

# Advaxis

**Investor Presentation**

Summer 2011



ADVAXIS

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# About Advaxis

Advaxis is a leader in developing the next generation of immunotherapies that harness the body's intrinsic immune ability to fight cancer and infectious diseases.

Advaxis' platform technology uses an already established human immune response to stimulate a more comprehensive immune attack than other immunotherapies and overcome tumor protection mechanisms—something no other immunotherapy does.



# The Advaxis Opportunity

1. Immunotherapy-Using the immune system to fight cancer is the most promising approach because:
  - It already works, naturally
  - It isn't poison
  - It works throughout the body
2. FDA is approving immunotherapies: Dendreon is now at \$5bn
3. Advaxis does what no other technology does:
  - Creates a strong immune attack using a vector our bodies respond to strongly. +300% killer T cells. Other stimulants. AND
  - Reduces the tumor defense against immune attack by 80%
4. Advaxis has delivered very promising results to date
  - 75% tumor elimination in animals
  - Good safety
  - Doubling of survival in very late stage, previously untreatable human cancer in its initial 15 patient study



# The Advaxis Opportunity

4. The Advaxis Technology is getting wide scientific acceptance
  - NCI sponsored clinical trial
  - Collaboration with top NCI vaccine investigator
  - Cancer Research UK running study at their expense
  - Collaborations with Wistar Institute, Roswell Cancer Center, City of Hope, Montefiore Cancer Center, Homeland Security
5. Two Phase II studies will begin to report in the next 6 months
  - Cervical cancer: leading killer of women under 45, WW
  - CIN, diagnosed in 500,000 American women, annually (prevalence of breast and prostate cancer, combined).
6. Why only a \$35-40MM market cap? We use a vector that we all eat several times a month, but only gets headlines when misuse causes food poisoning. We make it safe by weakening it by over 10,000 times. Over 100 patients dosed to date without serious side effects.



# Key Facts

## Areas of Focus

- Immunotherapy R&D
- Clinical development program: cervical dysplasia, cervical, head & neck, breast and prostate cancers
- Veterinary medicine program

## Innovative Platform Technology

### Multi-modal Active ImmunoTherapy (MAIT)

- Proprietary and versatile platform technology used to develop immunotherapies for cancer, infectious disease and parasitic disease
- Protected worldwide by more than 70 issued and pending patents

## Finances\*

- Expenses '11 (incl. clinical trials): \$10-12 million
- Market cap: \$40 million
- Shares outstanding: 214 million
- Average trading volume (3 months): 847,153
- 52 week range : \$.10 - \$.25

## Pipeline

- 1 immunotherapy in 4 Phase II clinical trials
- 2 immunotherapies in development for prostate and breast cancer
- 1 immunotherapy in development for canine osteosarcoma
- 1 for bovine hoof & mouth
- 15 constructs in discovery

## Key Partnerships & Collaborations

- NCI Gynecologic Oncology Group (GOG)
- Cancer Research UK
- NCI Vaccine Section
- Albert Einstein School of Medicine/Montefiore Medical Center
- University of British Columbia
- The Wistar Institute
- U.S. Department of Homeland Security



# Goals & Strategies

## Technology

- To use our proprietary, versatile platform (**MAIT**) as the foundation for a continuous pipeline of active immunotherapies that target multiple cancers and infectious diseases

## Clinical

- To demonstrate the safety and efficacy of our active immunotherapies through company- and government-sponsored trials and collaborations with leading institutions and organizations

## Shareholder

- To maximize value by leveraging the technology, developing improved constructs, out-licensing immunotherapies and building a broad, defensible patent portfolio



# MAIT (Multimodal Active ImmunoTherapy)

## Construct bioengineered strains of *Listeria monocytogenes* (*Lm*)

- Remove pathogenesis genes from *Lm*
- Results in an attenuated strain that is > 10,000 times attenuated than *Lm* wild type

## Fuse tumor antigens to *Lm*-LLO protein

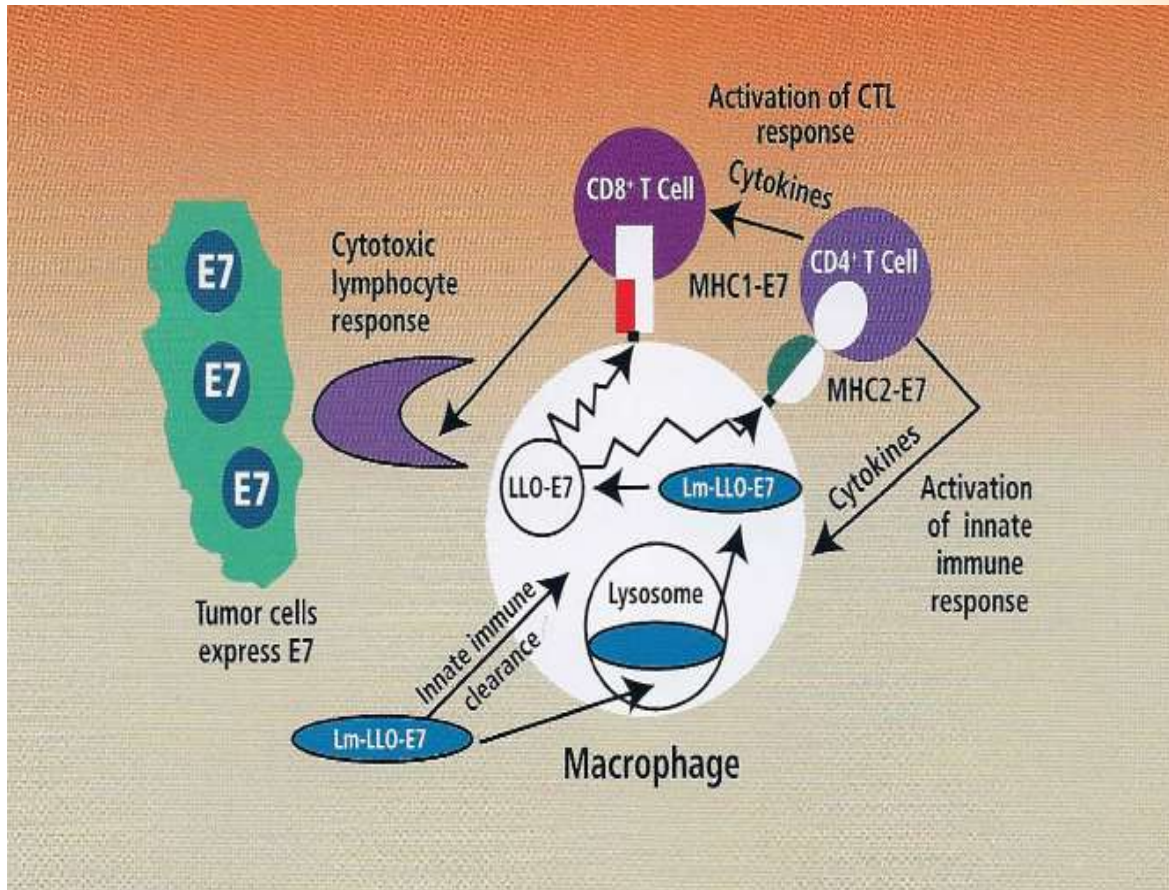
- *Listeria* secretes LLO that can perforate the phagosome membrane and escape into the cytosol
  - Stimulates the Class I or endogenous pathway
  - Transitions to TH2 and TH1 pathways

**Rapidly disseminate and degrade LLO-fusion proteins, increasing the rate and amount of Antigen fragments for MHC-1 incorporation**



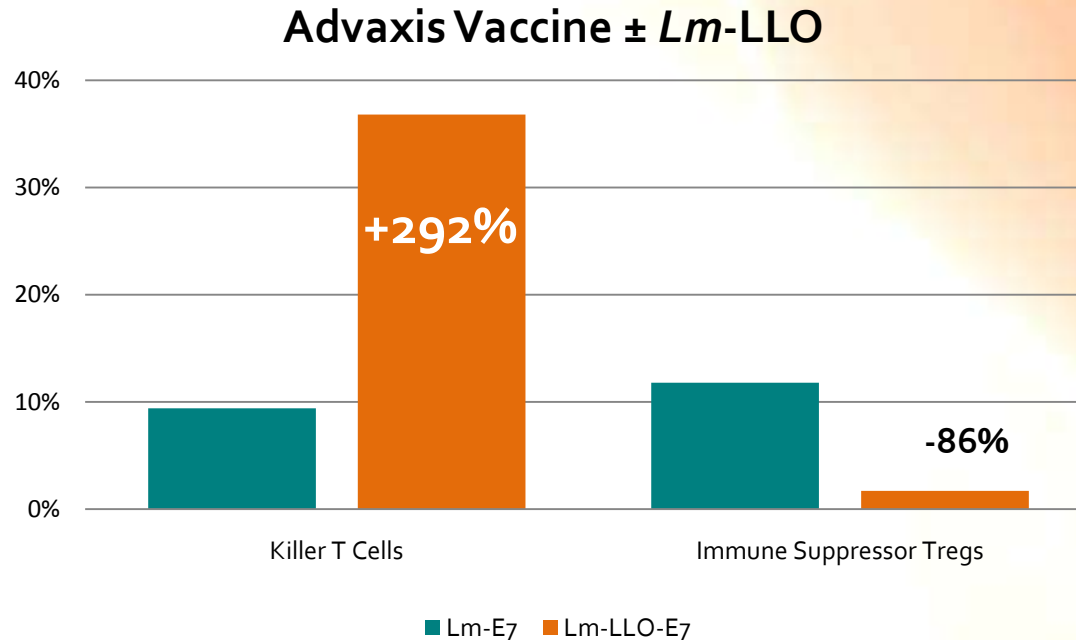
# MAIT Mechanism of Action

Vector acts as its own adjuvant; infects immune cells that initiate and direct an immune response, and secretes an adjuvant-antigen fusion protein from within the cell:



- Redirects immune response toward tumor antigens
- Stimulates both innate and adaptive immunity
- Changes the tumor microenvironment:
  - Increases cytotoxic tumor infiltrating lymphocytes (TIL)
  - Reduces immune suppressive T-regs and MDSCs

# Increasing the Kill Ratio Inside the Tumor



- Vaccine delivery of antigen alone is not effective.
- Vaccine delivery of *Lm*-LLO adjuvant antigen fusion protein significantly:
  - Increases tumor infiltrating killer T cells
  - Decreases immune suppressor TRegs
- With Advaxis *Lm*-LLO, the existing parity to an 20:1 ratio that is killer T cell heavy

# Publication Highlights

## Redirect immune response toward tumor antigens while stimulating both adaptive and innate immunity

- Shahabi V, Maciag PC, Rivera S, Wallecha A. Live, attenuated strains of *Listeria* and *Salmonella* as vaccine vectors in cancer treatment. *Bioeng Bugs*. 2010, 1(4): 235-239.
- Wood LM, Guirnalda PD, Seavy MM, Paterson Y. Cancer immunotherapy using *Listeria* monocytogenes and listerial virulence factors. *Immunol Res*. 2008; 42(1-3):233-245.

## Increase cytotoxic T-cells in the tumor to break antigenic tolerance

- Seavey MM, Maciag PC, Al-Rawi N, Sewell D, Paterson Y. An anti-vascular endothelial growth factor receptor 2/fetal liver kinase-1 *Listeria* monocytogenes anti-angiogenesis cancer vaccine for the treatment of primary and metastatic Her-2/neu+ breast tumors in a mouse model. *J Immunol*. 2009; 182 (9): 5537-46.
- Shahabi V, Reyes-Reyes M, Wallecha A, Rivera S, Paterson Y, Maciag P. Development of a *Listeria* monocytogenes based vaccine against prostate cancer. *Cancer Immunol Immunother*. 2008; 57(9):1301-13.
- Sewell DA, Pan ZK, Paterson Y. *Listeria*-based HPV-16 E7 vaccines limit autochthonous tumor growth in a transgenic mouse model for HPV-16 transformed tumors. *Vaccine*. 2008; 26(41):5315-20.
- Singh R, Paterson Y. In the FVB/N HER-2/neu transgenic mouse both peripheral and central tolerance limit the immune response targeting HER-2/neu induced by *Listeria* monocytogenes-based vaccines. *Cancer Immunol Immunother*. 2007; 56(6):927-38.

## Reduce suppressive T-cells in the tumor

- Hussain SF, Paterson Y. CD4+CD25+ regulatory T cells that secrete TGFbeta and IL-10 are preferentially induced by a vaccine vector. *J Immunother*. 2004; 27(5):339-46.

## Reduce numbers of myeloid suppressor cells in the tumor

- Reshma Singh, AACR Conference Dec/2010



# Clinical Pipeline

Construct	Indication	Pre-Clinical	Phase I	Phase II	Phase III	Collaboration
ADXS-HPV	CIN (Cervical Dysplasia), US 120 Patients					
	Cervical Cancer, US 67 patients					
	Cervical Cancer, India 110 patients					
	Head & Neck Cancer 27 patients					
ADXS-PSA	Prostate Cancer					
ADXS-HER2	Breast Cancer					
ADXS-HER2	Canine Osteosarcoma 18-20 companion dogs					
ADXS-PSA	Bovine Hoof & Mouth					



# Value Creation

## Clinical Development Targets

- Report survival data from Cervical Cancer (India) trial in Q4 2011
- Advance prostate and breast constructs to the clinic in Q4 2011
- Receive results from Cervical Dysplasia US (low dose) trial in Q2 2012
- Communicate pre-clinical and clinical data at key congresses and in peer-reviewed journals

## Business Development Targets

- License 1 immunotherapy for 2 indications by 2013
- License 2 immunotherapies per year beginning in 2015
- Expand and maintain intellectual property portfolio
- Position immunotherapies for potential licensing for late stage clinical development
- Develop strategic partnerships and co-funding relationships

## Financial Strategy

- Raise additional equity capital
- Strengthen balance sheet through conversion of debt to equity
- Leverage government sponsorship
- Increase share value and uplift to a higher exchange



# Intellectual Property

- **38 patents issued worldwide**
- **34 patents pending worldwide**
- **Compositions of matter, methods and use**
  - Attenuated strains of *Listeria* suitable for use as human vaccine vectors
  - Attenuated bioengineered strains of *Listeria* that secrete LLO-antigen or ActA-antigen fusion proteins
  - Truncated LLO and LLO-antigen fusion proteins (independent of *Lm*)
  - Patent No. EP-B1 790 835 – successfully defended in European Patent Court
    - Additional challenges to that patent are not permitted



# Pre-Clinical Results

**Therapeutic pre-clinical results presage clinical efficacy for all constructs tested to date:**

- **~75% tumor elimination in tumor-bearing animals**
- **~50% tumor elimination in transgenic animals**
- **Ability to prevent tumors in transgenic animals**
  - **Long-term protective immunity in responding animals; reinoculated tumor cells no longer grow**



# Disease Market

- Address unmet medical needs and provide alternatives to surgery, chemotherapy & radiation
- The estimated global market for immunotherapies will reach \$37.2B by 2012 with cancer vaccines forecast to reach over \$8B.\*

	Annual Diagnoses	
	US	Top 7 Markets
CIN 2/3	660,000	1,500,000
Cervical Cancer	24,400	50,000
Head & Neck Cancer	46,000	120,000
Prostate	440,000	1,000,000
Breast (HER2 <sup>+</sup> )	154,000	350,000



# Phase I Completed: Cervical Cancer

Construct	ADXS-HPV
Phase	I
Title	A Phase I Safety Study of ADXS-HPV in Patients with Advanced Carcinoma of the Cervix
# of Patients	15
Endpoints	Safety
Study Start/Completion	2006 – 2008
# of Sites and Where	3 sites: Serbia, Mexico, Israel
Sponsor	Advaxis
Status	Completed
Key Findings	Well-tolerated, MTD established



# Phase I Study: Safety

- 3 groups of 5 patients each were treated as in-patients for 5 days
  - 2 IV infusions; separated by three weeks ( $1 \times 10^9$ ,  $3.3 \times 10^9$ ,  $1 \times 10^{10}$  cfus)
- Ampicillin given after each dose
- Safety Profile
  - Cytokine mediated flu-like syndrome (fever, chills, headache, myalgia)
  - No serum Listeria at 2 days
  - No Shedding in feces or urine
  - DLT: grade 2 hypotension
  - AE responded to symptomatic treatment (no antibiotic needed)
- Well tolerated
- MTD established -  $1 \times 10^{10}$  cfus

# Phase I Study: Clinical Benefit

- Based on tumor assessments of 13/15 evaluable patients:

Tumor Response	# of Patients	%
Progressed	5	38.5%
Stable disease (minor response)	7 (3)	53.8% (23.1%)
Partial response	1	7.7%
Survival*	# of Patients	%
0 - 6 months	3	23.1%
6 months - 12 months	3	23.1%
> 12 months	7	53.8%
*Censored 1/1/11 as lost to follow up		

- Tumor response and stable disease with data suggestive of survival benefit.
- Positive clinical signal merited further clinical investigation
- Historical Gynecological Oncology Group (GOG) data associates disease severity with a 6-7 month prognosis and a 5% one-year survival.



# Phase II Update: CIN, US

Construct	ADXS-HPV
Phase	II
Title	A Randomized, Single Blind, Placebo Controlled Phase 2 Study to Assess the Safety of ADXS11-001 for the Treatment of Cervical Intraepithelial Neoplasia Grade 2/3
# of patients	120
Endpoints	Safety, efficacy determination by CIN remission at LEEP
Study start/completion	April 2010 – June 2013 Low dose: Q3 - Q4, 2011 Med dose: Q2 - Q3, 2012 High dose: Q1 - Q2, 2013
# of sites and where	Multicenter 15 sites, US only
Sponsor	Advaxis
Status	30 patients randomized
Key Findings	DSMB approved initial dose safe for study continuation



# Phase II Update: Cervical Cancer, India

Construct	ADXS=HPV
Phase	II
Title	A Randomized, Active Therapy Controlled Phase 2 Study to Assess the Safety and Efficacy of ADXS=HPV with and without Cisplatin as 2nd Line Therapy for the Treatment of Recurrent Cervix Cancer
# of patients	110
Endpoints	Safety & efficacy
Study start/completion	Nov 2010 – 2012 (LP/FV – Q4 2011)
# of sites and where	Multicenter > 15 sites, India only
Sponsor	Advaxis
Status	40 patients randomized, study ongoing
Key Findings	Over 70 doses given to 40 patients with no drug-related SAEs



# Phase II Update: Cervical Cancer, US

Construct	ADXS-HPV
Phase	II
Title	A Phase II Evaluation of ADXS-HPV in the Treatment of Persistent or Recurrent Squamous or Non-Squamous Cell Carcinoma of the Cervix
# of patients	67
Endpoints	Safety, efficacy and immunology
Study start/completion	Q2 2011 – Q4 2013
# of sites and location(s)	Multicenter, US only
Sponsor	NCI/GOG
Status	With local IRB's



# Phase I/II Update: Head & Neck Cancer, UK

Construct	ADXS-HPV
Phase	I/II
Title	A Phase I/II, Dose Escalation Trial of Recombinant <i>Listeria Monocytogenes (Lm)</i> -Based Vaccine in Patients with HPV-16 Oropharyngeal Carcinoma
# of patients	27
Endpoints	Safety, dose selection and immunology
Study start/completion	Q2 2011 – TBD
# of sites and location(s)	Multicenter, 3 sites, UK only
Sponsor	Cancer Research UK
Status	Pending study start approval

# Veterinary Program

- **Areas of focus**

Canine osteosarcoma, bovine hoof & mouth

- **Rationale**

Market expansion of proprietary immunotherapies to veterinary applications

- **Collaborators**

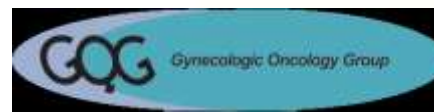
- University of Pennsylvania Veterinary School
- U.S. Department of Homeland Security, Science and Technology Directorate

- **Constructs used**

ADXS<sub>31-142</sub> and ADX<sub>31-164</sub>



# Papers & Conferences

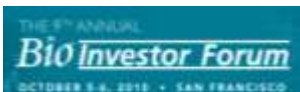


# The Investment Community



**“We are optimistic about the Company’s unique platform technology which has advantages over its peers... We believe Advaxis is heading in the right direction and we rate its shares Outperform.”**

*- Grant Zeng, CFA, Zacks Small-Cap Research, April 5, 2011*



ADVAXIS

# Management Team

## **Thomas A. Moore, *Chairman / CEO***

25 years experience in healthcare, executive management and business development. As CEO of Nelson Communications, engineering the sale of the company to *Publicis* Group for \$246 million. President of Procter & Gamble's (NYSE: PG) worldwide healthcare products business.

## **Mark J. Rosenblum, *CFO, Secretary, Senior VP***

25 years experience in accounting and financial leadership. VP, Chief Accounting Officer of Wellman, Inc., a \$1.2Bn chemical company; CFO and Secretary, HemoBioTech, Inc.

## **John Rothman, Ph.D., *Executive VP of Science & Operations***

30 years experience in drug development (infectious disease, gastroenterology, neurology, oncology and virology). Conducted first clinical trial of AIDS vaccine at Schering-Plough (NYSE: MRK). Led Roche, AG (OTCQX: RHHBY) global data collection, analysis and report writing.

## **Robert Petit, Ph.D., *VP Clinical Operations & Medical Affairs***

20 years experience in oncology drug development. US medical strategy lead for Yervoy® (Ipilimumab) program at Bristol Myers Squibb (NYSE: BMY) as the Director of Medical Strategy for new oncology products and Director of Global Clinical Research. VP of Clinical Development at MGI Pharma and Aesgen, Inc.



# Thank you!

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