# ADVAXIS IMMUNOTHERAPIES™

# **Corporate Presentation**

Nasdaq: ADXS June 2020

## **Forward-Looking Statements**

This presentation contains forward-looking statements that involve a number of risks and uncertainties. For those statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. The factors that could cause our actual results to differ materially include: the impact of the discontinuation on relationships related to the Aim2Cerv Study; the success and timing of our clinical trials, including subject accrual; our ability to avoid and quickly resolve any clinical holds; our ability to obtain and maintain regulatory approval and/or reimbursement of our product candidates for marketing; our ability to obtain the appropriate labeling of our products under any regulatory approval; our plans to develop and commercialize our products; the successful development and implementation of our sales and marketing campaigns; the size and growth of the potential markets for our product candidates and our ability to serve those markets; our ability to successfully compete in the potential markets for our product candidates, if commercialized; regulatory developments in the United States and other countries; the rate and degree of market acceptance of any of our product candidates; new products, product candidates or new uses for existing products or technologies introduced or announced by our competitors and the timing of these introductions or announcements; market conditions in the pharmaceutical and biotechnology sectors; our available cash, including to support current and planned clinical activities; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; our ability to obtain additional funding; our ability to obtain and maintain intellectual property protection for our product candidates; the success and timing of our preclinical studies including IND-enabling studies; the timing of our IND submissions; our ability to get FDA approval for study amendments; the timing of data read-outs; the ability of our product candidates to successfully perform in clinical trials; our ability to initiate, enroll, and execute pilots and clinical trials; our ability to maintain our existing collaborations; our ability to manufacture and the performance of third-party manufacturers; the performance of our clinical research organizations, clinical trial sponsors and clinical trial investigators; our ability to successfully implement our strategy; and, other risk factors identified from time to time in our reports filed with the SEC. Any forward-looking statements set forth in this presentation speak only as of the date of this presentation. We do not intend to update any of these forwardlooking statements to reflect events or circumstances that occur after the date hereof. Our fiscal year ends October 31. Throughout this presentation, all references to quarters and years are to the calendar quarters and years unless otherwise noted.

### **Corporate Overview**

### **Corporate Facts**

- Founded 2002; HQ in Princeton, NJ
- ~20 employees
- Cash runway anticipated into Q3 2021
- 61.6 million shares outstanding as of June 10, 2020

### **Platform Technology**

- Clinically validated, unique immuno-oncology platform
- Bacterial vector equipped with targeted (neo)antigens

### **Clinical Pipeline**

- ADXS-HOT: Off-the-shelf, tumor type-specific constructs
  - ADXS-503 in NSCLC in Phase 1/2 study
  - ADXS-504 in prostate cancer scheduled to enter clinic this year
- ADXS-PSA: Prostate cancer program
- ADXS-HPV (AXAL): HPV+ cancers

### **Upcoming Milestones**

- ADXS-503: Phase 1/2 combination with KEYTRUDA-clinical and immune/biomarker data for KEYTRUDA failures as well as first-line patients
- ADXS-504: Clinical trial initiation; initial data readout
- ADXS-PSA: Announcement of next steps

### **Investment Highlights**

Validated and Versatile I/O Platform, focused pipeline and several near-term milestones

### **Innovative Platform**

Proprietary bacterial vector/platform can elicit rapid and strong immunological activity

Legend: IND Investigational New Drug Application

Nearly 500 patients treated, manageable safety profile<sup>(1)</sup>

### **Clinical Signals**

- ➤ HOT Lung (ADXS-503):
  - 50% (3 of 6) of evaluable patients from the monotherapy arm, showed stable disease (SD) in a heavily pre-treated population
  - First two evaluable patients in combination arm (who previously progressed on pembrolizumab) showed substantial tumor shrinkage and sustained clinical benefit— One achieved a Partial Response (PR) with 60% tumor reduction (out to at least 16 weeks) and the other achieved durable SD (out to at least 25 weeks) with 25% reduction in a site lesion and both still on treatment
- PSA (ADXS-PSA): Phase 2 study in prostate cancer<sup>(2)</sup> showed prolonged survival in combination with pembrolizumab

### **Pipeline**

- ADXS-HOT: Trial in lung cancer initiated in February 2019, currently enrolling both pts. who have progressed on pembrolizumab as well as 1L pts.; IND clearance for prostate cancer; with another >10 constructs designed that can be moved into the clinic
- > ADXS-PSA: Evaluating next steps

## **Clinical Pipeline**

Program	Cancer Indication	IND	PHASE 1	PHASE 2	PHASE 3
ADXS-HOT	Non-Small Cell Lung Cancer (ADXS-503) in Combination with KEYTRUDA® (pembrolizumab)				
	Prostate Cancer (ADXS-504)	IND Cleared Jan 2020			
ADXS-PSA	Metastatic Prostate Cancer in Combination with KEYTRUDA® (pembrolizumab)				
ADXS-HPV (AXAL)	HPV+Lung Cancer (Taiwan Partner)			*	

★= Planned

**Advaxis Funded** 

Third Party Funded



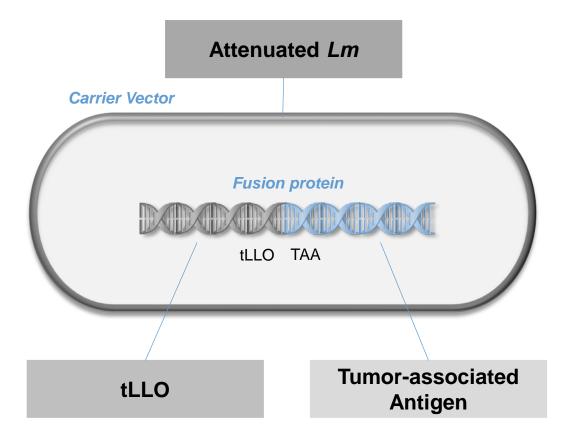


## Lm Platform Technology

Proprietary Antigen Delivery Platform which Activates the Immune System, Naturally

## Lm Platform Designed to Trigger Strong Immune Responses with Targeted Antigens

### **Three Core Components**

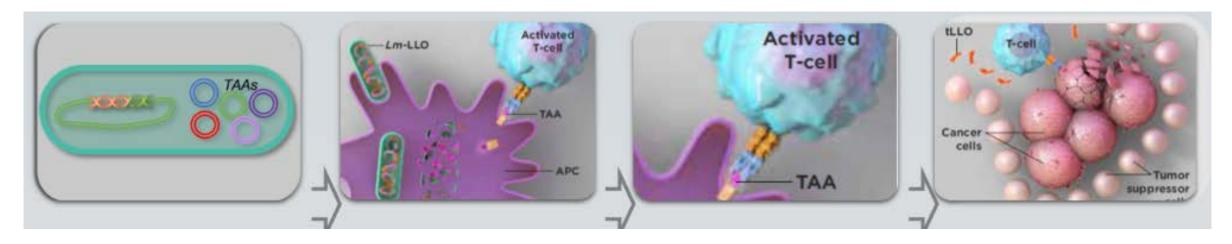


### **Comprehensive Immune Activity**

- Listeria monocytogenes (*Lm*) bacteria
  - Carrier vector; irreversibly attenuated<sup>(1)</sup>
  - Mimics infection and redirects immune response against cancer
  - Well understood and manageable safety profile
- tLLO
  - Adjuvant properties
  - Powerful CD8+ T cell response
  - Neutralizes Tregs & MDSCs that protect tumor
- Diverse antigens in different drug constructs
  - Cancer type-specific (HOT, PSA)
  - Patient-specific neoantigens (NEO)
  - Viral (HPV)

### Using the Body's Own Immune System to Fight Cancer

Harnessing the Unique Life Cycle of *Lm* in Antigen Presenting Cells (APCs)



Live attenuated strains of *Lm* are bioengineered to secrete antigenadjuvant fusion proteins

Upon infusion,
Bioengineered *Lm* are
phagocytosed by
APCs where fusion
protein is secreted
and processed –
presented to MHC
class I and II

Target peptides
presented on APC
surface stimulate
tumor associated
antigen (TAA) specific
CD4+ and CD8+ T
cells

Activated CD8+ T cells seek out and kill TAA-expressing cancer cells and modulated tumor microenvironment to overcome immune suppression

## Advaxis Technology Evolution: Higher Payloads, New Targets

### **ADXS-HPV (AXAL)**

Prolonged survival and complete responses in cervical and anal cancer patients and antigen spreading observed

#### **ADXS-PSA**

In combination with KEYTRUDA® prolonged survival in metastatic castration-resistant prostate cancer and antigen spreading

#### **ADXS-NEO**

Personalized,
patient-specific
candidates based on
sequencing of each
patient's tumor; early
data suggest rapid
and strong
immunogenicity and
antigen spreading

### **ADXS-HOT**

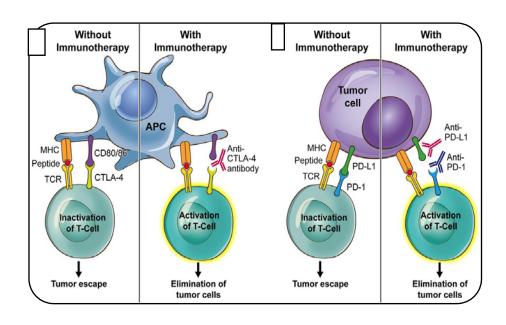
specific candidates based on "hotspot" mutations and proprietary cancer antigens with promising clinical data in ongoing lung cancer study; efficient priming by antigens and antigen spreading

Single antigen delivery platform

Multiple neoantigen delivery platform



## **Neoantigen-Directed Immunotherapies Can Transform Cancer Treatment**



- Immuno-oncology (I/O) treatments work to harness the power of individual's immune system
- Immune Checkpoint Inhibitors (ICIs) have dramatically altered the cancer treatment landscape but still only a minority of patients treated with ICIs have durable responses and improved outcomes leading to long-term survival
- Emerging data from studies of patients who successfully respond to ICIs show that most have pre-existing T cells against neoantigens
- Neoantigen-directed immunotherapies can build upon the success of ICIs, leading to durable outcomes with long-term survival to further transform cancer treatment paradigms

# A D V A X I S IMMUNOTHERAPIES™

## **ADXS-HOT**

Off-the-Shelf Hotspot Neoantigen-Directed Therapy

Phase 1/2 in Non-Small Cell Lung Cancer (ADXS-503)

IND cleared in Prostate Cancer (ADXS-504)

### **ADXS-HOT**

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



Hotspot mutations have demonstrated pre-clinical activity in Advaxis' *Lm* Technology<sup>1</sup>



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



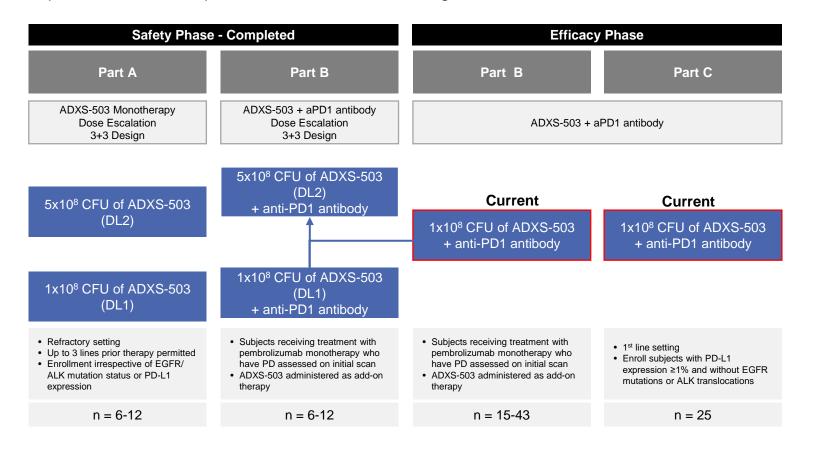
Off-the-shelf and available for patients to start treatment immediately

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

### **HOT Development Overview – Lung Phase 1/2 Clinical Trial**

ClinicalTrials.gov Identifier: NCT03847519

**Title**: 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

### **ADXS-503 Status Update and Results to Date**

- Part A, in monotherapy completed; Part B, in combination, completed enrollment at first dose level (DL1) and recently
  expanded to efficacy phase and to enroll up to 15 additional pts. in Part B DL1 (first part of Simon Two-stage study) and
  opened up Part C for first line pts.
- 10 patients dosed; 7 in the monotherapy arm and 3 thus far in Part B; 9 evaluable patients
- 3 patients dosed in combination arm who previously progressed on pembrolizumab with sustained and durable clinical benefit in first two patients, respectively:
  - 1 achieved partial response (PR) with 60% tumor reduction seen on 8-week scan and confirmed on 16-week scan;
     patient had received pembro for > 2 years with a best overall response of stable disease
  - 1 achieved **stable disease (SD) with a 25% reduction in target lesion** now out to 25 weeks, confirmed by radiographic scans; patient had received pembro for > 2 years with a best overall response of stable disease
- 50% (3 of 6) of evaluable patients from the monotherapy arm, from Part A, showed SD in a heavily pretreated patient population with patients failing up to 6 prior lines of therapy and most patients progressing on prior immunotherapy treatments
- Part A at 1X10<sup>8</sup> and 5X10<sup>8</sup> CFU monotherapy, as well as Part B DL1 in combination therapy, appeared safe and tolerable with only transient Grade 1–2 adverse events and no dose limiting toxicities; there were no added toxicities from combining ADXS-503 with pembrolizumab



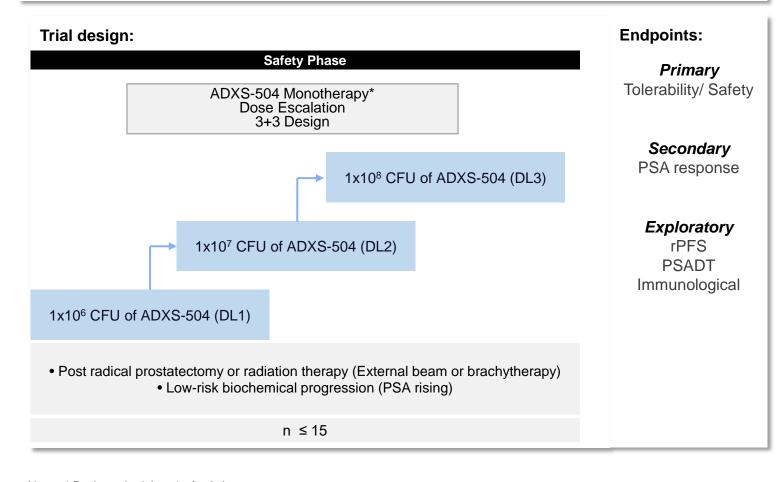
## **ADXS-503: Preliminary Immune and Biomarker Results**

7 patients evaluated to date: 6 in monotherapy and 1 in combination therapy, showing:

- Increased secretion of cytokines/chemokines for several hours after infusion consistent with immune activation
- Activation of cytotoxic- and memory- CD8+ T cells in patients treated with monotherapy and in one patient evaluated in combination therapy
- 100% efficient priming by antigens in ADXS-503 (7/7 patients)
- CD8+ T cells were generated against hot spot mutations and/or heteroclitic/wild-type tumor associated antigens
- Antigen spreading in 5 of 7 patients which increases potential of killing tumor cells

### ADXS-504 (HOT Prostate) in Biochemical Recurrent (BCR) Prostate Cancer

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



### **Potential benefits:**

- Delay progression after radical prostatectomy/radiotherapy in low risk-BCR patients
- Delay start of androgen deprivation therapy to decrease long term toxicity (e.g., sarcopenia, insulin insensitivity, fractures, CVD, weight gain)

Notes: \* Dosing schedule: q4w for 6 doses

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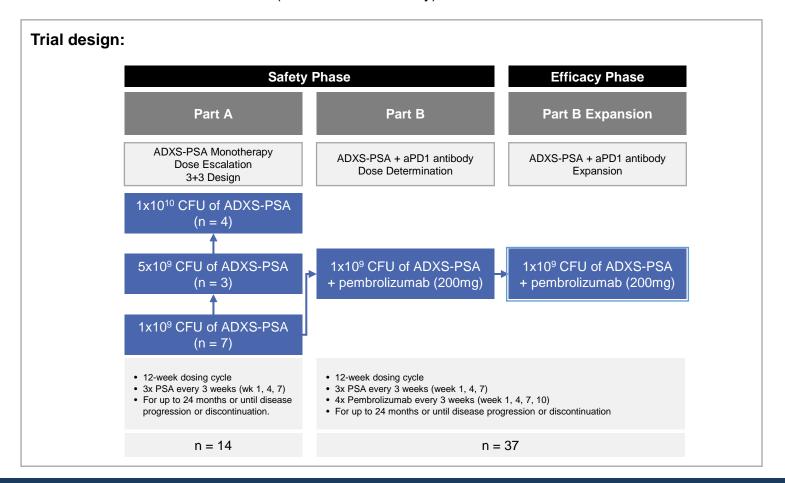
## **ADXS-PSA**

Prostate Cancer Therapy

### **PSA Development Overview – Phase 1/2 Clinical Trial**

### 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 (KEYNOTE-046 study)



### **Endpoints:**

#### **Primary**

Tolerability/Safety
RP2D

### Secondary

Anti-tumor activity
Progression-free survival
Overall survival
Effects on serum PSA
Immune correlative work

### **ADXS-PSA Highlights**

- Parts A and B are completed<sup>1</sup>
  - 1x10<sup>9</sup> +/- 200mg pembrolizumab established as R2PD
- Combination prolonged survival in combination with KEYTRUDA® (Part B):
  - Median OS (mOS) =33.7 months (15.4–NR) in patients who had failed chemotherapy or were chemotherapy-naïve
    - Despite MSI-H negative status and presence of visceral metastases
  - In patients with visceral metastases (n=11) mOS=16.4 months compared to:
    - Standard of care: mOS=11 months (estimated)
    - KEYTRUDA® alone<sup>2</sup>: mOS= **7.9 months** in PD-L1 negative; **9.5 months** in PD-L1 positive pts.
- Treatment-related adverse events (TRAEs) were mostly mild or moderate constitutional symptoms such as fever, chills, rigors, hypotension, nausea and fatigue, consistent with immune activation and manageable with standard care. One patient in the monotherapy arm was discontinued from the study due to a grade 4 TRAE related to cytokine release, which resolved within 24 hours using medical management.
- Collaboration with Merck & Co.



## **Lm** Safety

### Summary of ADXS-HPV (AXAL) Treatment-Related Adverse Events

Treatment-Related Adverse Events Reported ≥5% with ADXS11-001 (AXAL)

Monotherapy: n (%) Adverse Events (N=192)

Preferred Term	Any Grade	Grade 3/4
Chills	91 (47.4%)	0
Pyrexia	70 (36.5%)	3 (1.6%)
Nausea	54 (28.1%)	0
Vomiting	48 (25.0%)	1 (0.5%)
Hypotension	46 (24.0%)	12 (6.3%)
Headache	41 (21.4%)	0
Tachycardia	15 (7.8%)	0
Cytokine release syndrome	15 (7.8%)	7 (3.6%)
Gamma-glutamyltransferase increased	15 (7.8%)	3 (1.6%)
Dizziness	14 (7.3%)	0
Aspartate aminotransferase increased	13 (6.8%)	0
Back pain	12 (6.3%)	0
Myalgia	12 (6.3%)	0
Influenza like illness	11 (5.7%)	0
Blood alkaline phosphatase increased	11 (5.7%)	2 (1.0%)
Diarrhea	10 (5.2%)	1 (0.5%)
Pain	10 (5.2%)	0
Decreased appetite	10 (5.2%)	0

- The largest source of Lm safety data is from patients treated with AXAL monotherapy at 1X10<sup>9</sup> CFU<sup>1</sup>
- Treatment-related adverse events across
   AXAL trials were primarily Grade 1 and 2<sup>2</sup>
- Adverse Events generally occurred within hours and were transient in nature
  - manageable and reversible
- Standard premedication regimen has appeared to be adequate (e.g., diphenhydramine, NSAID, etc.)

## **Key Financial Information**

Balance Sheet <sup>1</sup>	
Cash, Cash Equivalents and Marketable Securities, as of April 30, 2020 Financing in January 2020 netted \$9.6 million	\$28.2MM
Shares Outstanding, as of June 10, 2020	61.6MM
Fully Diluted Shares Outstanding, as of June 10, 2020	67.9MM
Positive Cash Balance Anticipated Into Q3 2021	
Operating Expenses for the Quarter Ended April 30, 2020 <sup>1</sup>	
Research and Development Expenses*	\$3.9MM
General and Administrative Expenses*	\$2.6MM

\*Cash expenditures for the 12 month period May 2020 – April 2021 are expected to range between \$22M-\$24M <sup>1</sup> The Company's fiscal year ends October 31st



## **Anticipated Catalysts Over the Next 12 Months**

PROGRAM	COMPLETED/ANTICIPATED MILESTONES	TARGET
ADXS-503 (HOT NSCLC)	<ul> <li>Clinical and immunogenicity data from Part A cohort (safety, immune response)</li> <li>Clinical and immunogenicity data from Part B cohort (safety, immune response)</li> <li>Clinical and immunogenicity data from Part C cohort (safety, immune response)</li> </ul>	1H 2020* 2H 2020 1H 2021
ADXS-504 (HOT Prostate)	<ul> <li>Initiate clinical study</li> <li>Initial clinical and immunogenicity data</li> </ul>	2H 2020 1H 2021
ADXS-PSA	<ul> <li>Updated survival data in subset of patients (prolonged survival in patients with visceral metastases)</li> <li>Announce program next steps</li> </ul>	1H 2020* 2H 2020

<sup>\*</sup>Completed



## **Advaxis Management**

### Seasoned Management Team, Transaction Oriented

#### **Chief Executive Officer**



Kenneth A. Berlin

ROSETTAGENOMICS™



**Chief Financial Officer** 



**Molly** Henderson







**Chief Medical Officer** 



**Dr. Andres Gutierrez** 









Bristol-Myers Squibb Company

BIOMARIN

#### **Head of Scientific Advisory Board**



Dr. Robert Petit











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## Thank You