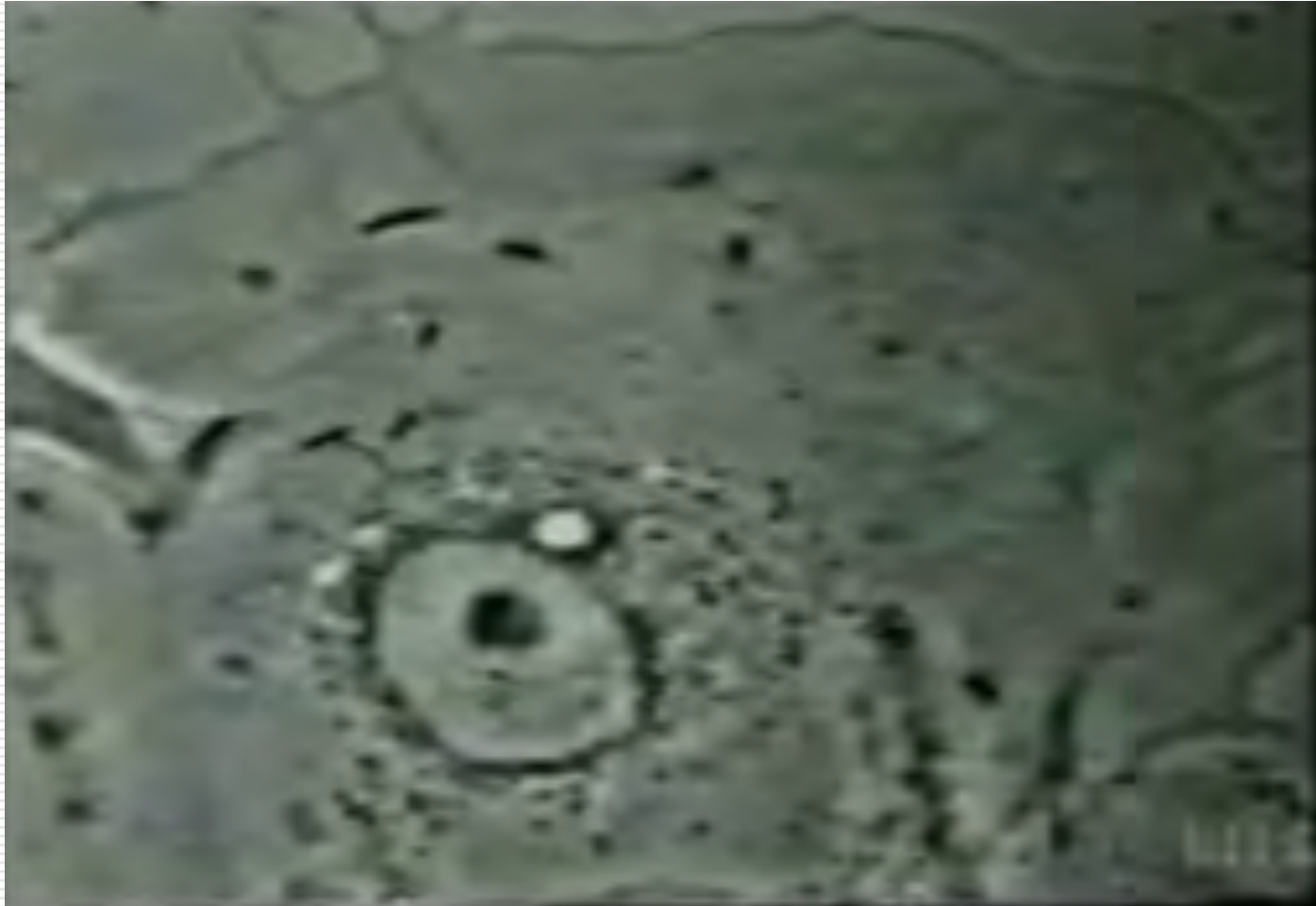




Lm*-LLO: Live Bioengineered *Listeria

Antigen-LLO Fusion Protein Secretion



Live wild type *Listeria* in action
inside a cell

Dr. John Rothman
Advaxis Inc.



Safe Harbor Statement

Statements made during the course of this presentation that state the Company's or management's intentions, hopes, beliefs, expectations or predictions of the future are forward-looking statements. It is important to note that the Company's actual results could differ materially from those projected in such forward-looking statements. This presentation only highlights some of the progress Advaxis has made to date. It is not meant to be a complete document as it represents only a portion of the company's presentation of its business.

Additional information and factors that could cause actual results to differ materially from those in the forward-looking statements are contained from time to time in the Company's SEC filings, including but not limited to the Company's report on Form 10-K for the year ended October 31, 2010. Copies (or more current versions) of this presentation may be obtained by contacting the Company or visiting the Company's website, www.advaxis.com.



Lm-LLO Immunotherapies

- Attenuated $\sim 1 \times 10^5$ times
- Secrete an antigen fused to a non-hemolytic, highly immunogenic fragment of LLO
 - 10-12 copies of fusion protein genes
- HPV agent is the 1st to reach the clinic
 - PSA and Her2 agents in 2012
- For the treatment of cancer, infectious disease, autoimmune disease

Our *Listeria* is 10,000-100,000 less pathogenic than wild-type *Listeria*



Bioengineered *Listeria*: Novel, Useful Therapeutic Modality

- Live metabolically competent *Listeria* is more complex than antibodies or synthetic molecules and engender a more complex immune response
- The immune response to *Listeria* is more comprehensive than to viruses, yeasts, & other bacteria.
 - Classical activity
 - Innate/adaptive – no adjuvant is needed
 - Newly discovered activities
 - Intratumoral immunosuppression
 - Activities not previously associated with immunity
 - Vascular & myeloid upregulation effects



***Lm*-LLO: Comprehensive Immunotherapy**

Many Integrated Mechanisms

1. Strong Innate Immune Effects

- Lm-LLO vaccines are cleared in SCID & IFN- γ KO mice

Innate & Adaptive Immunity
stimulated by the same agent

2. Strong Adaptive Immune Effects

- High titers of activated CD4⁺, CD8⁺, APC, and TIL

3. Brief Exposure Results in Immune Memory Consolidation

- Antibiotics immediately after dosing do not impair long term responses

4. Alteration of Tumor Microenvironment

- Reduces both Tregs and MDSC in tumors but not in other tissue, Many other effects

5. Bystander Effects

- Lm infection induces cytokine and chemokine secretion from non-infected cells adjacent to infected ones.

6. Synthesis of New Immune Cells, Maturation of Existing Cells

- Marrow, tissue and blood born effects

7. Upregulation of Tumor Chemokines & T Cell Chemokine Receptors

- CXCL8, 9 & 10 & CXCR3 in T cells in TDLN

8. Chemotaxis and Extravasation of Activated Immune Cells

- Chemokine mediated effects and effects directly on vascular endothelium increase TIL

9. Antigen Spreading

- Immunotherapy directed against one TAA result in immune activation against other TAA

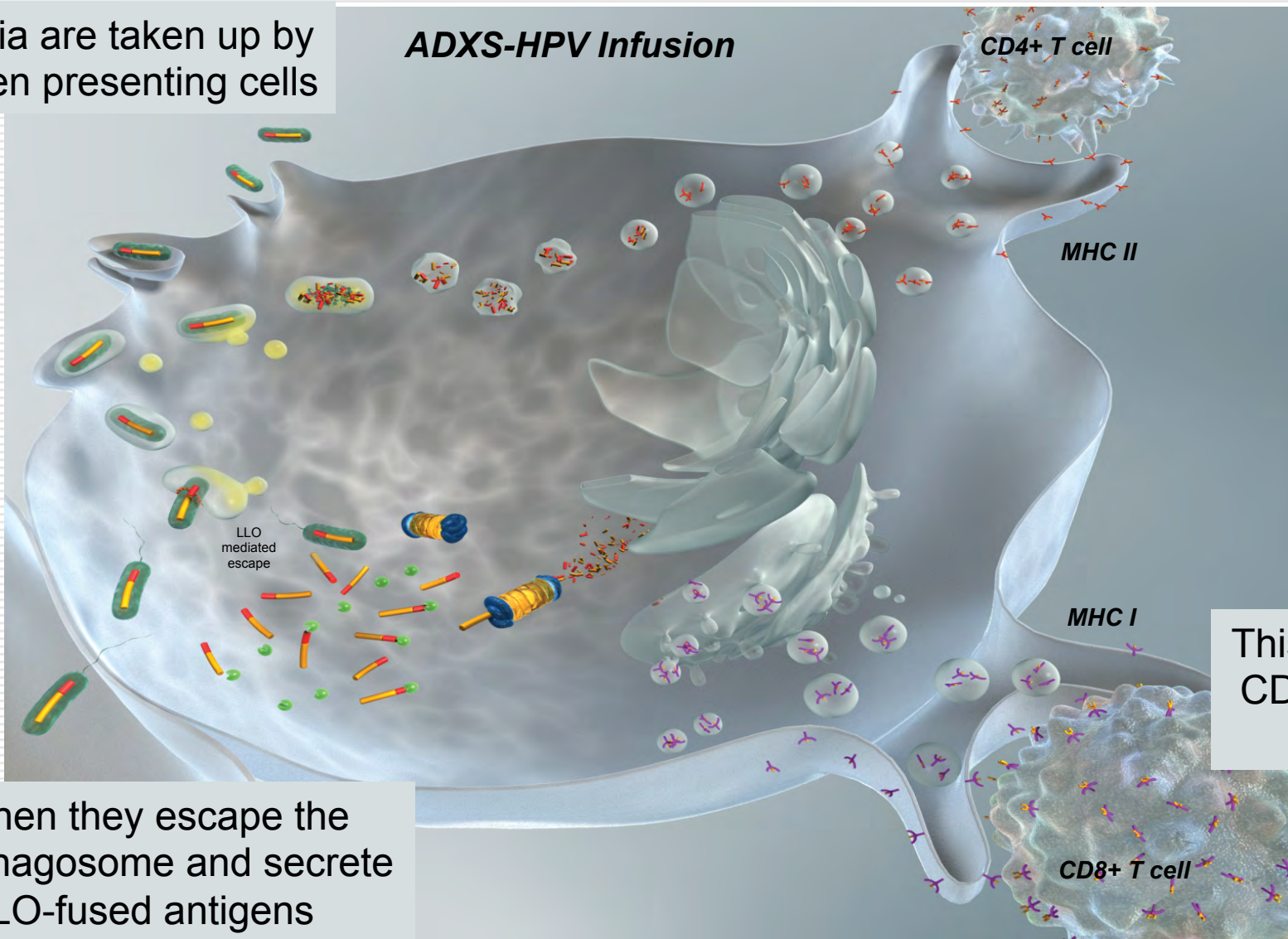
10. Predominant Cellular Immune Response. Little Antibody Formation.

- Not neutralized by humeral immunity, a useful property for cellular immune vaccine

Lm-LLO: Strong Adaptive Immune Effects

Listeria are taken up by antigen presenting cells

ADXS-HPV Infusion



Then they escape the phagosome and secrete LLO-fused antigens

This creates CD4 & CD8 cells

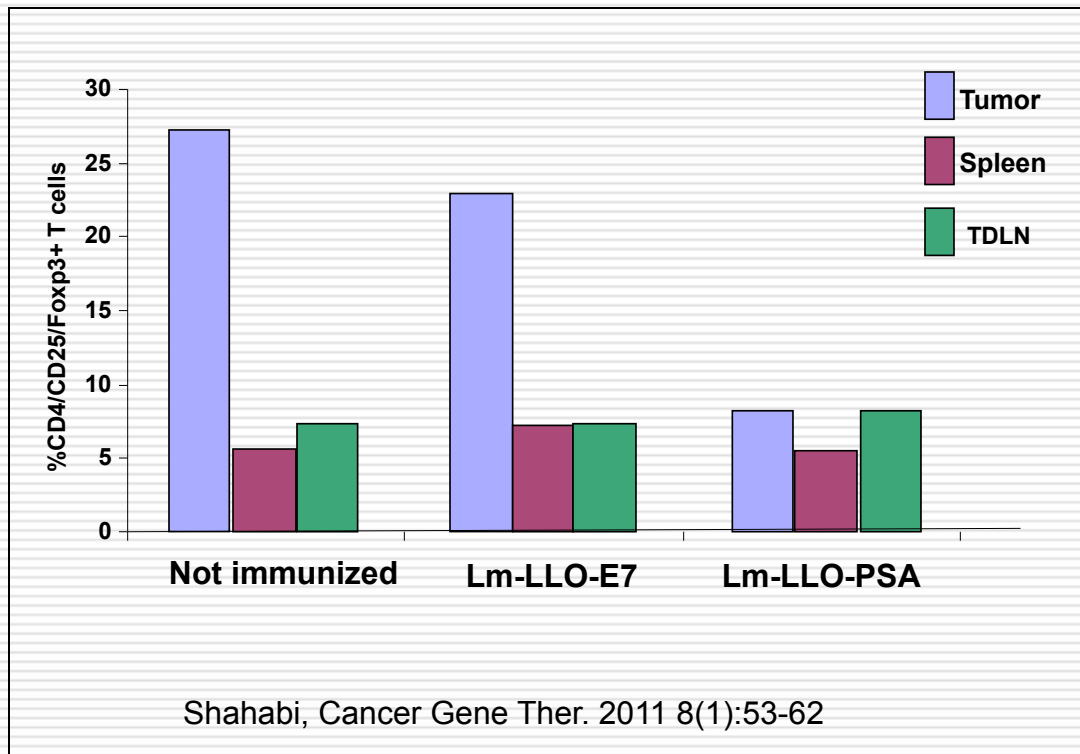


Lm-LLO Extensive Innate Effects

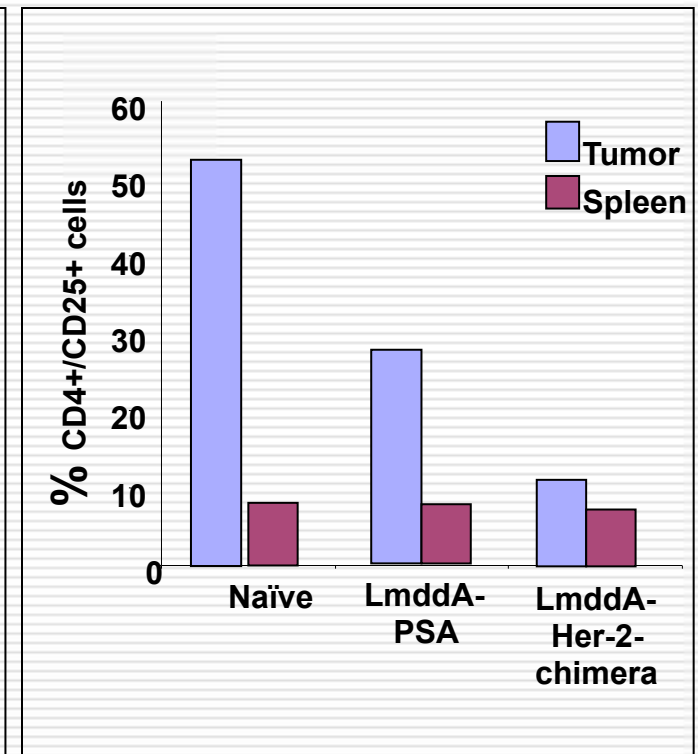
- **PAMP and DAMP Mediated Events**
 - NOD1 & 2, TLR 2, 4 & 5, 7, 9, NK- $\kappa\beta$, IL-2, IL-12, IFN- γ , TNF- α and NO mediated immune activation mechanisms
- **Systemic Innate Activation Including:**
 - Innate effects include mediation of:
 - IL-1 β , IL-2, IL-6, IL-8, IL-12, IL-15, IL-18, NOS generating NO, CSF-1, MCP-3, and MCP-1 IL-18. CCR2 IFN- γ TNF- β , caspase, TNF- α , type-1 interferon TRAIL, CD40, B7-H1 [PD-L1], CD86 [B7-2] and B7-DC [PD-L2]
 - Shift from Th-2 to Th-1 profile; M Φ -2 to M Φ -1, etc.
 - recruitment & activation of neutrophils, NK cells, mast cells, M Φ , conventional & plasmacytoid DC, CD4⁺, CD8⁺
- **Stimulation of Lymphopoiesis, Monopoiesis**
 - differentiation of undifferentiated immune cells to activated effector cells.
- **Facilitates Chemotaxis**
 - Increased extravasation of activated immune cells into tumors
 - CCR2, CXCL-8, CXCL-9, CXCL-10, CX3CL-1, MCP-1, MCP-3
- **Intra-Tumoral Effects**
 - reduction of Tregs & MDSC
 - Confined to tumor – not systemic as in CTLA4 blockade
 - T_{reg} cells & Th-17

Treg Reduction in PSA & cHer-2 Models

PSA

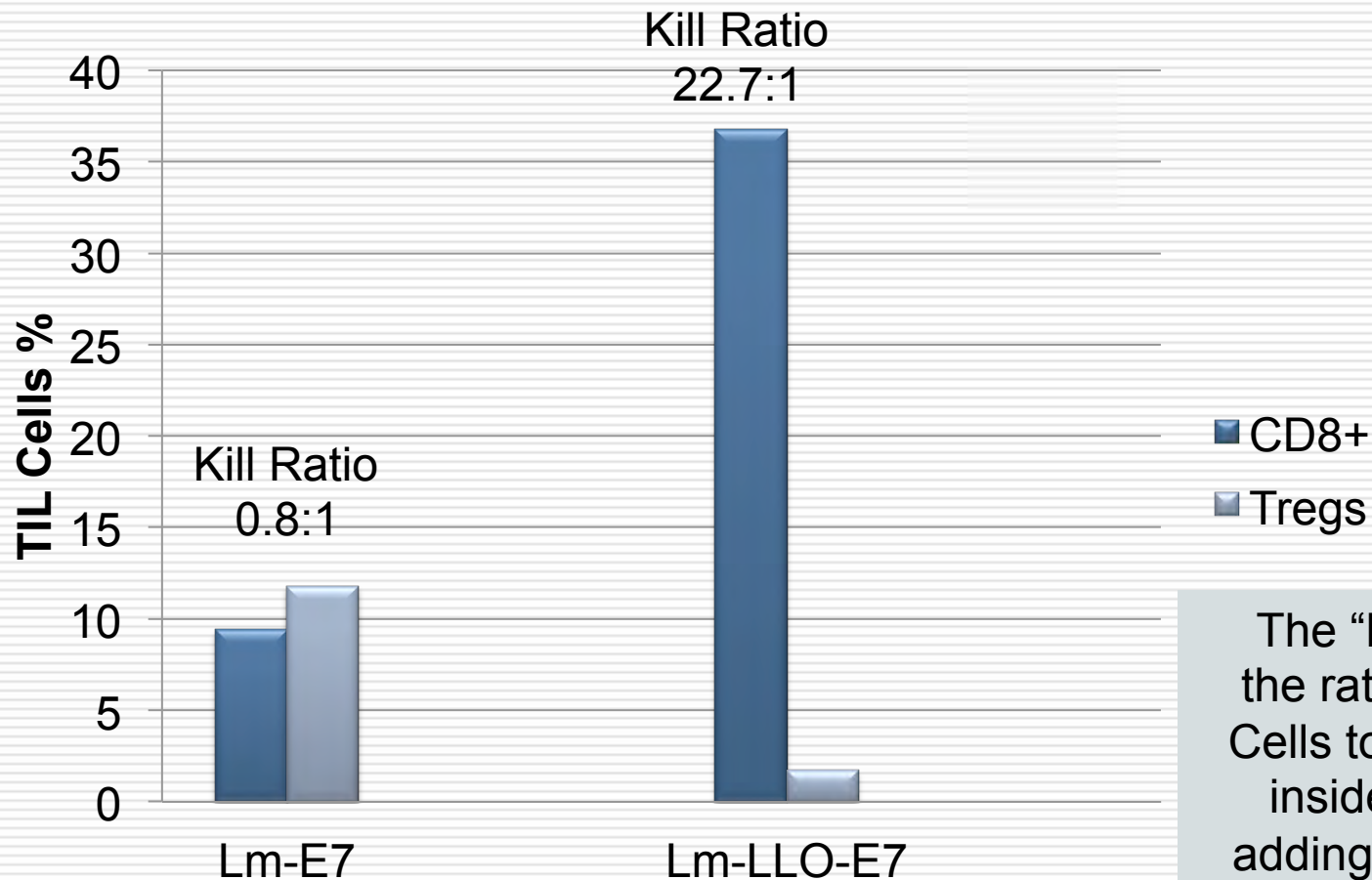


cHER2



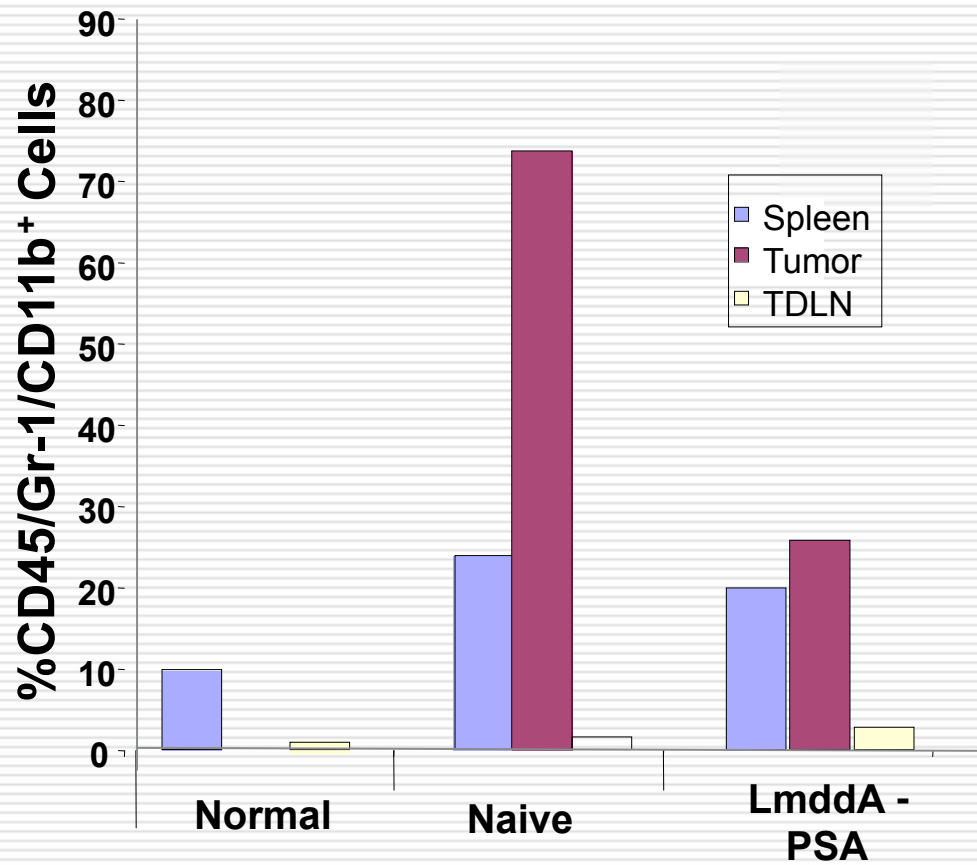
Tregulatory cells inhibit immune attack-protecting the tumor, reduction is specific to having the correct antigen

Lm-LLO-Antigen Fusion Protein is Necessary for Activity



The “Kill Ratio” is the ratio of killer T Cells to T-reg cells inside the tumor, adding LLO fusion proteins to *Listeria* causes the change

Lm-LLO Decrease MDSCs in tumors



MDSCs are another immune inhibiting cell, the effect is specific to the tumor, not general tissues



SAFETY

Lm-LLO Constructs Are Nonpathogenic

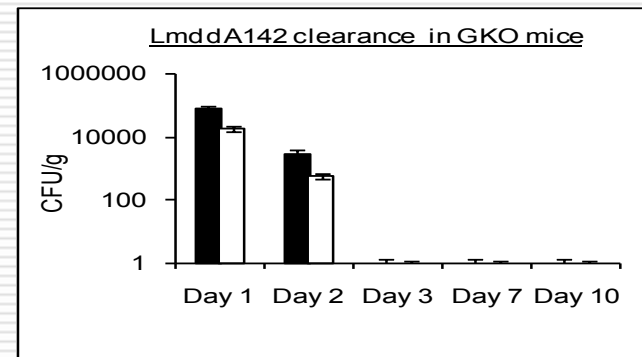
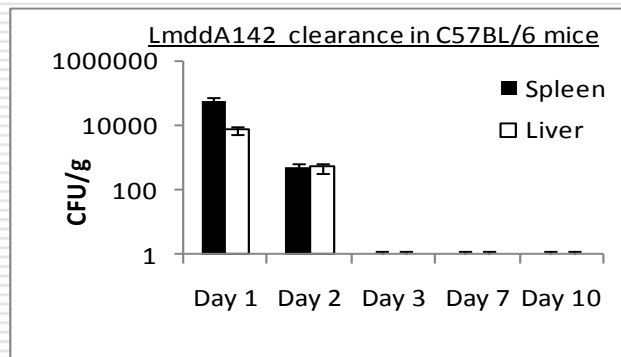
2 government regulatory agencies have designated *Lm*-LLO agent classification consistent with BSL-1/Risk Group 1 (non-pathogenic)

- **The US CDC Public Health Service waived PHS Import Permits**
 - “Based upon the review of your application, the material you wish to import contains non-infectious material (highly attenuated *Listeria* vaccine) and would not require a U.S. PHS Import Permit.”
- **German ZKBS designated a Risk Group 1**

SCID Mice Clear *Lm*-LLO Vaccines

- LD_{50} in C57BL/6 = 1×10^4 cfu. SCID mice challenged with 1×10^9 cfu
- All mice survived; 16% had low levels of detectable bacteria at 5d

G. Gunn Dissertation 2001



Dose = 1×10^8 cfu

Wallecha, A., et al. 2009. *Clinical & Vaccine Immunol.* 16(1):96-103

~362 doses in ~153 patients to-date



Phase 1



ADXS11-001 Targets HPV

- HPV is associated with 5-7% of all cancer
- Cervix cancer is the 2nd leading cancer killer of women in the world
 - 1st in women under 50
- Oropharyngeal head and neck cancer, anal, vulvar, penile and possibly some lung cancers
- Gardasil, Cervarix don't work in women with HPV

Cervical Cancer Treatment Failures

GOG 127 Series Studies

Table 1. Protocol 127: Probability of Surviving Progression-Free and Median Overall Survival by Study Section

Protocol 127 Study section	Agents studied	N of eligible Patients	Prob (PFS >6 months)*	Median Survival (months)**
B	Isotretinoin & Interferon	36	0.06 (0.04)	3.8
C	Cisplatin & Pentoxifylline	45	0.21 (0.06)	6.2
D	Altretamine	30	0.07 (0.05)	4.7
F	Topotecan	42	0.14 (0.05)	5.3
H	Etoposide	24	0.12 (0.07)	4.2
K	Gemcitabine	26	0.04 (0.04)	4.7

There are no study sections labeled A, E, G, I, J, or O. Results from studies L, M, N, P, and Q are pending.
 * Product-limit estimate of the cumulative probability of surviving progression-free greater than 6 months with standard error in parenthesis.
 ** Median overall survival.

Gynecologic
 Oncology
 Group Phase 2
 median survival
 data above and
 to the right

Because immunotherapies treat the immune system, which then exerts a therapeutic effect on disease a therapeutic immune responses frequently can take ~ 6mo to manifest



ADXS-HPV Phase 1 Study

- 1st Clinical trial of live attenuated *Lm* in humans
- 15 patients
 - Stage: recurrent or metastatic cervical cancer treatment failures
 - ECOG Performance Status: 1-4
- 3 groups of 5 patients each were treated as inpatients for 5 days
 - 2 IV infusions of the same dose at 3 week intervals
 - 1×10^9 , 3.3×10^9 , 1×10^{10} cfu
- 2 doses given
- Ampicillin given after each dose.

ADXS-HPV Phase I: AE Possibly or Probably Drug Related

# Patients with Possibly or Probably Treatment Related Adverse Events				
Study Population				
System Organ Class	1x10 ⁹	3.3x10 ⁹	1x10 ¹⁰	Total
Preferred Term (MedRa)	N=5	N=5	N=5	N=15
General Disorders				
Pyrexia	5	5	5	15
Chills	4	0	4	8
Asthenia	0	0	1	1
Fatigue	1	0	0	1
GI Disorders				
Vomiting	2	3	4	9
Nausea	3	1	1	5
Cardiac disorders				
Tachycardia	1	5	1	7
Nervous System Disorders				
Headache	3	1	3	7
Investigations				
γ-GT	0	2	3	5
Alkaline Phosphatase	0	1	2	3
ALT	0	0	1	1
AST	0	0	1	1
Conjugated Bilirubin	0	0	1	1
LDH	0	1	1	2
Lipase	0	0	1	1

- AEs associated with ADXS11-001 consisted of flu-like symptoms.
- Adverse events responded to over the counter agents such as NSAIDS and anti-histamines. Antibiotics were not needed to resolve side effects, indicating they were not infectious in nature.
- No clinically significant lab AE

ADXS11-001 Phase I: Efficacy

Progressive Disease	Group	Tumor Burden (%)
01-002	1x10 ⁹	+142.5
04-004	3.3x10 ⁹	+81.250
04-002	3.3x10 ⁹	+34.429
01-006	1x10 ¹⁰	+56.25
01-003	1x10 ⁹	+30
Stable		
04-006	1x10 ¹⁰	+17.778
01-001	1x10 ⁹	+17.5
04-001	1x10 ⁹	+10.989
01-005	1x10 ¹⁰	+7.407
03-001	3.3x10 ⁹	-19.355
01-004	1x10 ⁹	-20
01-007	1x10 ¹⁰	-20.833
PR		
04-003	3.3x10 ⁹	-32.484

- 13/15 treated patients were evaluable.
- 4/13 evaluable patients experienced reduction of their tumor mass
- 2 doses

	GOG Protocol 127 Series	ADXS11-001 Phase 1
Median Survival	~180 days	347 days
1 year Survival	~5%	53%

Pt. 01-004 & 04-003 had lesions disappear



Phase 2



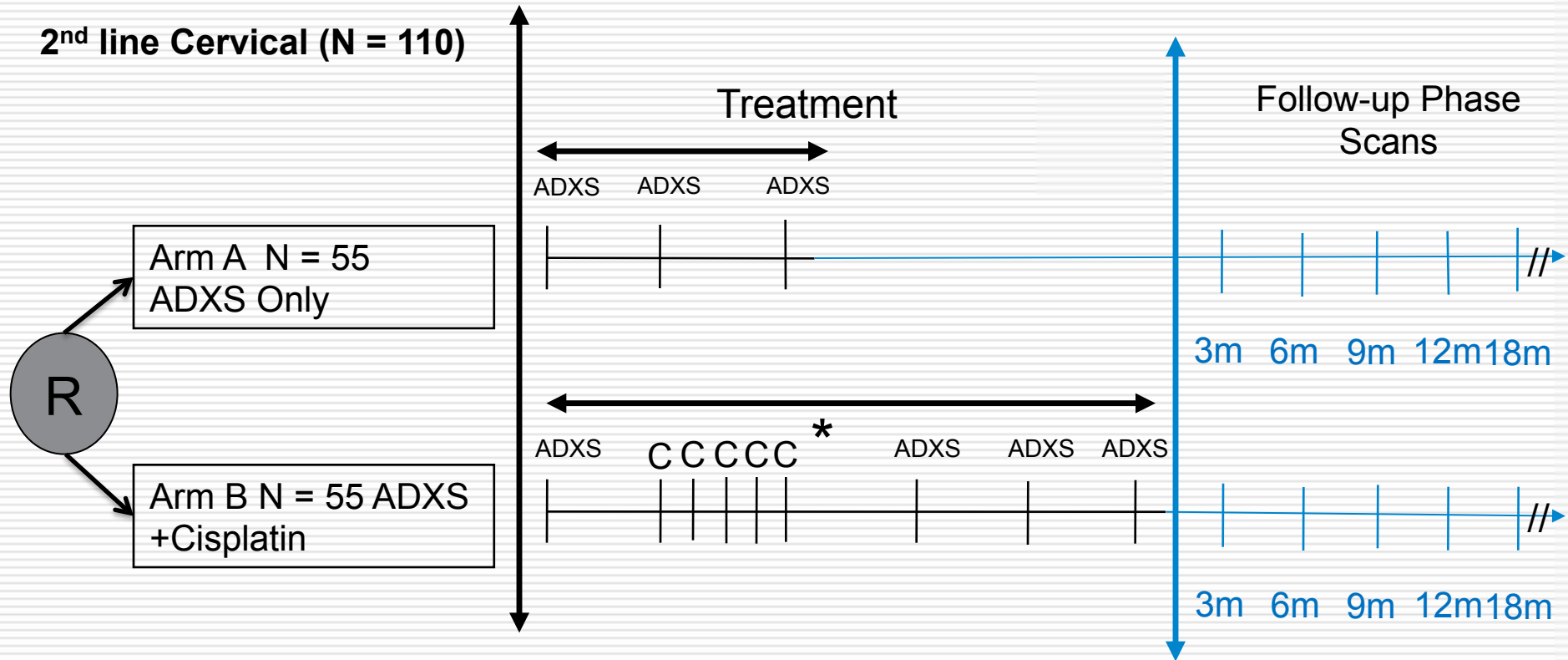
India Cervical Cancer Study Objectives

- To explore the safety and efficacy of ADXS11-001 in cervical cancer treatment failures
- To determine if ADXS11-001 can be combined with platinum chemotherapy in this patient population

Trial Design: Lm-LLO-E7-015

Cervical Cancer Cytotoxic Treatment Failures

2nd line Cervical (N = 110)



* Low dose cisplatin: 40mg/m²



India Cervical Cancer Trial

87 patients and 195 doses

30 subjects report 77 AEs related/ possibly related to study drug

- 39 Chills (in 23 patients)
- 10 Pyrexia (in 8 patients)
- 4 Vomiting (in 4 patients)
- 4 Nausea (in 4 patients)
- 3 Leukopenia
- 3 Headache (in 3 patients)
- 1 Influenza like illness
- 1 Hypertension, tachycardia & dyspnea (SAE)
- 1 Hyponatraemia
- 1 Constipation
- 1 Eosinophil count increased
- 1 Lymphocyte count decreased
- 1 Neutropenia
- 1 Neutrophil count decreased
- 1 Weight decreased
- 1 Stomatitis
- 1 Candidiasis
- 1 Bacterial perforation and peritonitis
- 1 Bleeding from node
- 1 Pain in Node

Grade 3-4 Toxicity of ADXS-HPV and GOG Single Agents in Recurrent/Refractory Cervical Cancer Tx Failures

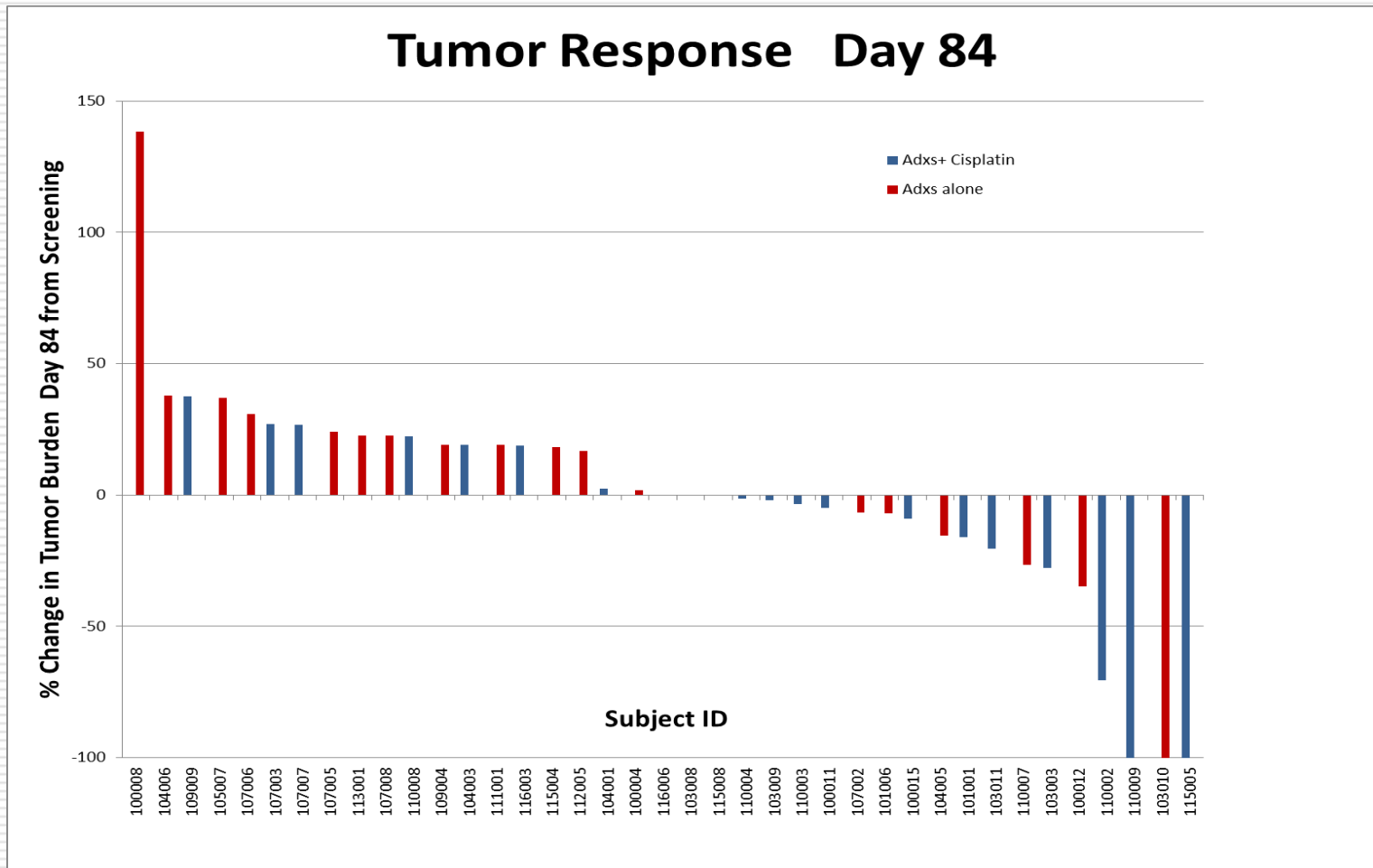
Trial	Regimen	# cycles	Resp. Rate	P. S.	# Grade 3-4 / # patients	Mean Related SAE / pt.	Median O.S. (Months)
ADXS-HPV	10 ⁹ cfu/mo x3, 4+CIS	1	10% *	0-2	1 / 87	0.01	TBD

*Study ongoing and enrolling - 3 CR, 4 PR's in first 70 patients to reach 3 months. 1/19/12

Trial	Regimen	# cycles	Resp. Rate	P. S.	# Grade 3-4 / # patients	Mean Related # SAE /pt. *	Median O.S. (Months)
GOG Ph 2							
GOG 127C Mannel 2000	Cisplatin 75 mg/m ² q21d + Pentoxifylline	3	10%	0-3	70 (52/18) / 44	1.59	6.2
GOG 127F Bookman 2000	Topotecan 1.5 mg/m ² dx5, q21d	2	12.5%	0-2	40 /(63) - total	1.57	5.3
GOG 127L Muggia 2003	Vinorelbine 30 mg/m ² d1, d8, q21d	2	14%	0-3	46 (24/18)/44	1.05	n.a.
GOG 128B Curtin 2001	Paclitaxel 170 mg/m ² q21d	5	31%	0-2	62 (28/34) / 42	1.48	3.8
GOG 127K Schidler 2000	Gemcitabine 800 mg/ m ² Wk x3, q4Wks	2	8%	0-2	Gr. 4 = 4/25 Gr 3 not reported	N.A.	4.9
GOG Ph 3							
Moore 2004	Cisplatin 50 mg/m ² q3w	4	19%	0-2	134 (67/33)/100	0.75	8.8
	Cisplatin 50 mg/m ² + Txl 135 mg/m ² q3w	5	36%	0-2	230 (136/94)/130	1.77	9.7 (ns)

Advaxis response rate is similar to short-term cytotoxic treatments. The SAE rate for Grade 3/4 is low to date.

Revised Day 84 Waterfall plot...



Tumor responses observed in both ADXS alone and ADXS+Cisplatin

RECIST Responses

Patient #	1 st LINE	Recurrence	Stage	Tx Arm	Tumor Burden/Size in mm					% Decrease
					Baseline	84 d	184 d	273 d	365 d	
115005	EBRT 50 Gy, #23	Cervix	2B	ADXS + CIS	30	0	0	0	N/A	-100
110009	Cisp+5FU EBRT (23#)	Cervix	1B	ADXS + CIS	23	0	N/A	N/A	N/A	-100
103010	Carbo + Endox	Vaginal	4A	ADXS	35	0	0	N/A	N/A	-100*
110002	EBRT 50 Gy #25	Peri-aorta Liver Lung	4B	ADXS + CIS	284 (n=10)	84 (n=5)	56 (n=3)	34 (n=2)	20 (n=1)	-93
101001	Carbo 5 FU + RT (50 Gy Cobalt)	Vaginal Mesenteric	4B	ADXS + CIS	50	42	44	20	N/A	-60
103012	Carbo + Endox, EBRT, 50gy 25#	Retroperitoneal Nodes	4B	ADXS = CIS	18	9	N/A	N/A	N/A	-50
100012	Carbo + Taxol + RT Pelvis	Cervical, Axilla, Vagina	4B	ADXS	164	107	N/A	N/A	N/A	-35%

Immune responses may be more durable than others seen in this population

Tumor reduction over time is generally regarded as an immunotherapy effect

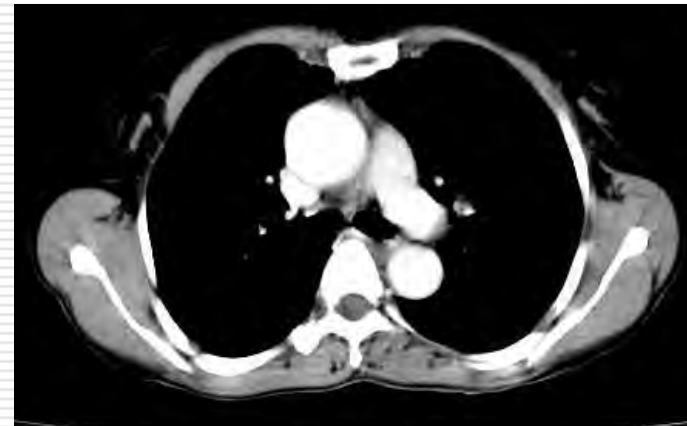
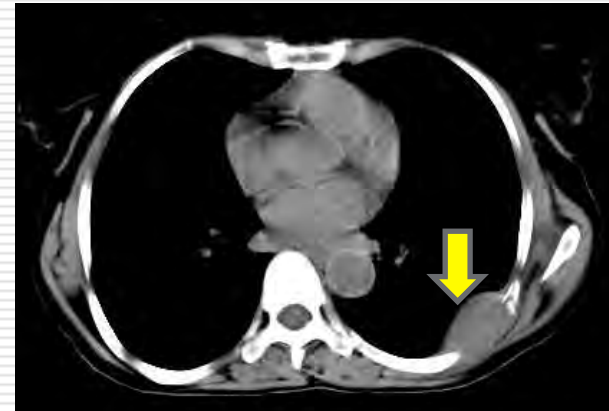
Lm-LLO-E7-15: Subject 110002

Target Lesion	Screening (mm)	Day 84 (mm)	Day 184 (mm)	Day 273 (mm)	Day 365 (mm)
TL#1 2nd Rib Metastasis	41	0	0	0	0
TL#2 Superior Mediastinal Node	24	21	27	20	20
TL#3 Right Pleural Nodule	32	0	0	0	0
TL#4 Liver Metastasis (Right Lobe)	57	28	19	14	0
TL#5 Left Para-aortic Node	32	17	10	0	0
TL#6 1st Right Para-aortic Node	24	6	0	0	0
TL#7 2nd Right Para-aortic Node	15	0	0	0	0
TL#8 Pre-aortic Node	27	12	0	0	0
TL#9 Left Iliac Node	14	0	0	0	0
TL#10 Right Iliac Node	18	0	0	0	0
Total	284	84	56	34	20

110002 target lesions have been reduced from 10 to 1 over a year

Lm-LLO-E7-15: Subject 110002

Resolution of Lung Metastasis on CT at 9 months



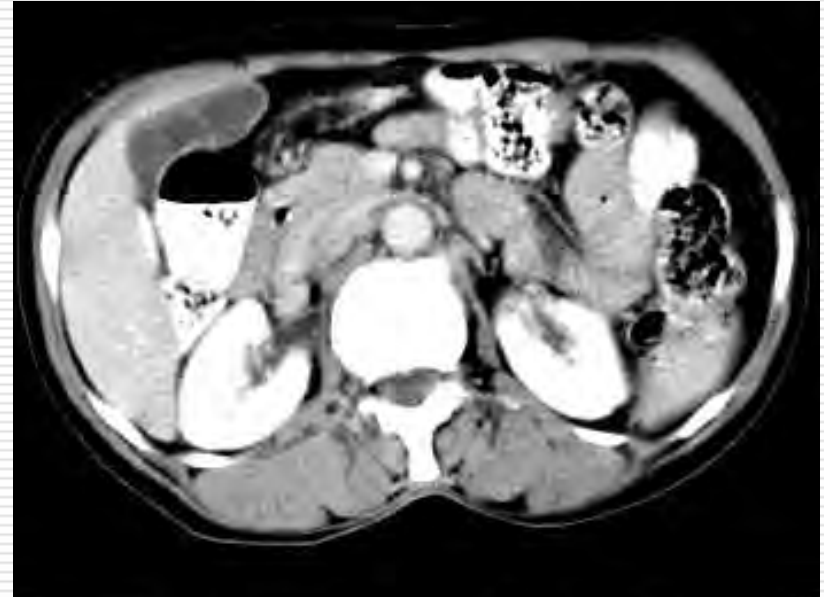
Lm-LLO-E7-15: Subject 110002

Resolution of Liver Metastasis on CT at 9 months



Lm-LLO-E7-15: Subject 110002

Resolution of Para-Aortic Lymph Nodes on CT at 9 months





Preliminary Survival

Preliminary Survival

January 20, 2012

	<u>6 mo.</u>	<u>9 mo.</u>	<u>12 mo.</u>
N	55	37	15
n Alive	34	15	6
% Alive	62	41	40



Ongoing Activities



Clinical Development Program

- **HPV-Associated Disease**
 - Cervical Cancer
 - India: ADXS-HPV +/- cisplatin; 110 patients 87 treated to date
 - GOG/NCI: 67 patients; 2 patient treated
 - CIN 2/3
 - US: 120 patients – 49 treated to date
 - Head and Neck Cancer (REALISTIC)
 - UK: 45 patients -- enrolling
- **PSA**
 - Phase 1
 - Hormone Refractory Prostate Cancer
- **cHER2**
 - Phase 1
 - HER2+ Expressing Cancer
 - Veterinary, Osteosarcoma in dogs: Penn Vet School - open

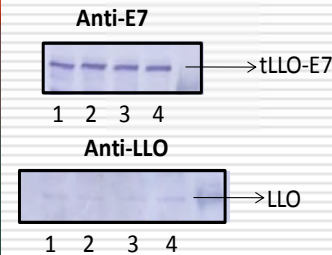
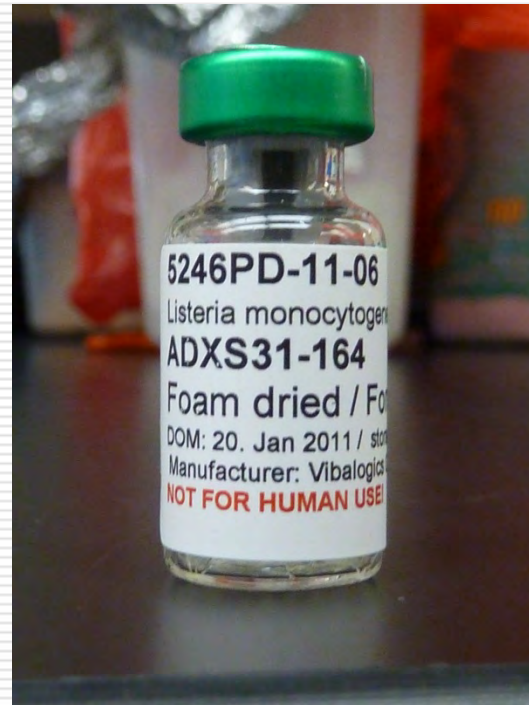
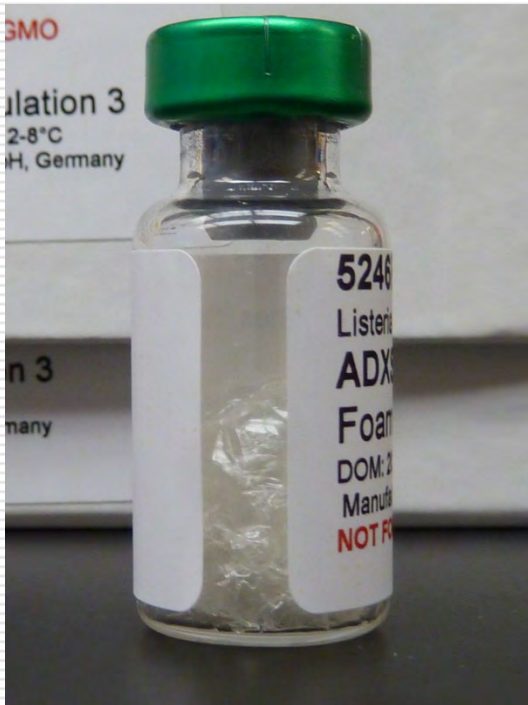


Intellectual Property

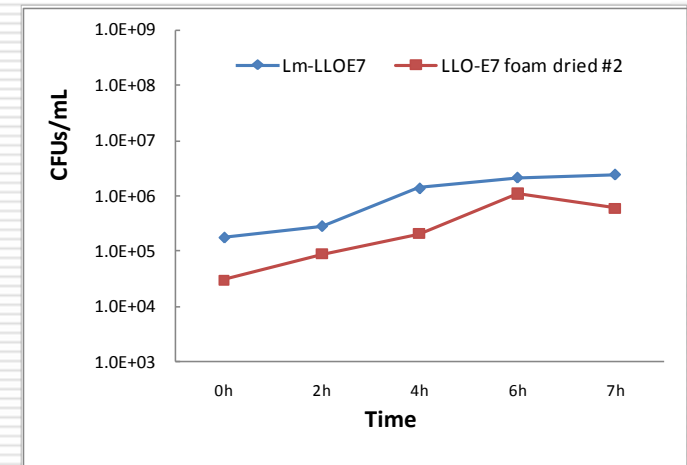
- **39 patents issued**
 - Composition of matter, methods and uses covering:
 - Live *Lm*
 - Four (4) different *Listeria* species for human use
 - LLO-antigen & ActA-antigen fusion proteins
 - Delivered by *Lm* or stand alone
 - Two (2) different families of adjuvant fusions
 - Safe, modified LLO
- **39 patents pending and/or ongoing application**
- **IP successfully defended in European Patent Court (Munich)**
 - No additional challenge of that patent permitted

Breaking the Cold Chain

Storage Stable Room Temp Material



- Lanes
1. Lm-LLO-E7 (lab)
 2. Foam-dried Formulation 1
 3. Foam-dried Formulation 2
 4. Foam-dried Formulation 3



APC infectivity

Multivalent 3rd & 4th Generation Vaccines

- Two methods
 - Genomic + epigenomic
 - multivalent plasmids

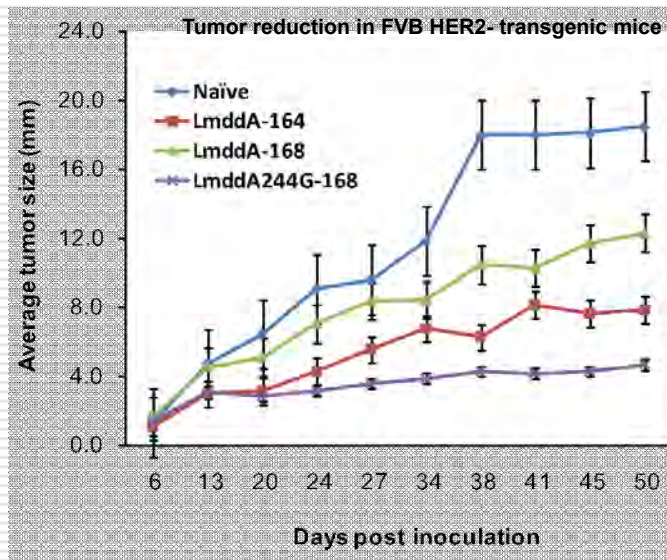


Fig.2: Vaccination with dual vaccine causes rapid reduction of tumor growth.

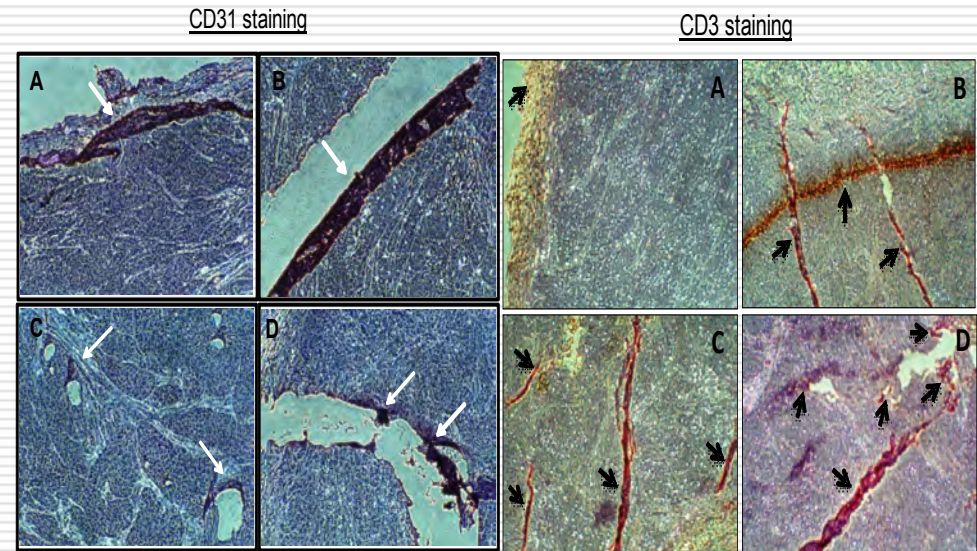


Fig 3. IHC staining of CD3 T cells and CD31 cells in tumors of naïve (A), LmddA164 (B), LmddA168 (C) and LmddA244G-168 (D).

Thank You

For Your Attention

