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NASDAQ: CLSN

May 2016

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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

Deep Pipeline and Multiple Technology Platforms

Focused and Capital Efficient Drug Development

Local/Regional Therapies in Cancer
Nanoparticle-Based Technology

Targeted Chemotherapy Programs

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

- Updated China Cohort from HEAT Study (Q3 -2016)
- Enrollment Completed in OPTIMA (2017)
- 1st Interim Efficacy Read-out (2018)

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

GEN-1 IL-12 Immuno-Oncology Programs

Phase I Neoadjuvant Therapy in Frontline Ovarian Cancer (2016)
Phase I/II Combination Therapy with Avastin in Platinum-Resistant Ovarian Cancer (2016-2017)

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Two Platforms to Drive Growth

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 Newly Diagnosed Ovarian Cancer
- Combination Study with Avastin and Doxil in Platinum-Resistant Ovarian Cancer

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Chemotherapy
ThermoDox®
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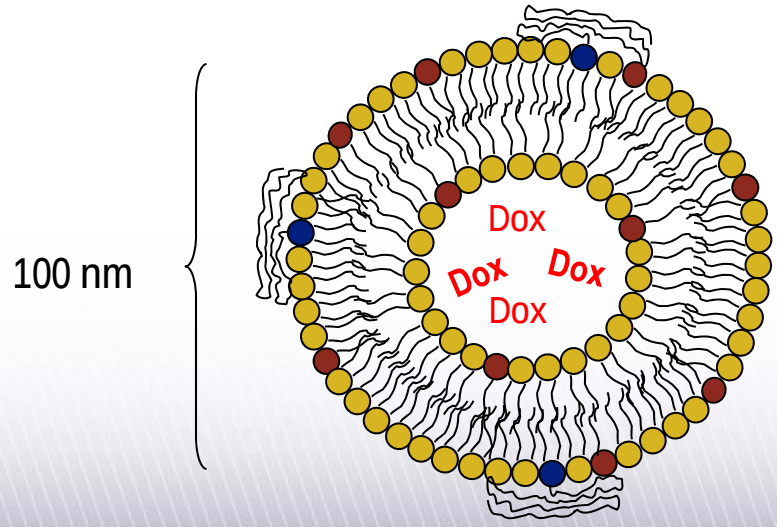
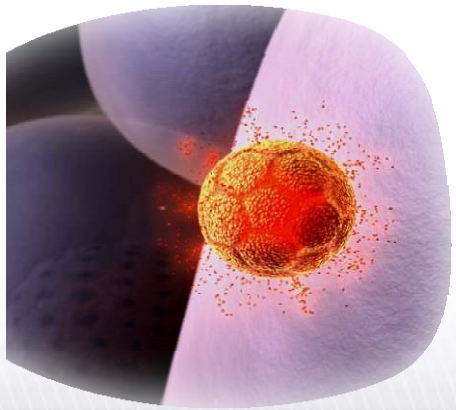
ThermoDox Design Principles

- Complete encapsulation of Doxorubicin HCl
- Release of the encapsulated Doxorubicin with mild thermal warming (> 40°C)
- Ability to provide adequate systemic circulation to allow Mononuclear Phagocytic System (MPS) and Enhanced Permeation and Retention (EPR) to concentrate at tumor target
- Heat-inducing medical devices to warm the target tumor - initiating a rapid drug release in the targeted tumor vasculature





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Hepatocellular Carcinoma

Large and Deadly Global Cancer

- **5th most prevalent**
  - 800,000 incidence worldwide; growing 5% annually
  - By 2020, expected to be the #1 cancer, surpassing lung 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
  - Cure, usually through surgery, is possible in less than 20% of patients
- **Local therapies include:**
  - RFA, TACE and radiation
  - RFA is the dominant treatment average 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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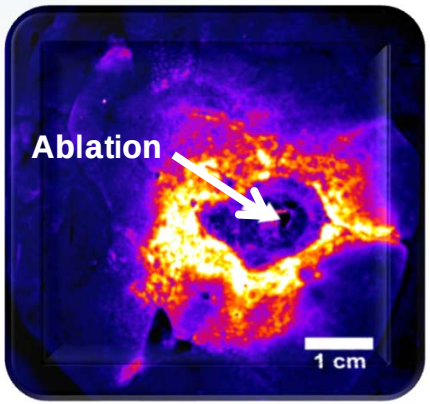
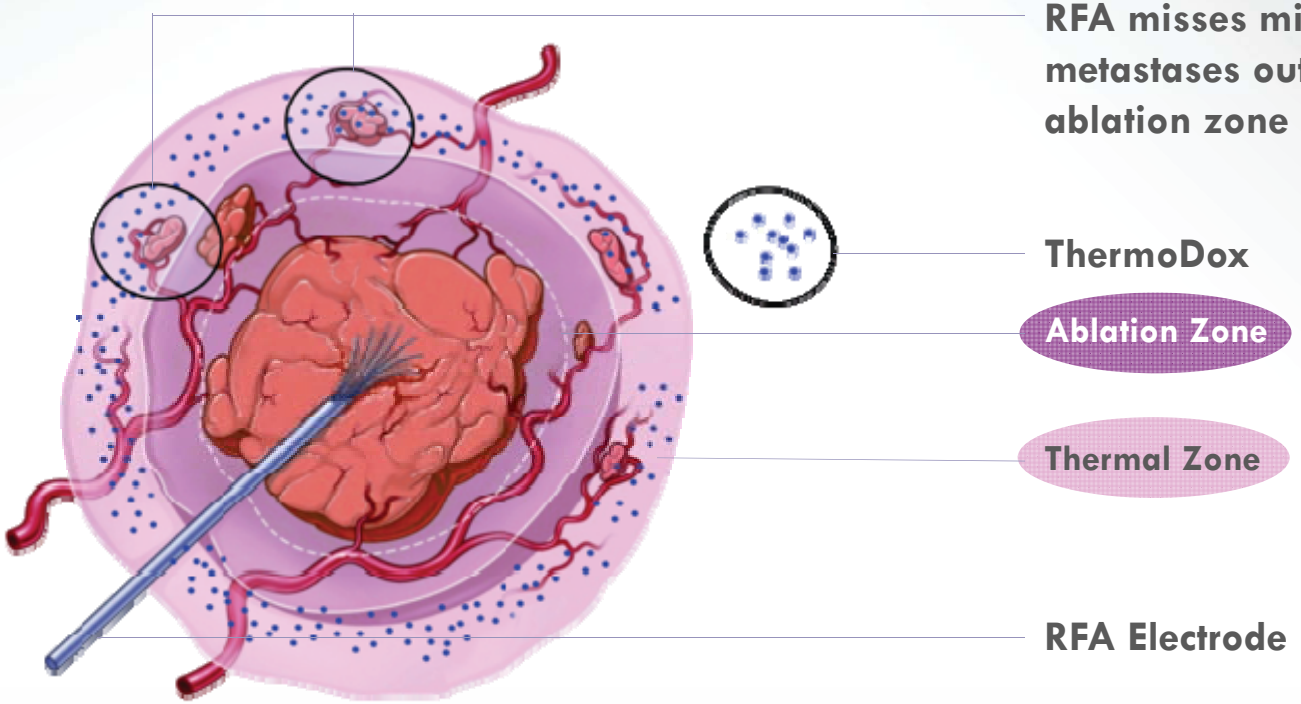
ThermoDox + RF Liver Ablation

Expanding the Treatment Zone Addresses RFA Limitations

ThermoDox
+
sRFA 45





- 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 metatases outside the ablation zone

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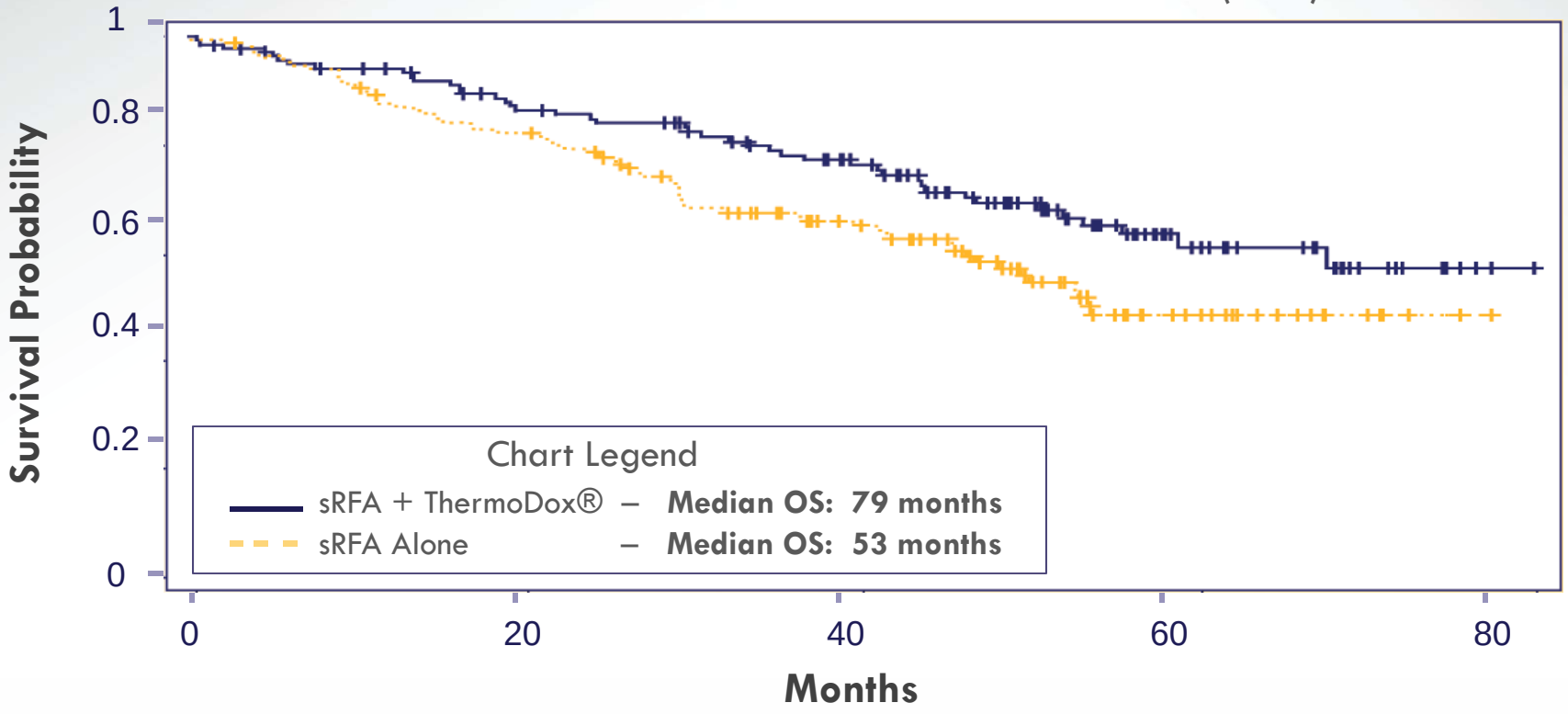
ThermoDox: HCC

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 for HCC

	HEAT STUDY	HEAT STUDY SUB-GROUP	OPTIMA STUDY DESIGN
Population	701 Patients	285 Patients	550 Patients
Eligibility	1 to 4 Lesions At least one 3 cm to 7 cm Child-Pugh A/B	Single Lesion 3 cm to 7 cm Child-Pugh A/B	Single Lesion 3 cm to 7 cm Child-Pugh A
Primary Endpoint	PFS (HR=0.75) 380 PFS Events	OS (HR=0.63) 79 month OS	OS (HR=0.75) 198 OS Events
Interim Endpoints	None	HR = 0.63 (Observed)	HR=0.61 (118 OS Events)* HR=0.70 (158 OS Events)*
Powering of Final Endpoint	33% Improvement in OS 80% Power/p-value 0.05	N/A	33% Improvement in OS 80% Power/p-value 0.05

* Minimal Alpha Spend - *O'Brien-Fleming stopping boundaries determined by means of the Lan-DeMets approach*

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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

DEB TACE – Doxorubicin Eluding Beads

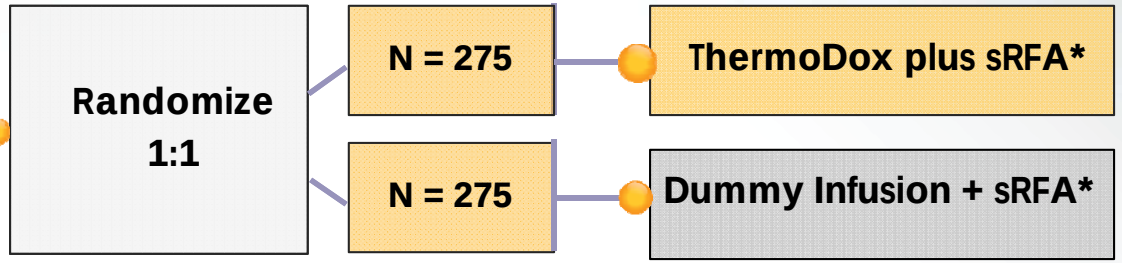
Phase III OPTIMA Study Design

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

*sRFA45 Standardized Radiofrequency Ablation > 45 minutes

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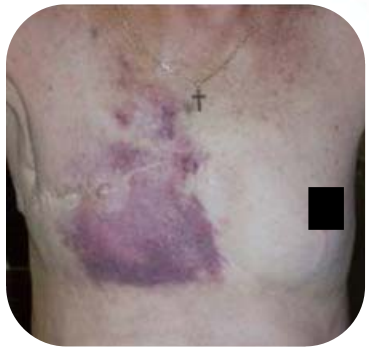
ThermoDox: RCW Breast Cancer

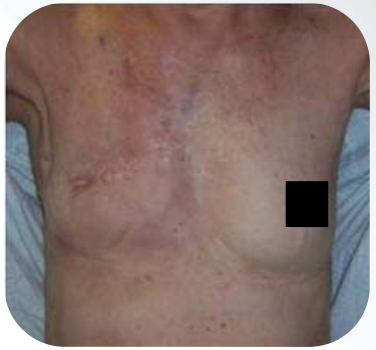
Difficult to Treat with Severe Complications

- 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

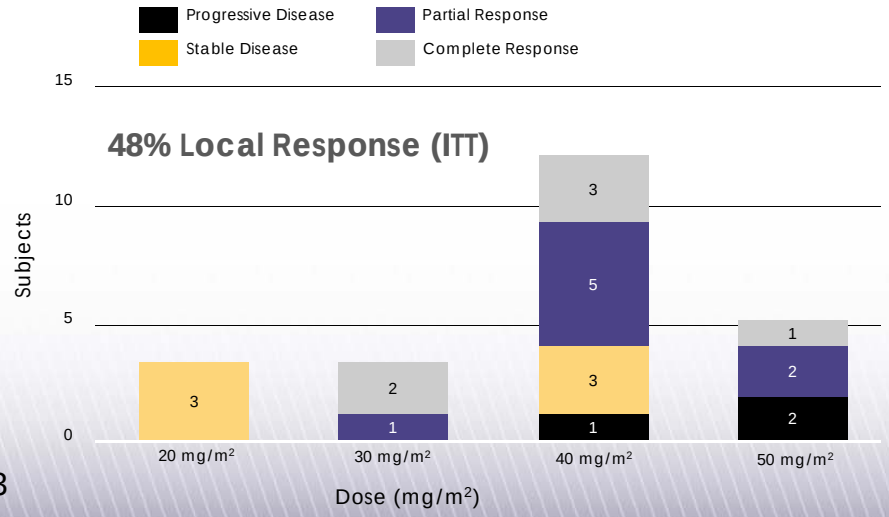
Limited Treatment Options



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

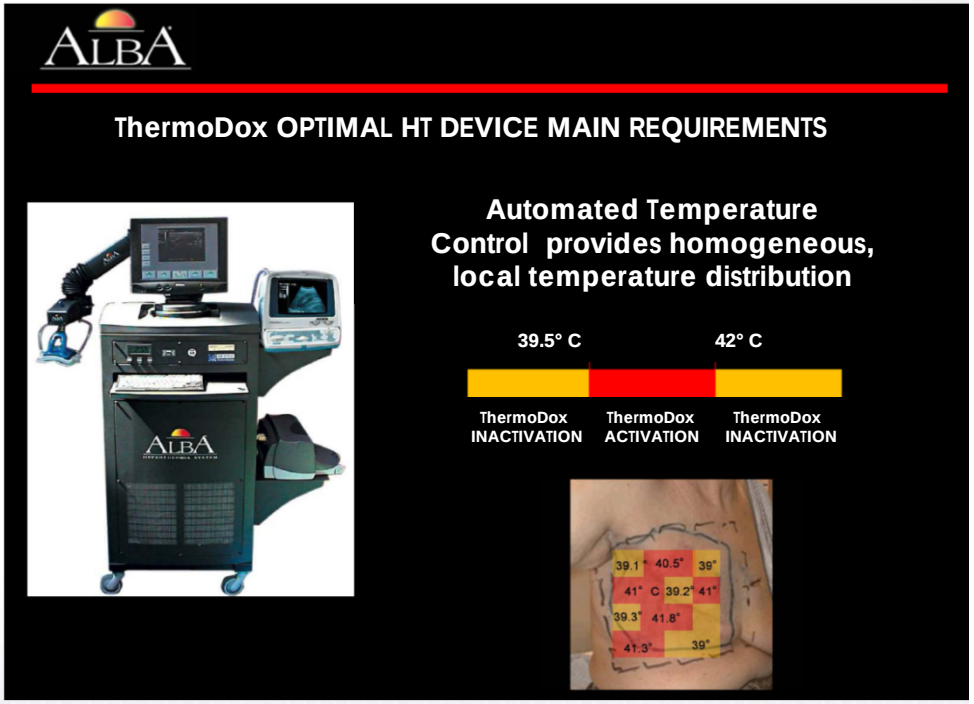
- Evaluate complete and partial response after 3 cycles of ThermoDox + Hyperthermia and Radiation Treatment (Tri-Modal Therapy)
- Evaluate loco-regional breast tumor control in patients undergoing Tri-Modal Therapy

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

GEN-1 Immunotherapy

Novel PPC Plasmid DNA Nanoparticle

Rationale for Local IL-12 Therapy with DNA Nanoparticles

- Local production of potent cytokine IL-12
- IL-12 recruits immune system with multiple mechanisms of action
- Avoids serious toxicities and poor pK associated with recombinant IL-12 protein

IL-12 Approaches Under Development

- ***Recombinant IL-12 Protein*** – Short half life; Systemic toxicities (Neumedicines – Low dose IL-12 protein for Lymphoma; Multiple Academic Institutions)
- ***Viral Vectors*** – Transfection efficiency; Ability to repeat dose (ZioPharm – melanoma; breast and brain cancer)
- ***Electroporation*** – Limited to intra-tumoral administration (Inovia and Oncosec – melanoma, head & neck, lung, pancreatic, prostate and breast cancer)
- **Non-Viral DNA Plasmid Nanoparticles** (GEN-1)
  - Persistent local delivery of IL-12 (up to one week)
  - IP administration and repeat dosing – Ovarian Cancer
  - Ideal for long-term maintenance therapy

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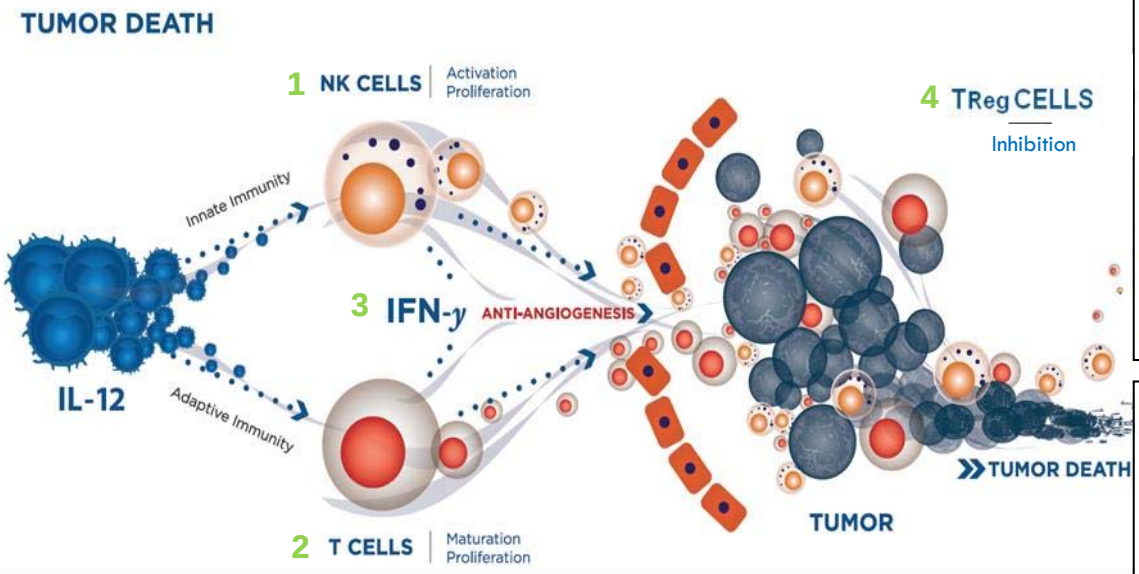
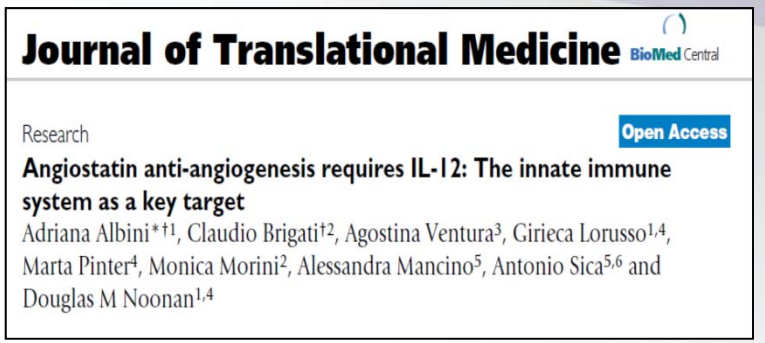
GEN-1 IL-12 Immunotherapy

Powerful Immune Modulating Agent

Multiple Mechanisms of Action

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



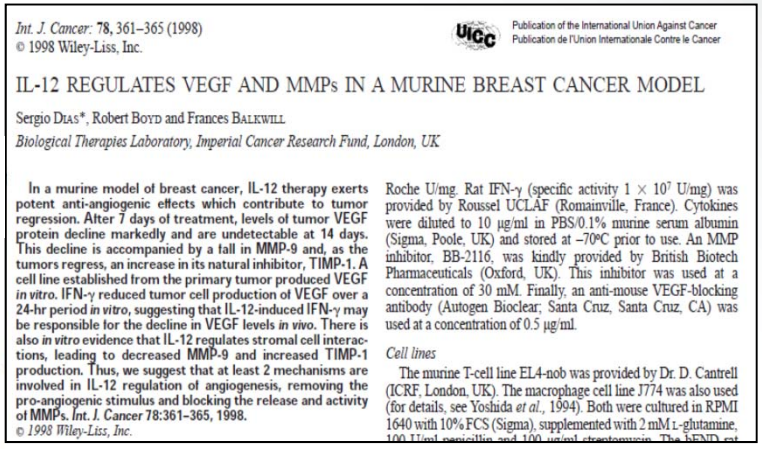


Journal of Translational Medicine BioMed Central

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)
© 1998 Wiley-Liss, Inc.

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

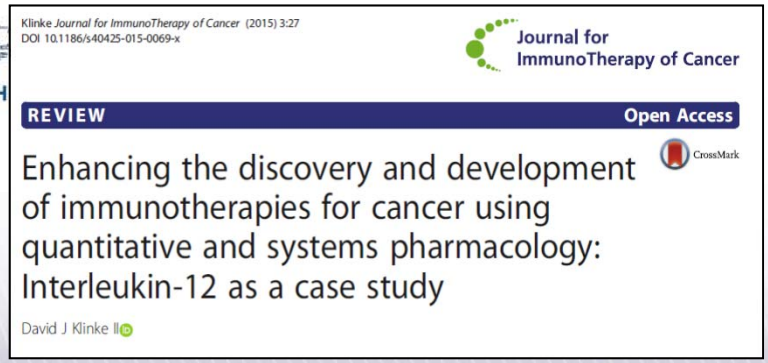
Biological Therapies Laboratory, Imperial Cancer Research Fund, London, UK

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.
© 1998 Wiley-Liss, Inc.

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,



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

Journal for ImmunoTherapy of Cancer

REVIEW Open Access

CrossMark

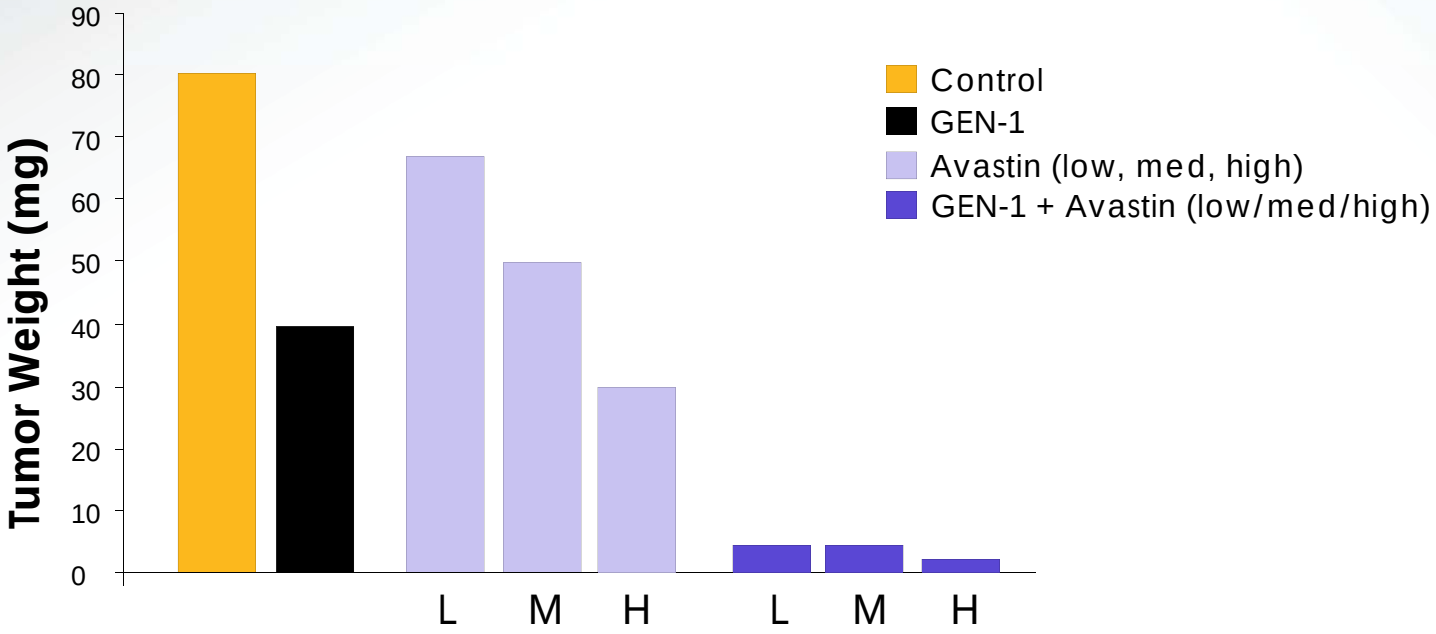
Enhancing the discovery and development of immunotherapies for cancer using quantitative and systems pharmacology: Interleukin-12 as a case study

David J Klinke II

GEN-1: Preclinical Studies

Combination with 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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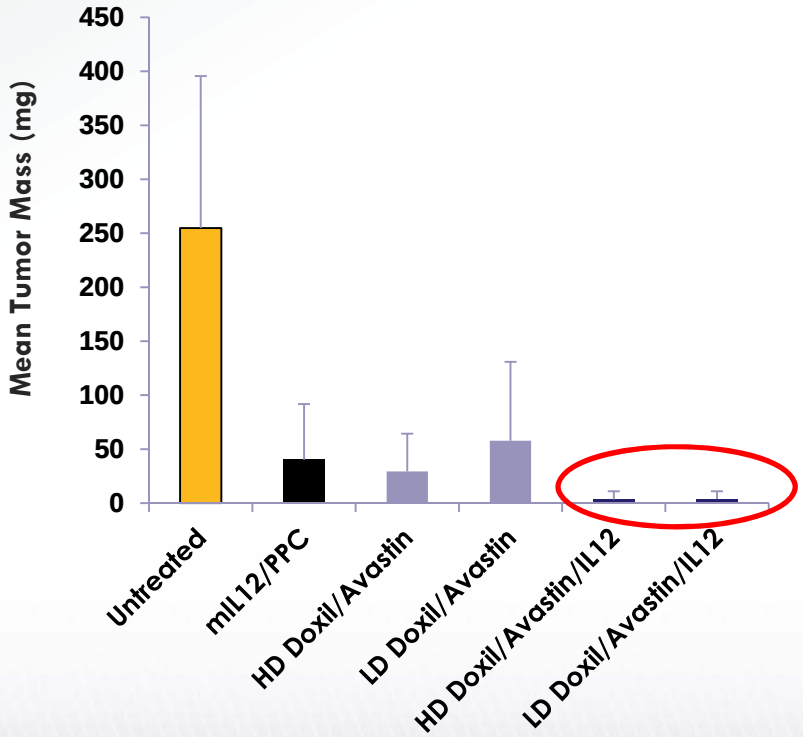
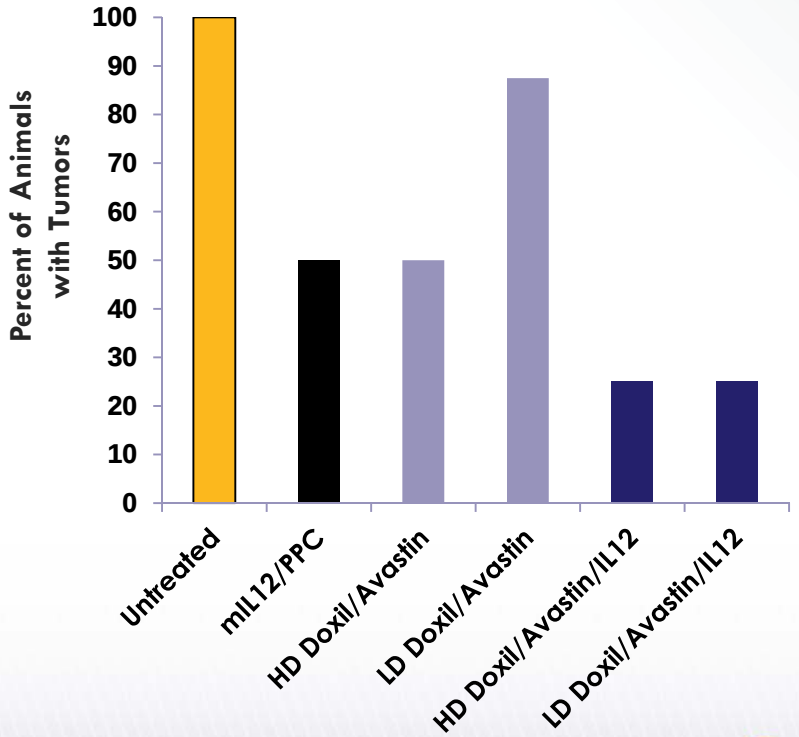
GEN-1: Preclinical Studies

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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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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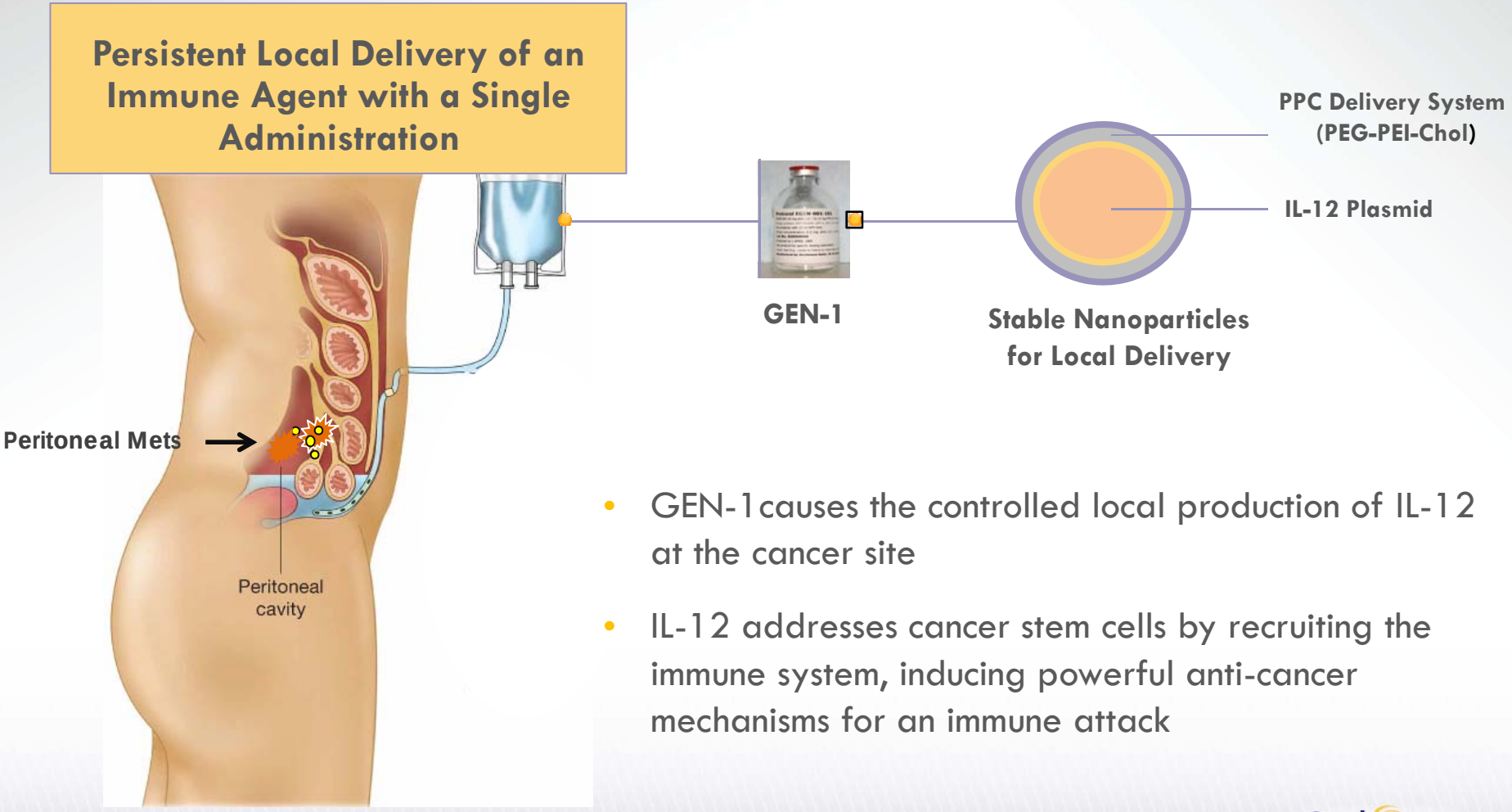
GEN-1 for Ovarian Cancer

Local Immunotherapy

Persistent Local Delivery of an Immune Agent with a Single Administration



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

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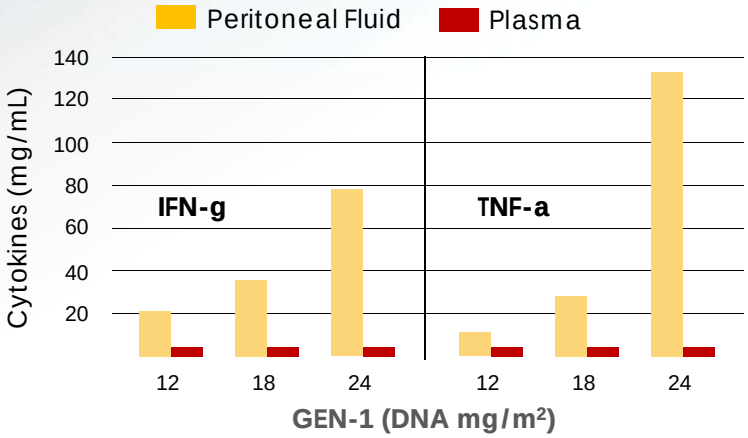
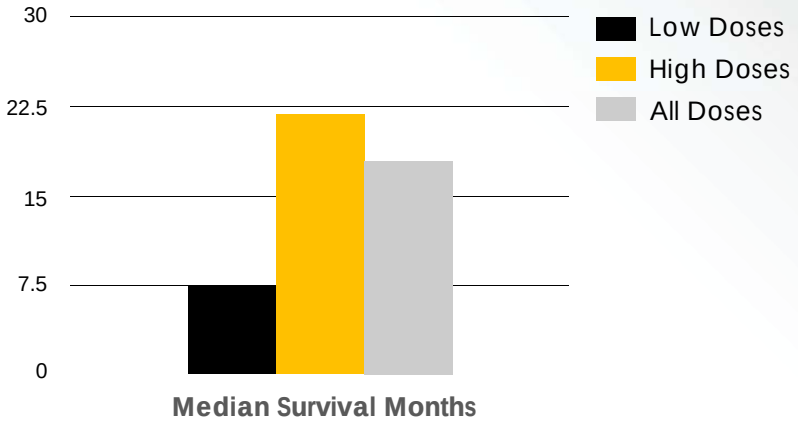
GEN-1 Immunotherapy

Clinical Experience To-Date

1 Convincing Evidence of Biological Activity



2 Single Agent Benefit



3 Lack of Overlapping Toxicities Allows for Combination Therapies

GEN-1 (IP)

- Gastrointestinal
- Low Grade Fever
- Chills
- Catheter Site Pain/Redness
- Abdominal Discomfort

Chemotherapy (IP)

- Cardiovascular, Hematological
- Metabolic, Neurologic
- Fever, Infection
- Urinary Problems, Gastrointestinal
- Hepatic, Fatigue, Metabolic, Pain

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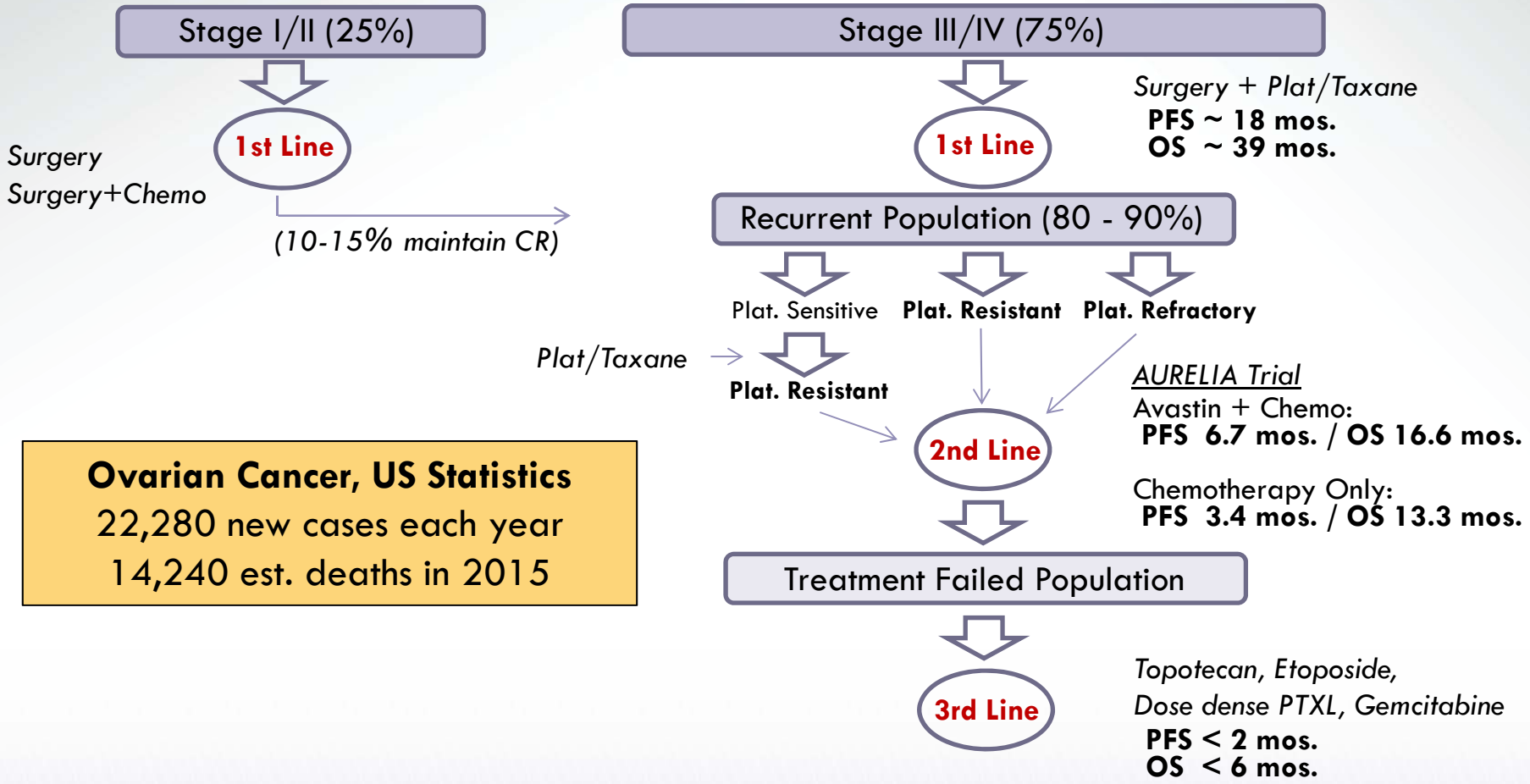
Ovarian Cancer Treatment Path



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

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GEN-1 + Doxil Phase 1b Trial

Platinum Resistant Ovarian Cancer

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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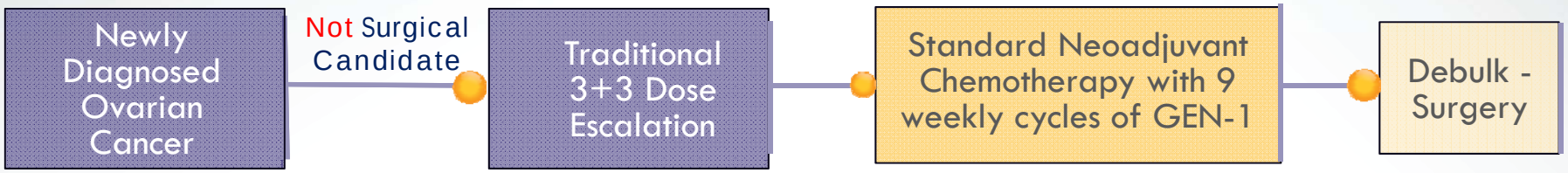
GEN-1: First Line Treatment in Ovarian Cancer

Phase I Study – First Patient Enrolled September 2015

The OVATION Study



Neoadjuvant Study in Newly Diagnosed Ovarian Cancer Patients	To determine safety, dose, and feasibility in target patient population
Primary Endpoint	Optimal Dose (Max or MTD)
Secondary Endpoints	pCR, PFS, ↑IFNγ, ↑IL-12, ↓VEGF

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OVATION Study

Clinical Experience To-Date

Cohort 1 36 mg/m²	FIGO Stage	Tumor Response RECIST	Surgical Debulking 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%	microPR
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

* 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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Platinum Resistant Ovarian Cancer

GEN-1 in Combination with Avastin + Doxil (SoC)

Clinical Data - Platinum Resistant Ovarian Cancer			
HISTORICAL	Doxil Only (Four Doxil Studies)	ORR (CR+PR)	**8-12%**
		CRR (CR+PR+SD)	**< 50%**
AURELIA TRIAL	Chemo Only	ORR (CR+PR)	**12%**
		CRR (CR+PR+SD)	n/a
	Chemo + Avastin	ORR (CR+PR)	**27%**
		CRR (CR+PR+SD)	n/a
Phase 1b GOG Study	Doxil + GEN-1 (Highest Dose Cohort)	ORR (CR+PR)	**29%**
		CRR (CR+PR+SD)	**86%**

Pre-Clinical Data - Presented at AACR 2016	Reduction in tumor burden
GEN-1 Alone	50%
Avastin Alone	39%
GEN-1 + Avastin	78%
GEN-1 + Avastin + Doxil	**92%**

1. Combining GEN-1 with Avastin + Doxil resulted in a > 98% decrease in tumor burden in animals compared to controls and a 92% decrease in tumor burden compared to animals treated only with Avastin and Doxil (p-Value < 0.01)
2. The combination of GEN-1 with Avastin and Doxil was well tolerated with no systemic toxicities
3. Plans for initiation of Phase I/II trial in Q4 - 2016

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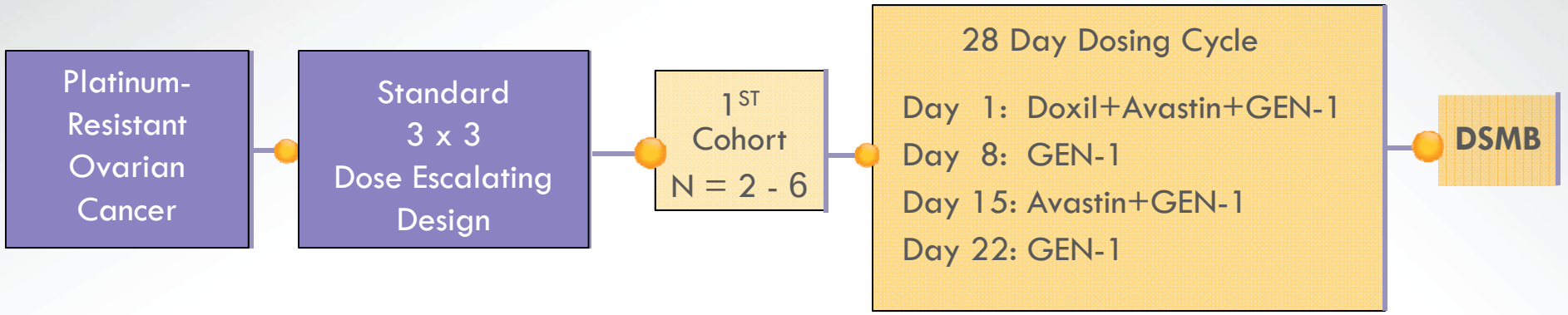
GEN-1 with Avastin and Doxil

Platinum – Resistant Recurrent Ovarian Cancer



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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GEN-1 + Avastin and Doxil

Statistical Rationale for Phase II Study Design

100 Patients Planned for Randomized Phase II Study

- **Primary Endpoint:**
  - 70 PFS events provide 80% Power
  - P-Value = 0.10
  - Minimum observed PFS HR ratio associated with a statistically significant result is 0.74 (~ 2.2 mos. v AURELIA)
  - Median PFS control is approximately 6.7 months from the AURELIA Study
- **Overall Survival:** OS follow up will continue until at least 60 events (deaths) are observed to provide a meaningful OS estimate (95% confidence interval of OS HR and associated medians)

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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)

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								

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Financial Overview

Cash & Investments (12/31/15)	$20.1 million
Estimated cash usage per month	~$1.3 million
Market Capitalization	$35 million
Common shares outstanding	23 million
Fully diluted shares outstanding	31 million
Avg Daily Trading Volume	~ 100,000

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