OS THERAPIES

Investor Presentation

February 2025

NYSE American: OSTX

Safe Harbor Statement

This document contains forward-looking statements. In addition, from time to time, we or our representatives may make forward-looking statements orally or in writing. We base these forward-looking statements on our expectations and projections about future events, which we derive from the information currently available to us. Such forward-looking statements relate to future events or our future performance, including: our financial performance and projections; our growth in revenue and earnings; and our business prospects and opportunities. You can identify forward-looking statements by those that are not historical in nature, particularly those that use terminology such as "may," "should," "expects," "anticipates," "contemplates," "estimates," "believes," "plans," "projected," "predicts," "potential," or "hopes" or the negative of these or similar terms. In evaluating these forward-looking statements, you should consider various factors, including: our ability to change the direction of the Company; our ability to keep pace with new technology and changing market needs; and the competitive environment of our business. These and other factors may cause our actual results to differ materially from any forward-looking statement. Forward-looking statements are only predictions. The forward-looking events discussed in this document and other statements made from time to time by us or our representatives, may not occur, and actual events and results may differ materially and are subject to risks, uncertainties and assumptions about us. We are not obligated to publicly update or revise any forward-looking statement, whether as a result of uncertainties and assumptions, the forward-looking events discussed in this document and other statements made from time to time by us or our representatives might not occur.

Risks Related To Our Business

Our business is subject to a number of risks you should be aware of before making an investment decision. These risks include the following:

- Our success is primarily dependent on the successful development, regulatory approval and commercialization of our lead product candidates which are in the early stages of development
- Our approach to the discovery and development of innovative products is novel, and unproven and may not result in marketable products
- We have no source of predictable revenue, have incurred significant losses since inception, may never become profitable and may incur substantial and increasing net losses for the foreseeable future as we continue the development of, and seek regulatory approvals for our product candidates
- If clinical trials of our product candidates fail to demonstrate safety and efficacy, we may be unable to obtain regulatory approvals to commercialize our product candidates
- We are subject to regulatory approval processes that are lengthy, time-consuming and unpredictable. We may not obtain approval for any of our product candidates from the FDA or foreign regulatory authorities
- Even if we obtain regulatory approval, the market may not be receptive to our product candidates
- We may not be able to establish collaborative partnerships with other pharmaceutical companies, through which we expect to complete development of, obtain marketing approval for and, if approved, manufacture and market our product candidates
- We may encounter difficulties satisfying the requirements of clinical trial protocols, including patient enrollment
- We may face competition from other companies in our field or claims from third parties alleging infringement of their intellectual property

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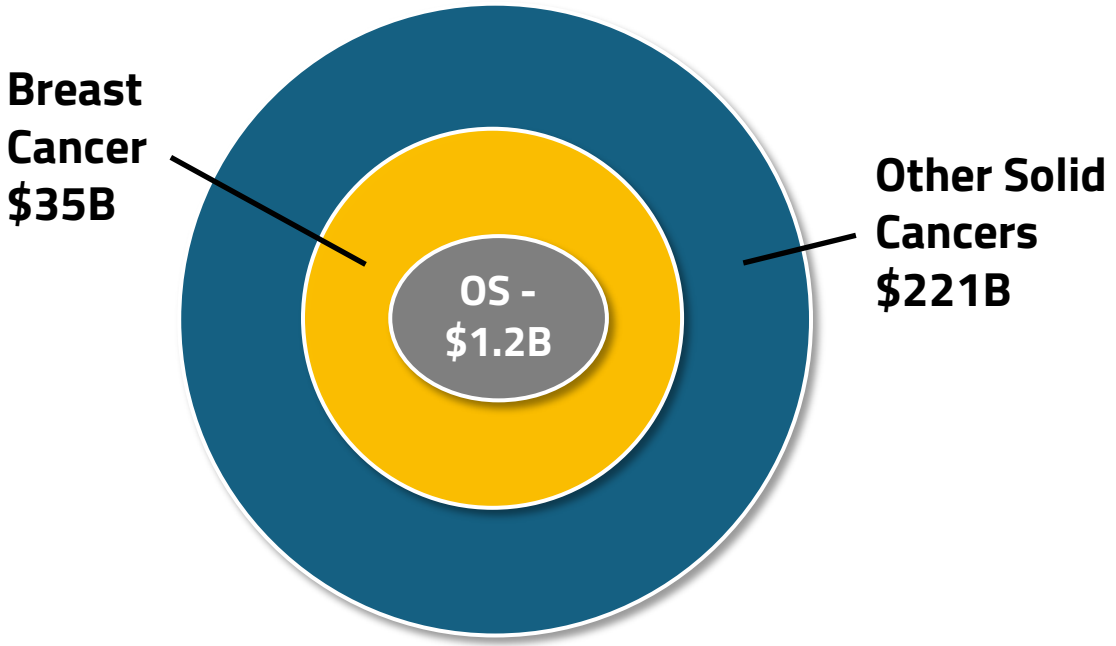
Immunotherapy and Precision Medicine for Cancer

OST-HER2: ***Listeria monocytogenes***

Ultra Orphan Lead Clinical Program in Osteosarcoma (OS) with follow-on application in Breast Cancer & Other Solid Tumor Cancers - $258B TAM

Solid Cancers TAM - $258B



OST-tADC: Next-gen *Tunable* Drug Conjugate (tADC) Unique Patented Silicone linker improves safety & efficacy

Investment Highlights

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Over $250 million has been invested in listeria platform to date

Multiple Near-Term Catalytic Milestones

- Type C Meeting with FDA & subsequent BLA submission for OST-HER2 in Human Osteosarcoma – **1H/25**
- Regulatory pathway to full approval for OST-HER2 in Canine Osteosarcoma – **1H/25**
- FDA Approval (accelerated/conditional) – **End of 2025**

Large Total Addressable Markets (TAM)

- Human (Adult + Pediatric) Osteosarcoma – **$1.2B**
  - Expected US Topline Revenue for OST-HER2 in osteosarcoma - **$500M+**
- Canine Osteosarcoma – **$150M+**

Osteosarcoma is a Rare Pediatric Disease - Priority Review Voucher (PRV)

- Osteosarcoma (Human and Animal): No new approvals in 40+ years
- Orphan Designation & Fast Track Designation granted by the FDA and EMA
- Rare Pediatric Disease Designation (RPDD) granted by FDA
- ***If OST-HER2 approved, value of PRV sale is ~$150M***

Market & Financial Summary	
Stock Price	$1.80
Shares Outstanding	~22M
Market Cap	$38.2M
Cash	**~$7M**
Monthly Cash Burn	**~$400K**
Time to Conditional FDA Approval & PRV	**~12 mo.**
Est. PRV Sale Proceeds	**~$150M**

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January 29, 2025

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OS Therapies Agrees to Acquire All Listeria Monotygenes-based Immuno-Oncology Programs and IP Assets from Ayala Pharmaceuticals, Adding Phase 2 Lung Cancer and Phase 1 Prostate Cancer Programs to Pipeline

- *Consolidates ownership of listeria monocytogenes-based immunotherapy IP*
- *Eliminates milestone payments and reduces future royalty obligations relating to OST-HER2 for osteosarcoma and other HER2-related indications*
- *Capital allocation focus remains on regulatory approval, priority review voucher (PRV) issuance and commercialization of OST-HER2 in osteosarcoma*
- *Previously disclosed $7.1M funding for OS therapies priced at $4.00/share provides cash runway into 2026 & precludes raises below $12.00 for 6 months*
- *Karim Galzahr appointed to OS Therapies Board of Directors*

Therapeutic Pipeline

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Listeria Immunotherapy Pipeline

Trial	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Approval	Launched
Osteosarcoma (OS) *(OST-HER2)*	***Positive Phase 2b Data. Targeting Accelerated Approval Q4/25***				✓ *Orphan drug designation* ✓ *Fast Track Designation* ✓ *Rare Pediatric Disease Designation*		
Non-Small Cell Lung Cancer* (NSCLC) *(OST-503)*	***Improving Sensitivity to Keytruda After Failure***						
Non-Small Cell Lung Cancer* (NSCLC) *(OST-503)*	***Frontline alone & in Combination w/Keytruda***						
Breast Cancer (BC) *(OST-HER2)*	***HER2+ BC in Combination w/HER2 Abs***						
Prostate Cancer* (PC) *(OST-504)*	***Biochemically Recurrent Disease***						
Canine OS *(OST-HER2)*	***USDA conditional approval achieved. Full approval path pending updated regulatory guidance***						

* = Pending close of Ayala asset acquisition

Therapeutic Pipeline

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Antibody Drug Conjugate Pipeline

Trial	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Approval	Launched
Ovarian Cancer *(OST-tADC)*							
Breast Cancer *(OST-tADC)*							
Other Solid Tumors *(OST-tADC)*							

OST-HER2: Background + New Data

OST-HER2: Originally Developed for Breast Cancer

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An Off-the-Shelf Immunotherapy "Cancer Vaccine"

Platform Inventor: Dr. Yvonne Patterson from U Penn

Lead Veterinarian: Dr. Nicola Mason from U Penn

- In 2002, Dr. Patterson worked extensively on Listeria vaccines and following her own breast cancer diagnosis sought to create a HER2 targeted listeria vaccine for breast cancer
- The rapidly changing therapeutic landscape in breast cancer following market introduction of Herceptin made the development of novel treatments very challenging given expanded use in various settings and biomarker challenges
- In 2016, Dr. Nicola Mason identified potential uses in Osteosarcoma in animals and successfully completed trials that led to veterinary approval
- Osteosarcoma became the lead human indication when OS Therapies was incorporated to rapidly gain FDA approval
- Now that OST-HER2 is on a path to approval in Osteosarcoma, there is renewed interest in Breast Cancer once it is on the market

Dr. Yvonne Patterson
Microbiologist

Dr. Nicola Mason
Veterinary Medicine

Perelman School of Medicine
University of Pennsylvania

POC DATA: CANINE OSTEOSARCOMA CLINICAL TRIAL

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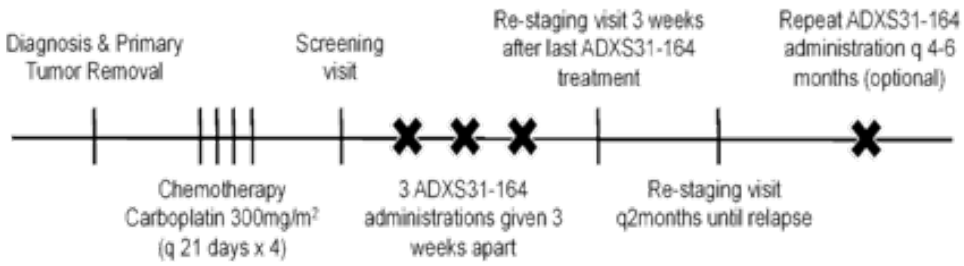
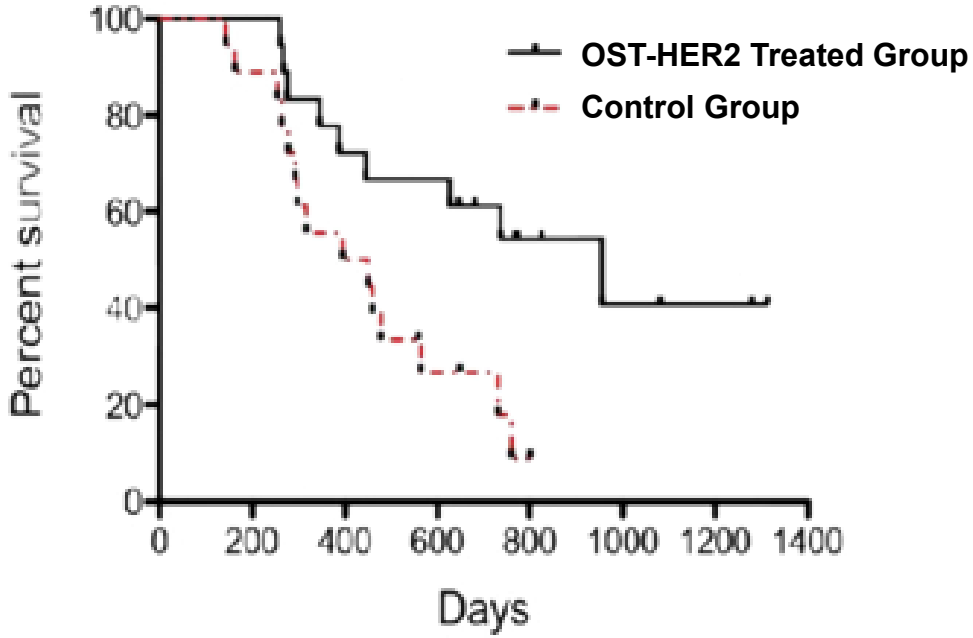
**USDA has granted provisional approval for OST-HER2 for the treatment of Canine Osteosarcoma*

DESIGN





ADDITIONAL DATA

	Median Disease-Free Interval (DFI - days)	Median Survival Time (MST - days)	1 Year Survival	2 Year Survival
OST-HER2 Treated Group	615	956	78%	67%
Historical Control Group	NR	423	55%	28%
Published Retrospective Studies	123-257	2017-321	35%	10-15%

Clin Cancer Res 2016;22:4380-4390; DOI: 10.1158/1078-0432.CCR-16-0088

Mechanism of Action (MOA)

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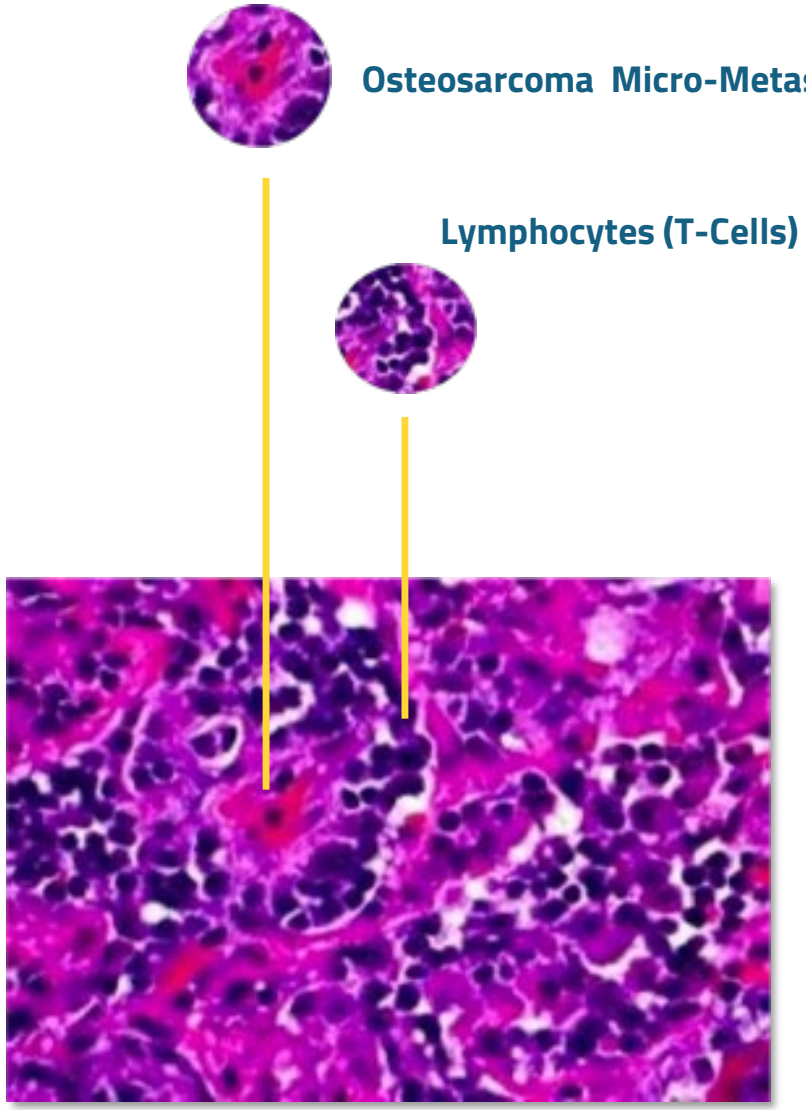
Lymphocytes (T-Cells) Kill Metastases (Cancer Cells)

- Proof-of-concept in Phase I & III canine study (p-value = .0007)
  - Previously received conditional USDA approval in Canine Osteosarcoma
- Intravenous OST-HER2 vector rapidly cleared by immune system's antigen presenting cells (APCs)
- APCs strongly activated to generate potent HER2 specific T-cell response
- T-Cells proliferate, travel through blood to hunt down the OS Micro-Metastasis
- Cancer cell contents spill out revealing additional cancer targets
  - Epitope Spreading
- New targets are taken up by the immune system
- T-Cells are generated against the new targets, repeating the cycle and extending the treatment effects



<u>*OSTX Safety vs. Advaxis Lm development: Antibiotic at 4h vs. 72h*</u>

- ***Exposure to 4h of Lm yields same immune response as 72h***

Osteosarcoma (Bone Cancer)

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No Treatments Available to Prevent or Delay Subsequent Recurrences

Global Death Rate Upon Recurrence/Metastasis is 80-90%

Crompton et al: Survival after recurrence of osteosarcoma: A 20-year experience at a single institution. August 2005: Pediatric Blood & Cancer. https://onlinelibrary.wiley.com/doi/abs/10.1002/pbc.20580

Osteosarcoma ("Bone Cancer") is a solid tumor of the bone

- 1,000 cases/year in US; 20,000 globally
- Most Cases Present In Patients 15-20 Years Of Age
- No New Treatments In Over 40 Years
- METS (Lung) In ~50%+ Of Patients
- High Lung METS Recurrence: Fatality Rate: ~ 90%
- Time To Mortality Upon METS Recurrence: ~12 Months
- Only Treatment for Recurrent METS: Lung METS Surgery
  - No drug therapy used (chemotherapy failed)
- Objective = Prevent Recurrence - Increase Overall Survival

Standard of Care (SOC):

- Primary OS – a) Amputation of leg, extremity b) orthopedic implant and highly toxic 9-month chemotherapy regimen with10% treatment-associated mortality
- Secondary OS / Recurrent Disease: None

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OST-HER2 Open Label Phase 2b Trial:

Enrollment Criteria

- 12-39 years old
- Recurred, resected metastatic (METS) Osteosarcoma
- 39 evaluable patients at 21 centers, single treatment arm – **FULL TREATMENT ARM COMPLETE**
- 52 Weeks on Study: Dosed 16 times every 3 weeks for 48 weeks with 4-week follow-up final visit
- **Primary Endpoint:** 12-month Event Free Survival (EFS) vs. Children's Oncology Group (COG) publication
- **Secondary Endpoint**: Overall Survival (OS)
- **Exploratory Endpoint #1**: 12-month EFS vs. Natural History Case Matched Database
- **Exploratory Endpoint #2:** OS vs. Leaving Publication

*FDA Feedback from June Breakthrough Therapy Designation Request

- Clinical indication meets criteria for Breakthrough Therapy Designation
- Need case matched controls to be able to clinically interpret positivity of data

*Exploratory Endpoint - Natural History Case Matched Database: Only Database Currently Available in US

- Patient Advocacy Group Collected under IRB (n=55)
- Many didn't meet the stringent enrollment criteria outlined above or had missing key data points (n=46)
- Only 9 evaluable subjects

OST-HER2 Phase 2b Trial: Data vs. COG Historical Control

Primary Efficacy Endpoint: Responders = 12-month Event Free Survival (EFS)

33% Responders in OST-HER2 Clinical Trial (n=39)

vs.

20% Responders in COG Publication Control[1] (n=42)

p=0.0158, 95% CI (0.185 - 0.481) favors OST-HER2 Treated Group*

1: Lagmay JP, Krailo MD, Dang H, et al: Outcome of patients with recurrent osteosarcoma enrolled in seven Phase II trials through Children's Cancer Group, Pediatric Oncology Group, and Children's Oncology Group: learning from the past to move forward. J Clin Oncol. 2016;34:3031-8.

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OST-HER2 Treated Patients: Subgroup Analyses

- **Female vs. Male: 47% vs. 20% (p=0.0604, n=39)**

  Positive trend – favors Female Group
  Known in published literature and from KOLs that females do better

- **2+ Prior Resections vs. 1 Prior Resections: 55% vs 25% (p= 0.0848, n=39)**

  Positive trend – favors 2+ prior resections vs. 1 resection
  Believed to be related to MOA of boosting immune function/memory

- **In 2+ Prior Resections Subgroup (n=11)**

  Resection Prior to Enrollment (Resection X) vs. Resection X-1: 55% vs. 27% (p=0.1935)

  Positive trend – favors OST-HER2 Treatment Vs. No Treatment
  Based on literature, each resection shows reduced likelihood of 12-month EFS. OST-HER2 treated patients show increased likelihood of 12-month EFS

1: Lagmay JP, Krailo MD, Dang H, et al: Outcome of patients with recurrent osteosarcoma enrolled in seven Phase II trials through Children's Cancer Group, Pediatric Oncology Group, and Children's Oncology Group: learning from the past to move forward. J Clin Oncol. 2016;34:3031-8.

OST-HER2 Phase 2b Trial: OST-HER2 Treated vs. Natural History

- **Secondary Efficacy Endpoints: Overall Survival (OS) vs. Leading Publication[2]**
  - 12-month OS: **91%** / 18-month OS: **80%** / 24-month OS: **61%**
  - *100% of Responders on OST-HER2 (12-month EFS) still alive: 100% (n=13)*
- **Exploratory Efficacy Endpoints vs. Natural History Database:**
  - 12-month Event Free Survival: **33% (n=39) vs. 11% (n=9) (p=0.1848)**
  - Time to Event in Non-Responders: **5.9 mo (n=26) Vs. 4.7 mo (n=8) (p=0.1454)**
- Exploratory Efficacy Endpoints vs. Leading Publication:
  - 12-month OS: **91% vs. 80% (p = 0.0700)**/ 24-month OS: **61% vs. 40% (p = 0.0576)**

OST-HER2 FDA Path: Requirements for BTD & Approval

- Create new natural history database of at least 39 case matched patients (to be named OST-400)
  - Collaborating with US, UK, EU Leading Osteosarcoma KOLs to access de-identified patient data
- Submit this Data to US FDA for Type C Meeting
- Continue to Monitor Responders (n=13) for continued extension of EFS

2: Osteosarcoma in adolescents and adults: survival analysis with and without lung metastases': Annals of Oncology 2009; 20: 1136–1141

Scientific Advisory Board for Osteosarcoma

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Peter M. Anderson, MD Cleveland Clinic	Doug S. Hawkins, MD Seattle Children's	Meenakshi Hedge, MD Texas Children's Hospital	Nabil M. Ahmed, MD Texas Children's Hospital
Department Of Pediatric Hematology, Oncology And Blood & Marrow Transplantation	Professor Of Pediatrics, Hematology/Oncology Division Center For Clinical And Translational Research	Assistant Professor, Department Of Pediatrics, Section Of Hematology - Oncology, Baylor College Of Medicine	Associate Professor, Department Of Pediatrics, Section Of Hematology-Oncology, Baylor College Of Medicine

Alejandro S. Cordero, MD UCSF	Brenda Weigel, MD University of Minnesota	Felafsa M. Wodajo, MD INOVA Healthcare System
Pediatric Malignancies - Cancer Genetics - Associate Professor Of Pediatrics	Professor, Division Of Pediatric Hematology And Oncology - Masonic Cancer Center	Orthopedics Surgery - Musculoskeletal Oncology

Commercialization and Partnerships

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OS Patient Advocacy

Miriam Cohen
Mother of OS Angel
Osteosarcoma Collaborative, Chair

Serena Subada
Osteosarcoma Patient
OST-HER2 Trial Participant

Mac Tichenor
Father of OS Angel
Osteosarcoma Institute, Chair

Olivia Egge
Osteosarcoma Patient
OS Therapies, Director Emerita

Tony Trent
Father of OS Angel
Tyler Trent Foundation

OST-HER2 Featured on CBS
60 Minutes **– Patient on Trial**
Interviewed by Anderson Cooper

https://www.youtube.com/watch?v=8wWeaGKT3Ak

Antibody Drug Conjugates (ADCs)

Dr. Jutta Wanner
Founding Scientist
BlinkBio & OS Therapies

Dr. Borys Shor
President & CEO
Manhattan Biosciences

Dr. Colin Goddard
Founding Scientist
BlinkBio & OS Therapies

OST Recently partnered with J&J Innovation for collaborative office/laboratory space at J-Labs

Commercialization

Chris Benecchi
Chief Business Officer
Sage Therapeutics

Scott Styles
Managing Partner
Styles Strategy

Edward Robb, DVM
Chief Strategy Officer
Anivive Animal Health

OST-HER2 – Breast Cancer Treatment

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Positive Preclinical & Phase 1 Results > Anticipate 2025 Phase 2 Trial – $30B TAM

Preclinical Studies

- In nonclinical studies, OST31-164 was found to cause regression of tumors in both a spontaneous HER2-expressing tumor model and in a metastatic breast cancer model in mice
- The reduction in tumor growth with OST31-164 was directly associated with the induction of HER2-specific immune responses
- HER2-specific CD8 T-cell responses are elicited by OST31-164

Phase 1 Trial Endpoints Met

Study Design

- Late stage advanced/metastatic Her2 expressing solid tumors (n=12)

Primary

- Dose limiting toxicity for OST31-164
  - Determined therapeutic dose: $1x10^9$ CFU

Secondary

- Efficacy signals
  - One patient left hospice care following treatment

OST-HER2 – Additional Cancer Clinical Targets

Solid Tumor Treatment Potential – Combined $35B TAM

HER2+ Solid Tumors

- Bladder, Breast Cancer, other HER2+ solid tumors
- OST-HER2 plus trastuzumab may prevent development of trastuzumab resistance in HER2+ solid tumors like Bladder, Breast, others

https://doi.org/10.1016/S1470-2045(07)70190-0

Esophageal

- Rationale: **OST-HER2 + trastuzumab may prevent development of trastuzumab resistance** in HER2+ gastroesophageal cancer and extend utility of trastuzumab after first progression

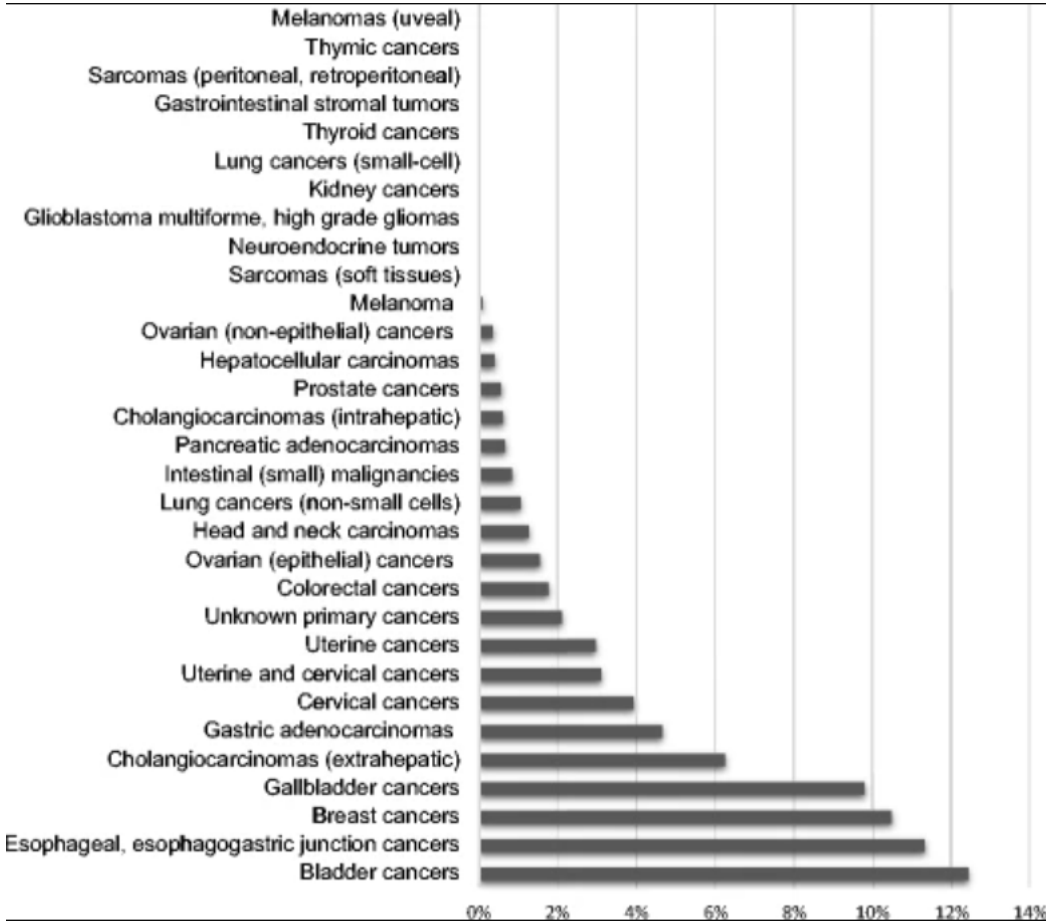
https://dx.doi.org/10.1186%2Fs13045-019-0737-2

Colorectal

- Rationale: 2-3% are HER2+, ICI have not been active in CRC except in DNA Mismatch Repair where there is high T cell infiltration Trastuzumab and lapatinib – 30% response rate in HER2 + CRC
- Increasing T cell infiltration with OST31-164 may improve activity of ICI in CRC, especially HER2+ CRC

https://ascopubs.org/doi/full/10.1200/PO.19.00154

HER2 positivity across cancers: analysis of 37,992 samples by IHC. IHC 3+ was considered HER2 IHC positive



Yan, M., Schwaederle, M., Arguello, D. *et al.* HER2 expression status in diverse cancers: review of results from 37,992 patients. *Cancer Metastasis Rev* **34,** 157–164 (2015). https://doi.org/10.1007/s10555-015-9552-6

OST-tADC Linker Platform

tADCs / tSM-DCs /tmRNA-DCs

OST-tADC – Product Overview

Potential to Displace Legacy Cancer Chemo Treatment

Interchangeable Ligands, Linkers, and Payloads – Tunable Drug Conjugate

- "Plug & Play" - Targeting Ligands, pH sensitive SiLinkers™ (silicon linkers), and multiple CAPed (Conditionally Active) Payloads
- Antibodies (ADC), small molecules (SM-DC) and mRNA therapeutics (mRNA-DC)

OST-tADC Program

- A platform technology with extensive flexibility and multiple licensing opportunities – without limiting OS Therapies therapeutic development
- Currently in pre-clinical studies and working toward 2-Week & GLP toxicity trials
- **Phase 1 trials for ovarian cancer are expected to begin in 2025**


BIOTECH

ASCO: Replacing chemotherapy with ADCs? AbbVie rebuilds next-gen assets after Rova-T flop

By Gabrielle Masson

Jun 4, 2024 11:26am

AbbVie | ASCO 2024 | ASCO | antibody drug conjugates

tADC Patented Silicon Linkers Design

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Patented OST SiLinker Pioneering Next-Gen ADCs

	Traditional VAL-CIT LINKER	Traditional GGFG LINKER	Next-Gen Silicone LINKER
% Payload at Released at Target Tumor Site	+	+	**+++**
Stability in Circulation	NO	Limited	**YES**
New IP for Old Payloads	NO	NO	**YES**
Premature Cathespin Cleavage	YES – Ubiquitous	YES – Macrophages	**NO**
Myelosuppresion	YES	NO	**NO**
Multiple Payloads per Linker	NO	NO	**YES**

Corporate Overview

Management Team – 100+ Years of Experience

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Paul Romness, MHP
President & *CEO - OS Therapies*

- 25 years of experience in the biopharma
  - Johnson & Johnson
  - Amgen
  - Boehringer Ingelheim
- 9 major product launches:
  - Oncology, surgery, HIV, FSD, COPD, IPF, CV & diabetes
- Masters of Health Policy from George Washington University Medical Center & B.S. in Finance from American University

Robert Petit, PhD
Chief Medical & Scientific Officer
Founding Scientist: OST-HER2

- Inventor & Founding Scientist behind OS Therapies' clinical-stage listeria cancer vaccine platform
- Large Pharma Experience: BMS, & Pharmacia
- Small Pharma Experience: MGI Pharma (Acquired by Otsuka), Advaxis, SARS Therapeutics, RGP Biotech & Orionis Biosciences
- MD from Ohio State University College of Medicine & BS in Life Science from Indiana State University
- Research interests: Oncology & Virology

Gerald Commissiong
Chief Business Officer

- 15 years of experience in biopharma
- Small Pharma Experience: Amarantus Bioscience Holdings, Avant Diagnostics, Todos Medical
- Specializes in M&A, Capital Raising, Strategic Planning and Investor Relations
- Therapeutic areas: Oncology, Neurology, Immunology and Regenerative Medicine
- BS in Management Science & Engineering from Stanford University

Jutta Wanner, PhD
Advisor
Founding Scientist: OST-tADC

- Inventor & Founding Scientist behind OS Therapies' tunable Drug Conjugate (tDC) platform (tADC, tSMDC and tmRNADC)
- Large Pharma Experience: Roche
- Small Pharma Experience: BlinkBio
- PhD from the University of Kansas w/ postdoc training at The Scripps Research Institute in San Diego
- Research interests: Oncology & Virology

- **Paul Romness was inspired to launch OS Therapies following the Osteosarcoma diagnosis of a close family friend**

Deep Pharmaceutical Experience And Successful Track Records

100+ Years Combined Experience

> 20 Product Launches

> 10 Licensing Deals

Global Sales

$35B+ Revlimid	**$30B+** Epoetin Alfa	**$30B+** Herceptin	**$20B+** Yervoy
$20B+ Spiriva	**$25B+** Retuxin	**$20B+** Pradaxa	**$8B+** Jardiance

Key Takeaways

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Catalyst Rich Advanced OST-HER2 Cancer Therapeutic Platform

Multiple Near-Term Clinical Milestones

- Phase 2b trial for OST-HER2 in Osteosarcoma positive data: Announced Jan 2025
- Path to Pivotal OST-HER2 Canine OS study to support full approval pending USDA alignment:1H/25
- Type C FDA Meeting & BLA Submission: 1H/25
- FDA Conditional Approval: End of 2025

Significant Market Opportunity

- TAM Human Osteosarcoma – $1.2B
- Market Opportunity for OST-HER2 in Osteosarcoma: $500M
- TAM Canine Osteosarcoma – $150M+
- tADC platform – $311 billion

Favorable Regulatory Review Process

- Osteosarcoma (Human and Animal): No new approvals in 40+ years
- Orphan, Fast Track, Rare Pediatric Disease Designations granted by the FDA and EMA for OST-HER2
- Priority Review Voucher – if OST-HER2 approved, PRV value = $80M-$120M

Experienced, Successful Leadership

- Proven management team with large & early-stage pharma experience with multiple successful product launches
- Expert OS scientific advisory board
- Strong patient advocacy & commercialization advisors

Thank You!

Paul Romness
President & CEO
par@ostherapies.com
(703) 541-9811


Appendix

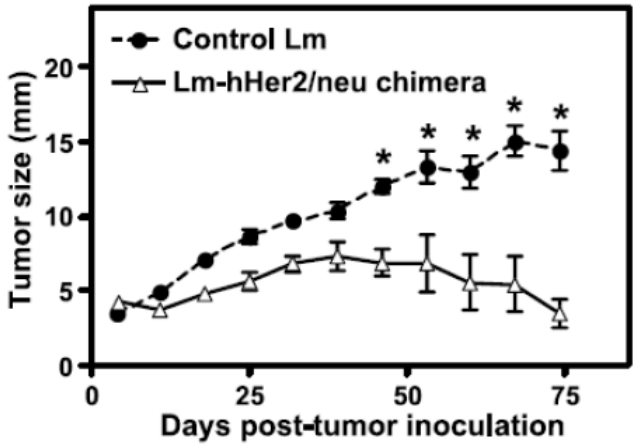
Animal Data: Inhibition of Growth of Breast Cancer Tumors

- Mouse Models of Breast Cancer
  - Fig 14 is a treatment model
  - Fig 15 is a prevention model

- Figure 14 shows Lm-LLO-chHER2 (OST-HER2 component) Anti-tumor activity against a foreign antigen of an established tumor in female FVB/N mice.

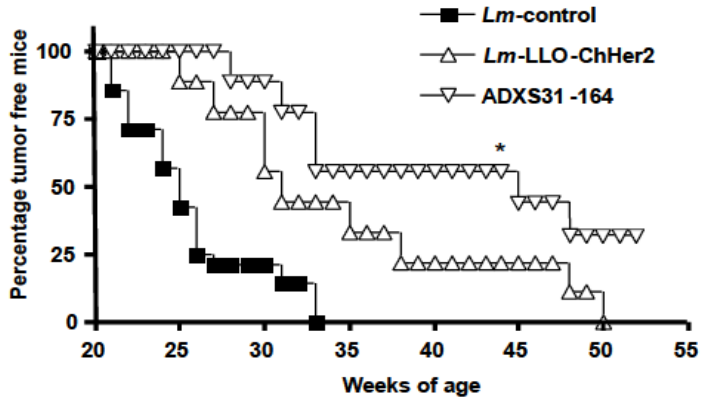
- The NT-2 tumor cell line was derived from a spontaneous mammary tumor in a rat HER2/neu transgenic FVB/N mouse and therefore expresses rat HER2.

Figure 14 **Tumor Inhibition by *Lm*-LLO-chHER2 or Lm-hHer2/neu chimera**



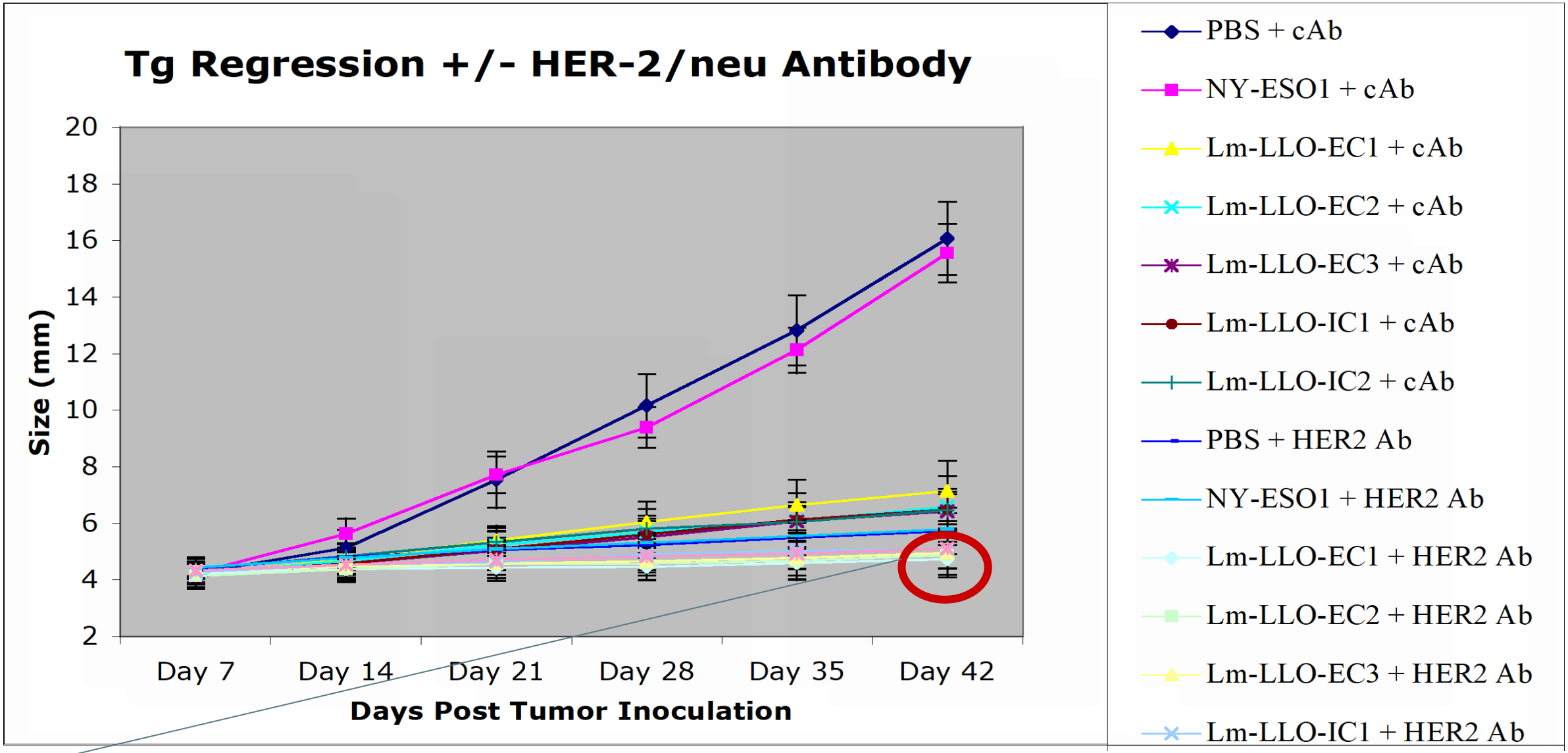
Tumor sizes are expressed by two perpendicular diameters of the tumors (mean ± SE), * denotes $P < 0.05$

Figure 15 **Prevention of Tumor Formation**



*denotes $P < 0.05$

Control Ab vs HER-2/neu Ab vs HER-2/neu Ab + OST-HER2



The Combination of OST-HER2 + HER2 Antibody (e.g. Herceptin, et al) shows strong improvement vs. HER2 Antibody alone (PBS + HER2 Ab)

Suppression of Growth of Metastatic Breast Cancer in the Brain

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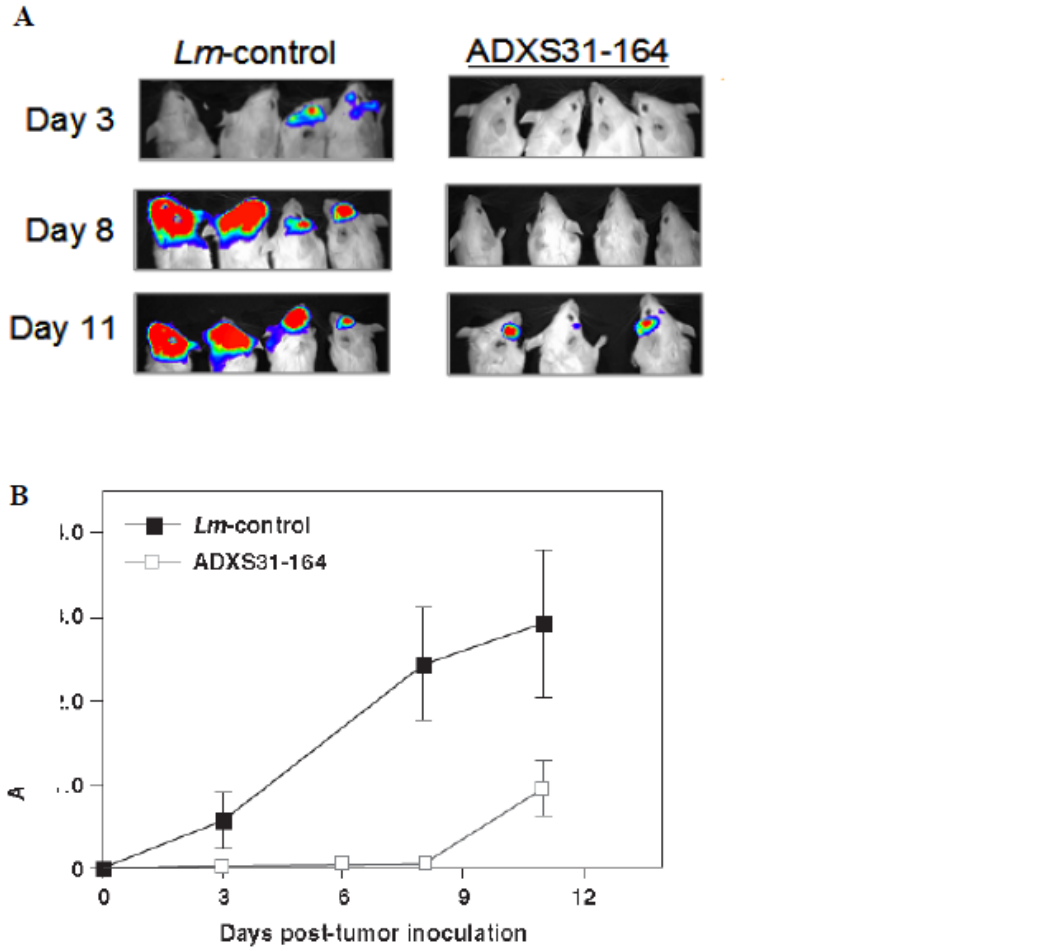
- In order to determine whether OST- could inhibit the growth of a metastatic breast cancer in the brain, BALB/c mice (n=4 animals/ group) were administered 5×10^8 CFU of OST-HER2 or Lm control by intraperitoneal injection once a week for three weeks.

- After the third injection, mouse breast carcinoma EMT6 cells stably transfected with luciferase (EMT6-Luc) were injected into the brains of anesthetized mice (5000cells/mouse).

- Tumor growth was detected in all control animals but none of the OST-HER2 treated animals.

Figure 16 **Delay of Breast Cancer Growth in the Brain**



A: Luciferase metabolizes into D-luciferin and photon by products are captured and displayed as body imaging heat map. B: Pixel intensity is graphed as number of photons per second per cm^2 of surface area, which is shown as average radiance.

Interview Highlights from Key Opinion Leader Experts

Consistently Enthusiastic And Positive, Confirming The Novelty Of The Lm Approach

"Canine and human osteosarcoma are the same disease genetically and as close as 2 diseases can be across to species and when we think of survival, the survival of the dog was because the *Lm* therapy was preventing the METS forming and this is usually what kills people and dogs with this disease."

Yvonne Paterson, PhD
Emeritus Professor of Microbiology at the University of Pennsylvania Perelman School of Medicine

Yvonne's laboratory was the first to show that the *Lm* bacterium could be used to target antigens to the MHC class I pathway for antigen processing with the induction of cytotoxic T cells and has pioneered the application of this organism in vaccine development over the past 15 years. They have shown that recombinant forms of this organism which have been transformed to express viral antigens from influenza, HIV and SIV are excellent vectors for inducing cell mediated immune responses both parenterally and at mucosal surfaces.
Furthermore, they've also applied this technology in the development of cancer vaccines that result in the induction of potent cell mediated immunity that can eliminate established macroscopic tumors even in the face of profound immune tolerance to the tumor-associated antigen.

"Overall, I think it's a really sound approach. I'm really excited about and I was *Listeria* skeptic for a long time until I started playing with it and now, I'm definitely a believer, I think that it is a really great platform compared to some of the other ones that are out there"

Adam Snook, PhD
Assistant professor at Thomas Jefferson University Hospital

Adam's research focuses on the discovery and clinical development of novel cancer immunotherapeutics.

"This approach is true exciting and very easy on the patient compared to other cancer therapy as *Lm* treatment would likely be an outpatient proceed, requiring on a short IV time, with potential for only short and transient issues with patients recovered from the treatment the next day rather than greater toxicities with Chemo or Check Point Inhibitors than can also be cumulative."

Dung Le, MD
Medical Oncologist at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine

Lm vector development and how pancreas cancer vaccines, combined with other agents, can elicit tumor-specific immune responses. She completed her training, fellowship, and residency at Johns Hopkins. Dr. Le has been involved in several trials on treatments for pancreatic cancer patients. Her work attempts to interrupt that signaling pathway, either by inhibiting negative signals that cancer cells use to turn off the immune system, or by accelerating the positive signals produced by immune system T-cells.

PATENTED TECHNOLOGY: OST-HER2

OS THERAPIES

- **21 Patents Issued: US, Japan, Austria, Belgium, Czech Republic, Germany, Denmark, Spain, Finland, France**
- **10 Patents Pending: China, India, Mexico, New Zealand, Taiwan, South Korea, Hong Kong**

Select Patents: Extended to 2033

Country	Status	Application Number	Patent Number	Filing Date	Application Type	Title
United States	Issued	12/945,386	9,084,747	November 12, 2010	Priority to 61/260,277	COMPOSITIONS AND METHODS FOR PREVENTION OF ESCAPE MUTATION IN THE TREATMENT OF HER2/NEU OVER-EXPRESSING TUMORS
United States	Issued	13/210,696	9,017,660	August 16, 2011		COMPOSITIONS AND METHODS FOR PREVENTION OF ESCAPE MUTATION IN THE TREATMENT OF HER2/NEU OVER-EXPRESSING TUMORS
Japan	Issued	2016-152578	6329211	November 12, 2010	Divisional of 2012-539021	USE OF RECOMBINANT LISTERIA STRAIN IN PREPARATION OF MEDICAMENT FOR DELAYING ONSET OF BRAIN OR MAMMARY TUMOR
United States	Issued	14/669,629	10,016,617	March 26, 2015	Continuation-in- part of U.S. 14/268,436	COMBINATION IMMUNO THERAPY AND RADIOTHERAPY FOR THE TREATMENT OF HER-2-POSITIVE CANCERS

Interview Highlights from Key Opinion Leader Experts

OST-tADC Platform Viewed As Differentiated Beyond Other ADC / TDC Players

"There's several different linkers and site specific conjugation technologies coming forward, but here's the key punchline, I'm coming to a lot of times with these technologies it's sort of here's the linker and here's a payload and one or two payloads. There's less plug and play and less adaptability. OS Therapies can manipulate each of these components and I think there's a growing appreciation that to have a platform that's widely applicable across many solid tumor types you need that kind of adaptability where one size doesn't fit all for all cancers or all tumors or all solid tumors that you're going to have to use one payload for ovarian and this might be different than the best payload for non- small cell lung."

Morris Rosenberg, PhD

Founder and Consultant, MRosenberg BioPharma Consulting

Morris has over 25 years experience in the development of therapeutic agents to treat a variety of human diseases. He has participated in the development and launch of Adcetris, Avonex, Angiomax, Xigris, and Forteo. He played a key role over the past decade, as part of the executive management team at Seattle Genetics, in building a commercial biopharmaceutical company focused on the development of antibody-drug conjugate technology for the treatment of cancer and autoimmune disorders.

"Overall, I very excited about what you are developing here as you show true innovation in 3 out of 4 of the key components of an ADC: 1. ligands; 2. Linkers, and; 3. Payloads."

Christoph Rader, PhD

Scripps Professor and Associate Dean, Skaggs Graduate School of Chemical and Biological Sciences, Department of Immunology and Microbiology

Christopher has focused on antibody target and drug discovery strategies toward more specific and more potent treatment options for cancer patients. Target discovery efforts are aimed at identifying new cell surface antigens suitable for monoclonal antibody (mAb) therapy of cancer.

"This is fascinating. I didn't expect to hear about small molecule, I hear about antibody, ADCs but this is fascinating to me that it's interesting."

Ravi Chari, PhD

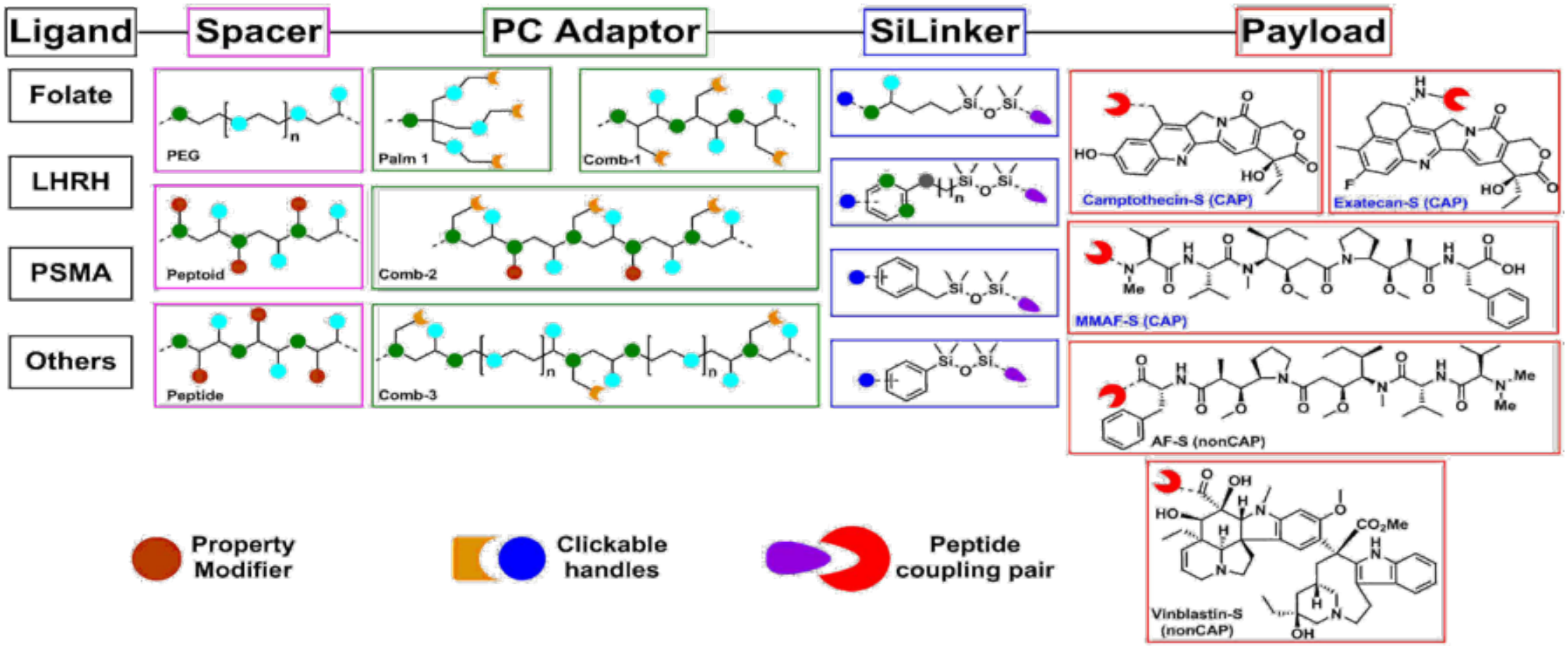
BioTechnology Consultant at RChari Consulting

Ravi assists organizations in design and optimization of ADCs (payload - including siRNAs, linkers, conjugation, analysis, biological evaluation and can also assist in patent drafting and technology evaluation.

OST-tADC PLATFORM IS "PLUG AND PLAY" AND "ADAPTABLE"

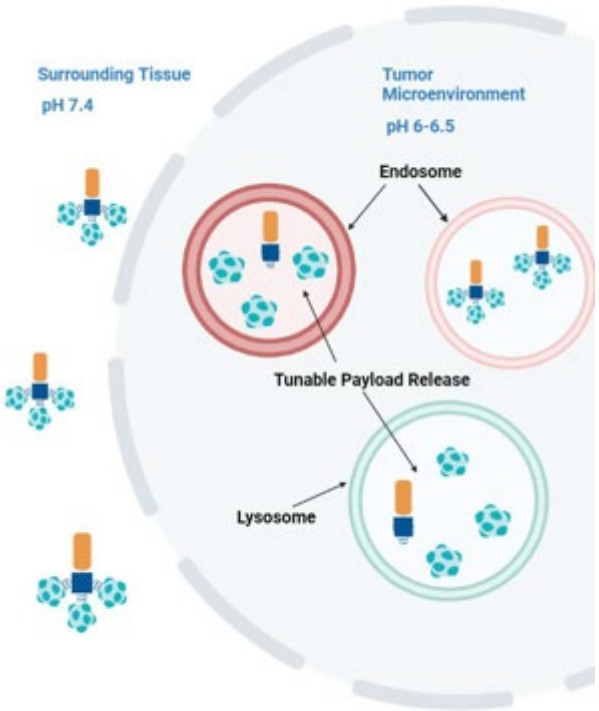
OS THERAPIES

Modular Approach is a Key Differentiator - Preferred Building Block Examples



CHEMICAL MODIFIERS ALLOW TUNABLE SiLINKERS CLEAVAGE

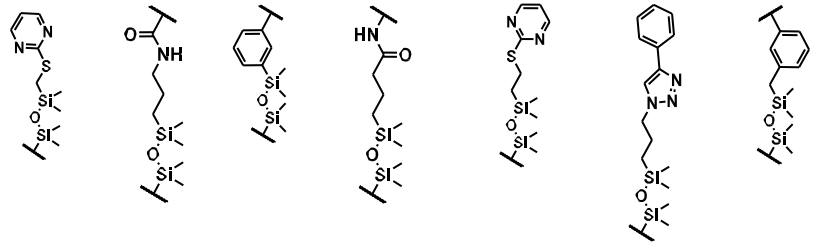
Payload Release can be Tuned to Occur Either in Endosome or Lysosome



Key Points

- Proximal functional groups influence the hydrolysis rate of the disilylether linkers
- We have demonstrated that rapid hydrolysis with the pyrimidine system *in vitro* translated to rapid linker cleavage in cells

Linkers which cleave more rapidly under slightly acidic conditions are ideal for small OST-TDC approach



	Pyrimidine	Amide	Phenyl	Carboxamide	Homologous Pyrimidine	Triazole	Benzyl
pH 7.4 $t_{1/2}$ (mins)	>600	6080	6170	>7920	9850	9134	>11520
pH 5 $t_{1/2}$ (mins)	2	77	307	95	480	445	1550

Stable SiLinkers can be used in ADCs to raise the Drug-to Antibody Ratio (DAR) to between 6 and 24 payloads per ADC

LCMS Hydrolysis studies were carried out in 50 mM HEPES buffer (pH 7.4 or pH 5) at 37 °C

PATENTED TECHNOLOGY: OST-tADC

The overarching platform claims protecting SiLinkers and Payload Cassettes are covered in US 9,931,407 issued in April 2018 which provides protection to the core platform into 2036.

Conditionally Active Payloads (CAPs) are covered in a broader payload patent filing from which two Track 1 filings (for MMAF-S and Exatecan-S) have already issued (US 10,064,880 and US 10,293,053, respectively); these filings are expected to protect our CAPs through at least 2037.


(12) **United States Patent**
Nguyen et al.

(10) **Patent No.: US 10,064,880 B2**
(45) **Date of Patent: Sep. 4, 2018**


(12) **United States Patent**
Foreman et al.

(10) **Patent No.: US 9,931,407 B2**
(45) **Date of Patent: Apr. 3, 2018**