LadRx Corp

OTCQB:LADX
CORPORATE OVERVIEW
June 2024
Non-Confidential

LadRx Corporation Safe Harbor Statement

THIS PRESENTATION CONTAINS FORWARD-LOOKING STATEMENTS THAT INVOLVE CERTAIN RISKS AND UNCERTAINTIES. SUCH STATEMENTS MAY BE PRECEDED BY THE WORDS "INTENDS," "MAY," "WILL," "PLANS," "EXPECTS," "ANTICIPATES," "PROJECTS," "PREDICTS," ESTIMATES," "AIMS," "BELIEVES," "HOPES," "POTENTIAL" OR SIMILAR WORDS. FORWARD-LOOKING STATEMENTS ARE BASED ON THE BELIEFS OF MANAGEMENT AS WELL AS CERTAIN ASSUMPTIONS MADE BY AND INFORMATION CURRENTLY AVAIALABLE TO MANAGEMENT, ARE NOT GUARANTEES OF FUTURE PERFORMANCE, AND ARE SUBJECT TO VARIOUS KNOWN AND UNKNOWN RISKS AND UNCERTAINTIES, MANY OF WHICH ARE BEYOND LADRX'S CONTROL, AND CANNOT BE PREDICTED OR QUANTIFIED AND CONSEQUENTLY, RESULTS MAY DIFFER MATERIALLY FROM THOSE EXPRESSED OR IMPLIED BY SUCH FORWARD-LOOKING STATEMENTS AS A RESULT OF VARIOUS RISKS AND UNCERTAINTIES, INCLUDING THOSE RISK FACTORS DISCUSSED IN THE ANNUAL AND QUARTERLY REPORTS THAT LADRX FILES WITH THE U.S. SECURITIES AND EXCHANGE COMMISSION. STATEMENTS CONTAINED HEREIN ARE MADE AS OF THE DATE OF THIS PRESENTATION UNLESS STATED OTHERWISE, AND NEITHER THIS PRESENTATION, NOR ANY SALE OF SECURITIES, SHALL UNDER ANY CIRCUMSTANCES CREATE AN IMPLICATION THAT THE INFORMATION CONTAINED HEREIN IS CORRECT AS OF ANY TIME AFTER SUCH DATE OR THAT INFORMATION WILL BE UPDATED OR REVISED TO REFLECT INFORMATION THAT SUBSEQUENTLY BECOMES AVAILABLE OR CHANGES OCCURRING AFTER THE DATE HEREOF. LADRX RESERVES THE RIGHT TO UPDATE, AMEND OR SUPPLEMENT THE INFORMATION AT ANY TIME IN ITS ABSOLUTE DISCRETION (WITHOUT INCURRING ANY OBLIGATION TO DO SO). INVESTORS AND SECURITY HOLDERS ARE URGED TO READ THESE DOCUMENTS FREE OF CHARGE ON THE SEC'S WEB SITE AT WWW.SEC.GOV. LADRX ASSUMES NO OBLIGATION TO PUBLICLY UPDATE OR REVISE ITS FORWARD-LOOKING STATEMENTS AS A RESULT OF NEW INFORMATION, FUTURE EVENTS OR OTHERWISE.

Management and Board

Stephen Snowdy, PhD
CEO

- Recently joined LadRx
- PhD Neurobiology University of North Carolina
- Full-cycle experience: napkin drawings to global product launch
- 20 years of experience in medical executive management
    - Venture capital
    - Medical devices
    - Pharma
    - IPO
    - Public company management

Gilad Gordon, MD
R&D/Regulatory Consultant

- Oncology development expert
- 30 years experience developing cancer treatments
- Directly responsible for 50 INDs, hundreds of clinical trials

John Caloz
CFO

- 30+ years of CFO experience in life sciences sector
- Occulogix, IRIS Int'l, Synarc, Phoenix Int'l Life Sciences

Board of Directors

- **Jennifer Simpson, PhD**

LadRx Chair of the Board. CEO of Panbela Therapeutics. Former CEO of Delcath, Oncology Lead at Imclone, Product Director Oncology Marketing at Ortho Biotech

- **Joel Caldwell**

Chair of Audit Committee. 30 years of experience in tax, finance, and auditing.

- **Cary J. Claiborne**

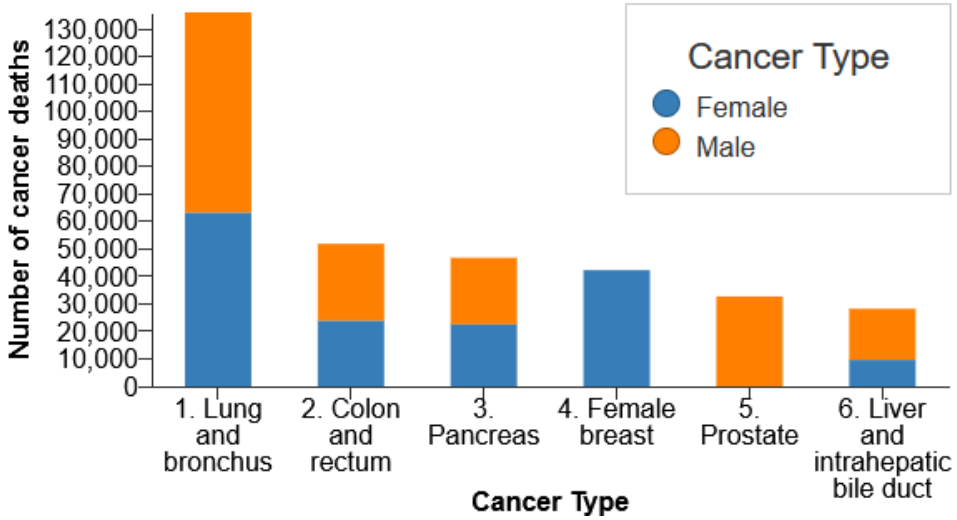
Chair of the Compensation Committee. CEO of Adial Pharmaceuticals Inc. Former CEO of Prosperity Capital Management, LLC.

Despite Progress, Cancer is a Massive Burden Needing Solutions

In 2019, cancer claimed over 10 million lives worldwide[1]

Leading attributable causes (approx. half of cancers are attributable) are smoking, alcohol use, and high BMI[1]

Cancer is the second leading cause of death in the US, behind heart disease[2]



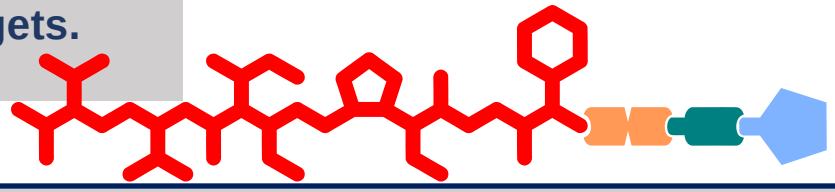
Graphs Adapted from Center for Disease Control, "An Update on Cancer in the United States"

1. "The Global Burden of Cancer…", The Lancet. August 20, 2022. 400:10352. 563-591
2. Center for Disease Control, "An Update on Cancer in the United States"

LadRx Corp

Investment Highlights

LadRx has developed elegant tumor targeting and release molecules called LADR that are based on small molecular entities (no complex antibodies or nanoparticles) allowing for higher dosing, lower off-target toxicity, and no need for screening patients for presence of antibody targets.



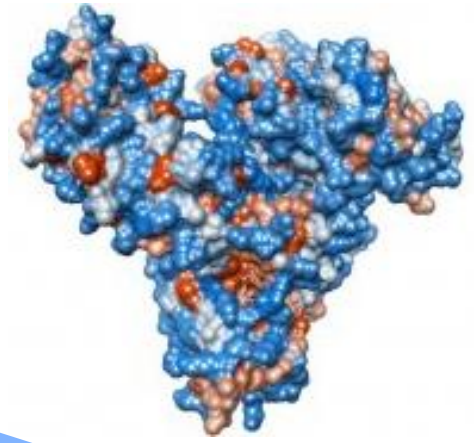
- First LADR drug aldoxorubicin showed promise in Phase II in soft tissue sarcoma, extending PFS with less cardiotoxicity than doxorubicin. Several additional human studies have confirmed cardiotox benefit. Well positioned for additional Phase II and III study
- Aldoxorubicin has orphan drug status in several cancers
- Next-gen LADR drug, LADR-7, has been manufactured under GMP, ready for IND filing in 3Q-4Q 2024 and FIH end of 2024
- Small and virtual to minimize cash use.
- Strong, broad, and global patent portfolio

*Cranmer, LD. OncoTargets and Therapy, 2019:12 2047-2062

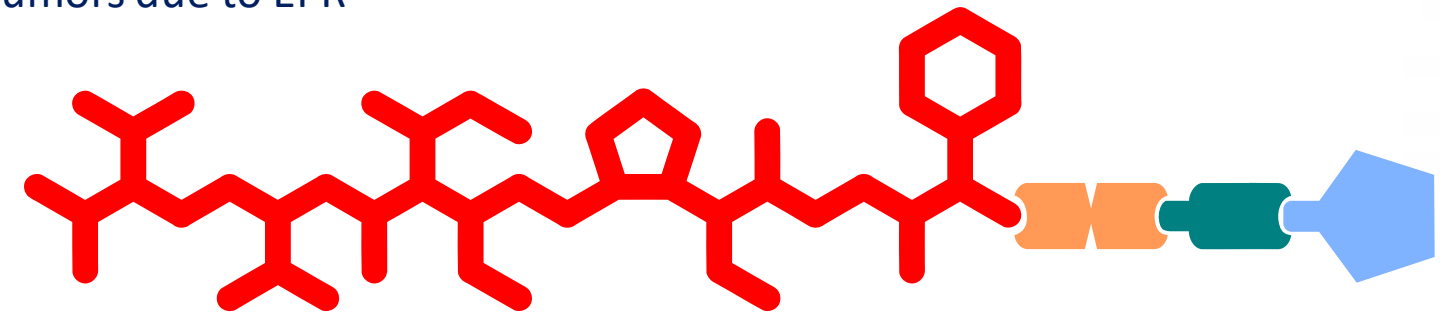
LADR=Linker-Activated Drug Release

LADR-based drugs take advantage of circulating albumin as trojan horse:

- Major source of amino acids for tumors*
- Tumors use as carrier for metabolites, hormones, nutrients*
- Undergoes macropinocytosis*
- Accumulates in tumors due to EPR*
- Long half life*



LADR:



Ultra High Potency Drug Payload

- Payloads are effective in the nanomolar range
- Similar to those used for approved ADCs (auristatins and maytansinoids)

Cleavable Linker

- Novel linker keeps the highly potent drug payload inactive until the conjugate reaches the tumor
- The linker is then cleaved when exposed to lower pH in tumor and intracellular environments

Targeting

- Ensures rapid and selective binding to circulating serum albumin
- Serum albumin transports the LADR™ drug to the tumor

* Kratz, F. Albumin as a drug carrier. J Cont Rel (2008) 132:171-183

Aldoxorubicin: 1st Gen LADR-Based Drug Has Proven Higher Dosing with Improved Safety in Human Trials Compared to Native Doxorubicin

Doxorubicin maximum dosing is 75 mg/m², limited mostly by cardiotoxicity[1]

When attached to LADR backbone, doxorubicin has been dosed in humans at 250 equiv mg/m² (3.3x higher), with lower cardiotoxicity[2]

- **LADR allows for 3X higher dosing or more of doxorubicin**
- **Aldoxorubicin crosses the Blood-Brain Barrier**
- **Tumor targeting and release with the simplicity of a small molecule**
- **In the case of next-gen LADRs 7-10, maximum doses are ~10 higher than that of non-LADR versions**

[1]accessdata.fda.gov

[2]Gong, J, Hendifar, A. et al. Aldoxorubicin: A tumor-targeted doxorubicin conjugate for sarcomas. Drug Dev Des Ther (2018) 12:777-786

Aldoxorubicin-Early Clinical Experience

Phase I

- No tox up to 200 mg/m^2 dose equivalence (DE)
- 260 mg/m^2 Grade 2 mucositis anemia, grade 3 neutropenia/leukocytopenia
- 340 mg/m^2 DE determined to be MTD
- RP2D: 260 mg/m^2 DE every 3 weeks (3.5X conventional doxorubicin dosing)
- No cardiac effects noted, even at 1,650 mg/m^2 DE, which is higher than doxorubicin dose that causes cardiotoxicity in > 50% of patients

Phase IA/IIB

- Metastatic solid tumors, aldox+gemcitabine
- Thrombocytopenia was the dose-limiting toxicity
- No cardiotoxicity, 6/27 had >10% reduction in LVEF
- PR2D 200mg/m^2 (150 mg/m^2 DE) and 500 mg/m^2 gemcitabine
- 20% PR in pts receiving > 260mg/m^2 DE (350mg/m^2)
- ORR 29% in those receiving less than 260 mg/m^2
- ORR 38% in those receiving at least 260 mg/m^2

Aldoxorubicin-Phase II in Soft Tissue Sarcoma

Structure

- Advanced Soft Tissue Sarcoma versus doxorubicin, randomized 2:1
- 21-day cycle for 6-8 cycles
- Aldoxorubicin 260 mg/m^2 DE (350 mg/m2) vs doxorubicin 75 mg/m^2 DE
- 126 pts primary endpoint PFS
- Patients could have received up to 225 mg/m2 doxorubicin, but must have been treatment-naive for advanced disease.

Results

- 86 in aldoxorubicin group, 40 in doxorubicin
- 6% of patients had received prior doxorubicin
- Primary endpoint met: Investigator mPFS 8.3m vs 4.6m (central mPFS 5.6m vs 2.7m)
- 12% of aldoxorubicin group versus 29% of doxorubicin group experienced LVEF decrease greater than 10%. Serum troponin unchanged in aldoxorubicin group, elevated in doxorubicin group for up to 5 months
- Not powered to assess OS
- Grade 3-4 tox more frequent in aldoxorubicin group (80% vs 58%)

Aldoxorubicin-Phase III in Soft Tissue Sarcoma

Structure

- Structure very different from successful Phase II
- 433 patients, randomized 1:1 to aldoxorubicin at 260 mg/m^2 DE on 21-day cycle versus investigators choice among 3 regimens that included, 1) dacarbazine, pazopanib, gemcitabine/docetaxel; 2) doxorubicin; or 3) ifosfomade
- Included patients who had relapsed or been refractory to initial systemic therapy

Results

- 2/3 of patients in each group had received prior doxorubicin
- Liposarcomas and leiomyosarcomas were 55% of aldoxorubicin group and 59% of control group
- PFS (primary endpoint) 4.1m vs 2.96, not statistically significant
- PFS in L-sarcomas was significant at 5.3m vs 2.96m
- OS and ORR not improved
- Decrease in LVEF > 20% in 8/213 (3.8%) aldoxorubicin subjects, 4/43 (9.3%) in doxorubicin subjects.
- Decrease in LVEF <50% was seen in 9/213 (4%) aldoxorubicin subjects versus 9/47 (19%) of doxorubicin subjects.

Comments

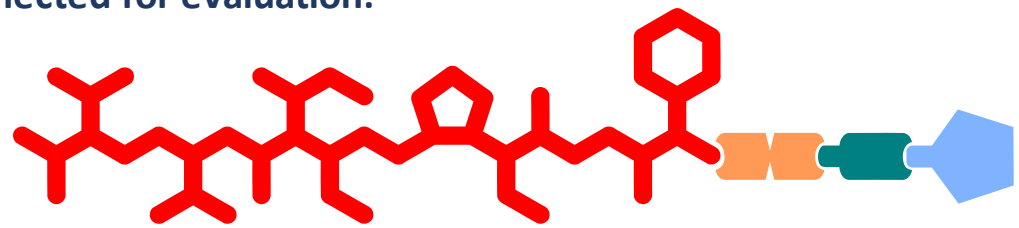
- 47/215 in control group received doxorubicin, and could be assumed to not have failed doxorubicin prior (else investigator would not choose doxorubicin for that subject), compared to active group, in which 2/3 could be assumed to have failed/recurred after doxorubicin treatment
- Remainder of control group received therapies that are not cross-resistant with doxorubicin

Aldoxorubicin-Other Trials

Additional trials have been conducted with aldoxorubicin in glioblastoma, Kaposi sarcoma, small-cell lung cancer, and others. Limited data and information are available for these trials, though LadRx will update this page as we gain access to the data, following the return of aldoxorubicin to LadRx from Immunity Bio.

Next-Gen LADRs : LADR 7, 8, 9, 10

- High-throughput screening yielded four compounds selected for evaluation:
  - LADR 7: Auristatin-E with Ketone Linker
  - LADR 8: Auristatin-E with Ester Linker
  - LADR 9: Maytansine with Ketone Linker
  - LADR 10: Maytansine with Ester Linker



- Auristatins and Maytansinoids are highly potent microtubulin inhibitors with IC50 values in the low nanomolar range. They are too toxic to use as untargeted drugs with systemic exposure.

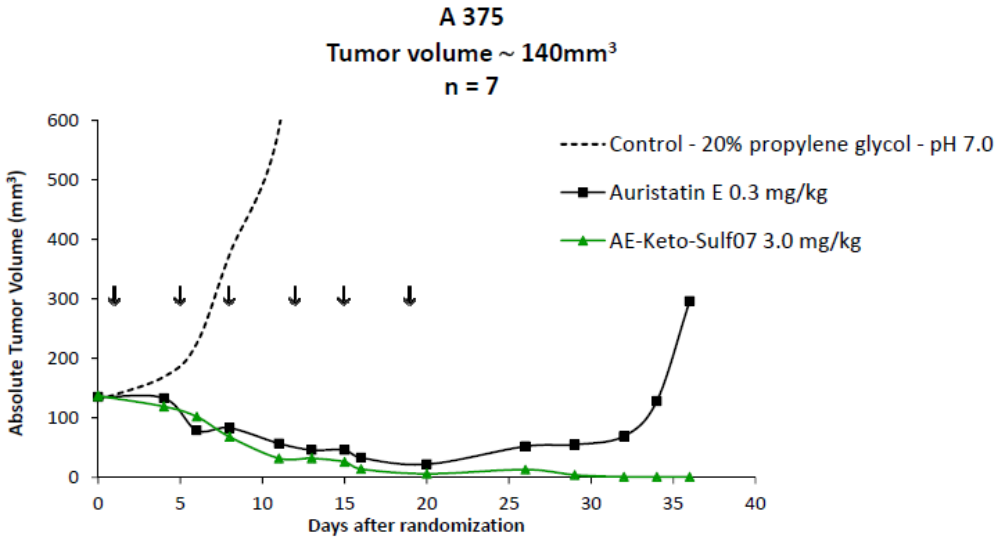
- Auristatin-E and Maytansine are currently approved in the form of ADCs as Adcetris ($700m sales in 2021, SeaGen) and Kadcyla ($2b sales in 2021, Genentech)

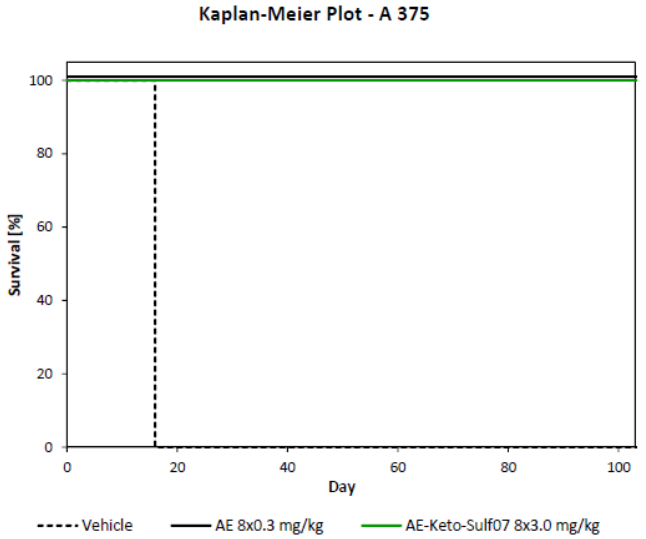
  - Adcetris: Hodgkin Lymphoma 3rd line+ or failed ASCT, Systemic Anaplastic Large Cell Lymphoma 2nd line+

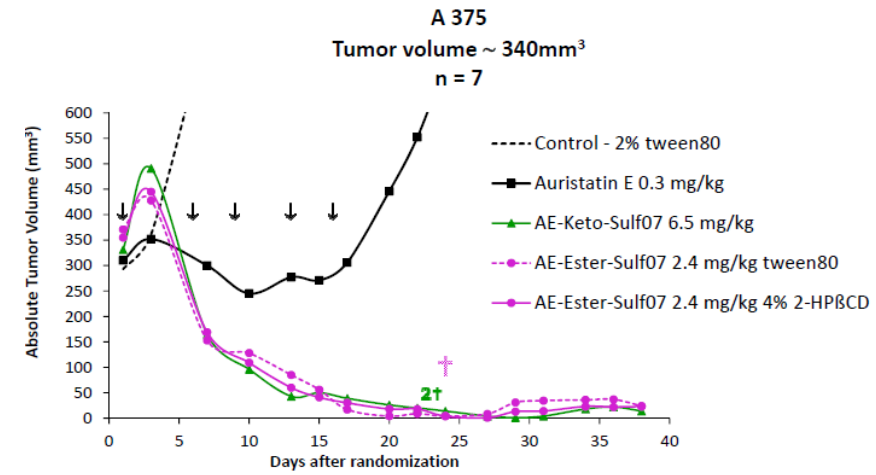
  - Kadcyla: HER2 Positive MBC 2nd Line+

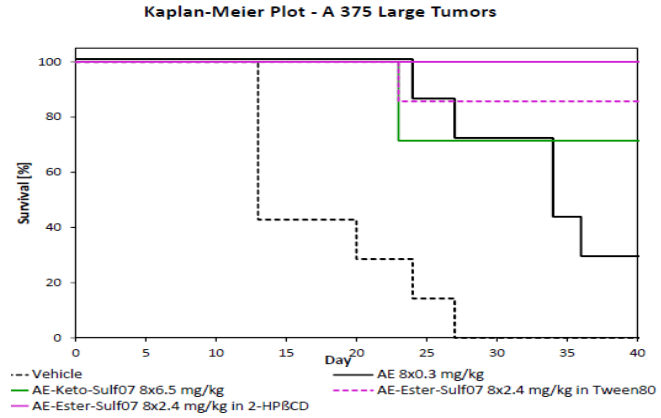
  - LADR system capable of delivery many times as much chemotoxin compared to antibodies

LADRs 7 and 8 are powerful anti-cancer drugs in multiple PDX/CDX cancer models: Melanoma

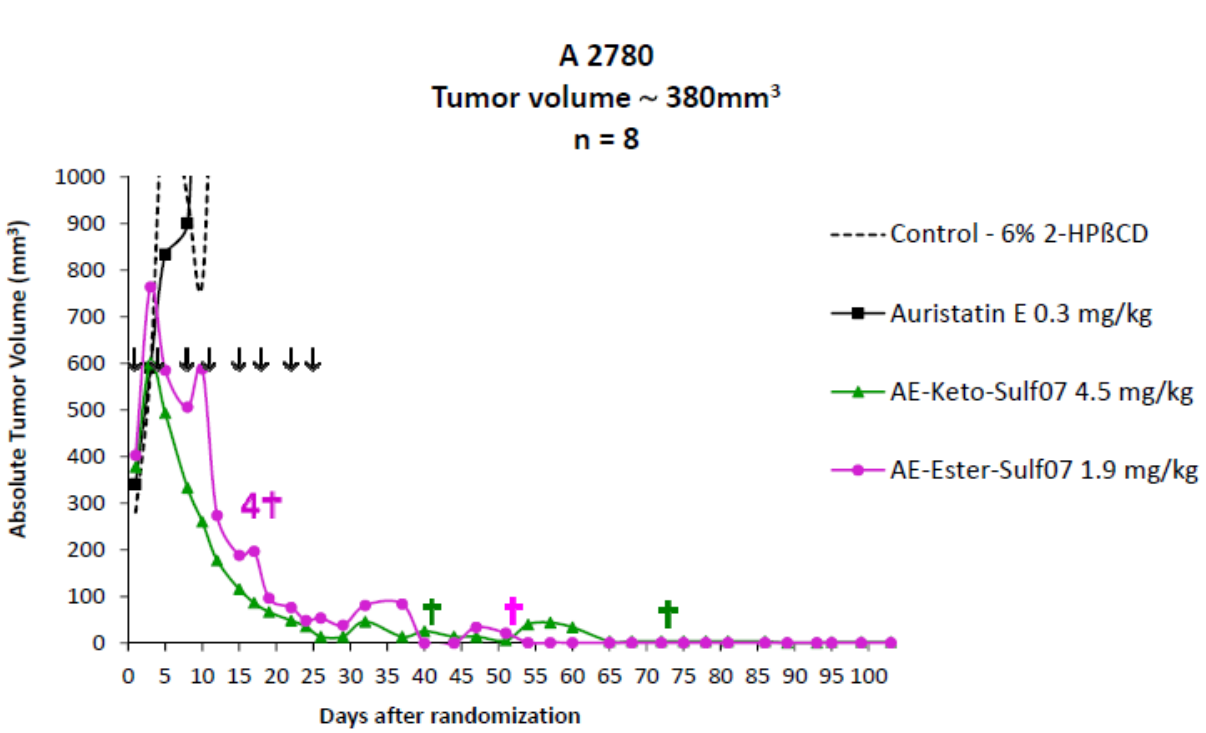


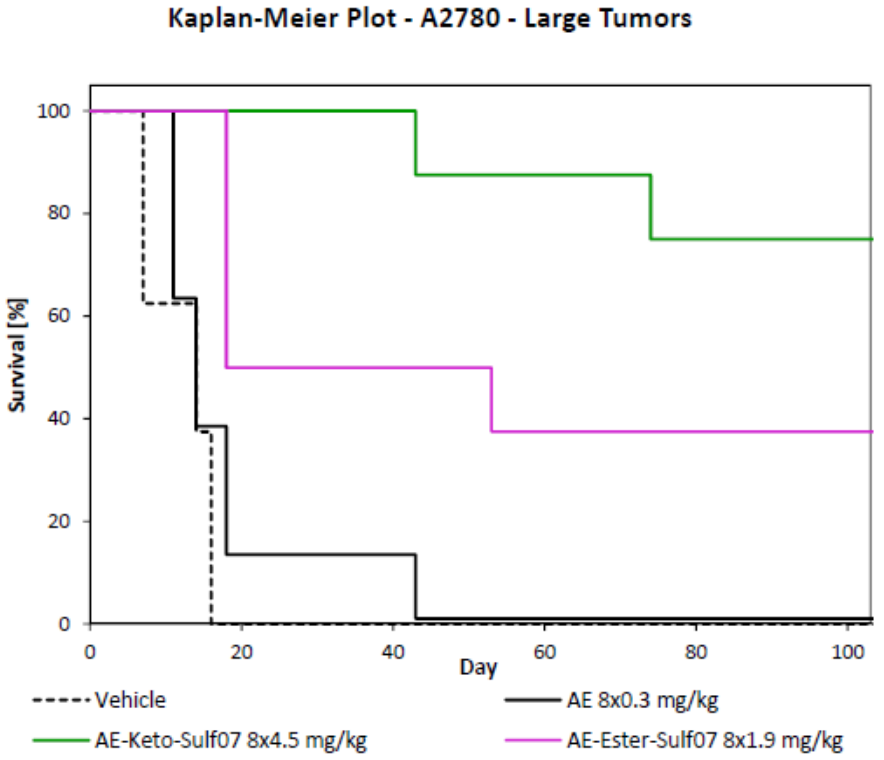




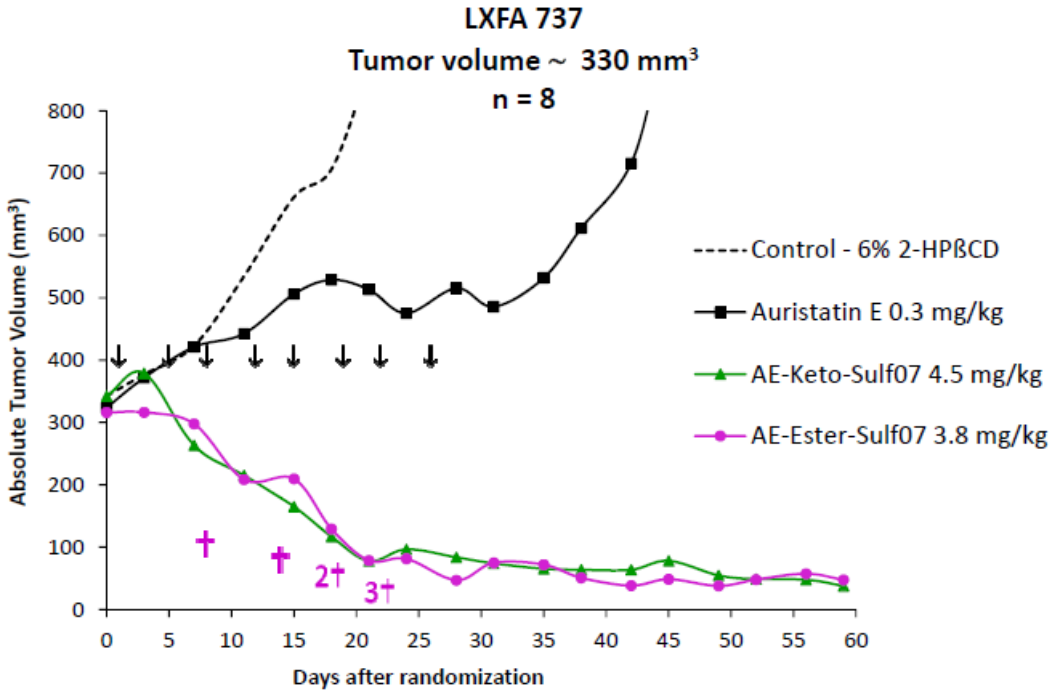


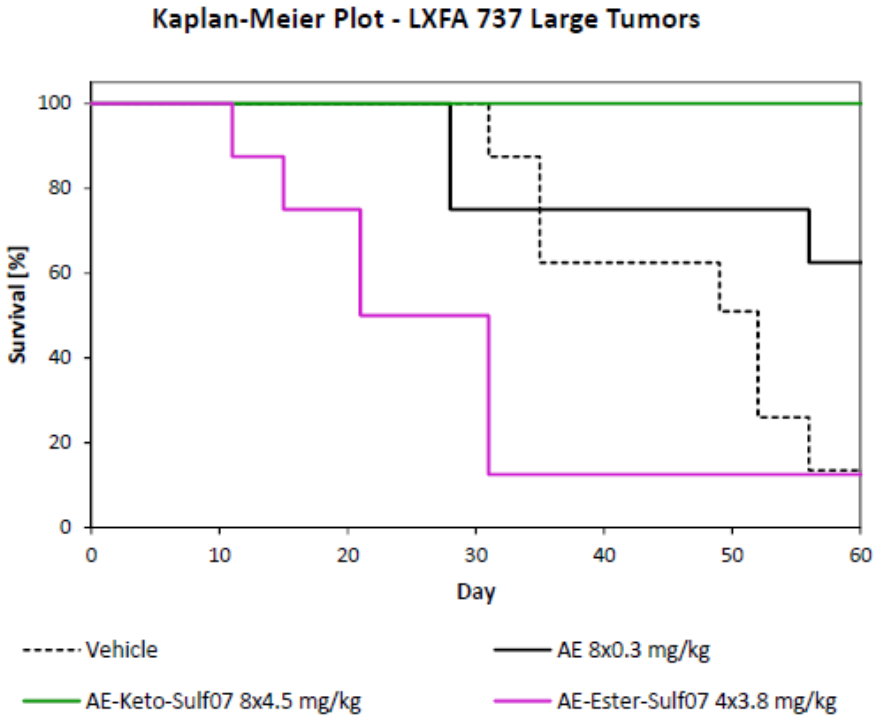
LADRs 7 and 8 are powerful anti-cancer drugs in multiple PDX/CDX cancer models: Ovarian





LADRs 7 and 8 are powerful anti-cancer drugs in multiple PDX/CDX cancer models: Non-Small Cell Lung Cancer





LadRx Corp

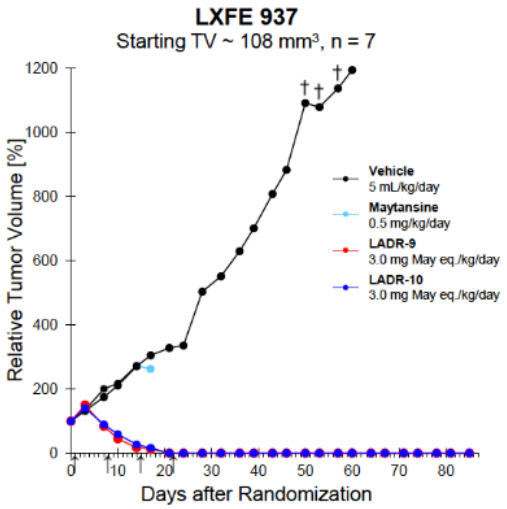
…As are LADRs 9 and 10

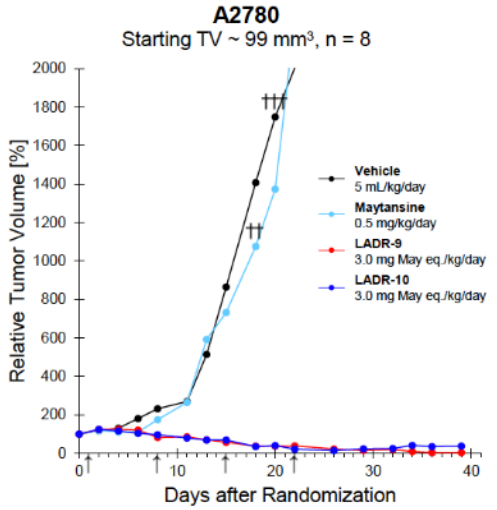
Overview of the antitumor activity of maytansine and both albumin-binding drugs in various human PDX and CDX xenograft tumor models in nude mice

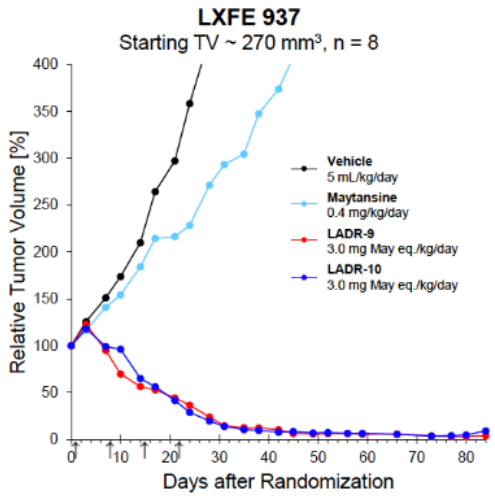
maintained complete remission
complete remission
partial remission
stable disease
partial progressive disease
progressive disease
toxic dose
not available

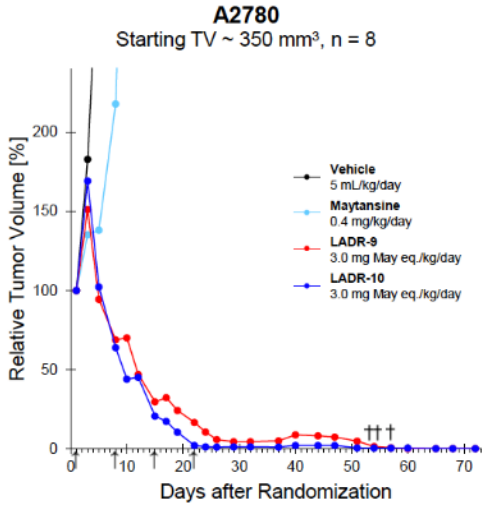
		Median start tumor volume [mm³]	Number of animals per group	Days of observation after last treatment	Maytansine 0.4 mg/kg (1xqWx4)	Maytansine 0.5 mg/kg (1xqWx4)	LADR-9 2.0 mg May eq./kg (1xqWx4)	LADR-9 3.0 mg May eq./kg (1xqWx4)	LADR-10 2.0 mg May eq./kg (1xqWx4)	LADR-10 3.0 mg May eq./kg (1xqWx4)	
Lung	LXFE 937	108	7	63		(7/-)		(-/-)	(1/2)	(-/-)	*
		270	8	63	(-/7)			(2/-)		(-/-)	*
	LXFA 737	331	8	37	(1/-)			(4/-)		(1/-)	
Breast	MDA-MB 231	76	7	41		(-/1)	(1/-)		(-/-)		
	MDA-MB 468	73	7	35		(7/-)		(3/-)		(7/-)	
		87	7	39	(3/-)			(-/-)		(1/-)	
Ovarian	A2780	99	8	17		(-/8)		(2/-)		(2/-)	*
		350	8	51	(-/7)			(-/2)		(-/1)	*
Renal	RXF 631	109	7	42		(-/4)			(-/-)		
		98	7	34	(-/1)			(-/-)		(-/-)	
Head & Neck	HN 10114	103	1	36							
	HN 10913	117	1	32							
	HN 11142	110	1	39							
	HN 11269B	115	1	36							
	HN 11204B	99	1	31							

The experiments were evaluated based on the T/C values (by LOCF; MCR <5 %, CR 5-10 %, PR >10-50 %, SD >50-75 %,>75-125 % PP, >125 % PD). The compounds were administered i.v. in a solution of 20 % propylene glycol in 10 mM sodium phosphate buffer (pH 7.0). The pattern fill (dots) indicates a regrowth of tumors towards the end of the experiment. In parentheses, the number of deaths related to toxicity and tumor growth, respectively, are shown. *denotes the experiments shown in detail.









LadRx Corp

All Four LADR Candidates Meet Initial Development Criteria

	Auristatin LADR™s (LADR-7 and LADR-8)	Maytansinoid LADR™s (LADR-9 and LADR-10)
Selective Binding to Albumin and Stable in Plasma	✓	✓
Payload Releases at pH 4	✓	✓
Robust Anti-Tumor Activity in Multiple Tumor Types	✓	✓
Durable Responses Averaged 60–90 Days	✓	✓
Demonstrated Superiority Over Control Group With Parent Compounds	✓	✓
Highly Effective Even in Large Tumor Models	✓	✓
Initial Toxicology Results do not Preclude Continued Development	✓	✓

Next-gen LADR Drug, LADR-7, Nearing IND

- ✓ Stability in plasma (mouse, rat, dog, monkey, human)
- ✓ pH-dependent release
- ✓ Rat and mouse MTD
- ✓ In-vitro efficacy
- ✓ In-vivo efficacy (small and large tumor PDX and CDX)
- ✓ Non-GLP rodent tox
- ✓ CMC
- ✓ Manufacturing of clinical batch under Good Manufacturing Practices (GMP)

GLP tox is in progress

IND filing expected 3Q-4Q2024, ready for first-in-human dosing by end of 2024

Business Status of Arimoclomol and Aldoxorubicin

Xoma, Inc.

In 2023, LadRx transferred the economic rights to aldoxorubicin and arimoclomol in exchange for certain payments from Xoma to LadRx:

- ✓ **$5M gross proceeds upon closing**
- ✓ **$1M upon acceptance by FDA of arimoclomol NDA**
- **$1M upon first commercial sale of arimoclomol (possibly FY2024)**

Aldoxorubicin

In June of 2024, LadRx and NantCell (Immunity Bio) mutually terminated the license of aldoxorubicin, with the asset fully returned to LadRx, as Immunity Bio focuses on immunotherapy. Xoma, Inc. retains the rights to a small single-digit royalty if LadRx commercializes aldoxorubicin, and a mid-single digit percentage of any licensing/partnering revenue that LadRx receives on aldoxorubicin. LadRx is evaluating the pathways for partnering and/or the continued clinical development of aldoxorubicin

Summary

LadRx has developed a targeted delivery platform for chemotherapeutic agents that takes advantage of the concentration of albumin in solid tumors. Being small molecules, the agents are easier/cheaper to manufacture than macromolecules, confer solubility, cross the blood-brain barrier, and are not limited in use by tumor markers.

LadRx has also developed highly potent chemotherapeutic agents to couple with its LADR delivery platform, and demonstrated high potency and safety in multiple in-vitro and in-vivo cancer models

The first-gen LADR asset, Aldoxorubicin, has demonstrated proof-of-concept of the LADR platform in humans; this LADR form of doxorubicin is delivered to human subjects at 3X the dosing used for native doxorubicin, and met its endpoints in a Phase II study in soft-tissue sarcomas. Aldoxorubicin is ready for further Phase II or Phase III studies

The next-gen LADR product LADR-7 has now been manufactured under GMP, clinical material is in hand, and preparations are being made for an IND submission approximately 3Q-4Q2024, and clinical entry approximately the end of 2024