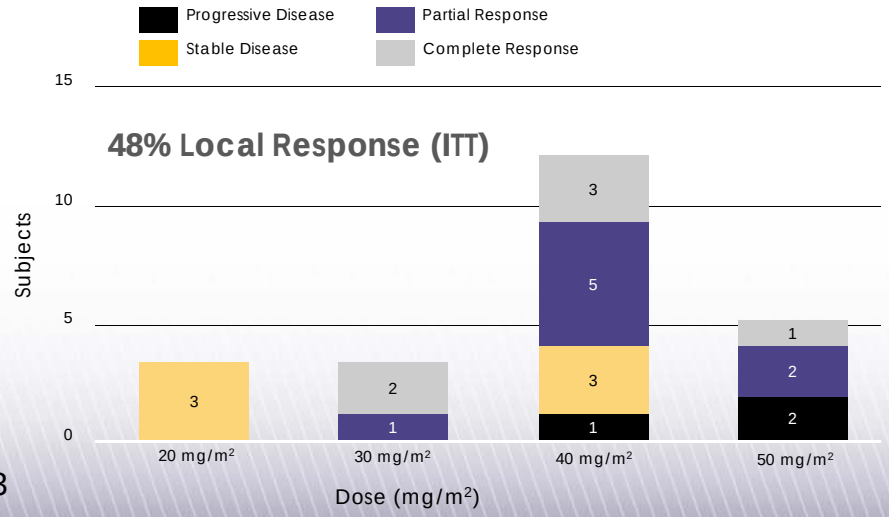
Limited Treatment Options



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)

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ThermoDox: Euro-DIGNITY Study

ThermoDox + Hyperthermia + Radiation

Primary Objectives

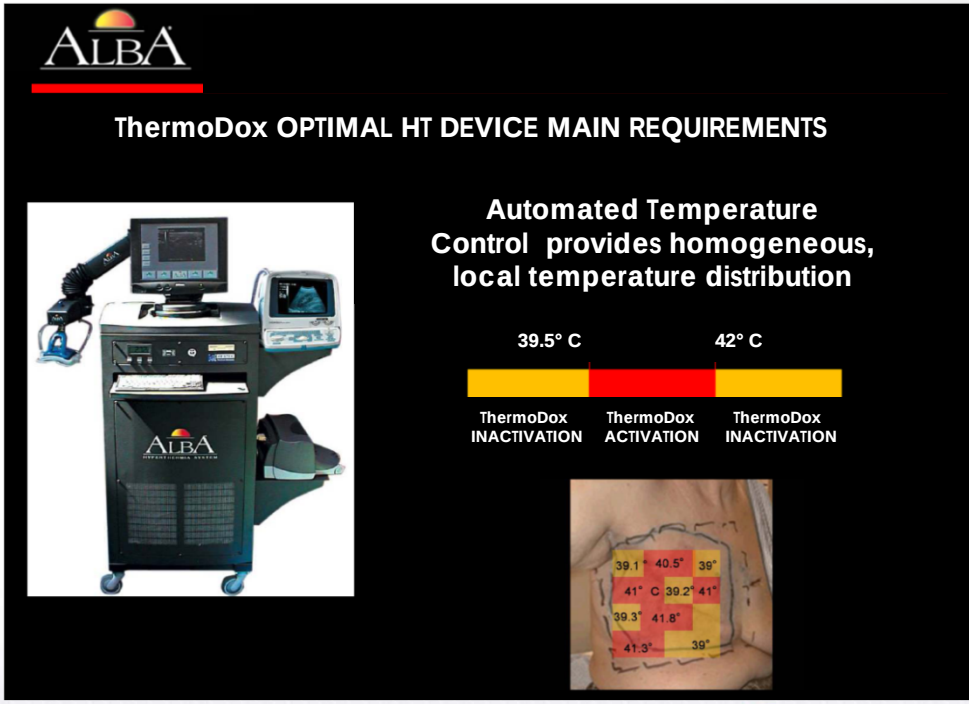
- Evaluate complete and partial response after 3 cycles of ThermoDox + Hyperthermia and Radiation Treatment (Tri-Modal Therapy)
- Evaluate loco-regional breast tumor control in patients undergoing Tri-Modal Therapy

70 patients to be enrolled

Open Label Design

Study Timelines

- Site Activation: 1st Half – 2016
- Interim Efficacy Assessment: Q1 – 2017
- Recruitment Period: 2016 – 2017
- LP/LV through Follow-Up: 2018



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GEN-1

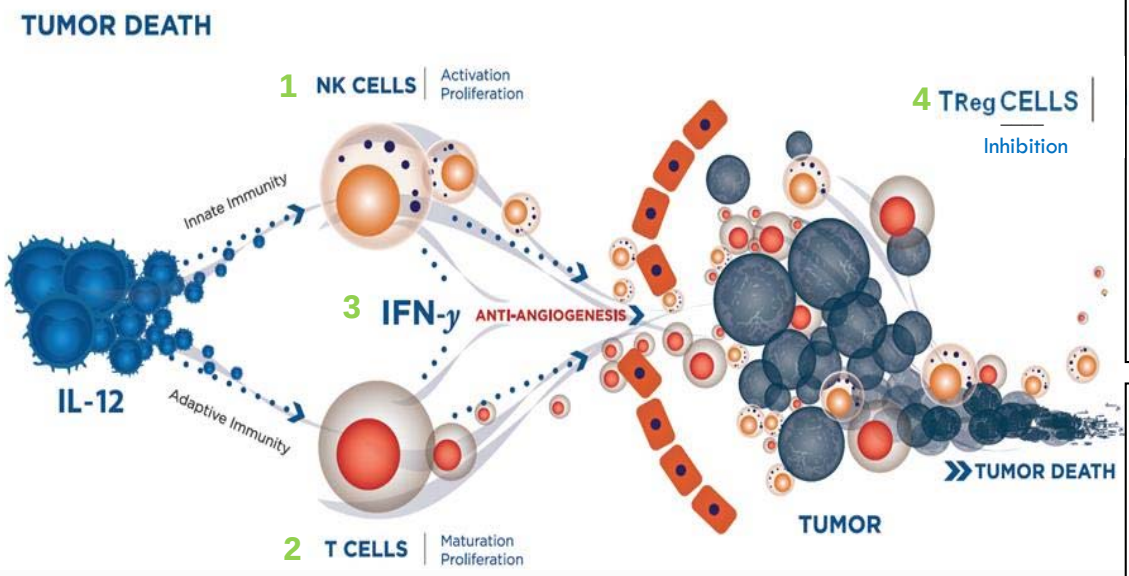
IL-12 Immuno-Oncology Program

IL-12 Immunotherapy

Powerful Immune Modulating Agent

Multiple Mechanisms of Action

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



Journal of Translational Medicine BioMed Central

Research Open Access

Angiostatin anti-angiogenesis requires IL-12: The innate immune system as a key target

Adriana Albini*†1, Claudio Brigati†2, Agostina Ventura3, Girieca Lorusso1,4, Marta Pinter4, Monica Morini2, Alessandra Mancino5, Antonio Sica5,6 and Douglas M Noonan1,4

Int. J. Cancer: 78, 361–365 (1998)

Publication of the International Union Against Cancer
Publication de l'Union Internationale Contre le Cancer

IL-12 REGULATES VEGF AND MMPs IN A MURINE BREAST CANCER MODEL

Sergio DIAS*, Robert BOYD and Frances BALKWILL
Biological Therapies Laboratory, Imperial Cancer Research Fund, London, UK

In a murine model of breast cancer, IL-12 therapy exerts potent anti-angiogenic effects which contribute to tumor regression. After 7 days of treatment, levels of tumor VEGF protein decline markedly and are undetectable at 14 days. This decline is accompanied by a fall in MMP-9 and, as the tumors regress, an increase in its natural inhibitor, TIMP-1. A cell line established from the primary tumor produced VEGF *in vitro*. IFN-γ reduced tumor cell production of VEGF over a 24-hr period *in vitro*, suggesting that IL-12-induced IFN-γ may be responsible for the decline in VEGF levels *in vivo*. There is also *in vitro* evidence that IL-12 regulates stromal cell interactions, leading to decreased MMP-9 and increased TIMP-1 production. Thus, we suggest that at least 2 mechanisms are involved in IL-12 regulation of angiogenesis, removing the pro-angiogenic stimulus and blocking the release and activity of MMPs. *Int. J. Cancer* 78:361–365, 1998.

Roche U/mg. Rat IFN-γ (specific activity 1×10^7 U/mg) was provided by Roussel UCLAF (Romainville, France). Cytokines were diluted to 10 μg/ml in PBS/0.1% murine serum albumin (Sigma, Poole, UK) and stored at –70°C prior to use. An MMP inhibitor, BB-2116, was kindly provided by British Biotech Pharmaceuticals (Oxford, UK). This inhibitor was used at a concentration of 30 mM. Finally, an anti-mouse VEGF-blocking antibody (Autogen Bioclear; Santa Cruz, Santa Cruz, CA) was used at a concentration of 0.5 μg/ml.

Cell lines

The murine T-cell line EL4-nob was provided by Dr. D. Cantrell (ICRF, London, UK). The macrophage cell line J774 was also used (for details, see Yoshida *et al.*, 1994). Both were cultured in RPMI 1640 with 10% FCS (Sigma), supplemented with 2 mM L-glutamine, 100 U/ml penicillin and 100 μg/ml streptomycin. The hEND cel

Klinke *Journal for ImmunoTherapy of Cancer* (2015) 3:27
DOI 10.1186/s40425-015-0069-x

Journal for ImmunoTherapy of Cancer

REVIEW Open Access

Enhancing the discovery and development of immunotherapies for cancer using quantitative and systems pharmacology: Interleukin-12 as a case study

David J Klinke II

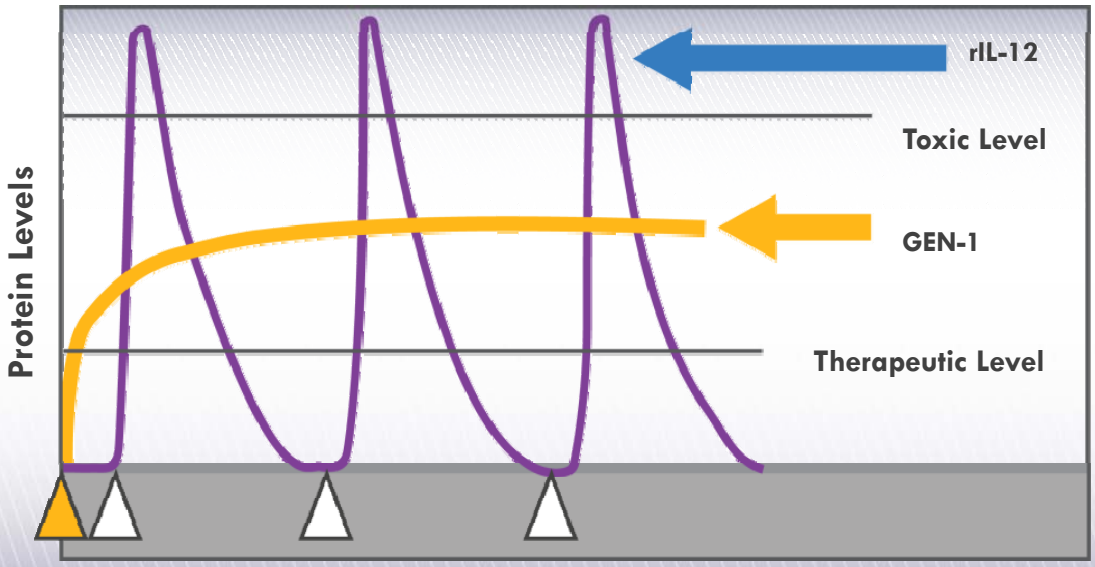
GEN-1

Novel "Polymer - Interluken12 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-1is an effective alternative to rIL-12 Poor PK



100 nm

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Ovarian Cancer

Large and Deadly Global Cancer

- **8th 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
- **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

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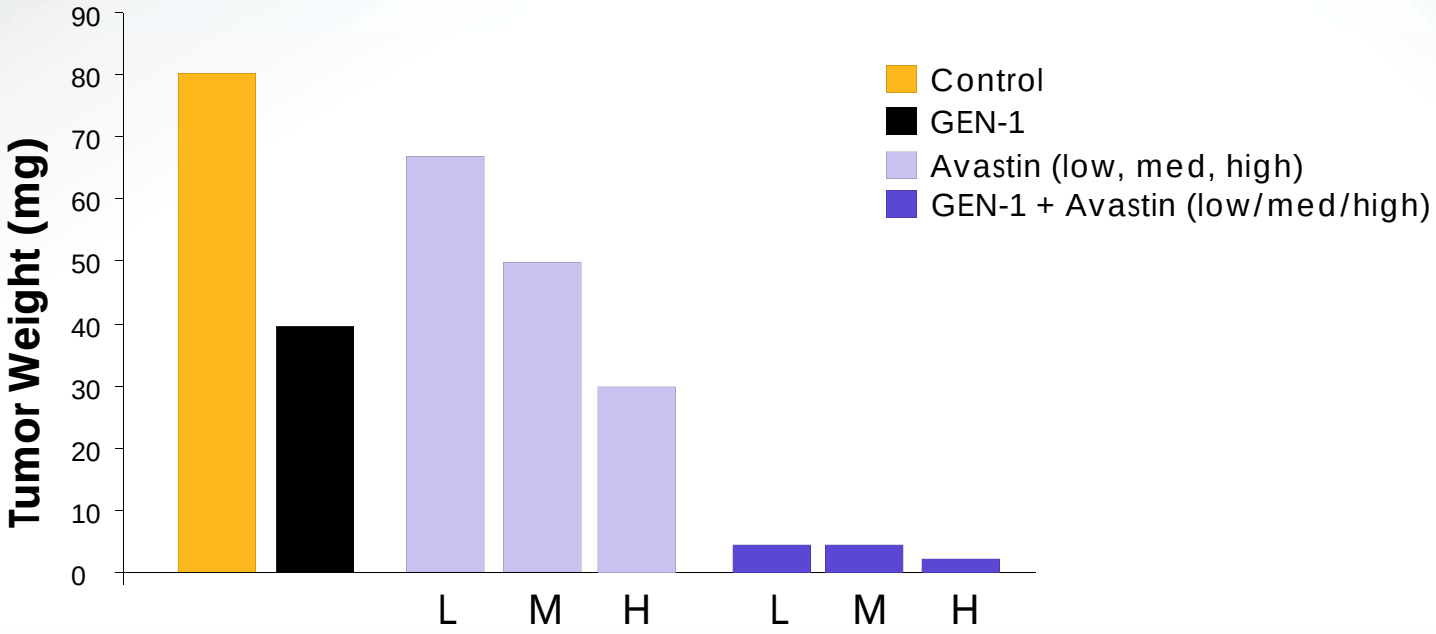
GEN-1 Preclinical Studies

Combination with Avastin

- As a single agent, Gen-1is comparable to Avastin
- Combining GEN-1with Avastin Yields Dramatic Improvement Activity



7 x 10^6 SKOV3 human ovarian cancer cells were implanted IP. Avastin treatment at three different doses (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.

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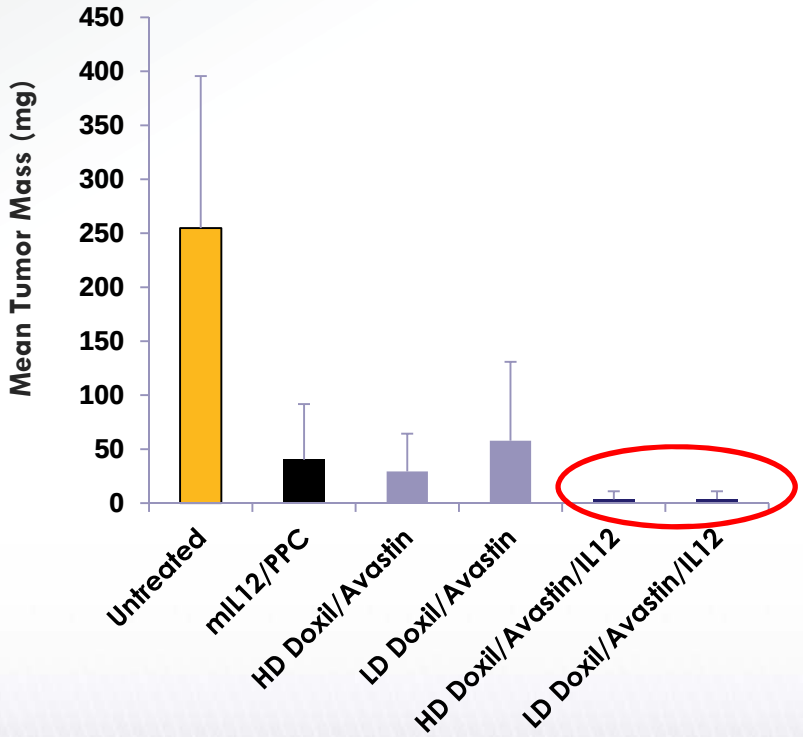
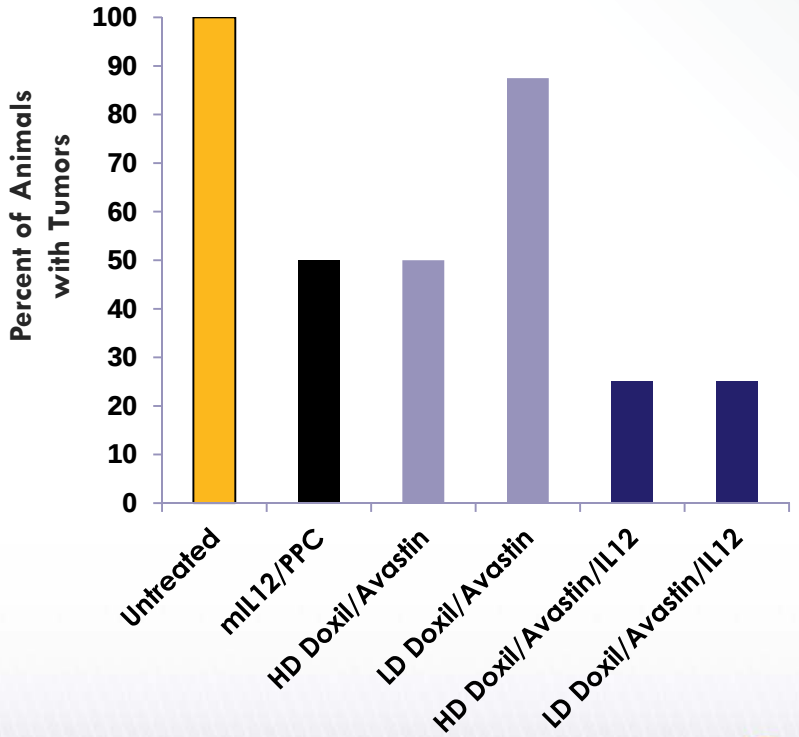
GEN-1 Preclinical Studies

GEN-1 + Doxil + Avastin

- Doxil + Avastin is SoC for platinum-resistant ovarian cancer (2nd line)
- GEN-1 + Doxil +Avastin Treatment Resulted in a > 98% Reduction in Tumor Burden Compared to Untreated Animals





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

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

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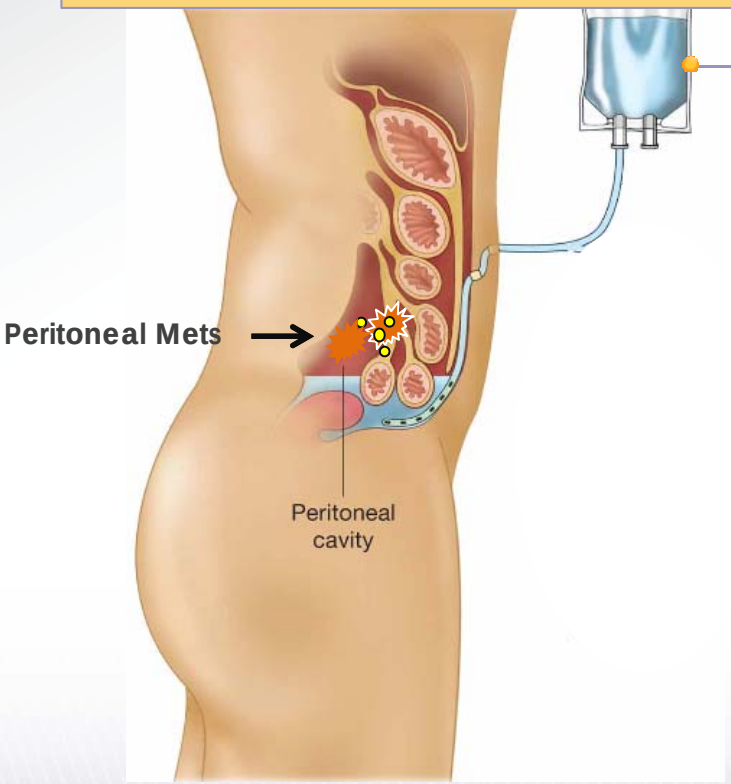
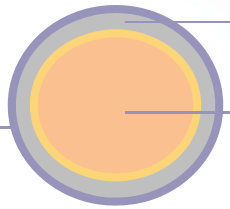
GEN-1 for Ovarian Cancer

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-1causes 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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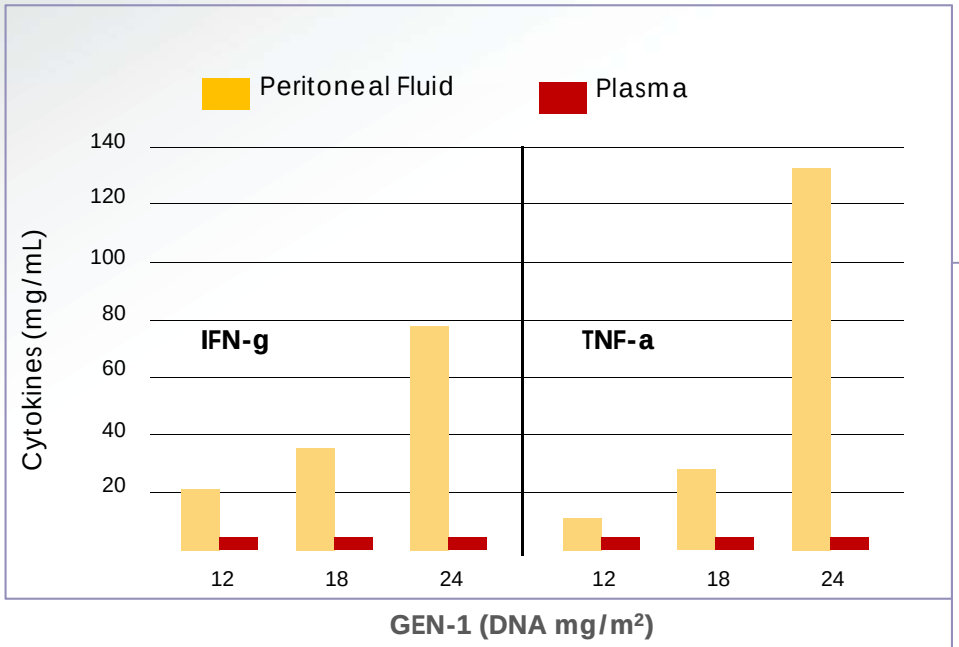
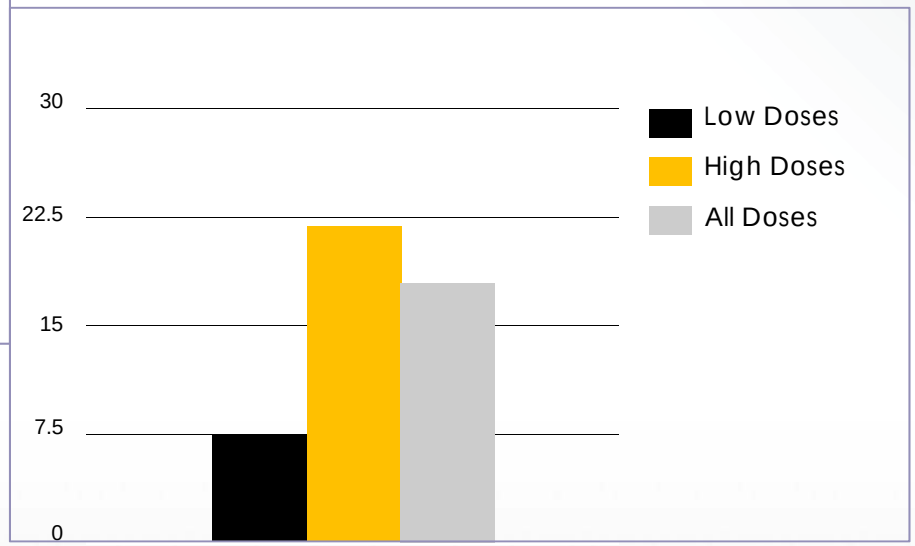
GEN-1 Immunotherapy

Clinical Experience To-Date

Biological Activity



Single Agent Benefit



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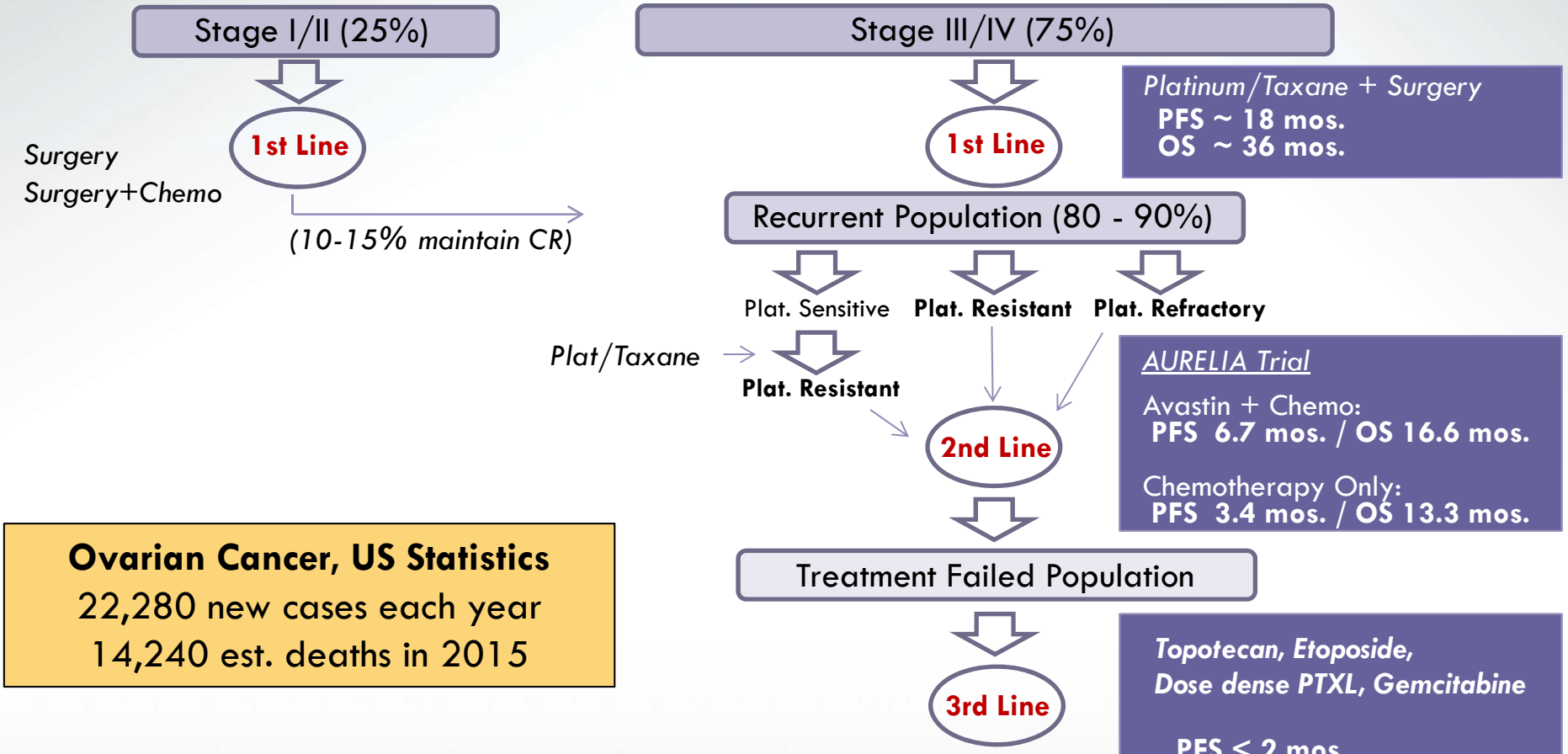
Ovarian Cancer Treatment Path



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

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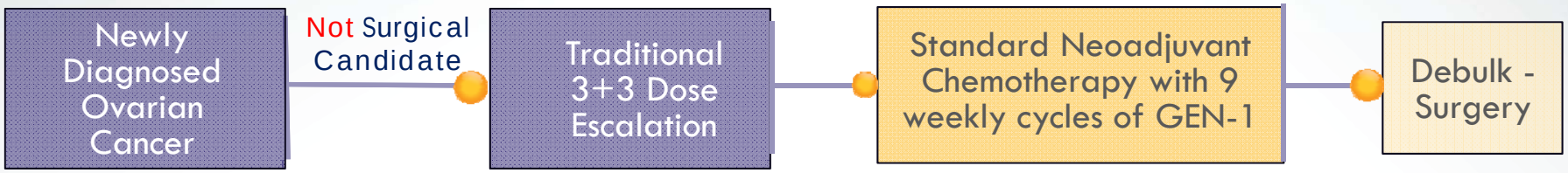
GEN-1 Phase I Study

1st 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	cOR, pCR, PFS, ↑IFNγ, ↑IL-12, ↓VEGF and Tumor-specific T-cell response CD4+,CD8+

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OVATION Study

Clinical Experience To-Date

Cohort 1 36 mg/m²	FIGO Stage	Tumor Response RECIST	Surgical De-bulking Status	CA-125 Levels (U/mL) *			Pathological Results **
				Baseline	Post TX	2 Weeks Post TX	
OV01-01 (01)	IV	Stable Disease	Optimal R1	362.0	9.0 -97.5%	6.4 -98.2%	macroPR
OV01-02 (02)	IIIB	Stable Disease	R0	246.0	28.0 -88.6%	7.9 -96.8%	microPR
OV01-04 (05)	IIIC	Complete Response	R0	423.0	64.4 -84.8%	16.3 -96.1%	Complete Pathological Response (pCR)

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

** In a 332 patient GOG Study, pCR's were seen in only 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)

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GEN-1 + Doxil Phase 1b Trial

2nd Line (completed Dec. 2014)

GEN-1 (mg/m^2)	Doxil (mg/m^2)
24	40
36	40
36	50

Clinical Observations

- All doses well tolerated with no DLTs
- Clear dose responses at 36 mg/m^2 dose
  - CRR (SD+PR+CR) (all doses): **> 50%**
  - CRR (SD+PR+CR) at highest dose: **86%**
- Compares favorably to single agent Doxil in 4 previous studies:
  - CRR (SD+PR+CR) **< 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-γ and TNF-α: ~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 IFNγ and TNF-α in plasma

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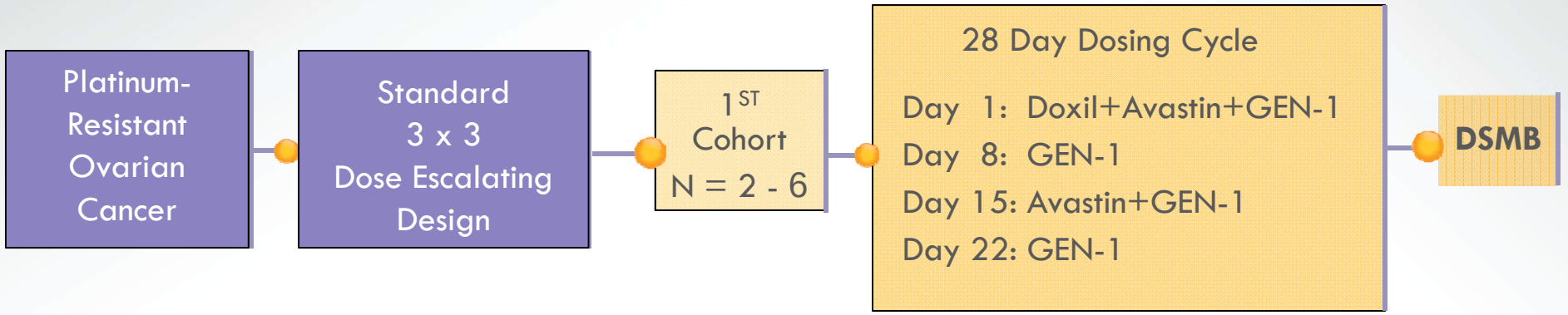
GEN-1 + Avastin and Doxil Trial Design

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

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Strong Patent and Regulatory Protection

ThermoDox (LTSL)

Composition of Matter Patent (2021)

Method Patents (2026)

Orphan Drug Designation for HCC

- U.S. - 7 year exclusivity
- Europe -10 year exclusivity
- Eligible for 5 year Hatch-Waxman (2031)
- No immediate ANDA route to registration

GEN-1 (TheraPlas)

Composition of Matter Patent (2027)

Methods Patents (2017)

Orphan Designation for Ovarian and GBM

- U.S. 7 year exclusivity
- No ANDA route to registration

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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)	OPTIMA 50% Complete				OPTIMA Enrollment Complete			1st Interim Efficacy Endpoint	
Euro-DIGNITY STUDY			Initiate Enrollment			1st Efficacy Assessment (24 pts)		Enrollment Complete		Final Data Assessment (70 pts)		
GEN-1												
OVATION STUDY		Efficacy & TR Data from Cohorts 1 & 2		Final Data from OVATION								
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	Initiate Phase 2 Study			
TheraSilence												
Lung Cancer		Pre-Clin Data (Collaboration w/ RNA company		Potential Co-Development Collaboration								

Corporate Information

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