Advaxis, Inc. – Company Overview

Chris Duke

Chief Operating Officer

Cervix Cancer Education Symposium, February 2018, Bucharest

Advaxis Overview

Advaxis is a biotechnology company developing immunotherapies that enlist the body's own immune system to fight cancer. We discover, develop and make better medicines through innovative sciences.

Company overview

Founded: March 2002

Headquarters: Princeton, New Jersey, U.S.

Cash on hand*: $89.4M (no debt)

Products: 5 development-stage therapies based on the proprietary *Lm* Technology™

Partnerships: BMS** (ADXS-DUAL), AstraZeneca** (AXAL), Merck** (ADXS-PSA), Amgen (ADXS-NEO)

Product overview

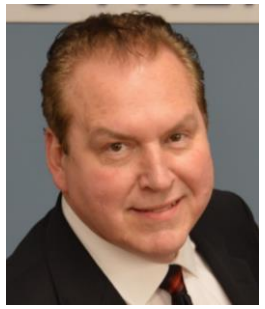
HPV-associated cancers	Cervical (CC), anal, head & neck **Products:** axalimogene filolisbac (AXAL) (Phase 3), ADXS-DUAL
HER2-associated cancers	HER2 expressing solid tumors **Products:** ADXS-HER2 (Phase 2)
PSA-associated cancers	Prostate **Products:** ADXS-PSA (Phase 2)
Neoantigen program	Multiple cancers **Products:** ADXS-NEO (Phase 1)
Hot-spot mutations	Multiple cancers **Products:** ADXS-HOT (Pre-IND)

Note: * As of July 31, 2017. **Clinical trial collaboration (drug only).

Who is Advaxis?
Experienced Management Team

Anthony Lombardo
Interim Chief Executive Officer

GE Healthcare · Philips · Bracco · ALI Technologies · EZEM



Robert Petit
Chief Scientific Officer

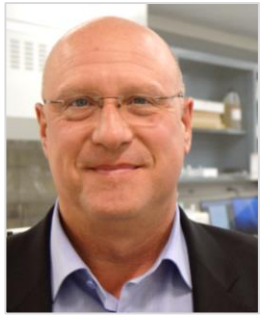
Bristol-Myers Squibb Company · Pharmacia · MGI Pharma · Aesgen

Sara Bonstein
Chief Financial Officer

ImClone Systems Incorporated · Lilly · Johnson & Johnson

Chris Duke
Chief Operating Officer

NPS Pharma · Amicus Therapeutics



Michael Grace
VP, Technical Operations

NPS Pharma · Schering-Plough/USA · Bristol-Myers Squibb Company

Thomas Hare
Sr. VP, Product Development

PRAHEALTHSCIENCES · Incyte · Bristol-Myers Squibb Company

Robert Ashworth
Sr. VP, Regulatory, Quality & Compliance

NPS Pharma · Otsuka · Forest Laboratories, Inc.

Ranya Dajani
VP, Business

Bristol-Myers Squibb Company

There is a delicate balance that determines the ability of the immune system to identify and destroy cancer

Immune system does not recognize cancer

Immune responses are blocked or are too weak

Immune system recognizes cancer

Immune system attacks cancer

Priming of the immune system (1)

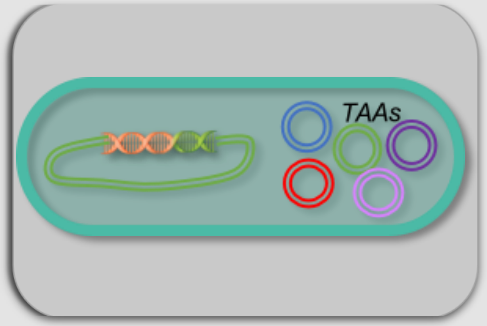
Access to strong T cells (2)

Reducing suppressive effects in the TME (3)

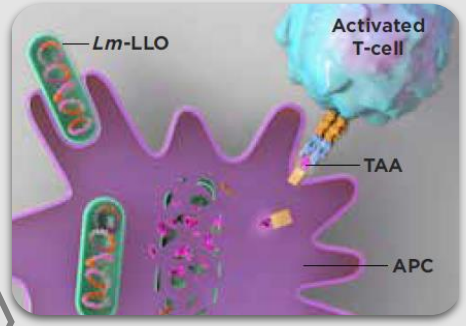
Three elements are required to shift the balance in favor of the immune system defeating cancer

Lm Technology:

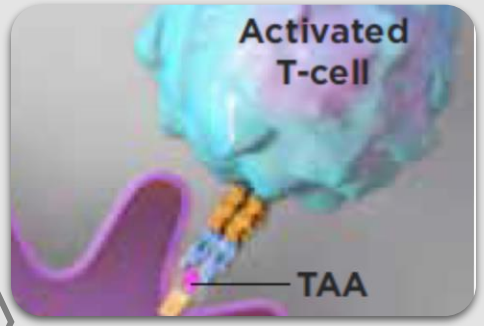
Lm Technology in antigen-presenting cells can lead to an anti-tumor immune response



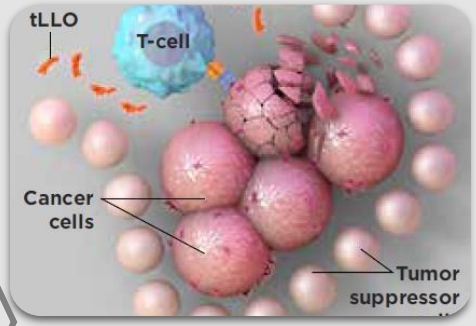
Live, attenuated strains of *Lm* are bioengineered to secrete an antigen-adjuvant fusion protein consisting of truncated fragment of listeriolysin O (tLLO), which has adjuvant properties, and one or more TAAs



Upon infusion into the patient, bioengineered *Lm* is phagocytosed by APCs, where the fusion protein is secreted by the *Lm*, processed, and presented onto MHC class I and II molecules



Target peptides presented on the surface of the APCs stimulate TAA-specific $CD4^+$ and $CD8^+$ T cells



Activated $CD8^+$ T cells seek out and kill TAA-expressing cancer cells, and modulate the tumor microenvironment to overcome immune suppression

APC, antigen-presenting cell; Lm, Listeria monocytogenes; MHC, major histocompatibility complex; TAA, tumor-associated antigen.

Lm Technology Features

Multifaceted mechanism	Multiple immunotherapy mechanisms: potent innate immune stimulation via TLRs and PAMPs including the STING receptor, strong $CD8^+$ and $CD4^+$ T cell responses, epitope spreading, and immune suppression by disabling Tregs and MDSCs in the TME
No neutralizing antibodies	Unique intracellular lifecycle of Listeria avoids neutralizing antibodies, allowing for repeat dosing
Synergies with other immunotherapies	Demonstrated synergies with checkpoint inhibitors, costimulatory agonists and others based on preclinical models
Flexible/adaptable platform	Large capacity; can be adapted to target many tumor types and evolve with innovations in the field of immuno-oncology; 3 ongoing clinical programs; Listeria is irreversibly attenuated
Manageable safety profile	Flu-like symptoms have been transient and associated with infusion

MDSCs, myeloid derived suppressor cells; PAMPs, pathogen-associated molecular patterns; TLR, toll-like receptor; STING, stimulator of interferon genes; TME. Tumor microenvironment.

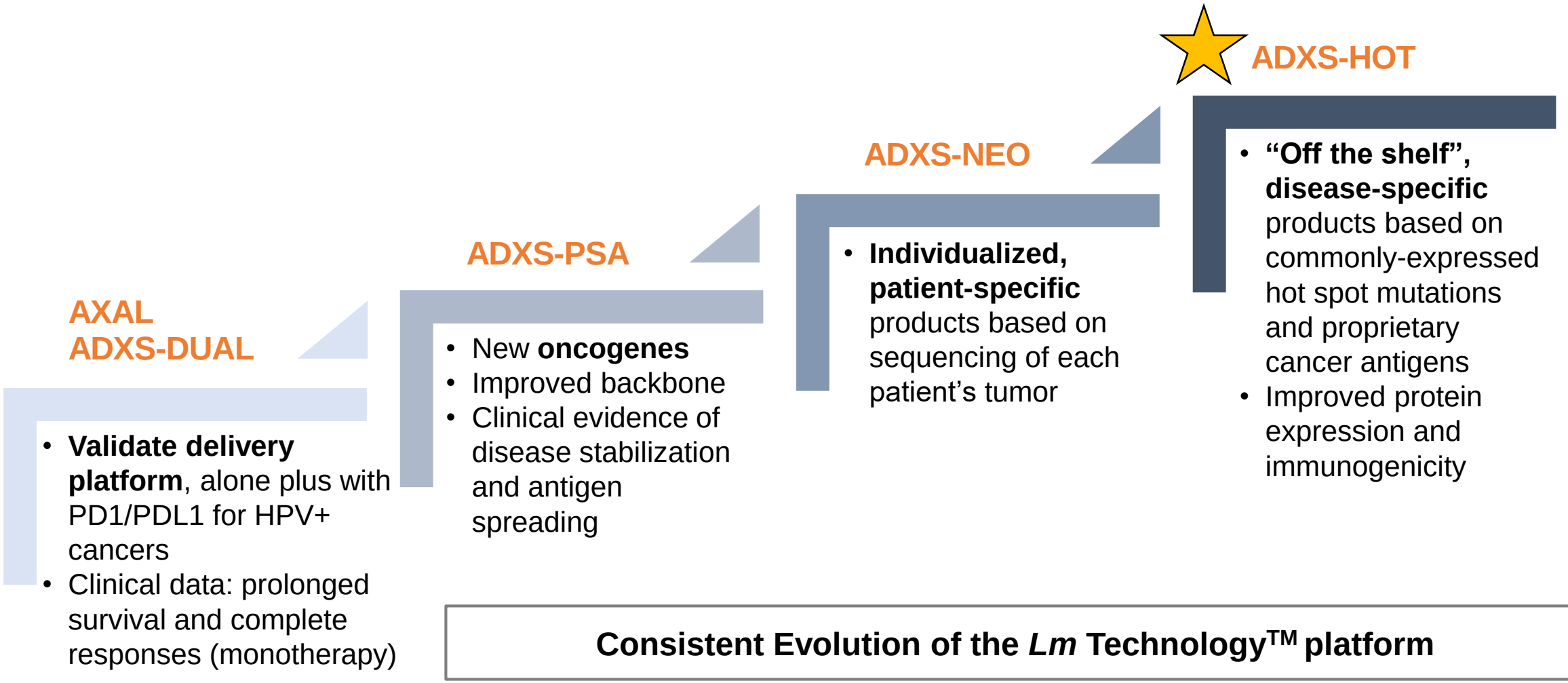
Clinical Trial Programs – In Progress and Planned

GYNECOLOGIC CANCER INTERGROUP
An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

	CANCER INDICATION	PARTNER	IND	PHASE 1	PHASE 2	PHASE 3
AXALIMOGENE FILOLISBAC	High-Risk, Locally Advanced Cervical					
	Metastatic Cervical Combination with IMFINZI™ (durvalumab)	AstraZeneca				
ADXS-DUAL	Metastatic Cervical Combination with OPDIVO® (nivolumab)	Bristol-Myers Squibb				★ Begin 1H ‘18
	Locally Advanced HPV+ Head & Neck Cancer				★ 2018	
ADXS-NEO	Multiple Cancers by Targeting Personal Neoantigens	AMGEN		★ Begin 1H ‘18		
ADXS-HOT	Multiple Cancers by Targeting Shared Hotspot Mutations		★ Filings ‘18			
ADXS-PSA	Metastatic Prostate Combination with KEYTRUDA® (pembrolizumab)	MERCK				

Advaxis Funded | **Partner Funded** | **Investigator-Sponsored Trial** | ★ = Planned

Lm Technology™ has the potential to expand the reach of immunotherapy



AXAL in Recurrent / Metastatic Cervical Cancer
GOG-0265 Open-Label Phase 2 Simon 2-Stage Study

GYNECOLOGIC CANCER INTERGROUP
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FDA Orphan

EU ATMP

Two-stage Trial Design

Eligibility

Persistent or recurrent squamous or nonsquamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix.

Stage 1
- n=26
- Axalimogene Filolisbac
- q28d X 3

Safety, tolerability and efficacy hurdle met for initiation of Stage 2

Stage 2
- n=37
- Axalimogene Filolisbac
- q28d until progressive disease, unacceptable toxicity, or consent withdrawn

Primary Endpoints:
- 12-month overall survival rate
- Safety & Tolerability

Secondary Endpoints:
- Progression-free survival
- Overall survival
- Objective response rate

Trial start: May 2011
Expected completion: Completed
Partner: GOG

Study sponsored by Advaxis and Cancer Therapy Evaluation Program and coordinated by the Gynecologic Oncology Group (GOG) in collaboration with the National Cancer Institute.

NIH NATIONAL CANCER INSTITUTE

NIH NATIONAL CANCER INSTITUTE DCTD Division of Cancer Treatment & Diagnosis
CTEP Cancer Therapy Evaluation Program

GOG Gynecologic Oncology Group

https://clinicaltrials.gov/ct2/show/record/NCT01266460 Tewari KS, et al. *Curr Oncol Rep*. 2005;7:419-434.
On October 24, 2016, Advaxis announced early closure of stage 2.

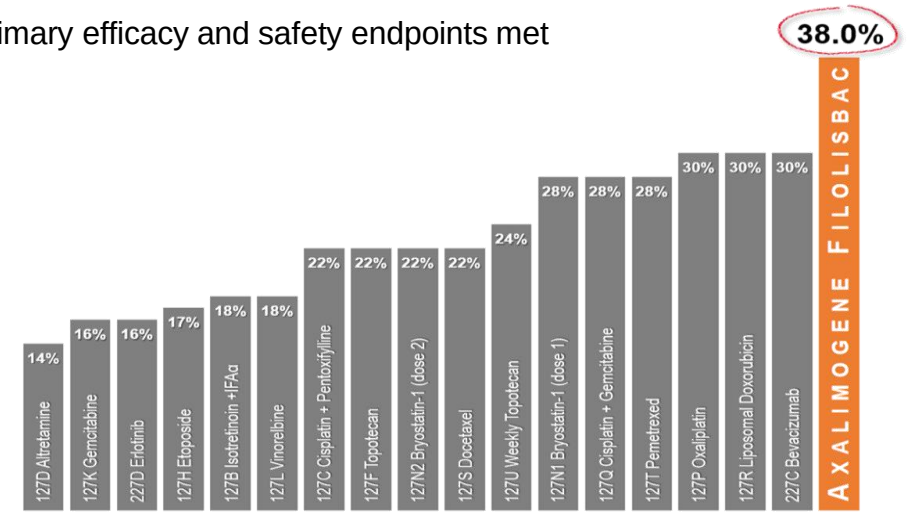
Cervical Cancer and AXAL: Strong Clinical Data in Phase 2 Study
GOG-0265 Open-Label Phase 2 Simon 2-Stage Study

Phase 2 Study in India: Prolonged Survival and Tumor Response in Randomized, Multicenter Phase 2 Study in Recurrent/ Refractory CC Illustrated the Promise of *Lm* Technology[1]

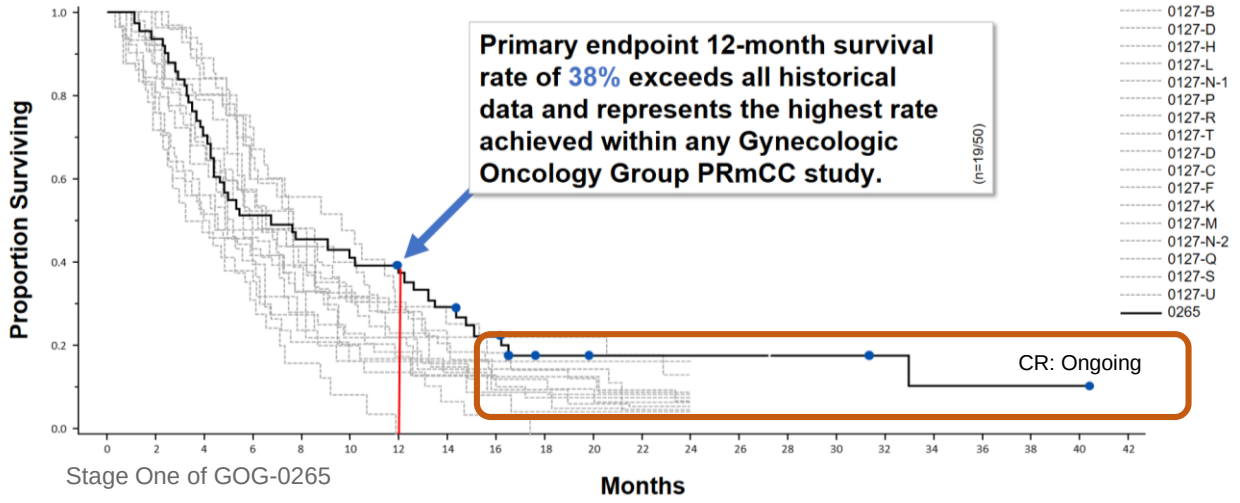
- ✓ 34.9% 12-month survival rate (38/109), 3 durable CRs observed

GOG-0265: Unprecedented improvement of survival rates in Recurrent / Metastatic Cervical Cancer Confirmed the Findings[2]

- ✓ 38.0% (95% CI 24.7% - 52.8%) 12-month survival rate (19/50); highest achieved to-date in GOG PRmCC studies to date, 1 durable CR observed
  - ✓ GOG Model-Predicted 12 month survival was 24.5%, based on the characteristics of patients in 0265
- ✓ Primary efficacy and safety endpoints met



Source: GOG-0265 Clinical Study



Stage One of GOG-0265

This strong body of clinical evidence of safety and efficacy led to decision to file for conditional approval in the EU in Q1 2018*

PRmCC=Persistent Recurrent Metastatic Cervical Cancer; GOG= Gynecological Oncology Group; CR= complete response

1. Data Presented at ASCO 2014. 2. Data presented at SGO 2017.

*The submission of the EU filing has been delayed in order to provide additional information requested by the regulatory authorities.

AXAL in Recurrent / Metastatic Cervical Cancer

GOG-0265 Complete Response, Ongoing, for 55-Year-old Patient

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An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

FDA Orphan

EU ATMP

Diagnosis: squamous cell cancer of the cervix

2006

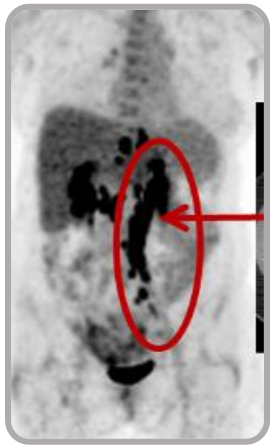
2007

Radical hysterectomy

Pelvic recurrence

2014

Treated with:
paclitaxel/carboplatin
bevacizumab
pelvic radiation

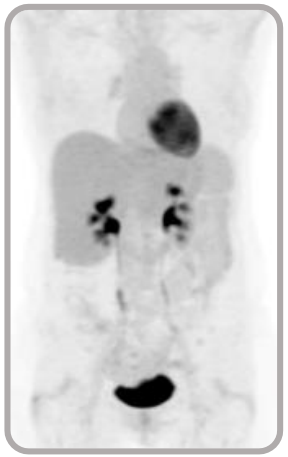


Systemic recurrence

June 2015
Enrolled in GOG-0265

2015
July | Aug. | Sept.

Dose 1 Axalimogene
Dose 2 Filolisbac
Dose 3



May 2016
Complete response

May 2017
Ongoing

Treatment-related AEs: Grade 1-2 fatigue, chills, fever, nausea and Grade 3 hypotension, cytokine release syndrome; No Grade 4-5 TRAEs reported

https://clinicaltrials.gov/ct2/show/record/NCT01266460

Results may not be typical; further study is warranted.

GOG-0265 Treatment-Emergent Adverse Event Summary

All treated patients (n=50) experienced ≥1 AE; safety findings from both stages of the study were consistent

AE	GRADE 1–4	GRADE 1–2	GRADE 3	GRADE 4
Patients with ≥1 TRAE, n (%)	48 (96)	28 (56)	18 (36)	2 (4)*
TRAEs occurring in ≥30% of patients				
Fatigue	26 (52)	26 (52)	-	-
Chills	26 (52)	26 (52)	-	-
Anemia	24 (48)	19 (38)	5 (10)	-
Nausea	16 (32)	16 (32)	-	-
Fever	15 (30)	15 (30)	-	-

*The observed grade 4 TRAEs recorded in 2 patients were considered possibly related (lung infection [klebsiella related] and hyponatremia [syndrome of inappropriate antidiuretic hormone secretion symptoms; same patient) to treatment.

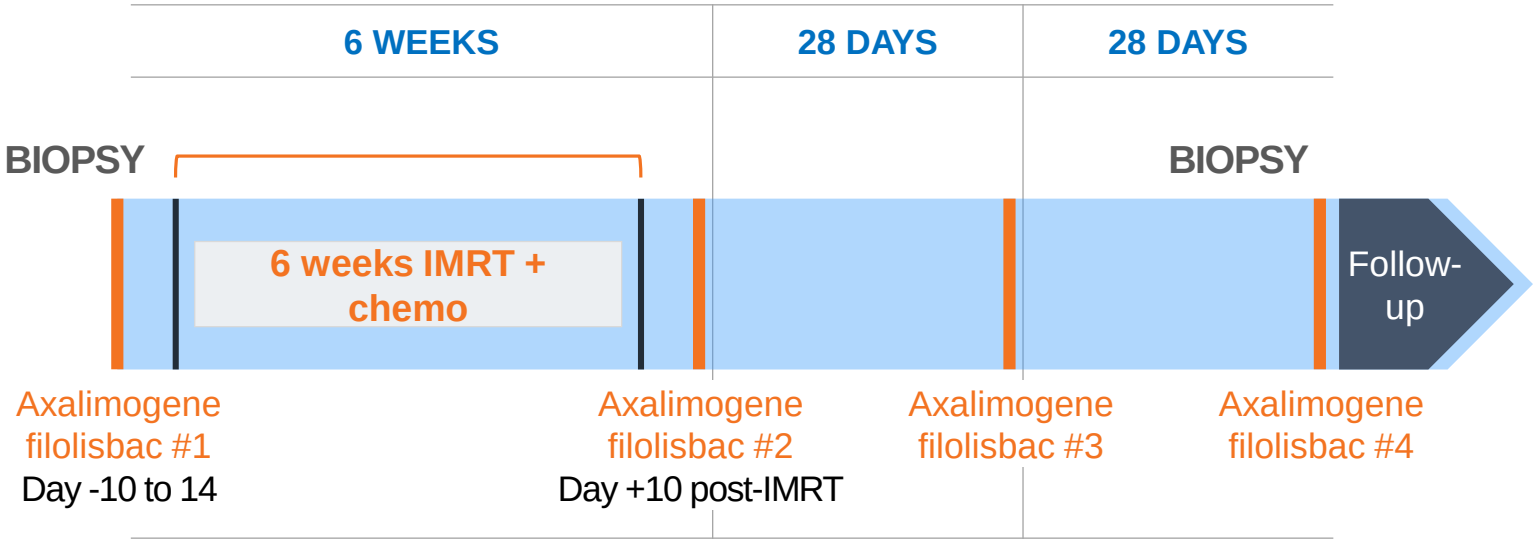
AE= adverse event; TRAE= treatment-related AE.

Phase 1/2 BrUOG Study in High Risk Advanced Anal Cancer with Axalimogene Filolisbac + Mitomycin, 5-FU and Radiation

Axalimogene Filolisbac

1×10^9 cfu × 4 (1 prior to chemoRT and 3 after, q28 days) as a 500-mL infusion over 30 min

- N = 25
- Primary Stage 2–3 anal cancer
- High risk of recurrence
- HPV positive

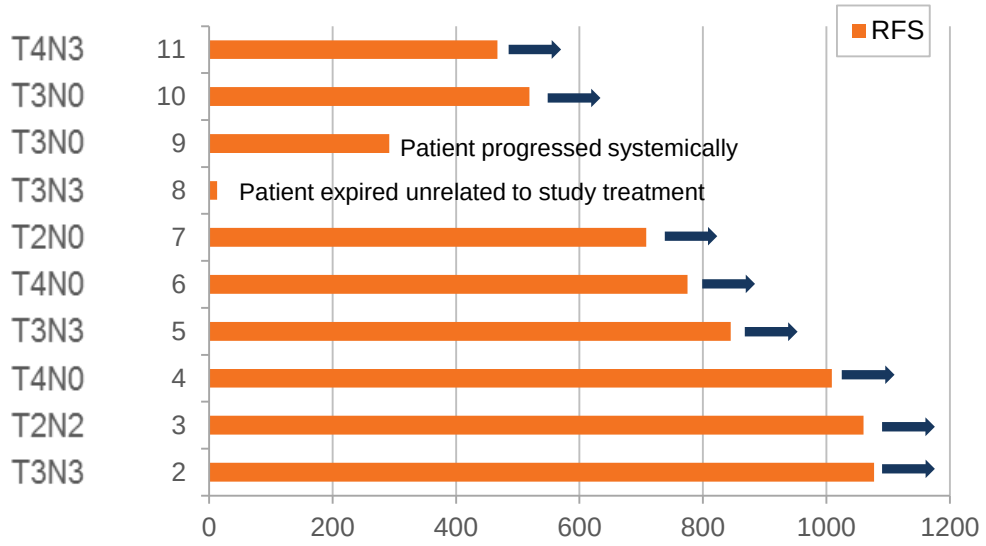


Primary efficacy endpoint is 6-month CR rate

Safran et at., Poster Presentation at ASCO 2016
Manuscript accepted for publication in the *International J of Radiation Oncology*
BrUOG, Brown University Oncology Group.

Phase 1/2 BrUOG Study in High Risk Advanced Anal Cancer with Axalimogene Filolisbac + Mitomycin, 5-FU and Radiation

Relapse Free Survival Data



Relapse-Free Survival (Days)*
Median Follow-up 42 months

Note: Patient #1 enrolled but was never treated on study

TRAE	N (%)	
	Grade 2	Grade 3
Chills/Rigors	4 (40)	2 (20)
Fatigue	1 (10)	0
Pyrexia	3 (30)	0
Headache	1 (10)	0
Flu-like symptoms	1 (10)	0
Pain (back/neck)	0	1 (10)
Hypotension	2 (20)	0
Hypertension	0	1 (10)

There were no Grade 4 adverse events

Summary

- 11 total patients enrolled
- All patients who completed RT and received treatment achieved a CR at **six months** (N = 9)
- 8/9 patients (89%) were recurrence free at a median follow up of 42 months
- Safety profile consistent with previous clinical experience

Safran et at., Poster Presentation at ASCO 2016
Manuscript accepted for publication in the *International J of Radiation Oncology* *BrUOG, Brown University Oncology Group. CR, Complete response; TRAE, Treatment related adverse events

AXAL in High-Risk, Locally Advanced Cervical Cancer

AIM2CERV Phase 3 Study as Adjuvant Monotherapy to Prevent Recurrence in High-Risk Cervical Cancer

GYNECOLOGIC CANCER INTERGROUP
An Organization of International Cooperative Groups for Clinical Trials in Gynecologic Cancers

FDA Orphan
FDA SPA
FDA FastTrack

Trial Design

Eligibility

- HRLACC
- FIGO stage I–II with positive pelvic nodes
- FIGO stage III–IVA
- Any FIGO stage with para-aortic nodes

Treatment with Cisplatin

Treatment with cisplatin (at least 4-weeks exposure) and radiation (minimum 40-Gy external beam radiation therapy)

R

Treatment with Axalimogene Filolisbac

- n=300
- 1 X 10^9 CFU
- Up to 1 year

Placebo IV

- n=150
- Up to 1 year

Primary Endpoint:

- Disease-free survival

Secondary Outcome Measures:

- Safety & Tolerability
- Overall survival

Baseline tumor imaging must be performed within 28 days prior to the first study treatment infusion

"Just as we need options to prevent HPV-related cancers, there is a significant need for more therapeutic options to treat those with cancer. No woman should die from cervical cancer."

Deborah Arrindell
Vice President, Health Policy
asha American Sexual Health Association

AIM2CERV – Axalimogene Filolisbac Immunotherapy Following Chemo/Radiation in Patients who have High Risk Locally Advanced Cervical Cancer (HRLACC)

1. Herzog T, et al. SITC 2016. Poster 145. https://clinicaltrials.gov/ct2/show/NCT02853604

SPA= Special Protocol Assessment; FIGO= International Federation of Gynecology and Obstetrics; HRLACC= high-risk locally advanced cervical cancer; IV= intravenous.

AIM2CERV: Ph 3 study has been initiated and will be launched in ~20 countries, with expected completion in 2020/2021

450 Patients with HRLA CC

~20 Countries

~150 Global sites

Basis for obtaining full EMA approval of AXAL in metastatic/recurrent CC patients

July 2016
FDA Special Protocol Assessment

Q3 2016
Initiate Study Start-up

Q1 2017
First patient enrolled

Ex-US sites to open

1H 2018
50% patient enrollment*

4Q 2018
Last patient enrolled*

2020 / 2021
Study completed

Trial start:	Sep 2016
Expected completion:	2020 / 2021
Partner:	GOG

Event-driven study: 184 events (recurrence or death due to any cause) required prior to efficacy analysis

Combination with durvalumab: a Ph 2 study of AXAL combined with durvalumab in metastatic cervical and HNC is under way

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Part 1: Cervical and head & neck cancer

Dose escalation / Dose determination

- n=11 enrolled/treated to date
- Axal: 1x10^9 (fixed) and durvalumab: 3+3 dose-confirmation

Dose Level 1: 3 mg/kg, n=5 cervical cancer

Dose Level 2: 10 mg/kg, n=3; cervical cancer; n=3; HPV+ squamous cell cancer of head and neck

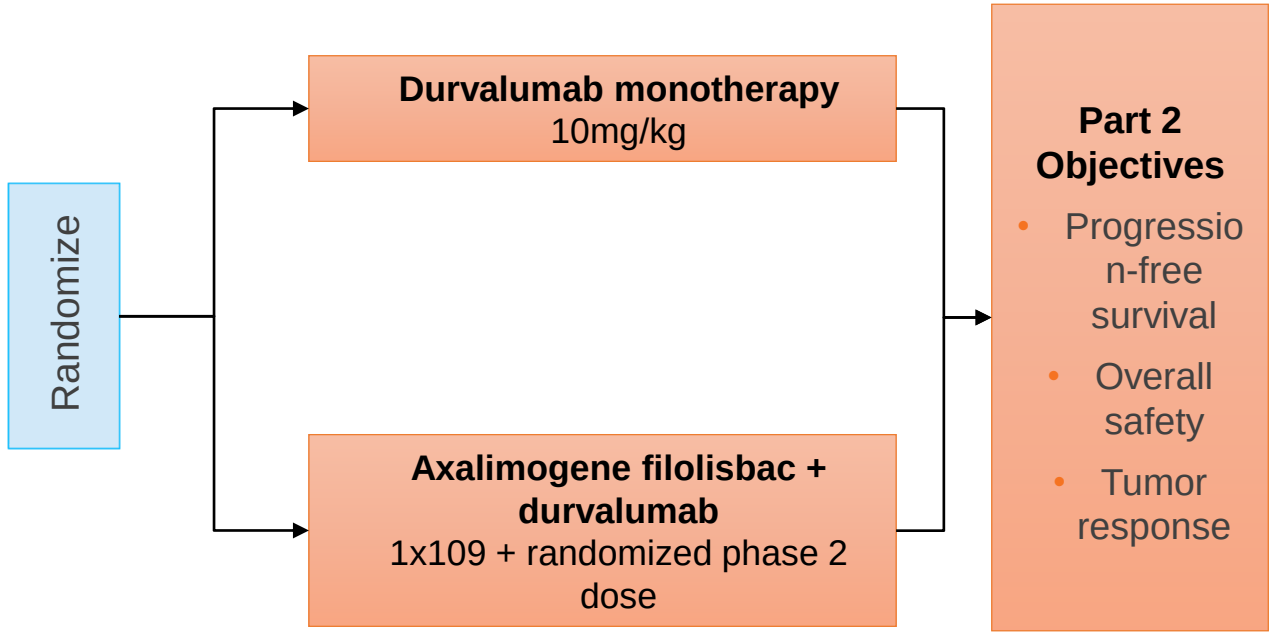
Part 1 Objectives

- Safety
- Tolerability
- Randomized phase 2 dose

Expansion Phase

- n=20
- Axal + durvalumab (randomized phase 2 dose) in squamous cell cancer of head and neck only

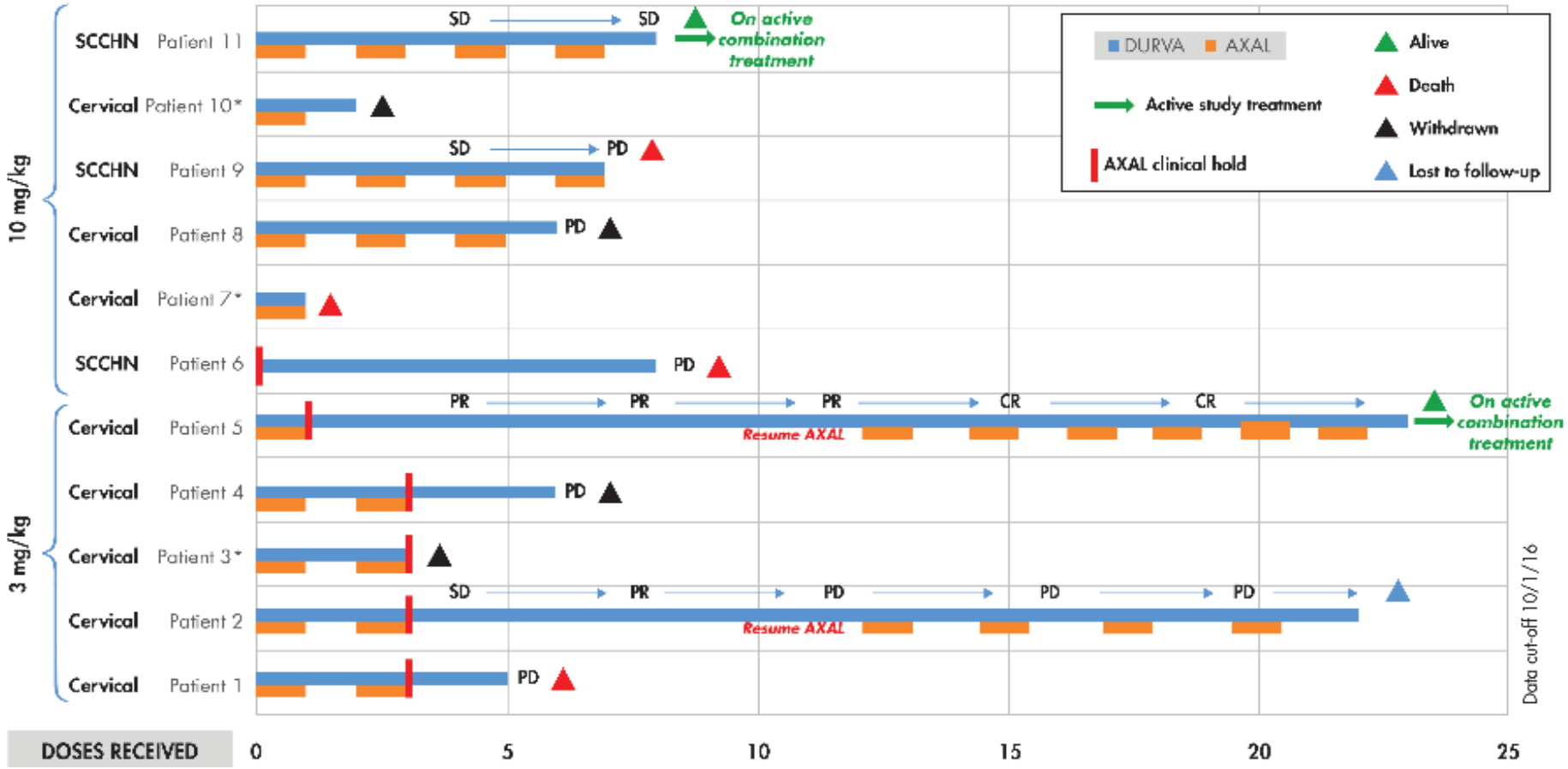
Part 2: Cervical Cancer



Trial start:	Aug 2015
Expected completion:	n/a
Partner:	Astra Zeneca

Combination with durvalumab: preliminary data indicate encouraging antitumor activity with 1 complete response to date

Patient disposition, treatment received, and response assessment



Preliminary Safety Findings:

- TRAEs included chills and/or rigor, nausea, hypotension, diarrhea, fatigue, tachycardia & headache
- 2 patients experienced grade 3 chills and/or rigors; 1 patient experienced grade 3 diarrhea; 1 patient experienced grade 4 hypotension.

Note: *In 3 patients (Patients 3, 7, and 10) no response assessment was made because a post-baseline scan was not obtained prior to elective study withdrawal.

ADVANCE Clinical Trial - Design

ADXS-602 + nivolumab compared with investigator's choice of chemotherapy in second-line recurrent, persistent, or metastatic cervical cancer (PRmCC)

Patient Population (N=~500)

- PRmCC
- Failed or ineligible to receive first-line chemotherapy
  - +/- bevacizumab

Safety Run-In Phase

ADXS-602

plus

Nivolumab (480mg)

Every 4 weeks

If safe and tolerable, proceed to Randomiz-ation Phase

R

Treatment A

ADXS-602 monotherapy

Treatment B

Nivolumab monotherapy

Treatment C

ADXS-602 + nivolumab

Treatment D

Investigator choice single agent chemotherapy

Statistical Analysis

Primary statistical analysis (**C vs. D**) will be on combination arm vs. single agent chemotherapy

Note: Study design not yet final

ADVANCE Study Endpoints

Co-primary	• Duration of overall survival (OS) • Objective response rate (ORR)
Secondary	• Duration of progression-free survival (PFS) • Duration of response (DOR) • Disease control rate (DCR) • 6-, 12-, 18- and 24-month OS rates • Patient reported outcomes (PROs): EQ-5D-5L, FACT-Cx and BPI questionnaires • Safety and tolerability
Exploratory	• Correlates of immune response from blood samples • HPV genotypes and PD-L1 expression in tumor tissue

MAA for Conditional Approval of AXAL in Europe to be Submitted Q1 2018

Conditional MAA for AXAL in Europe	• AXAL is a product for the treatment of metastatic cervical cancer: a life-threatening disease, within scope of products eligible for conditional approval • AXAL addresses a high unmet medical need • The GOG-0265 study demonstrates positive benefit-risk balance • AIM2CERV study will provide the required confirmatory clinical data supporting conditional approval
Key regulatory steps completed	• Scientific Advice from PEI (Germany) and MPA (Sweden) • Advanced therapy medicinal product (ATMP) for cervical cancer designation by the Committee for Advanced Therapies (CAT) • ATMP certificate for quality (manufacturing) and non-clinical data by CAT • Committee for Medicinal Products for Human Use (CHMP) confirmation of eligibility for Union Marketing Authorization (centralized procedure) • Rapporteurs assigned and pre-submission meeting held
Anticipated timeline	• The submission targeted for February, 2018 • Positive opinion by CHMP is expected early 2019

HPV Program Summary:
AXAL and ADXS-DUAL for the treatment of HPV-associated cancers

Based on proprietary Lm technology	• Axalimogene filolisbac (AXAL, ADXS11-001) and ADXS-DUAL are novel immunotherapies for the treatment of HPV-associated cancers (cervical, anal and head & neck) • Both utilize the proprietary *Lm* Technology™ antigen delivery system
Developing a next-generation improved therapy	• Next-generation ADXS-DUAL includes additional HPV antigens to provide stronger coverage against Alpha-7 HPV strains which are most prevalent in recurrent cervical cancer. ADXS-DUAL may create more potent T-cell responses for patients with metastatic cervical cancer
Clinical trials	• Ph 2 study with AXAL monotherapy in metastatic cervical cancer (GOG-0265 - completed) • Ongoing: Ph 3 trial with AXAL in high-risk locally advanced (HRLA) cervical cancer (AIM2CERV); Ph 1/2 with AXAL in head & neck and anal cancer • Planned for H1 2018: ADXS-DUAL trial to begin in patients with metastatic cervical cancer, in combination with BMS's *Opdivo* (registration quality study)
Regulatory successes and plans	• Plan to file regulatory application with EMA in Q1 2018 with potential for conditional approval in Q1 2019 • Results from AIM2CERV are expected to lead to full EMA approval of AXAL in cervical cancer (data readout expected in 2020/2021 for HRLA) and global approval in other countries