ADVAXIS
IMMUNOTHERAPIES™

Clinical Updates for Advaxis' Pipeline of *Lm*-based Immunotherapies in Oncology

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IO360

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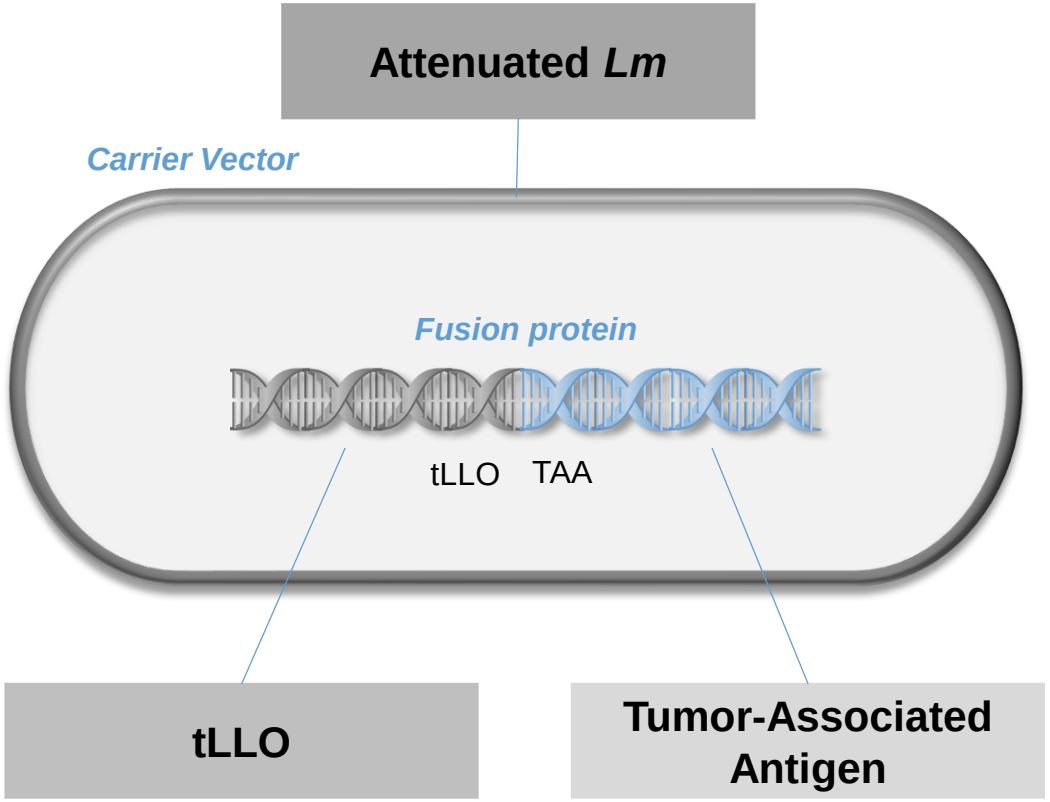
Lm Platform Designed to Trigger Strong Immune Responses against Targeted Antigens

Three Core Components

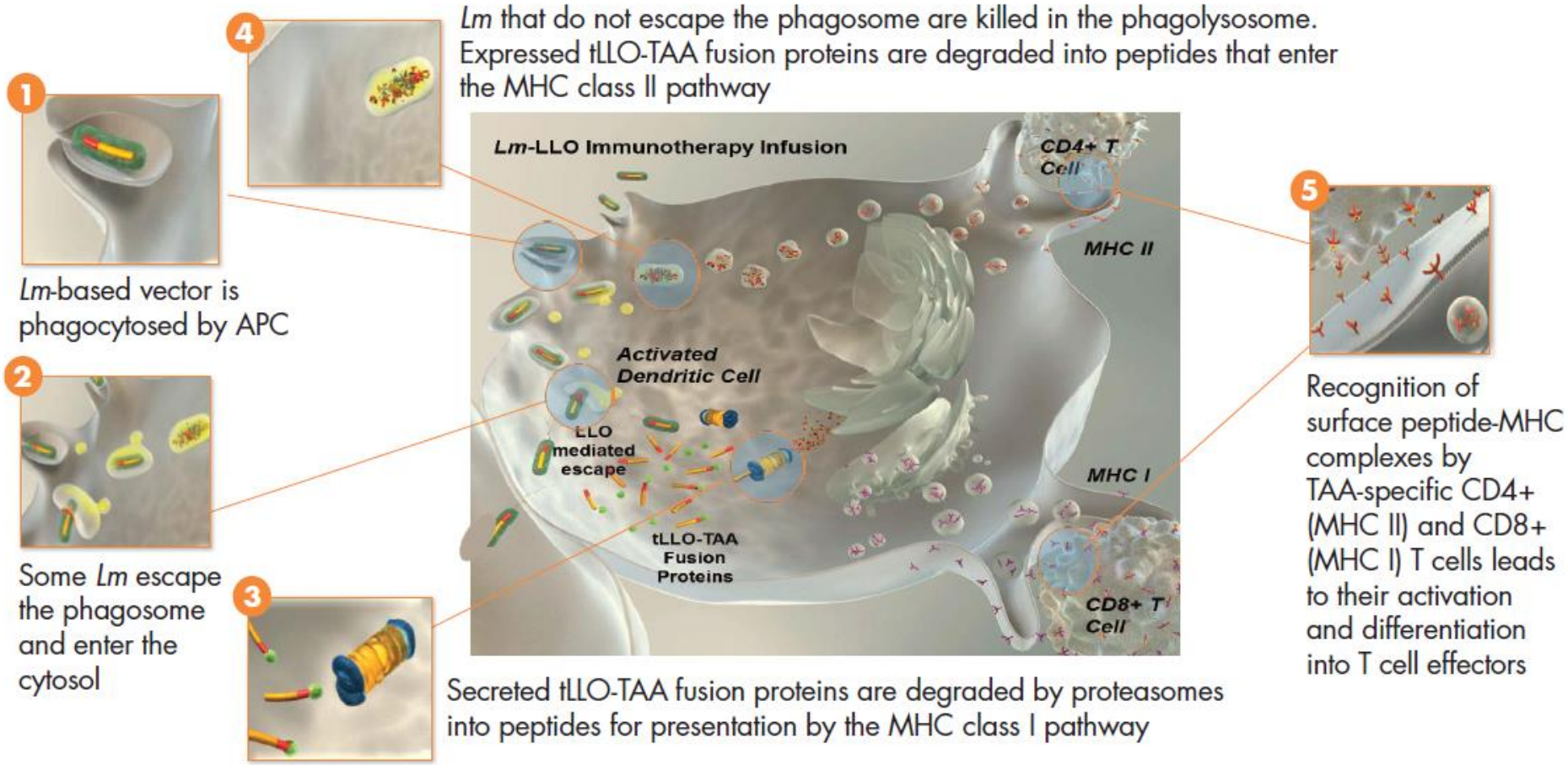


Comprehensive Immune Activity

- Listeria monocytogenes (*Lm*) bacteria
  - Carrier vector; irreversibly attenuated(1)
  - Tropism to spleen, lymph nodes, liver, lung, primary tumor & metastasis
  - Well understood and manageable safety profile, to date
- tLLO
  - Adjuvant properties
  - Neutralize Tregs & MDSCs protecting the tumor
- Diverse tumor-associated antigens
  - Viral antigens (HPV+)
  - Cancer type-specific (PSA, HOT)
  - Patient-specific neoantigens (NEO)
  - Powerful CD8+ T cell response and antigen spreading

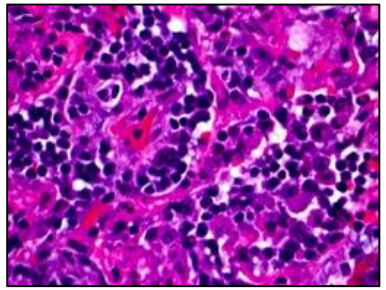
Legend: MDSC myeloid-derived suppressor cell | TAA tumor associated antigen | tLLO truncated fragment of listeriolysin O | Treg regulatory T cell.
Note: (1) attenuation renders the bacteria “harmless” to administrate.

Lm Technology™: Overview – Harnessing Unique Life Cycle of *Lm* in APCs

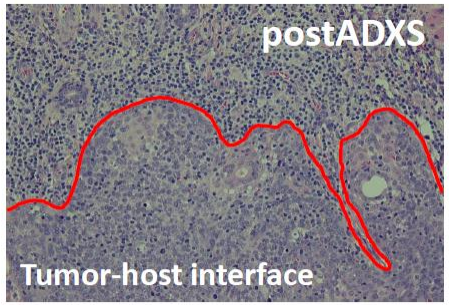


Legend: APC antigen-presenting cell | Lm Listeria monocytogenes | MHC major histocompatibility complex | TAA tumor-associated antigen | tLLO, truncated listeriolysin O.

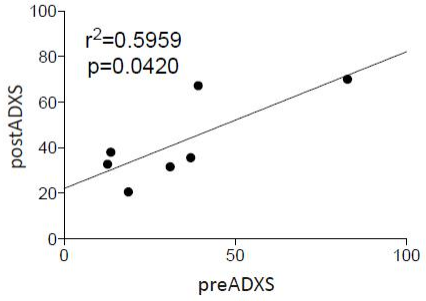
Lm effects on primary tumor and establishment of metastases

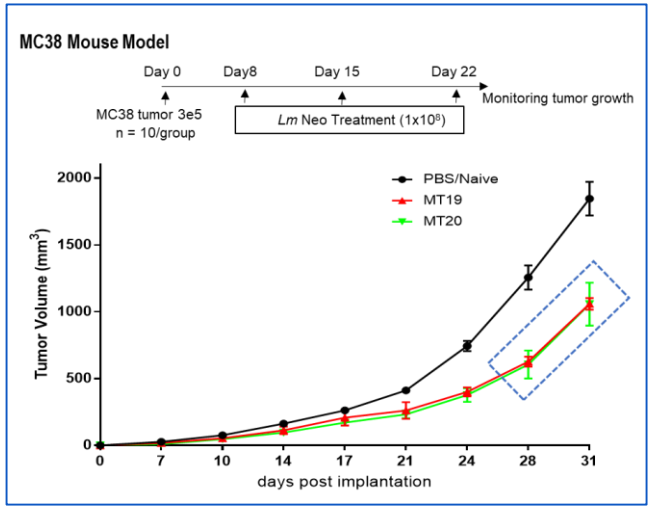


Canine osteoasarcoma with T cell infiltration after ADXS-HER2 therapy

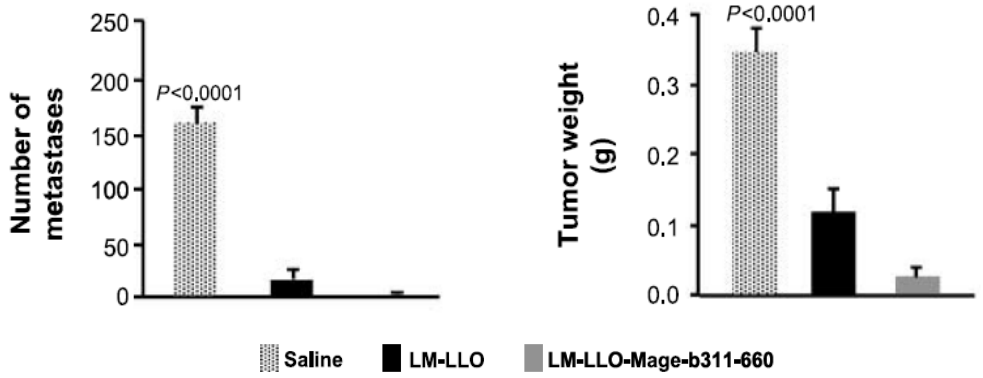


Pre/postADXS TIL

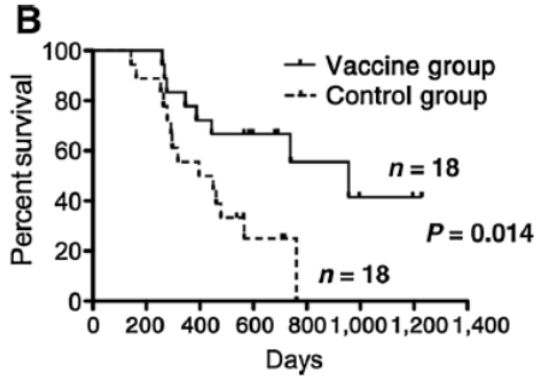




Frequency of metastases and tumor weight after a combination of one preventive and two therapeutic immunizations in BALB/c mice injected with 4T1 tumor cells



Disease-free survival in dogs with osteosarcoma without preexisting metastatic disease treated with ADXS-HER-2 and historical controls



Krupar R et.al., Advaxis Meeting_AACR 2016; Phee H. et.al.,European Neoantigen Summit, 2018; Kim SH et.al., Cancer Res 2009, 69:5860; Mason NJ et.al, CCR ,2016, 22

Combination with Checkpoints and Co-Stims May Improve Outcomes

Checkpoint Inhibitors:
PD-1/PD-L1
CTLA-4
TIGIT

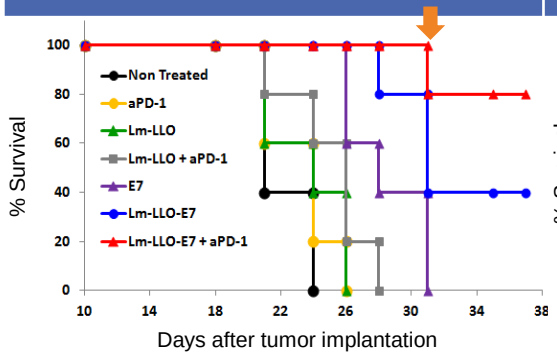
Co-stimulatory agonists:
CD137/41BB
OX40
GITR

TME acting agents:
CSF1R
HDAC1 inhibitor
CCR8
PEG rHuPH20(1)

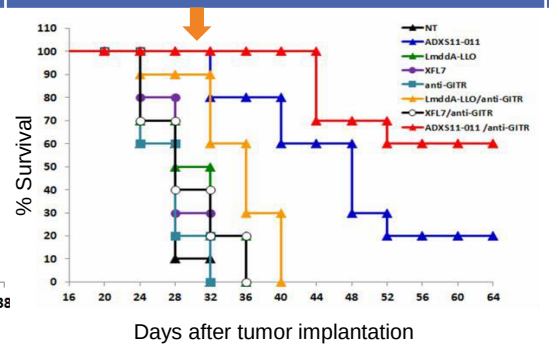
Standard-of-care regimens:
Chemotherapy
Radiation

Selected Examples

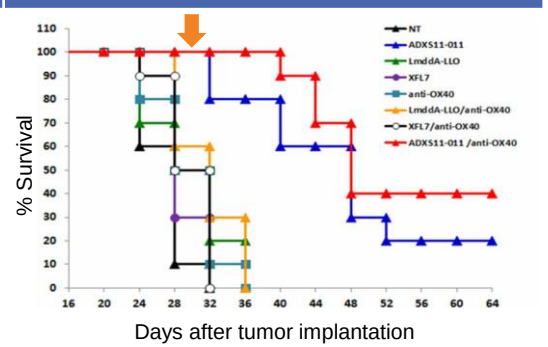
AXAL + aPD-1



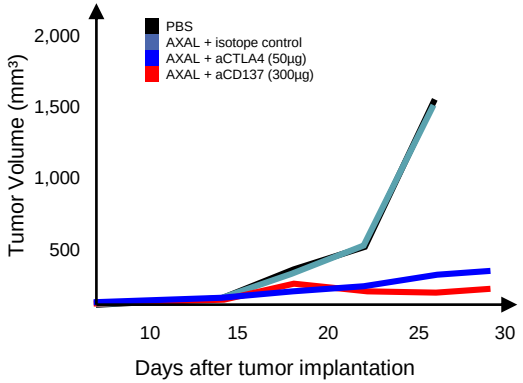
AXAL + aGITR



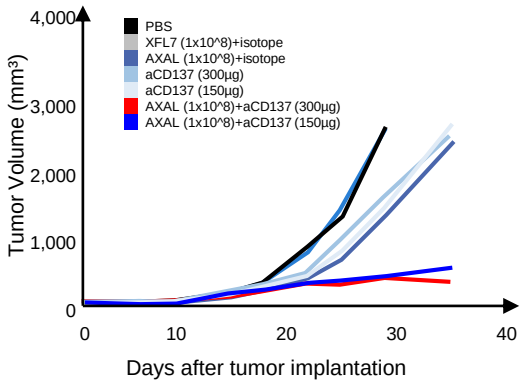
AXAL + aOX-40



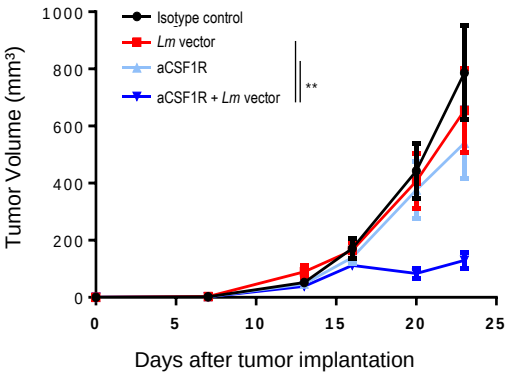
AXAL + aCTLA4



AXAL + aCD137



AXAL + CSF1R



CPI, checkpoint inhibitor; TME, tumor micro-environment.
(1) In collaboration with Halozyme.

Mkrtichyan M et.al., J Immunotherapy Ca, 2013, 1:15; Shrimali R et.al., J Immunotherapy Ca, 2017, 5:64; Kosoff RE et.al., SITC Annual Meeting 2016

Our Development Strategy

The Past…

Asset Centric

- **ADXS-HPV**
  - HPV+ cancers: cervical, anal & head and neck
- **ADXS-HER2**
  - Breast cancer and sarcomas
- **ADXS-PSA**
  - Advanced prostate cancer
- **ADXS-NEO**
  - Personalized multi-neoantigen immunotherapy
  - TMB approach: NSCLC > CRC > head and neck
- **ADXS-HOT (n >10)**
  - Off-the-shelf, tumor type-specific immunotherapy
  - **> 10** discrete constructs have been designed

PoC studies with monotherapy in late stage patients with high tumor burden

The Present…

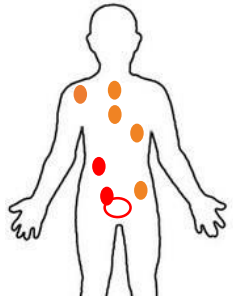
Disease/Patient Centric

- **ADXS-PSA:**
  - KN-046: Phase 1/2 monotherapy data and combination data with Keytruda in Metastatic Castration Resistant Prostate Cancer - Completed
- **ADXS-504:**
  - Phase 1/2 monotherapy data in prostate cancer patients with biochemical recurrence after radical therapy – IST
- **ADXS-503:**
  - Phase 1/2 monotherapy data and combination data with Keytruda in NSCLC – Ongoing

Prolong PFS/OS by selecting pts in earlier stages of the disease and by using combination therapy

Positioning of ADXS-PSA in the Prostate Cancer Treatment Landscape

ADXS-PSA expresses a truncated fragment of the listeriolysin (tLLO) fused to human PSA



Metastases
- Bone
- Measurable/visceral

Metastatic Castration Resistant Prostate Cancer

Local Therapies
Androgen Deprivation
Secondary Hormonal Therapies
Enza
Sipuleucel-T
Abiraterone
Radium 223
Docetaxel
Post Chemo
Abiraterone
Enzalutamide
Cabazitaxel
Palliative Chemo
PSA level
Olaparib, pembrolizumab (MSI-H)

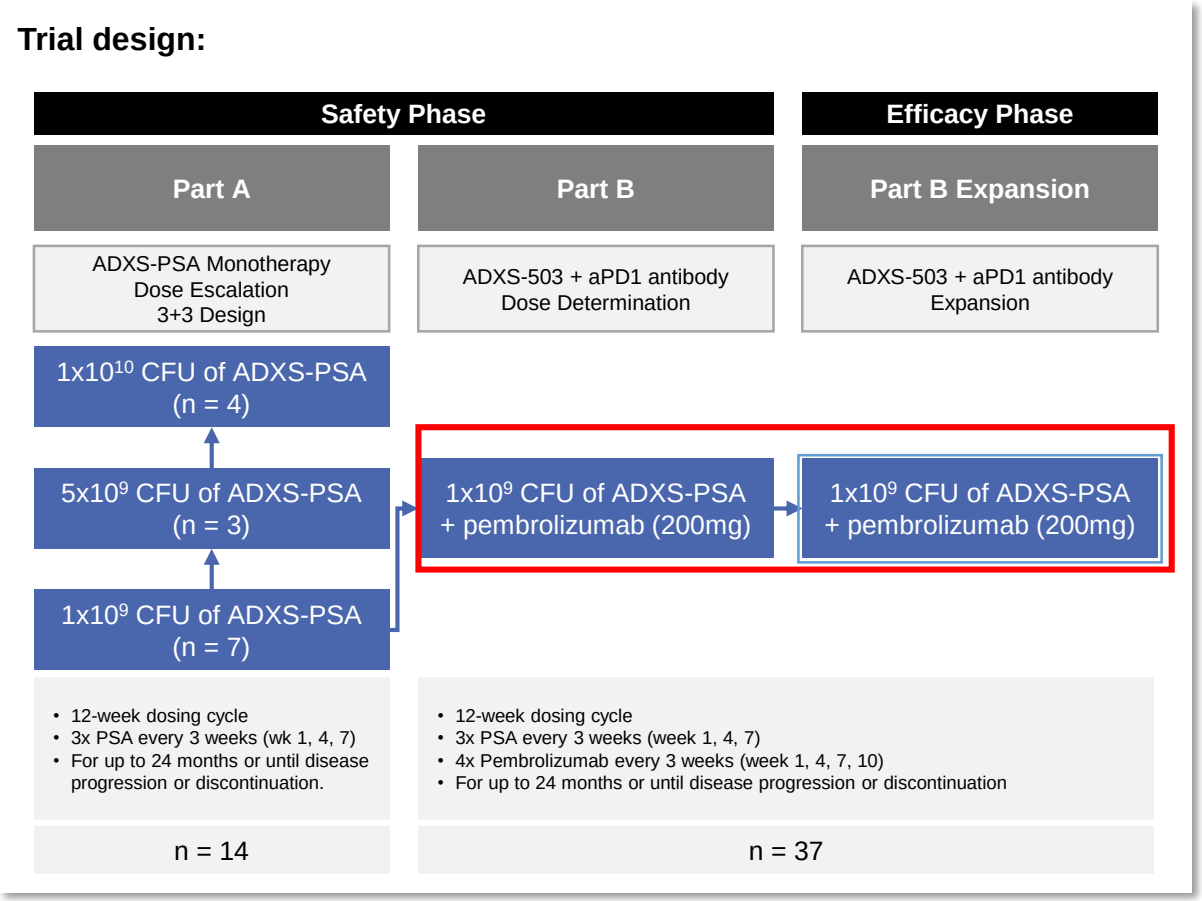
Symptoms	**Asymptomatic**	**Symptomatic**
Metastases	**Non-metastatic**	**Metastatic**
Castration	**Sensitive**	**Resistant**

KEYNOTE-046 ± Pembrolizumab in mCRPC

ClinicalTrials.gov Identifier: NCT02325557

Title: A Phase 1/2 Dose-Escalation and Safety Study of ADXS31-142 Alone and in Combination With Pembrolizumab in Patients With Previously Treated Metastatic Castration-Resistant Prostate Cancer

Trial design:



- **Keynote-046 PhI/II study**
  - Parts A - ADXS-PSA Monotherapy
  - Part B - ADXS-PSA $1x10^9$ CFU +/- 200mg pembrolizumab established as R2PD
- **Part B-combination might be associated with prolonged survival**
  - MSI-H negative status
  - visceral metastases ~30%
  - prior chemotherapy ~60%
  - prior NGHAs ~90%

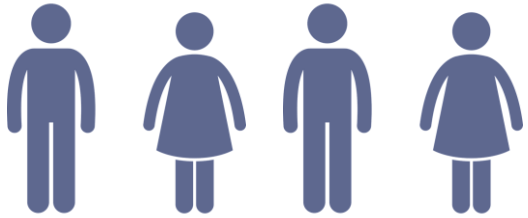
	N	Events	Median	95% CI
Overall	37	16	33.7	15.4-33.6
No prior docetaxel	17	3	NR	15.1-NR
Post-docetaxel	20	13	16.0	6.4 -34.6
Prior visceral mets	11	6	16.4	4.0-NR
No visceral mets	26	10	33.7	15.1-NR

Reference: Stein MN et al, ASCO GU Symposium 2020; Hayes SM et.al., SITC Annual Meeting 2017; Hayes SM et.al., Keystone Symposia 2019.
Legend: CFU Colony-Forming Unit | NGHA next generation hormonal agent | R2PD recommended phase 2 dose.
*

ADXS-HOT PROGRAM

Targeting Multiple Hotspots, OFAs and CTAs Increases Patient Applicability and Clinical Activity Potential

Hotspot mutations have demonstrated **pre-clinical activity** in Advaxis' *Lm* Technology[1]



ADXS-HOT constructs target both public, or shared, hotspot neoantigens and multiple proprietary tumor associated antigen targets, including oncofetal antigens (OFAs) and cancer testis antigens (CTAs)

Over 10 drug candidates designed using this approach

CD8 + T cell activity vs. hotspot mutations has been documented in a personalized neoantigen vaccine program, ADXS-NEO

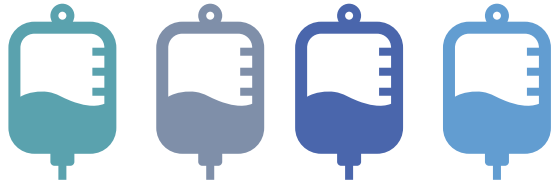
coverage of nearly

100%

ADXS-HOT constructs can include **over 30 antigen targets** and are designed to allow for multiple shots on goal to control the tumor in nearly all patients

Antigen spreading could further increase the potential number of targets

Can be used as **monotherapy and/or in combination** with other cancer treatments like checkpoint inhibitors



Off-the-shelf and available for patients to start treatment immediately

Manufactured in bulk with good stability keeping **cost of goods low** vs. "individualized" products

1. Data on file, Advaxis, Inc. 2019

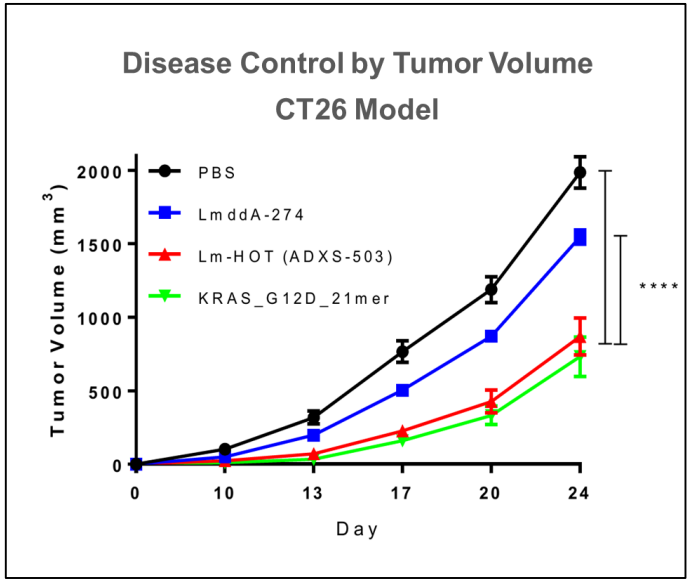
HOT ADXS-503 in metastatic NSCLC

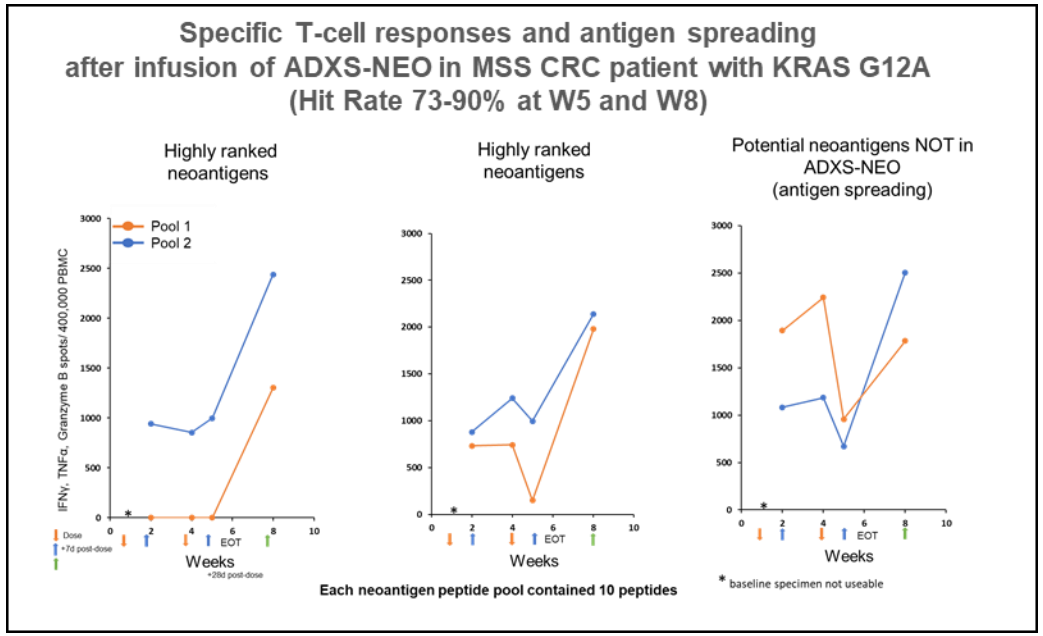
Off-The-Shelf *Lm*-vector Designed to Trigger Strong Anti-Tumoral Immune Responses with Targeted Antigens

ADXS-503 expresses a truncated fragment of the listeriolysin (tLLO) fused to highly prevalent antigens in cancer genes:

11 hot spots in:
KRAS, EGFR, U2AF1, BRAF, PIK3CA and TP53

11 oncofetal & cancer testis:
CEACAM5, STEAP1, RNF43, MAGE A6, NYESO1, GAGE1

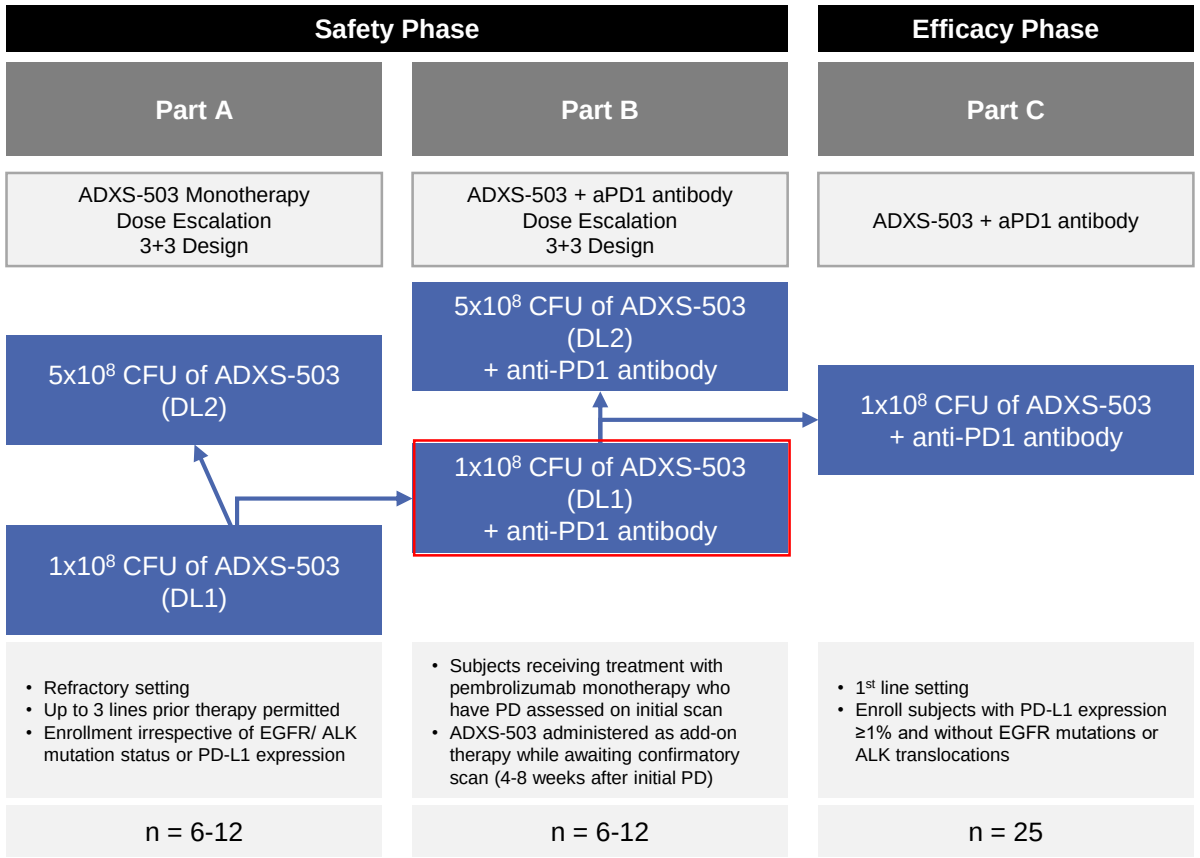




Data on file, Advaxis, Inc. 2019; Hecht JR et.al., AACR Annual Meeting, 2019

ADXS-503 ± Pembrolizumab in recurrent & first line therapy of NSCLC

Tithe: A Phase 1/2, Open-Label Study of ADXS-503 Alone and in Combination with Pembrolizumab in Subjects with Metastatic Squamous or Non-Squamous Non-Small Cell Lung Cancer



Endpoints:

Primary
Tolerability/ Safety

Secondary
Clinical activity
RP2D

Exploratory
Immunological

ClinicalTrials.gov Identifier: NCT03847519

Preliminary Results

- **Part A, in monotherapy and Part B, in combination with Pembrolizumab**
  - **Completed Part A (n= 7)**
    - No dose limiting toxicities observed
    - Most AEs were grade 1-2 chills, fever and nausea; reversible and manageable
    - SD observed in 3 pts
  - **Currently enrolling patients in Part B (n=2)**
    - Safe and tolerable in 2 pts treated at DL-1
    - One SD and one PR observed
- **Immune-correlative work in progress**

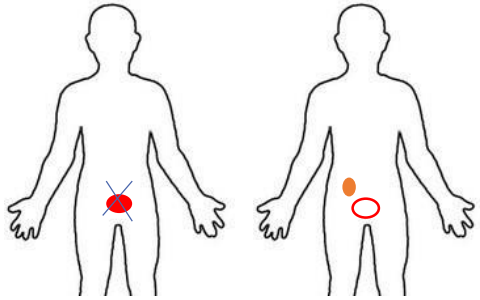
Carlisle J et.al., IASLC 2020 TTLC Meeting. Santa Monica, CA . 20 Feb 2020.
Legend: CFU Colony-Forming Unit | DL dose level | NSCLC non-small cell lung cancer | RP2D recommended phase 2 dose | DL dose level.

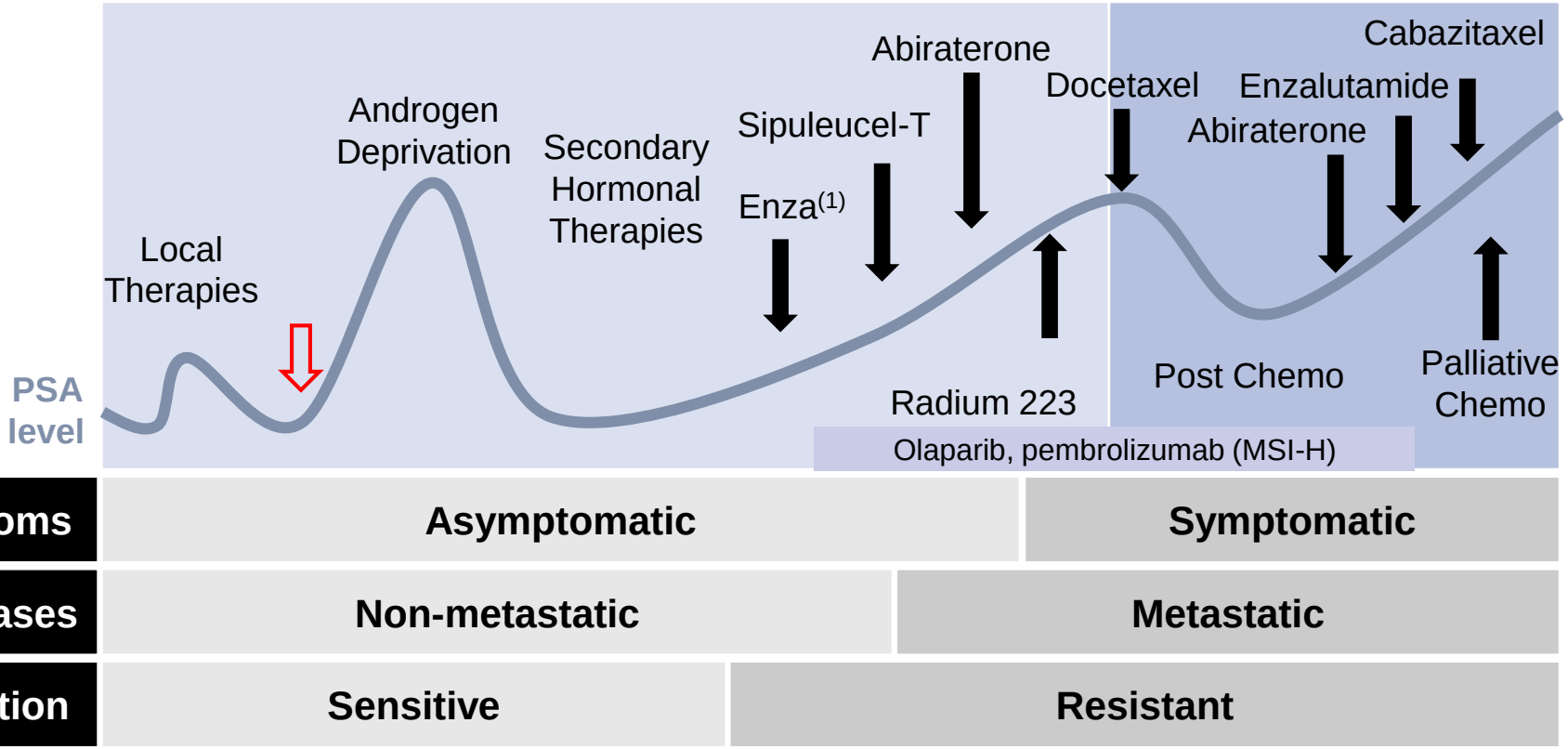
HOT ADXS-504 in the Prostate Cancer Treatment Landscape

ADXS-504 expresses a truncated fragment of the listeriolysin (tLLO) fused to highly prevalent antigens in cancer genes:

14 hot spots in:
CHEK2, RGPD8, ANKRD36C, SPOP, AR

10 oncofetal & cancer testis in:
PSA, PSMA, STEAP, SART3, RNF43, PAGE4, CEACAM5, SSX2, MAGEA4

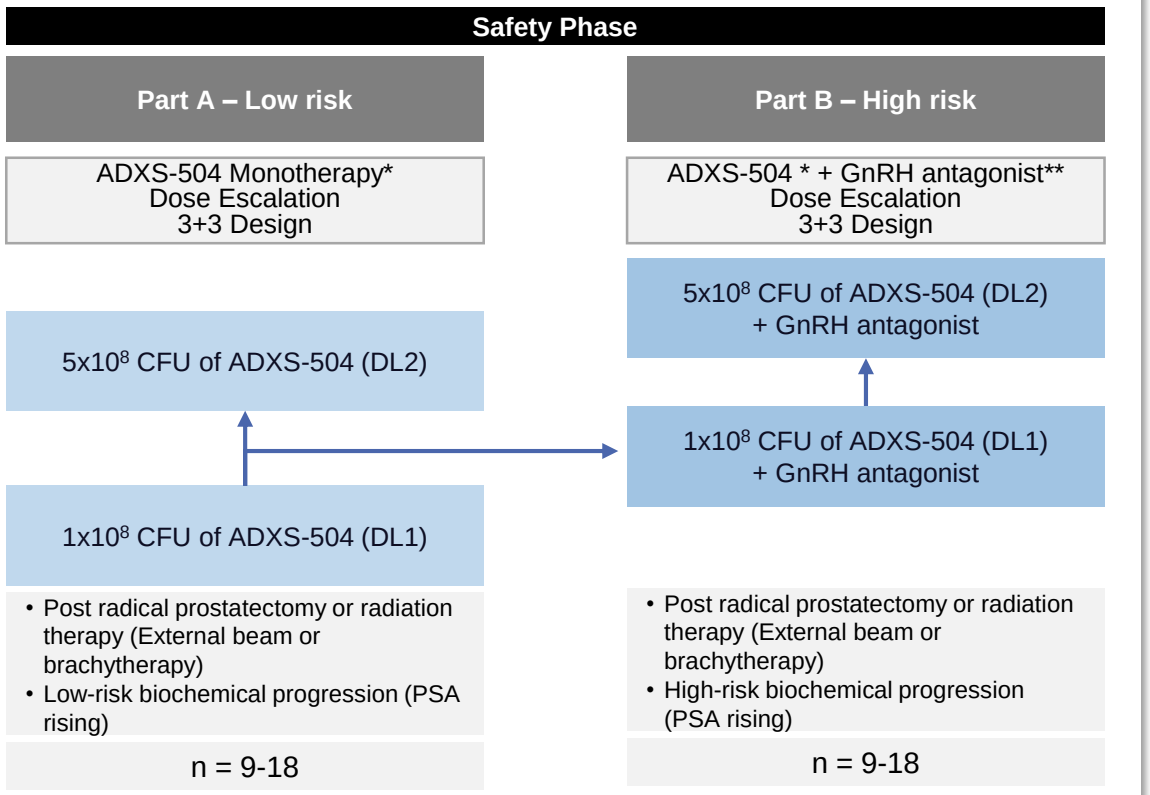




ADXS-504 in Biochemically Recurrent Prostate Cancer

Title: A Phase 1 Study of ADXS-504, a Cancer Type Specific Immunotherapy in Subjects with Biochemically Recurrent Prostate Cancer

Trial design:



Endpoints:

Primary
Tolerability/ Safety

Secondary
PSA response

Exploratory
rPFS
PSADT
Immunological

Potential benefits:

- To delay progression after radical prostatectomy/ radiotherapy
  - Low risk patients: monotherapy
  - High risk patients: combination with degarelix (gonadotropin-releasing hormone (GnRH) receptor antagonist)(1)
- To delay ADT hormone therapy and decrease long term toxicity, e.g., sarcopenia, insulin insensitivity, fractures, CVD, weight gain, etc.

Notes: * Dosing schedule: q4w for 6 doses | ** Dosing schedule: 4 doses only | (1) Alternative GnRH could be used.
Legend: ADT androgen deprivation therapy.

Our gratitude…

To our patients and their families

To our experts

ADXS-PSA
Dr. Mark N. Stein, Columbia University
Dr. Naomi Haas, UPenn
Dr. Lawrence Fong, UCSF
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Dr. Elaine T. Lam, U. Colorado University

ADXS-503
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Dr. Jonathan W. Goldman, UCLA
Dr. Thomas Stinchcombe, Duke Cancer I.
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