



LadRx Corp

**OTCQB:LADX
CORPORATE OVERVIEW
December 2024
Non-Confidential**

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Management and Board



Stephen Snowdy, PhD
CEO

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



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

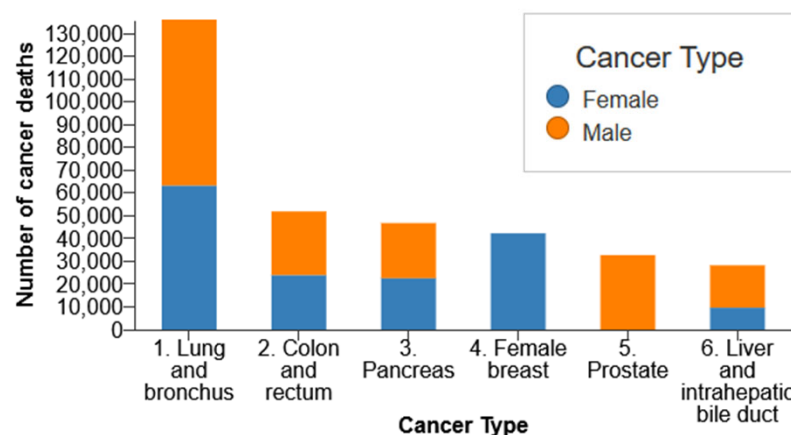
- **Jennifer Simpson, PhD**
LadRx Chair of the Board. CEO of Panbela Therapeutics. Former CEO of Delcath, Oncology Lead at Imclone, Product Director Oncology Marketing at Ortho Biotech
- **Joel Caldwell**
Chair of Audit Committee. 30 years of experience in tax, finance, and auditing.
- **Cary J. Claiborne**
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 worldwide¹

Leading attributable causes (approx. half of cancers are attributable) are smoking, alcohol use, and high BMI¹

Cancer is the second leading cause of death in the US, behind heart disease²

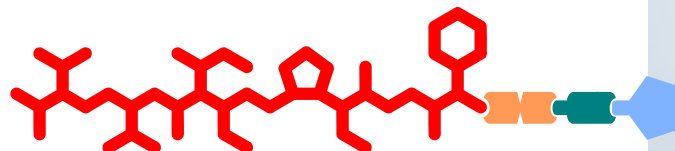


Graphs Adapted from Center for Disease Control, "An Update on Cancer in the United States"

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"

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. With LADR, no need to screen patients for targets.



- First LADR drug aldoxorubicin (targeted analog of doxorubicin) met primary endpoint 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 NDA under 505(b)(2), market launch ready in 18 months from funding if 505(b)(2) NDA successful. Out-licensed for \$340+ million in milestones/royalties, recently reclaimed due to a narrowing of focus by the licensee
- Aldoxorubicin has orphan drug status in soft tissue sarcoma, ovarian cancer, small cell lung cancer, pancreatic cancer, and glioblastoma.
- Several next-gen LADR drugs. LADR-7 has been manufactured under GMP, GLP tox complete, ready for IND filing in 4Q 2024 and FIH Phase I end of 2024/early 2025
- Simplified cap structure; no debt, no warrants, no preferred shares, only Common Shares outstanding
- Small and virtual to minimize cash use.
- Strong, broad, and global patent portfolio

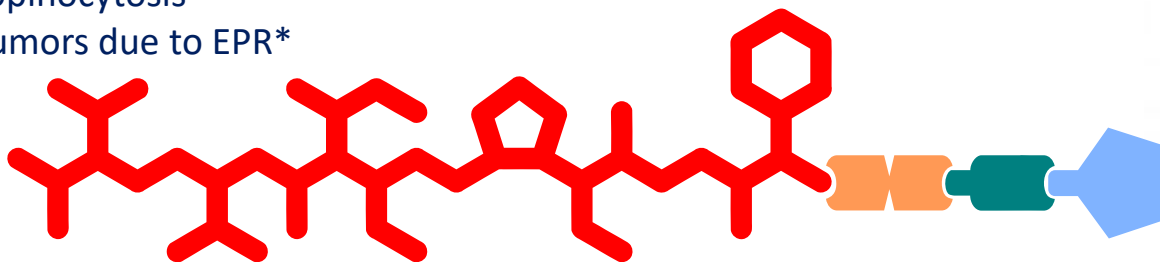
*Cranmer, LD. OncoTargets and Therapy, 2019:12 2047-2062

LADR=Linker-Activated Drug Release

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

- Most abundant protein in blood
- 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 cardiotoxicity¹

When attached to LADR backbone, doxorubicin has been dosed in humans at 250 equiv mg/m² (3.3x higher), with lower cardiotoxicity²

- 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

¹accessdata.fda.gov

²Gong, 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

- Inclusion of up to 700 mg/m² prior doxorubicin or epirubicin
- No tox up to 200 mg/m² dose equivalence (DE)
- 260 mg/m² Grade 2 mucositis, anemia, grade 3 neutropenia/leukocytopenia
- 340 mg/m² DE determined to be MTD
- RP2D: 260 mg/m² DE every 3 weeks (3.5X conventional doxorubicin dosing)
- No cardiac effects noted, even at 1,650 mg/m² DE, which is higher than doxorubicin dose that causes cardiotoxicity in > 50% of patients
- Demonstrated much lower rate of clearance than doxorubicin

Phase IB/II

- Metastatic solid tumors, aldox+gemcitabine
- Thrombocytopenia was the dose-limiting toxicity
- No cardiotoxicity, 6/27 had >10% reduction in LVEF
- PR2D 200mg/m² (150 mg/m² DE) and 500 mg/m² gemcitabine
- 20% PR in pts receiving > 260mg/m² DE (350mg/m²)
- ORR 29% in those receiving less than 260 mg/m²
- ORR 38% in those receiving at least 260 mg/m²

Aldoxorubicin-Phase II in Soft Tissue Sarcoma

Structure

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

Results

- 86 in aldoxorubicin group, 40 in doxorubicin
- 10% of pts had received prior adjuvant systemic therapy, some presumably 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/m² DE on 21-day cycle versus investigators choice among 3 regimens that included, 1) dacarbazine, pazopanib, gemcitabine/docetaxel; 2) doxorubicin; or 3) ifosfomide
- 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
- ORR was doubled, Disease Control Rate (ORR+SD) was statistically 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

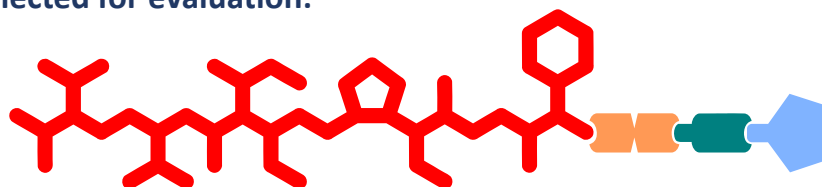
Plan for Aldoxorubicin: NDA under 505(b)(2)

- Doxorubicin sells approximately \$1B per year, and is dose limited by cardiotoxicity
- Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act allows for marketing approval of drugs that employ an active ingredient of an already approved drug (the “reference drug”), but in a new structure or formulation. Because many of the studies required of a marketed drug were performed for the reference drug, the 505(b)(2) pathway provides an abbreviated path to market
- Aldoxorubicin is a tumor-targeted prodrug of doxorubicin, and has over 600 patients worth of data to support the requirements under 505(b)(2)
- LadRx has communicated with the FDA with regard to what data would be required for NDA allowance of aldoxorubicin under 505(b)(2), and the Company does not feel additional human studies would be required (some limited animal studies likely are required, and final plan subject to FDA review)
- LadRx plans on beginning the 505(b)(2) activities early in 2025, and expects that aldoxorubicin could receive marketing approval as early as 18 months from funding (pre-NDA meeting, non-clinical studies, NDA filing).
- The Company believes that published data regarding aldoxorubicin will drive adoption and use over doxorubicin

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

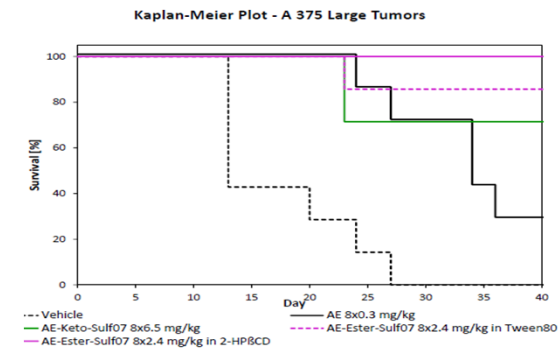
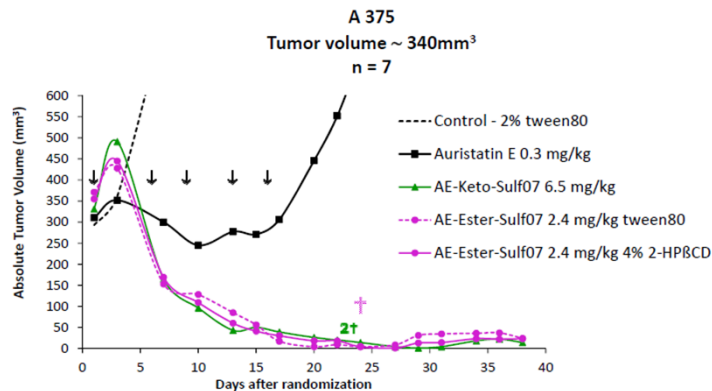
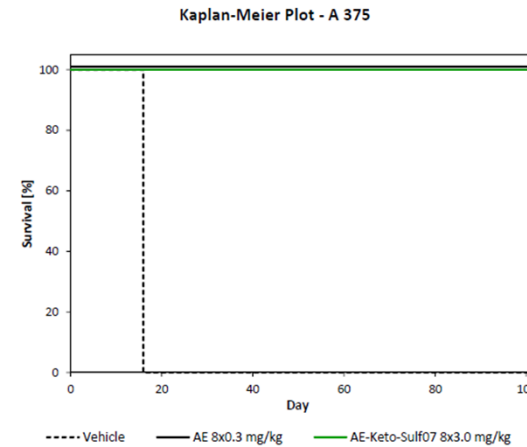
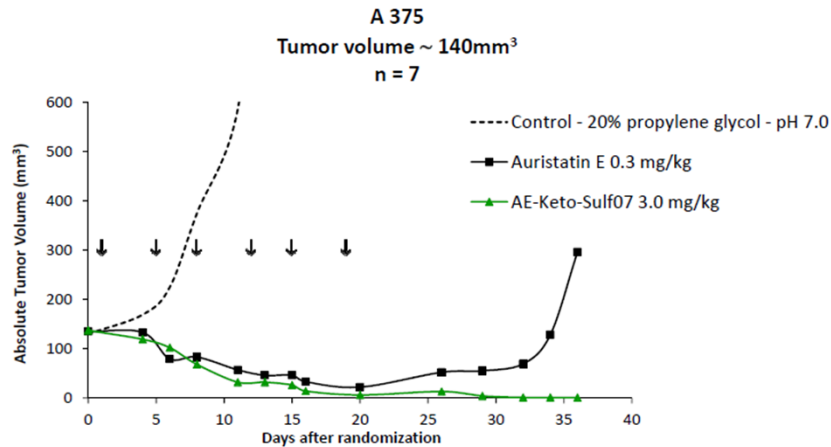
- High-throughput screening yielded four compounds selected for evaluation:

- 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

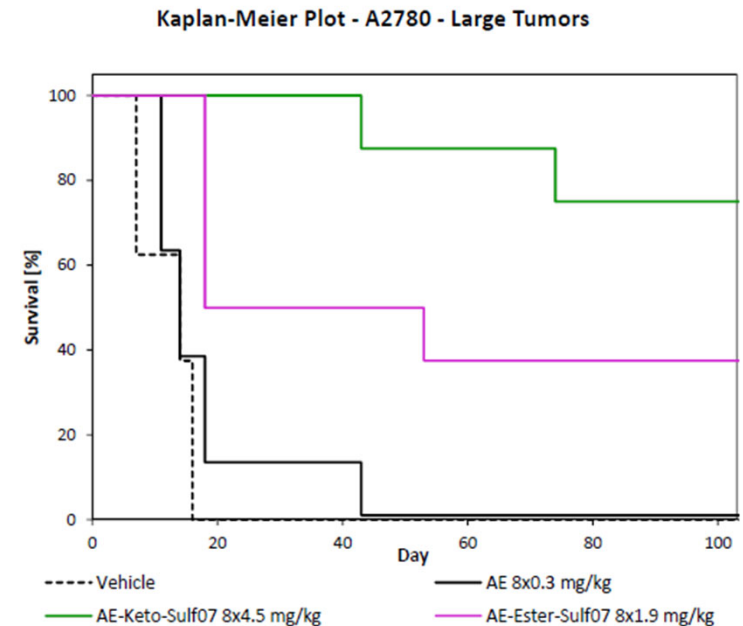
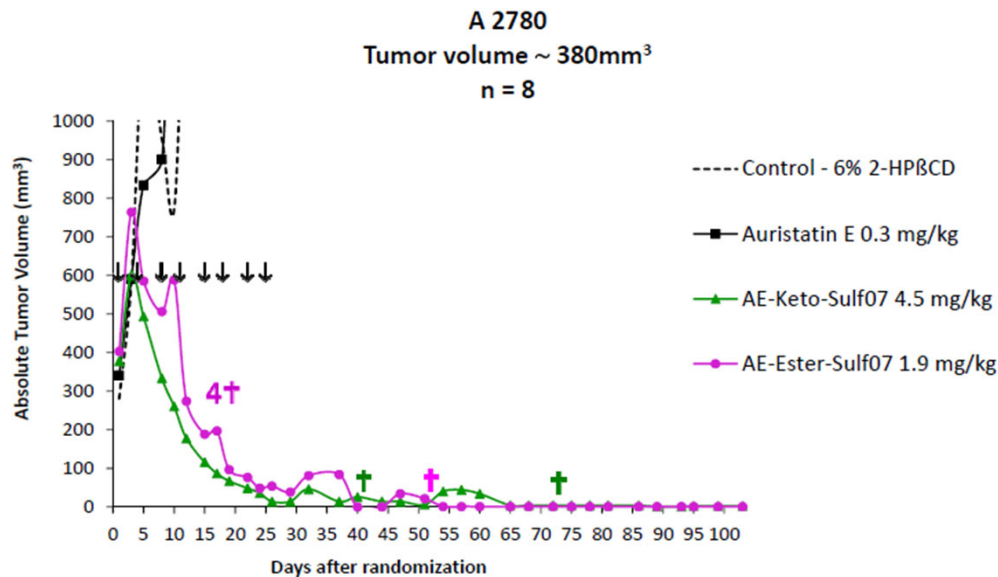


- Auristatins and Maytansinoids are highly potent microtubulin inhibitors with IC50 values in the low nanomolar range. They are too toxic to use as untargeted drugs with systemic exposure.
- Auristatin and Maytansine are currently approved in the form of ADCs as Adcetris (\$700m sales in 2021, SeaGen) and Kadcyra (\$2b sales in 2021, Genentech)
 - Adcetris: Hodgkin Lymphoma 3rd line+ or failed ASCT, Systemic Anaplastic Large Cell Lymphoma 2nd line+
 - Kadcyra: HER2 Positive MBC 2nd Line+
 - LADR system capable of delivering several fold more chemotoxin compared to antibodies

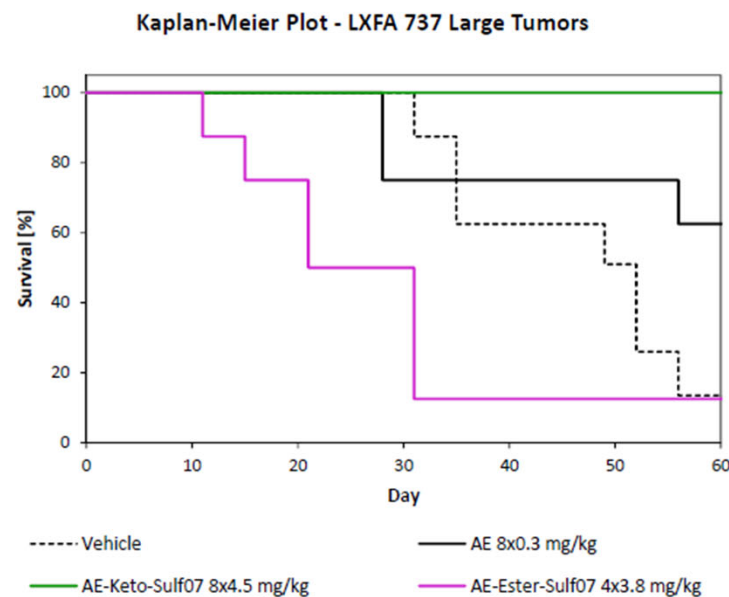
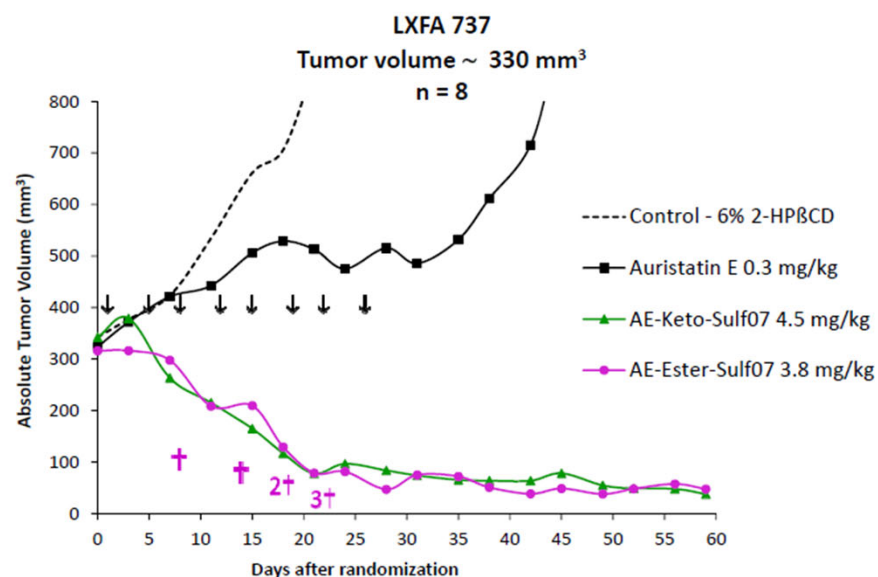
LADRs 7 and 8 are powerful anti-cancer drugs in multiple PDX/CDX cancer models: Melanoma



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



...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

					Median start tumor volume [mm ³]			Number of animals per group			Days of observation after last treatment			Maytansine			LADR-9			LADR-10		
														0.4 mg/kg (1xqWx4)			2.0 mg May eq/kg (1xqWx4)			2.0 mg May eq/kg (1xqWx4)		
														0.5 mg/kg (1xqWx4)			3.0 mg May eq/kg (1xqWx4)			3.0 mg May eq/kg (1xqWx4)		

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, Near IND Readiness

- ✓ 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 completed

First in human dosing approximately 5 months from funding

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. LadRx is preparing for NDA submission under 505(b)(2)

The next-gen LADR product LADR-7 has now been manufactured under GMP, clinical material is in hand. Human trials are expected to commence approximately 5 months after funding

LadRx Corp capital structure consists only of Common Shares, no debt, warrants, or preferred and is very capital efficient
