LadRx Corp

OTCQB:LADX
CORPORATE OVERVIEW
July 2023
Non-Confidential

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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**

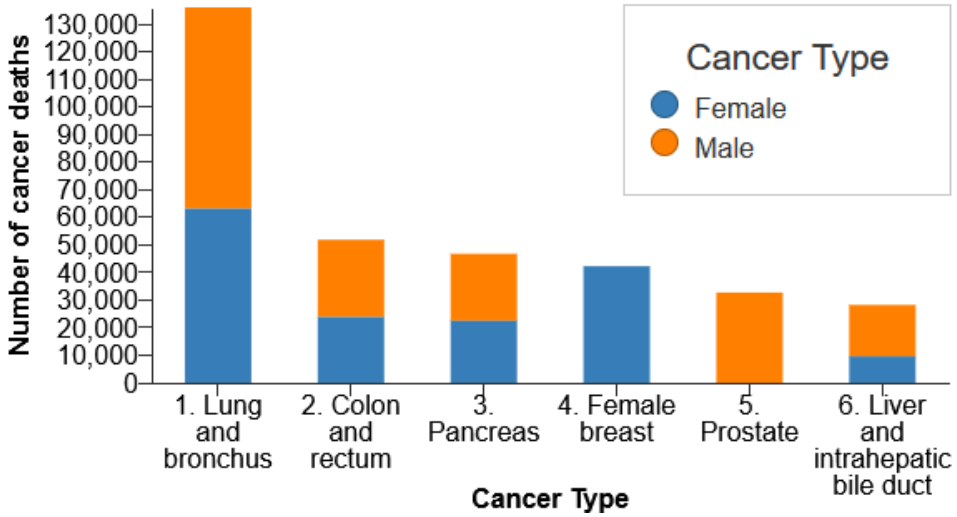
Chair of the Compensation Committee. CEO of Adial Pharmaceuticals Inc. Former CEO of Prosperity Capital Management, LLC.

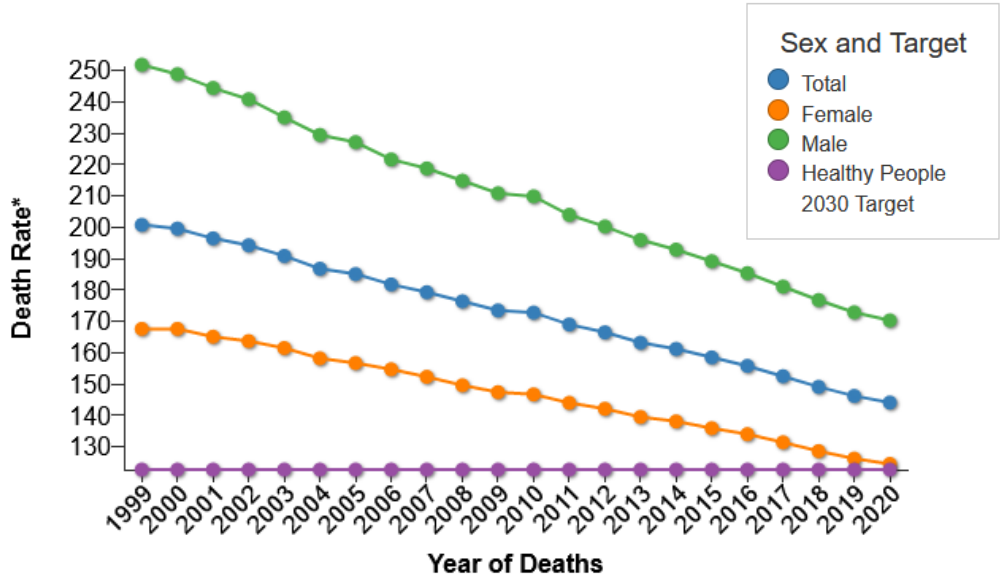
Despite Progress, Cancer is a Massive Burden

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"

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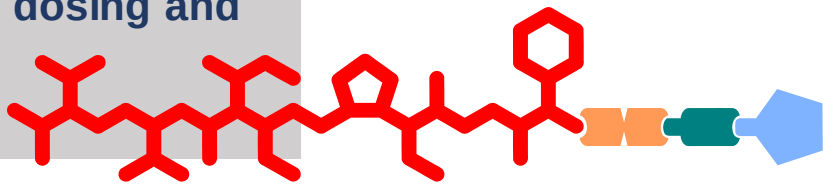
Investment Highlights

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 and lower off-target tox

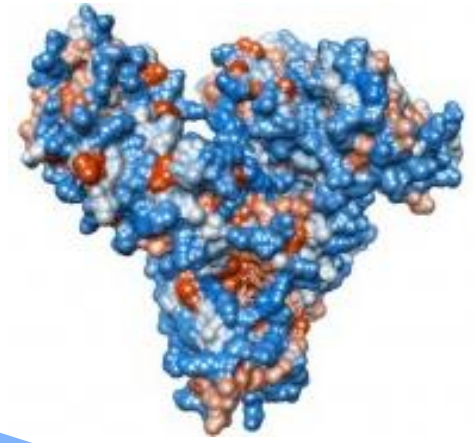


- First LADR drug Aldoxorubicin was licensed to Immunity Bio and is in human trial for pancreatic cancer
- Next-gen LADR-based drugs are nearing readiness for IND
- Small and virtual to minimize cash use
- Strong, broad, and global patent portfolio

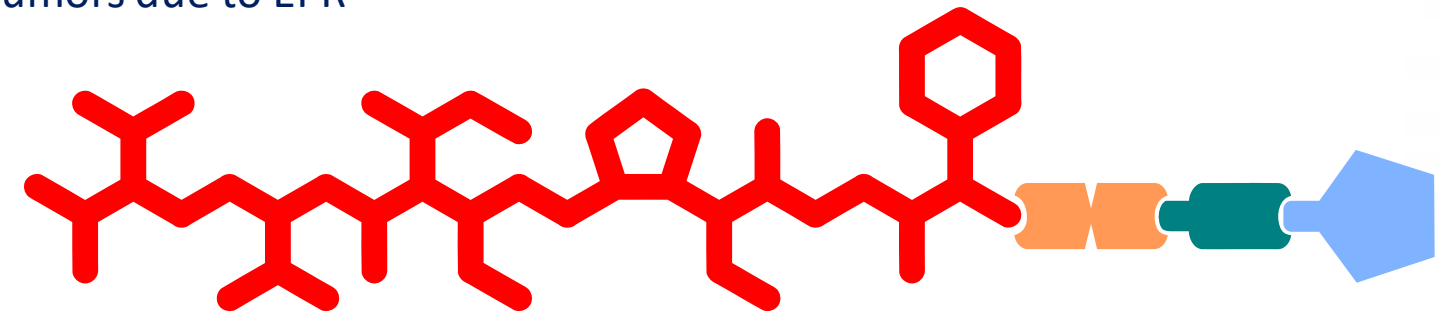
LADR=Linker-Activated Drug Release

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 toxicity, including lower cardiotoxicity[2]

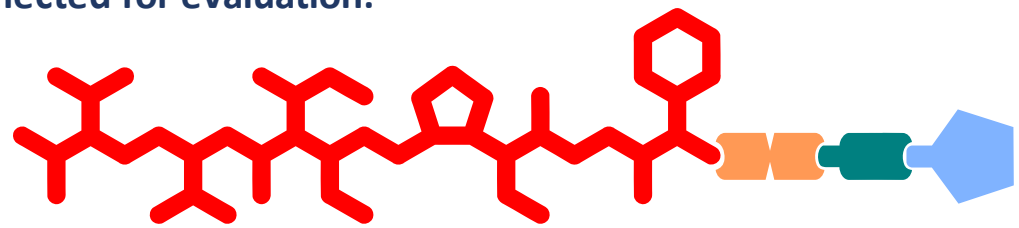
- **LADR allows for 3X higher dosing or more of doxorubicin**
- **Aldoxorubicin crosses the Blood-Brain Barrier**
- **Tumor targeting and release with the simplicity of a small molecule**
- **In the case of next-gen LADRs 7-10, maximum doses are ~10 higher than that of non-LADR versions**

[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

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.

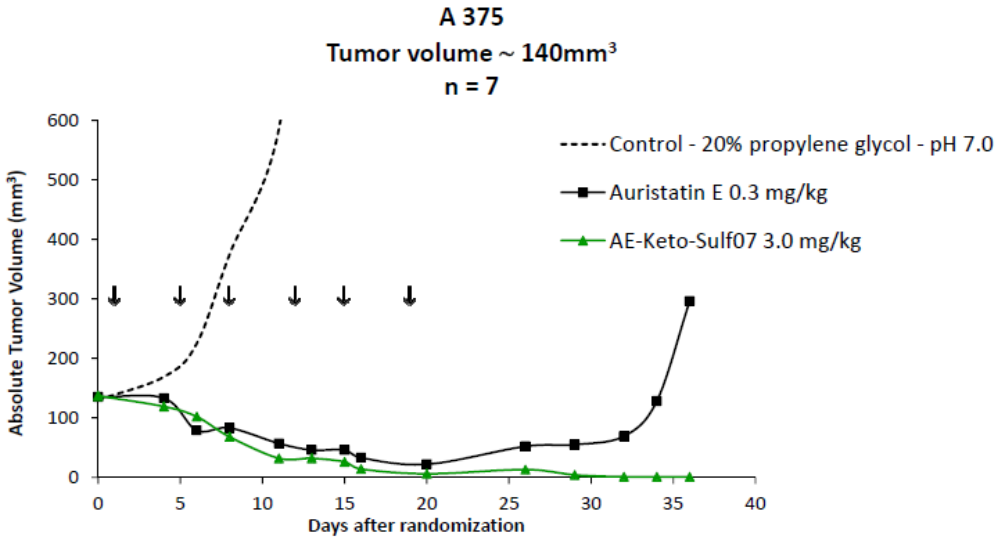
- Auristatin-E and Maytansine are currently approved in the form of ADCs as Adcetris ($700m sales in 2021, SeaGen) and Kadcyla ($2b sales in 2021, Genentech)

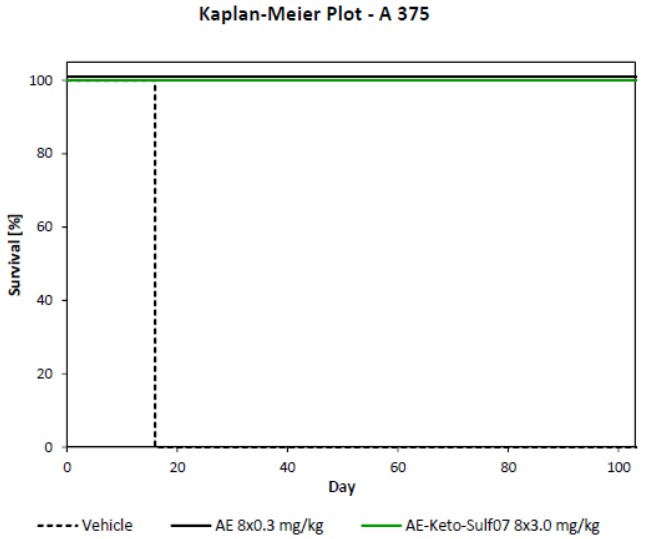
  - Adcetris: Hodgkin Lymphoma 3rd line+ or failed ASCT, Systemic Anaplastic Large Cell Lymphoma 2nd line+

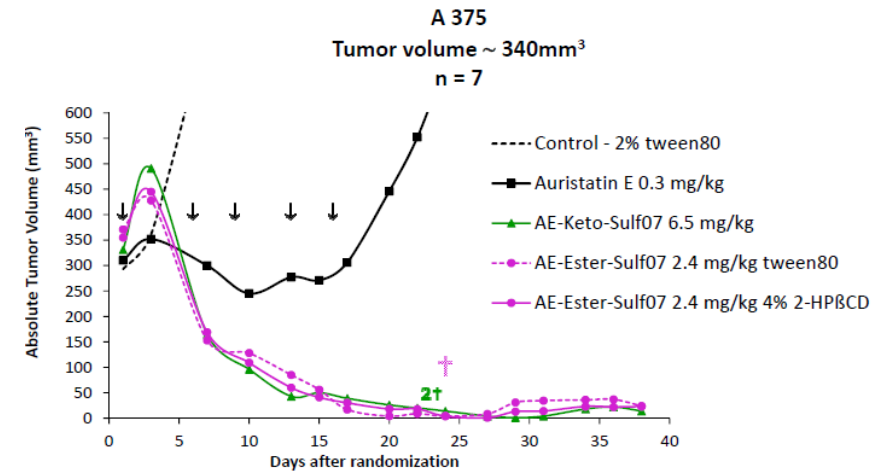
  - Kadcyla: HER2 Positive MBC 2nd Line+

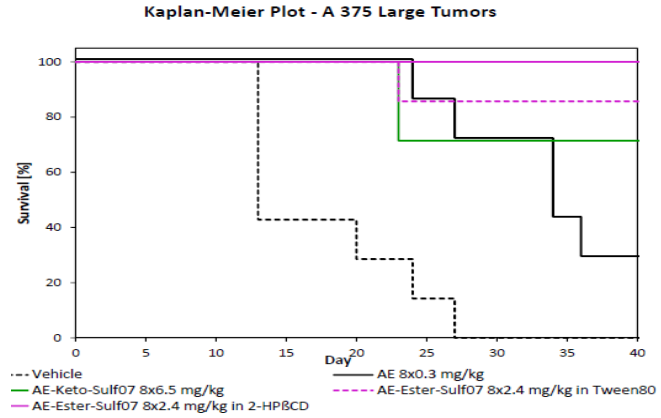
  - LADR system capable of delivery many times as much chemotoxin compared to antibodies

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

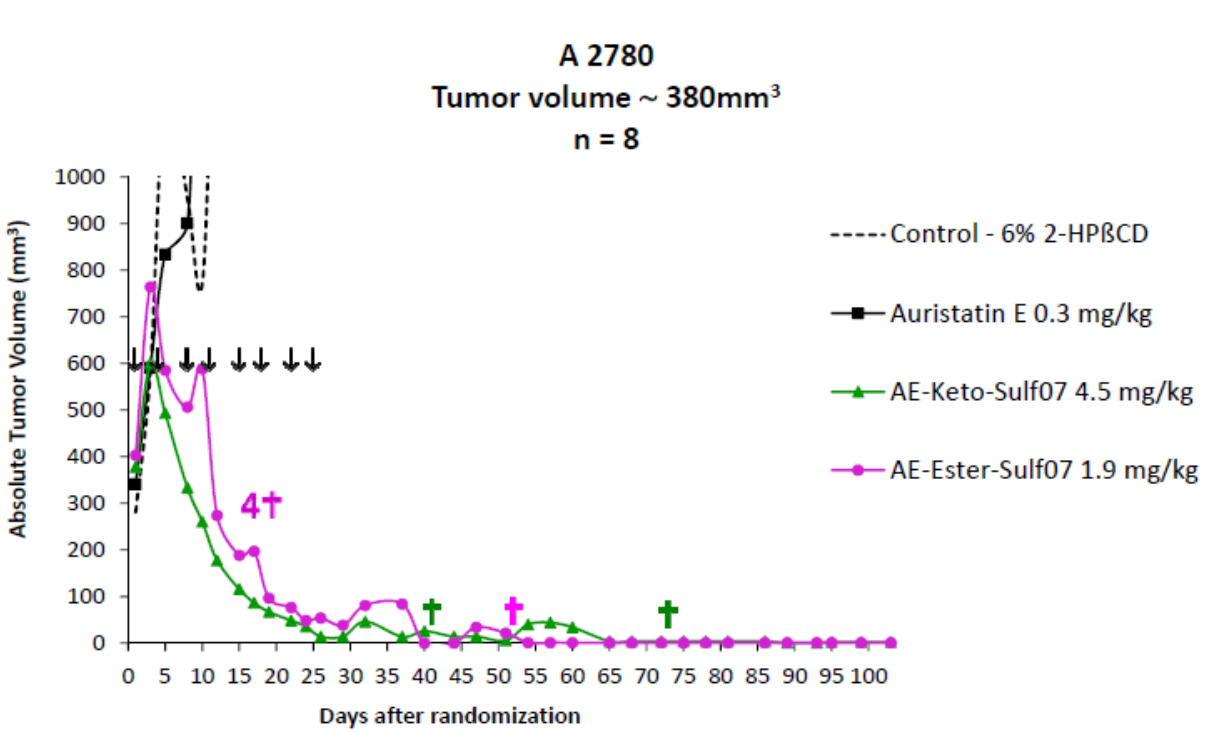


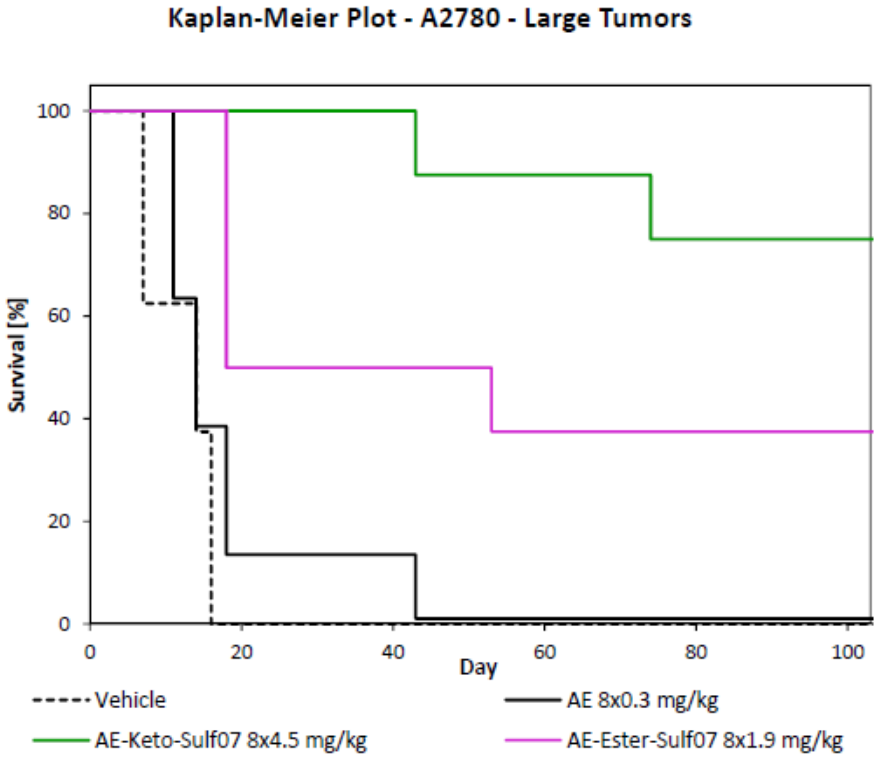




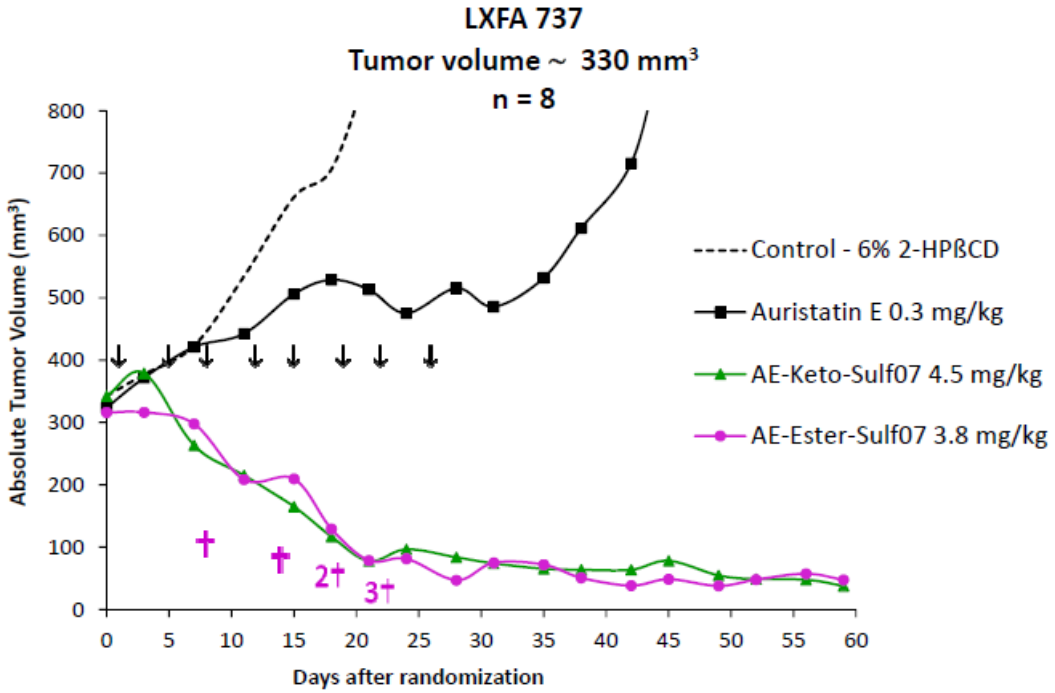


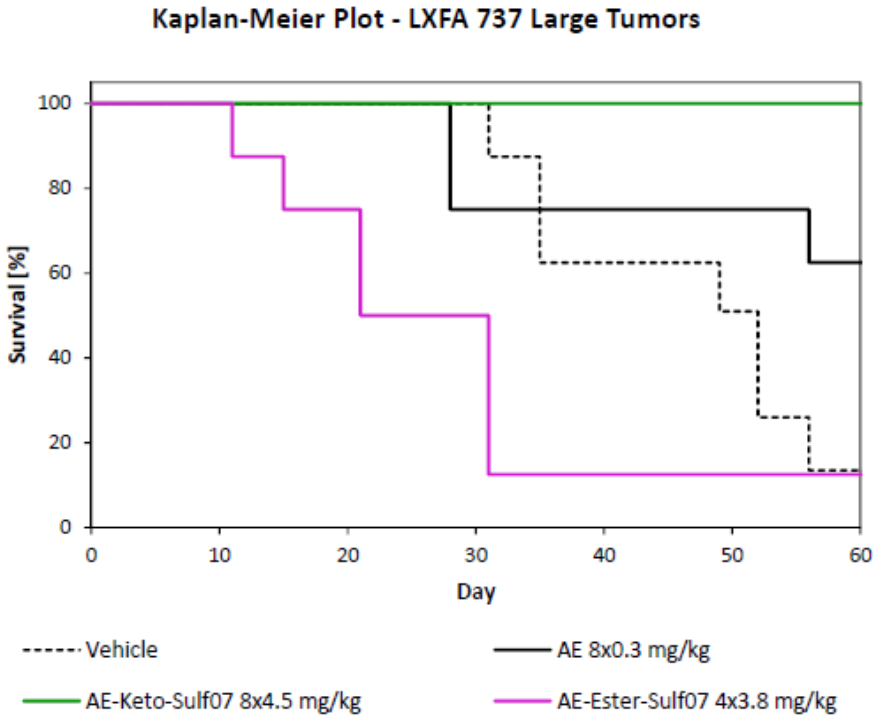
LADRs 7 and 8 are powerful anti-cancer drugs in multiple PDX/CDX cancer models: Ovarian





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





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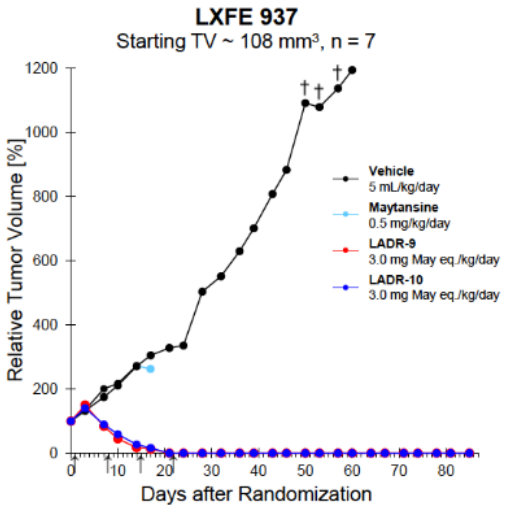
…As are LADRs 9 and 10

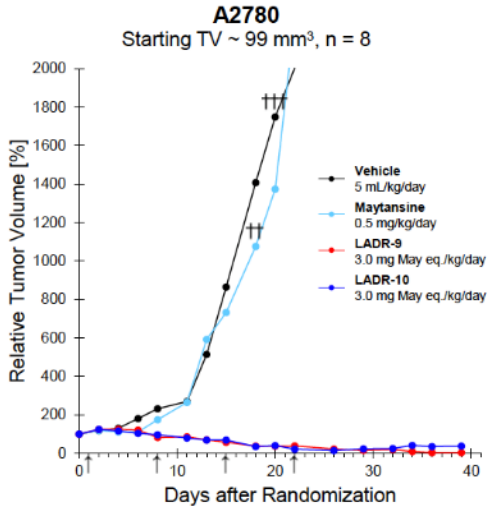
Overview of the antitumor activity of maytansine and both albumin-binding drugs in various human PDX and CDX xenograft tumor models in nude mice

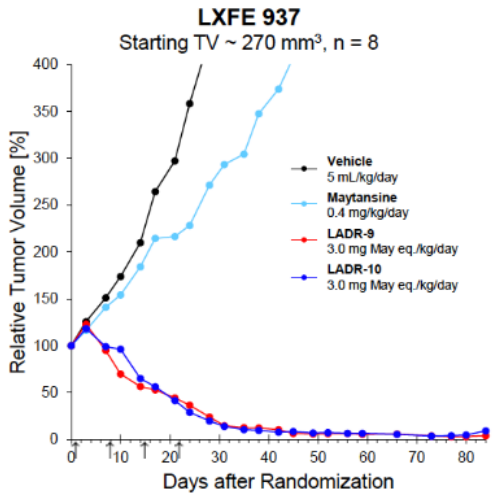
maintained complete remission
complete remission
partial remission
stable disease
partial progressive disease
progressive disease
toxic dose
not available

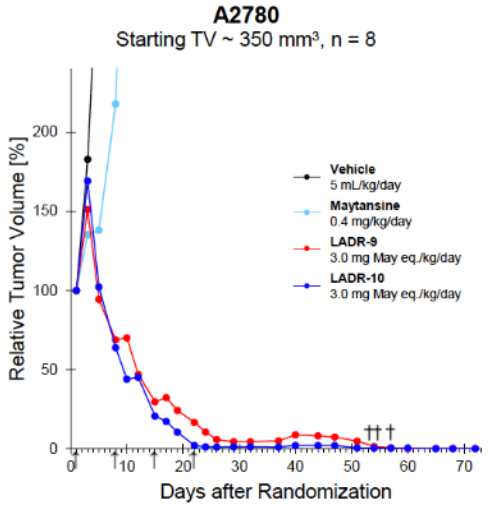
		Median start tumor volume [mm³]	Number of animals per group	Days of observation after last treatment	Maytansine 0.4 mg/kg (1xqWx4)	Maytansine 0.5 mg/kg (1xqWx4)	LADR-9 2.0 mg May eq./kg (1xqWx4)	LADR-9 3.0 mg May eq./kg (1xqWx4)	LADR-10 2.0 mg May eq./kg (1xqWx4)	LADR-10 3.0 mg May eq./kg (1xqWx4)	
Lung	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.









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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 Progress Towards 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

  GLP Mfg Run

  GLP rodent tox

Time to IND 12-18 months from project funding

Status of Arimoclomol and Aldoxorubicin

In June 2023, LadRx entered an agreement with Xoma, Inc. in which economic rights to arimoclomol and aldoxorubicin were transferred to Xoma, Inc.

In exchange for the economic rights to arimoclomol and aldoxorubicin, LadRx received or will receive:

- **$5M gross proceeds upon closing**
- **$1M upon acceptance by FDA of arimoclomol NDA (possibly Q4_2023)**
- **$1M upon first commercial sale of arimoclomol (possibly FY2024)**
- **$4M upon NDA approval by FDA of aldoxorubicin**

Xoma will be responsible for future licensing and milestone obligations owed by LadRx Related to arimoclomol and aldoxorubicin

Summary

LadRx has developed an efficient 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, and cross the blood-brain barrier.

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, with decreased toxicity

The next-gen LADR product LADR-7 is close to readiness for IND