LeonaBio

Corporate Presentation

March 2026

Disclaimer

This presentation and any accompanying oral commentary contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "on track," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance and financial condition, business plans and objectives, our ability to obtain funding for our operations, including funding necessary to develop and commercialize our drug candidates and funding necessary for the payment of future milestone and other payments that may be earned by our collaboration partners, timing and success of our planned or future development activities, our ability to obtain regulatory approval, the potential therapeutic benefits and economic value of (1) ATH-1105 as a potential treatment for Alzheimer's disease, Parkinson's disease, Parkinson's disease dementia, amyotrophic lateral sclerosis, neuropathic pain and other neurodegenerative diseases and disorders, and (2) lasofoxifene as a potential treatment for breast cancer, the anticipated reporting of data, the potential learnings from preclinical studies and other nonclinical data and clinical studies and their ability to inform and improve future clinical development plans and to demonstrate the safety and efficacy of our drug candidates, our ability to initiate and successfully advance clinical trials for the development of our product candidates, the rate and degree of market acceptance of our drug candidates, anticipated milestone timelines, such as the timing of data releases, and our ability to meet such timelines, our plans related to commercializing our drug candidates, if approved, the success of competing therapies that are or may become available, potential growth opportunities, our plans for any potential financing, strategic transaction, or partnership, including for ATH-1105 and lasofoxifene, competitive position, and industry environment and potential market opportunities. We do not undertake any duty to update these forward-looking statements.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors, including, but not limited to, risks associated with the possible failure to realize certain anticipated benefits of the license relating to lasofoxifene and the recent private placement financing, including with respect to future financial and operating results; the data from preclinical and clinical trials may not support the safety, efficacy and tolerability of our drug candidates; development of drug candidates may cease or be delayed; regulatory authorities could object to protocols, amendments and other submissions; future potential regulatory milestones for drug candidates, including those related to current and planned clinical studies, may be insufficient to support regulatory submissions or approval; whether our trials are sufficiently powered to meet the planned endpoints; we may not be able to recruit sufficient patients for our clinical trials; the outcome of legal proceedings that may in the future be instituted against us, our directors and officers; possible negative interactions of our drug candidates with other treatments; U.S. Food and Drug Administration ("FDA") regulatory delays and uncertainty and new policies, including executive orders, changes in the leadership of federal agencies such as the FDA and U.S. Securities and Exchange Commission ("SEC"), staff layoffs, budget cuts to agency programs and research, and changes in drug pricing controls; our assumptions regarding our financial condition and the sufficiency of our cash, cash equivalents and investments to fund our planned operations may be incorrect; adverse conditions in the general domestic and global economic markets, including as a result of tariffs; the impact of competition; the impact of drug candidate development and clinical activities on operating expenses; the impact of new or changing laws and regulations; as well as the other risks detailed in our filings with the SEC from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described in greater detail in our filings with the SEC may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and readers are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

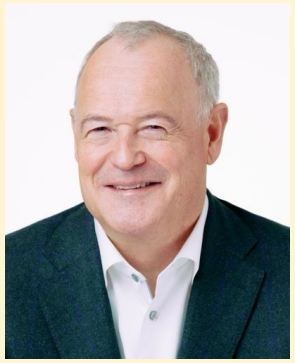
By attending or receiving this presentation you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of our business. This presentation contains estimates, projections and other information concerning market, industry and other data. We obtained this data from our own internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties, including governmental agencies. These data involve a number of assumptions and limitations, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed in our filings with the SEC. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. While we believe such information is generally reliable, we have not independently verified any third-party information.

This presentation concerns drug candidates that are under clinical investigation and which have not yet been approved for marketing by the FDA. The drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

We announce material information to the public through a variety of means, including filings with the SEC, press releases, public conference calls, our website (www.leonabio.com/), our investor relations website (investors.leonabio.com), and our news site (investors.leonabio.com/news-and-events/press-releases). We use these channels, as well as social media, including our X account (@leonabioinc) and Facebook page (https://www.facebook.com/leonabioinc/), to communicate with investors and the public about LeonaBio, our products, and other matters. Therefore, we encourage investors, the media, and others interested in LeonaBio to review the information we make public in these locations, as such information could be deemed to be material information.

Management team with significant drug development and approval experience

LEADERSHIP



Mark Litton, PhD
President and CEO

Javier San Martin, MD
CMO

Kevin Church, PhD
CSO

Mark Worthington, JD
General Counsel

Robert Renninger
CFO

Mark Kubik
CBO

David Portman, MD
CEO, Sermonix
(consultant)

Select prior companies

arrowhead pharmaceuticals

ultragenyx

Seagen

Lilly

AMGEN

ALDER BIOPHARMACEUTICALS → Lundbeck

CELLTECH → ucb

Approved therapies

prolia (denosumab) injection

DOJOLVI TRIHEPTANOIN

Vectibix (panitumumab)

PADCEV enfortumab vedotin-ejfv

Margenza (margetuximab-cmkb)

FORTÉO teriparatide (rDNA origin) injection

CRYSVITA burosumab injection

EVENITY (romosozumab-aqqg)

EVISTA raloxifene HCl

ADCETRIS brentuximab vedotin

vyepti

Mepsevii

POLIVY polatuzumab vedotin-piiq

tivdak tisotumab vedotin-tftv

ZENAPAX® (Daclizumab)

Collectively involved in multiple developed products and exits

Expected key inflection points within ~2 years

✓ **Lasofoxifene**

- Phase 3 registrational study ongoing with >50% enrolled

Topline results expected in 2H2027

✓ **ATH-1105**

- Phase 2 POC study in ALS planned to start in 2H2026

Topline results expected 2027

Exciting opportunity in metastatic breast cancer

LATE-STAGE PROGRAM DIVERSIFIES PIPELINE

LARGE MARKET OPPORTUNITY

- ER+/HER2- disease remains most common breast cancer subtype[1]
- Represents approximately 70% of all breast cancers[1]
- Global metastatic ER+/HER2- market expected to grow from ~$10.9B in 2025 to ~$15.9B by 2029[2]

DIFFERENTIATED MECHANISM OF ACTION

- Designed to overcome resistance that limits current endocrine agents[3,4,5]
- Tissue-selective pharmacology[6]
- Strong combinability profile[7]

POSITIVE PHASE 2 DATA

- Demonstrated compelling signals of clinical activity[7,8]
- Achieved 13 months of progression free survival (PFS)[7]
- Favorable safety profile and well tolerated with potential QoL benefits[6,7,8]

STRATEGIC FIT

- Right company and team to bring this program forward
- Builds on LeonaBio's late-stage development infrastructure
- Leverages deep regulatory and development expertise of LeonaBio leadership

Sources: 1. NCI. Retrieved from *https://seer.cancer.gov/statfacts/html/breast-subtypes.html;* 2. Research and Markets. Retrieved from: *https://www.researchandmarkets.com/reports/6076080/metastatic-hrher2-breast-cancer-global-market;* 3. Venetis et al. *Cancer Treat Rev 2023;* 4. Laine et al. *Breast Cancer Res 2021; 5.* Adreano et al, *Mol Cancer Ther 2020;* 6. Goldfarb et al, *Clinical Breast Cancer 2024*; 7. Damodaran et. al, *Annals of Oncology 2023;* 8. Goetz et. al, *Annals of Oncology 2023*

Lasofoxifene for the potential treatment of metastatic breast cancer

Small molecule selective estrogen receptor modulator (SERM)

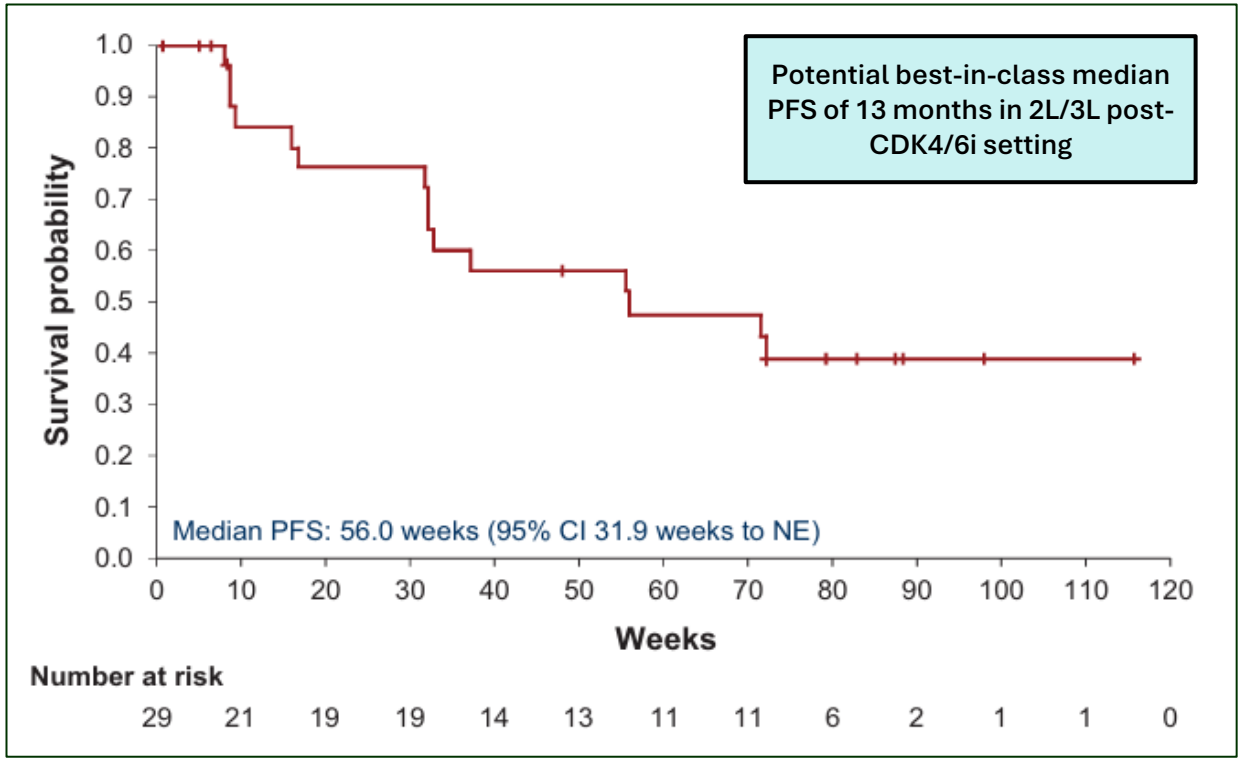
Lasofoxifene: Differentiated SERM for mESR1+ metastatic breast cancer

DESIGNED TO OVERCOME RESISTANCE, IMPROVE QOL, AND REDEFINE THE STANDARD OF CARE AS THE ENDOCRINE PARTNER OF CHOICE

Key Differentiators:

- Potential best-in-class combination efficacy (13 months PFS)[1]
- Recent outcomes (EMBER-3, EvERA) validate the combination approach to 2L+ mBC[2,3]
- Active against WT and mutant ESR1 where SoC can fail
  - Reduced new onset breast cancer by 83% in a large prevention trial[4]
- As the only SERM in the 2L+ mESR1 space, advantages in tolerability, QoL, and additional clinical benefits (bone, urogenital health)[5,6]

Lasofoxifene + Abema combo led to a potential best-in-class median PFS in a heavily pre-treated mESR1 population in Phase 2 ELAINE-2 trial[2]



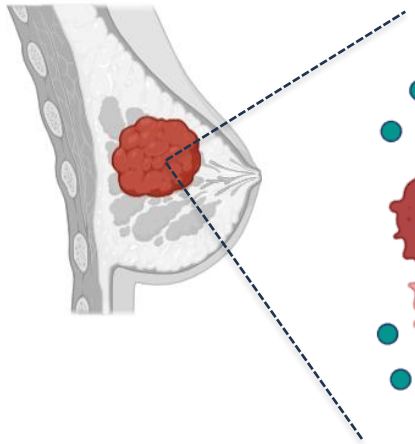
FDA-aligned registrational Phase 3 trial is ongoing

LeonaBio

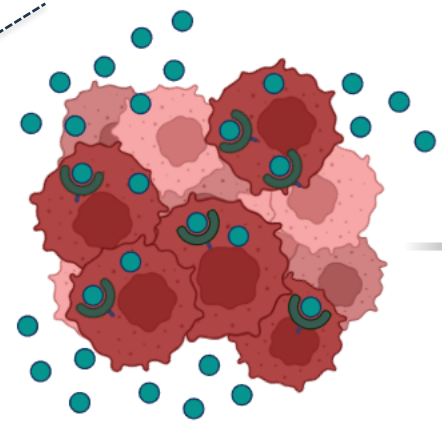
Sources: 1. Damodaran et. al, *Annals of Oncology, 2023; 2.* Jhaveri et al *NEMJ 2024; 3.* Mayer et al, *ESMO 2025;* 4. LaCroix et al, *J Natl Cancer Inst, 2010;* 5. Goldfarb et al, *Clinical Breast Cancer 2024*; 6. Cummings et al. *NEJM 2010;*

Treatment-resistant ER+ breast cancer is a critical unmet need

Global ER+ breast cancer ~1.6M patients[1,2*] → **30% progress to mBC[3] ~480k patients** → **40% acquire ESR1 mutations[4] ~192k patients**

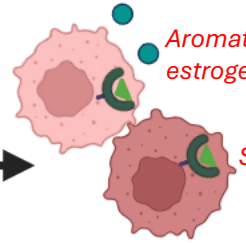


~70% of breast cancers are driven by estrogen receptor signaling (ER+)[2]



1. Initial Tumor
ER+ tumors depend on estrogen signaling via estrogen receptor (ESR1) to grow and survive

2. Therapy response (1L)
1L endocrine therapies (AIs, SERMs, SERDs) are highly effective at shrinking and stabilizing tumor cells

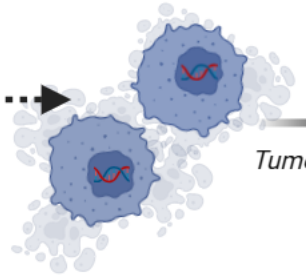


Aromatase inhibitors (AIs) inhibit estrogen production

SERMs inactivate ESR1

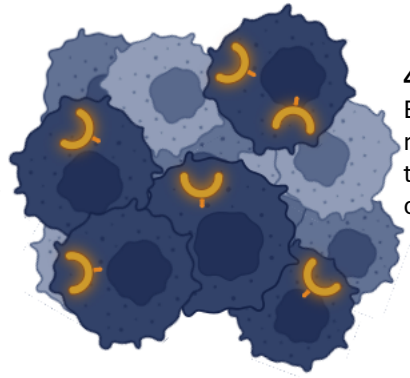
Endocrine therapy

Therapy-induced dormancy

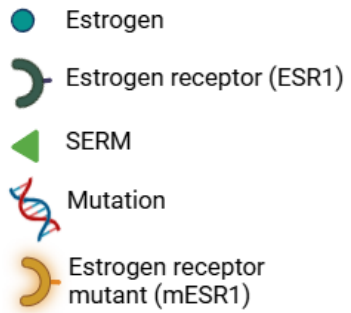


3. Tumor cell dormancy
In response to effective therapies, a portion of tumor cells enter a "quiet" state where they rewire survival pathways via ESR1 activating mutations

Tumor adaptation



4. Tumor resistance
ESR1 mutated tumor cells are resistant to endocrine therapies; lasofoxifene overcomes this resistance



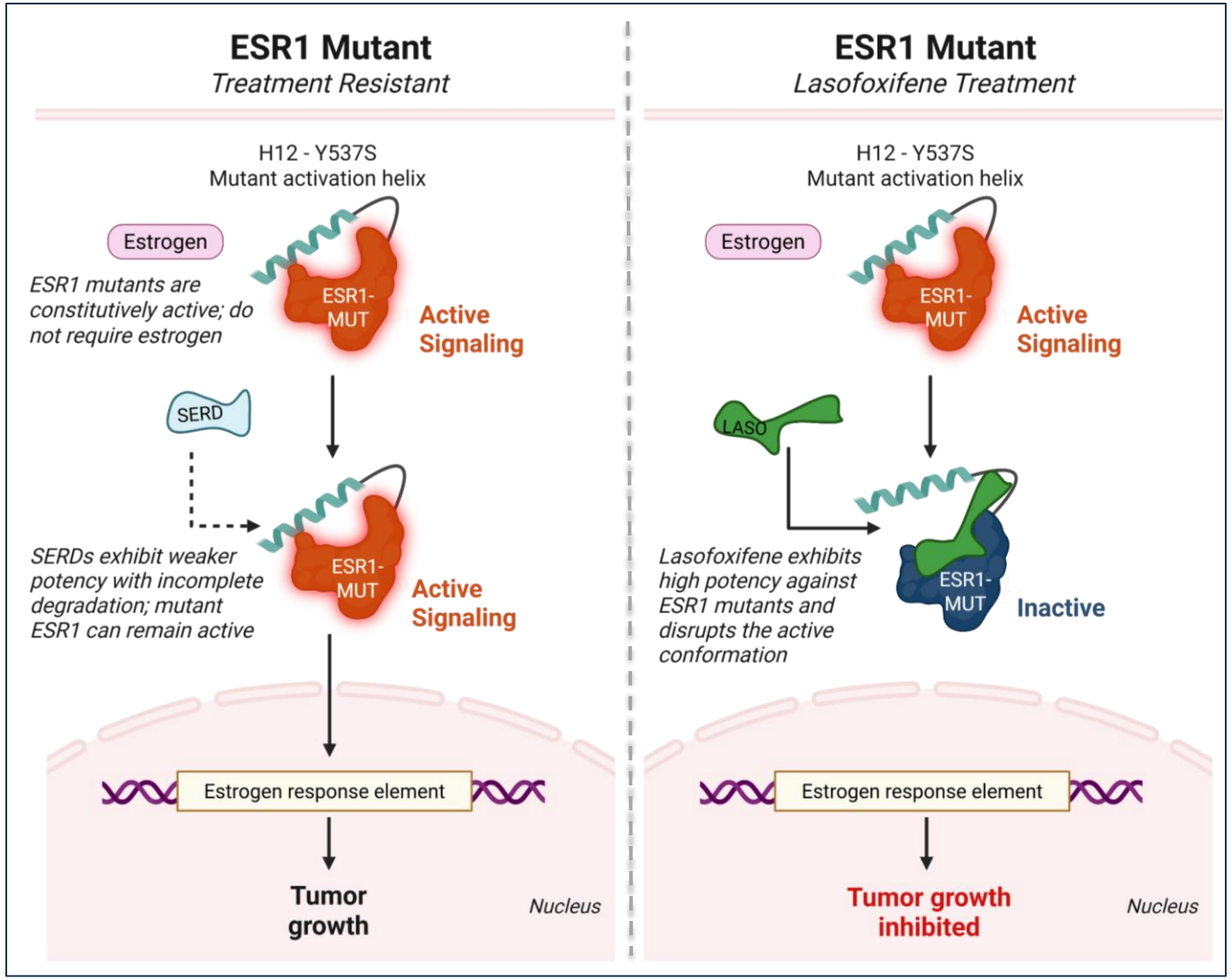
ESR1 activating mutations cause resistance to current therapies; lasofoxifene addresses this critical unmet need

**1.6M estimated using global breast cancer incidence (2.3M; Bray et al) and ER+ prevalence (~70%; NCI)*

Sources: 1. Bray et al. *American Cancer Society 2022;* 2. NCI. *Retrieved from https://seer.cancer.gov/statfacts/html/breast-subtypes.html; 3.* OncLive. *Retrieved from https://www.onclive.com/view/targeted-agents-expand-the-hr-her2-metastatic-breast-cancer-treatment-arena*; 4. Venetis et al. *Cancer Treat Rev 2023.*

Lasofoxifene is a SERM that blocks ESR1 breast cancer signaling even in the presence of mutations

- Active ESR1 signaling drives tumor growth and metastasis in ER+ breast cancer[1]
- Current endocrine therapies (SERDs, SERMs) aim to inhibit ESR1 signaling[2]
- ESR1 mutations cause resistance to endocrine therapies[3]
- Structural features of lasofoxifene inhibit mutant ESR1, overcoming resistance[4,5]



Sources: 1. Miziak et al. *Cancers (Basel) 2023*; 2. Cao et al. *Front Pharmacol 2024*; 3. Venetis et al. *Cancer Treat Rev 2023;* 4. Laine et al. *Breast Cancer Res 2021; 5.* Adreano et al, *Mol Cancer Ther 2020.*

Lasofoxifene retains potency against ESR1 mutations, overcoming a key driver of endocrine resistance

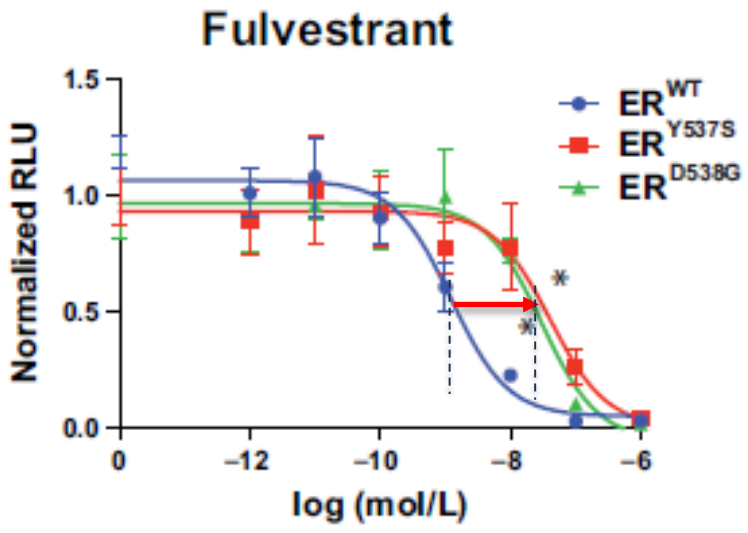
OUTPERFORMS SOC SERDS AND SERMS ACROSS ESR1 MUTATIONS, SUSTAINING INHIBITORY POTENCY, AND DRIVING SUPERIOR ANTI-TUMOR ACTIVITY

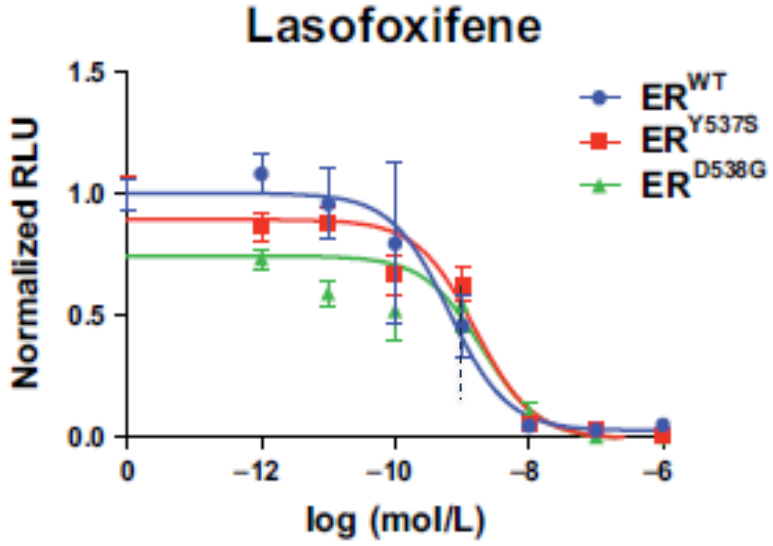
Competitors (e.g., fulvestrant) lose potency against mutant ESR1 → resistance

Lasofoxifene maintains similar potency against WT and mutant ESR1 → sustained inhibition

→

Superior anti-tumor activity in ESR-1 mutant breast cancer models





Adapted from Adreano et al, *Mol Cancer Ther 2020*

Inhibition of proliferation of CAMA-1 ESR1^{Y537S}	
Drug	IC_{50} (nM) ↓
Lasofoxifene	1.9
Vepdegestrant	22
Elacestrant	90
4OH-Tamoxifen	14
Fulvestrant	15
Imlunestrant	13
OP-1250	14

Adapted from Parisian et. al, *Mol Cancer Ther, 2023*

Affinity assay: Tested in luciferase reporter lines transfected with WT or mutant versions of ESR1. ESR1 was stimulated with a constant concentration of 17β-estradiol and inhibition of activation was assessed by reduction in luciferase reporter signal.

Cell proliferation assay: ESR1-mutant cells treated with antiestrogen in the presence of 100 pmol/L E2. Proliferation assessed by CyQUANTreagent is normalized to E2-treated vehicle.

Unique lasofoxifene MOA and pre-clinical data establish PoC in ESR1 mutations

- Lasofoxifene reduces tumor growth in *in vivo* animal models and maintains potency in lines with mutated estrogen receptors[1,2]
- Long half-life (6 days), excellent bioavailability, and volume of distribution optimizes receptor antagonism and tumor engagement[2,3]
- No receptor degradation necessary and lack of DDIs potentially allow for favorable dosing, tolerability, and combinability characteristics

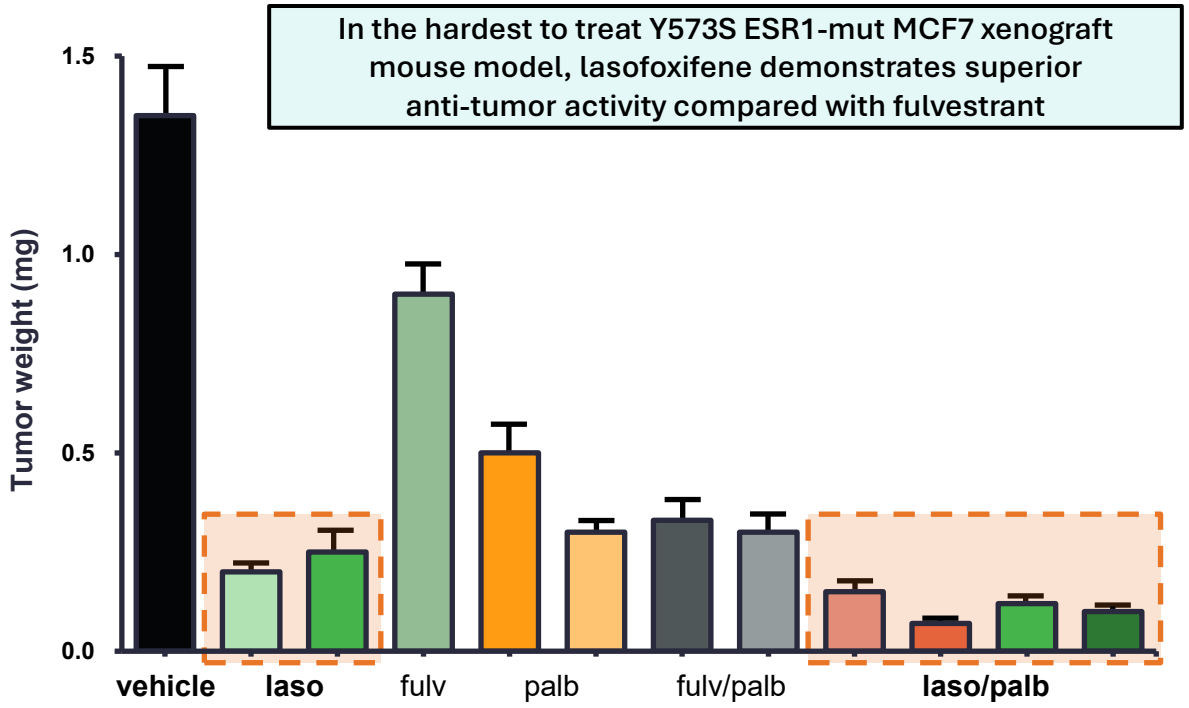


***Figure**: Effect of combination therapies on primary tumor growth in the Y537S ERα mutant model*

Adapted from Laine et. al, *Breast Cancer Ther, 2021*

Figure: Multiple bars under the same group denote different dose combinations

1. Adreano et al, *Mol Cancer Ther 2020;* 2. Laine et al *Breast Cancer Res 2021*; 3. Gennari, *Expert Opin Pharmacother 2009*

ELAINE Program: Stepwise validation toward a new standard of care

ESTABLISHING LASOFOXIFENE AS THE NEXT-GENERATION ENDOCRINE BACKBONE FOR ER+ METASTATIC BREAST CANCER

ELAINE-1	ELAINE-2	ELAINE-3
Proof of Concept (Complete)	*Combination Study (Complete)*	*Registrational Trial (Ongoing)*
Randomized Ph2 trial to demonstrate lasofoxifene's targeted mechanism and establish its activity vs SoC fulvestrant in mutant ESR1+ metastatic breast cancer	Ph2 single-arm study trial to evaluate efficacy of lasofoxifene + abemaciclib (CDK4/6 inhibition) in mutant ESR1+ metastatic breast cancer	Global Ph3 pivotal trial to confirm lasofoxifene's superiority in combination vs SoC fulvestrant and establish laso as new 2L/3L standard of care

Building on an extensive safety database, a systematic step-wise clinical development plan was designed to establish confidence in lasofoxifene through proof-of-concept (ELAINE-1) and a combination study (ELAINE-2), leading to a registrational Phase 3 trial to confirm superiority and establish lasofoxifene as a new standard of care for ER+ metastatic breast cancer

LeonaBio

ELAINE-1: Increased PFS and anti-tumor activity with lasofoxifene compared to SoC fulvestrant in mESR1 population

LASOFOXIFENE CLINICAL ACTIVITY VS. FULVESTRANT (SOC) IN ESR1-MUTANT BREAST CANCER IN A POC PHASE 2 STUDY

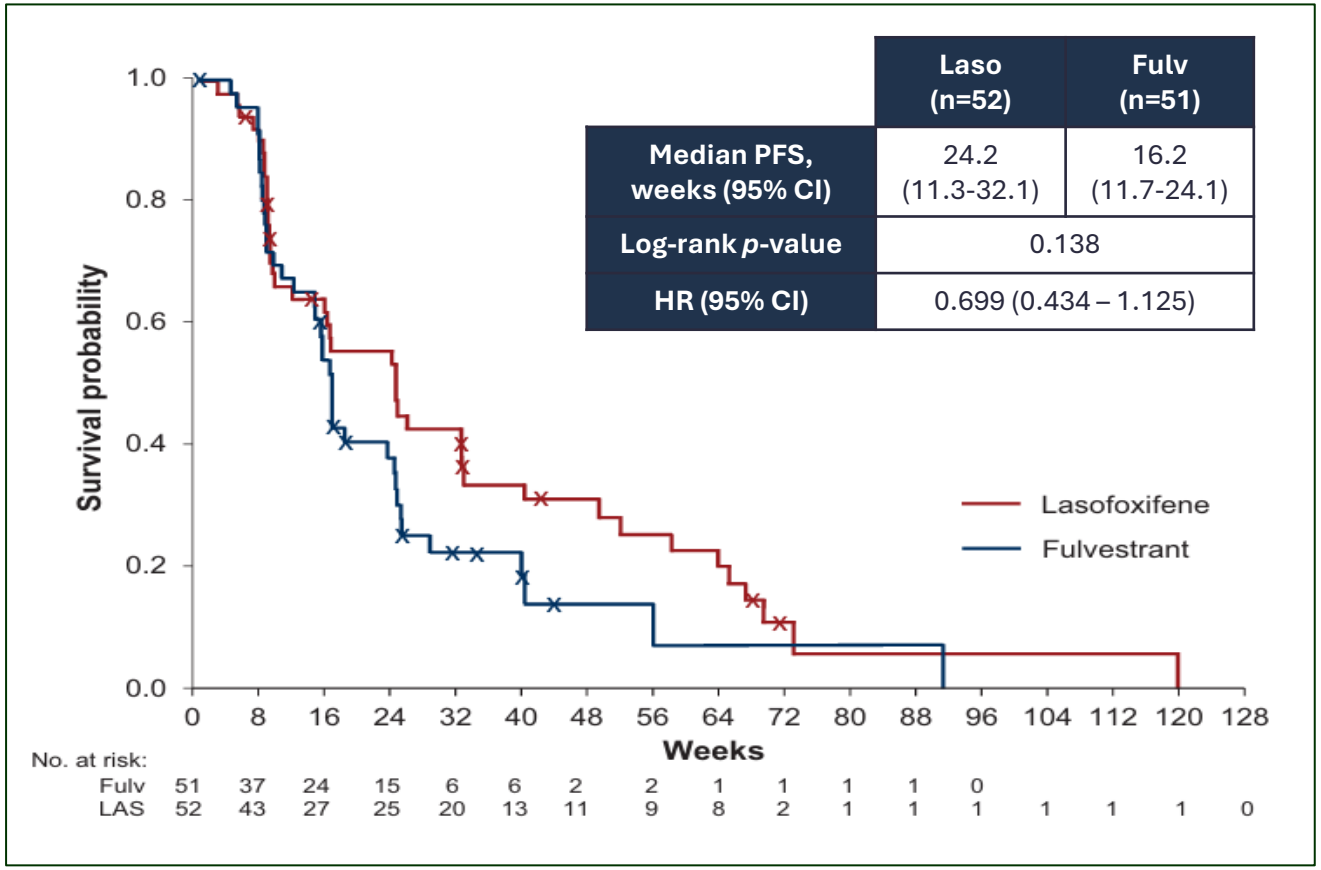
ELAINE-1

Proof of Concept

Clear efficacy advantage: Lasofoxifene delivered longer progression-free survival and higher tumor response rates vs SoC fulvestrant.

Validated targeted approach: ctDNA confirm lasofoxifene's direct activity against ESR1 mutations.

Strong differentiation: Well-tolerated with added quality-of-life benefits, including improvement in urogenital symptoms.



	Laso (n=52)	Fulv (n=51)
Median PFS, weeks (95% CI)	24.2 (11.3-32.1)	16.2 (11.7-24.1)
Log-rank *p*-value	0.138	
HR (95% CI)	0.699 (0.434 – 1.125)	

***Figure**: Kaplan-Meier estimates of progression-free survival*

	Laso	Fulv
CBR	37%	22%
ORR	13%	3%

***Table**: Tumor response rates for lasofoxifene vs fulvestrant*

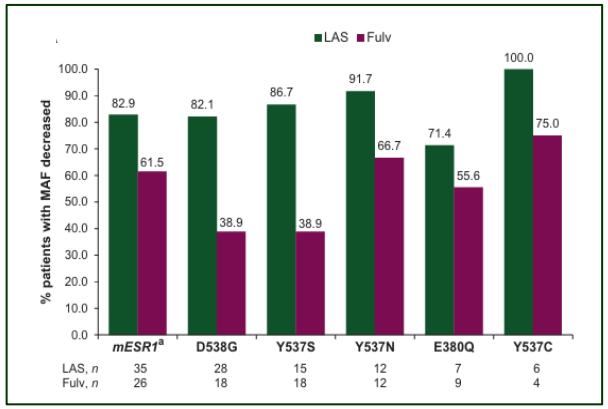


***Figure**: Proportions of patients with ESR1 mutant allele fraction decreased with lasofoxifene treatment*

HR, Hazard ratio

Source: Goetz et. al, *Annals of Oncology 2023.*

ELAINE-2: Demonstrated potential best-in-class 13 months PFS with lasofoxifene combination with abemaciclib in a heavily pre-treated mESR1 population

LASOFOXIFENE COMBINATION WITH CDK4/6I ABEMACICLIB IN ESR1-MUTANT BREAST CANCER, 100% PRIOR CDK4/6I (PHASE 2)

ELAINE-2

Combination Study

Potential best-in-class durability: Laso+Abema delivered 13-month (56 weeks) median PFS – among the longest seen in 2L/3L post-CDK4/6i.

Strong efficacy: High tumor response (56% ORR, 66% CBR) with durable disease control

Robust biology: Deep ctDNA and ESR1 clearance correlated with PFS, with benefits extending even to patients with co-mutations.

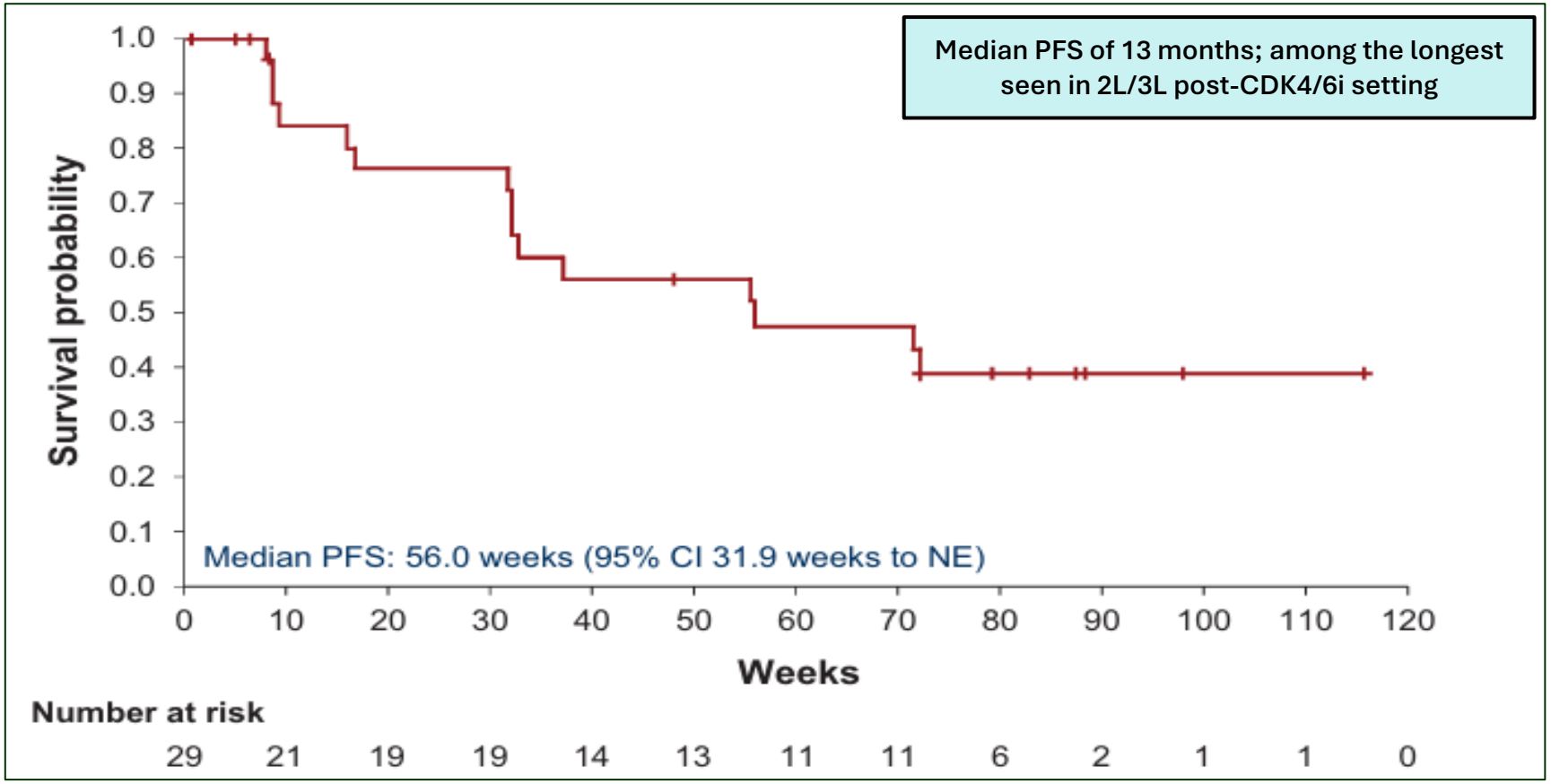


***Figure**: Kaplan-Meier estimates of progression-free survival*

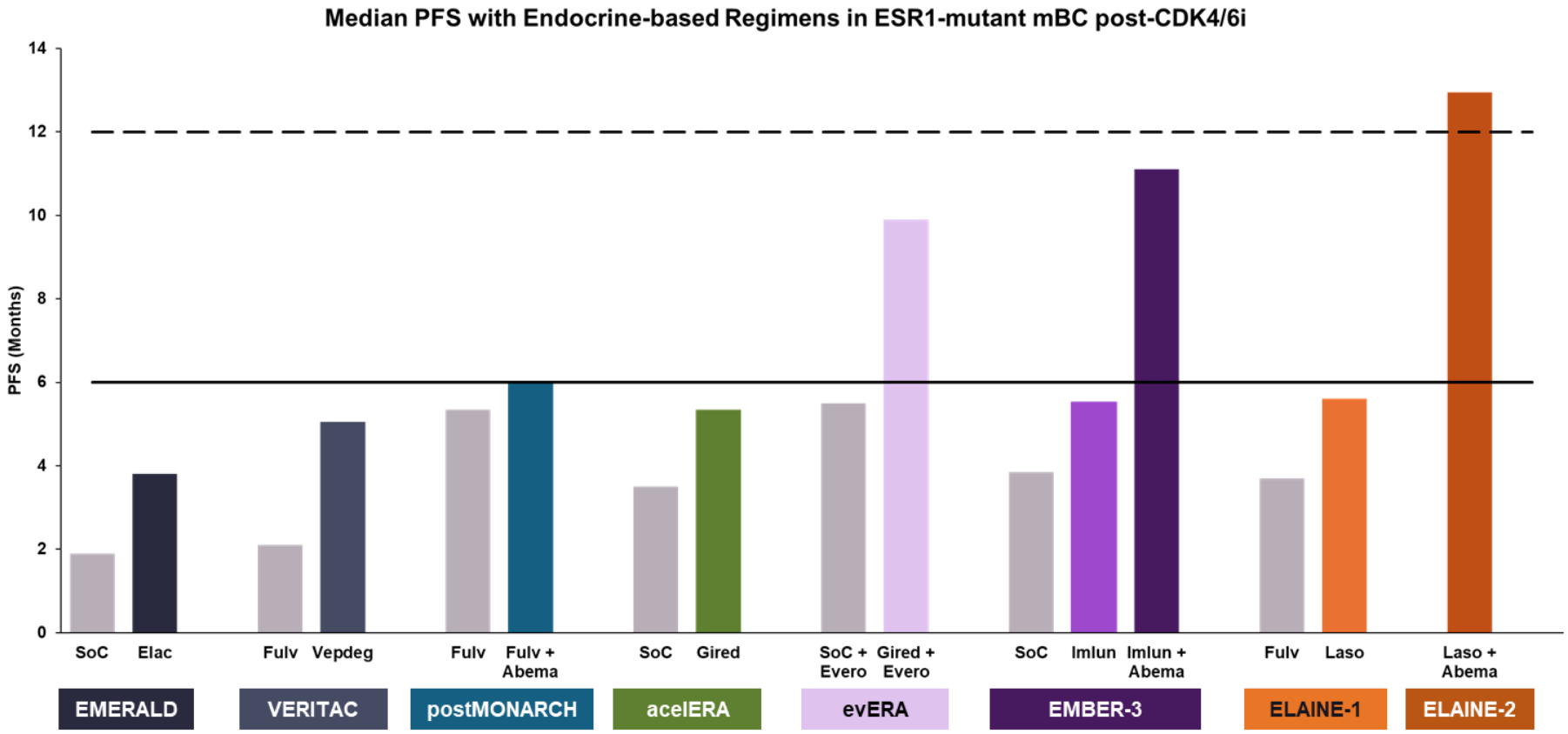
No head-to-head trials have been conducted comparing lasofoxifene combination regimens to SoC combination regimens. Therefore, such data may not be directly comparable due to differences in trial protocols, dosing regimens, and patient populations. Accordingly, these cross-trial comparisons should not be relied on.

Source: Damodaran et. al, *Annals of Oncology 2023*.

Treatment landscape is shifting toward combination regimen

EMERGING DATA SUPPORT COMBINATION ENDOCRINE APPROACHES IN CDK4/6 INHIBITOR–PRETREATED ER+ BREAST CANCER

- In the 2L+ space, endocrine monotherapy approaches appear to reach a ceiling of ~6 months PFS
- Durable disease control is increasingly pursued through biomarker-driven combination strategies, rather than next-generation endocrine monotherapy alone
  - With combination therapy, safety and tolerability become even more important
- With combination therapy, particularly laso + abema, median PFS can extend beyond 12 months, surpassing the one-year benchmark in 2L+ post-CDK4/6 ESR1-mutant disease
  - No stacking of toxicity, laso + abema was well-tolerated with favorable safety profile



Abema, abemaciclib; Elac, elsacestrant; Evero, everolimus; Fulv, fulvestrant; Gired, girdestrant; Imlun, imlunestrant; Laso, lasofoxifene; SoC, standard-of-care; Vepdeg, vepdegestrant

Comparisons are based on independently published study results. No head-to-head trials have been conducted comparing lasofoxifene combination regimens to SoC combination regimens. Therefore, such data may not be directly comparable due to differences in trial protocols, dosing regimens, and patient populations. Accordingly, these cross-trial comparisons should not be relied on. Sources: EMERALD – Bardia et al, *SABCS 2021*; VERITAC – Campone et al, *NEMJ 2025*; postMONARCH – Kalinsky et al, JCO 2024; acelERA – Martin et al, *ESMO 2022*; evERA – Mayer et al, *ESMO 2025*; EMBER-3 – Jhaveri et al *NEMJ 2024*; ELAINE-1, Goetz et al, *Annals of Oncology 2023*; ELAINE-2 – Damodaran et. al, *Annals of Oncology 2023*

LeonaBio

ELAINE-3: Registrational trial of lasofoxifene in mESR1 population

FDA-ALIGNED PH3 REGISTRATIONAL TRIAL TO ESTABLISH IMPROVED EFFICACY OF LASOFOXIFENE + ABEMACICLIB COMPARED TO CURRENT SOC COMBINATION

Screening (30 days)

Key Inclusion Criteria

- Pre- or post- menopausal women or men
- Positive ESR1 mutation
- Locally advanced or metastatic ER+/HER2- breast cancer
- Measurable disease
- Evidence of progression on AI with either palbociclib or ribociclib

Randomization (1:1)

Stratification Factors:

1. Visceral vs. non-visceral disease
2. Prior chemotherapy in metastatic setting
3. Prior use of palbociclib or ribociclib

Treatment Period (up to 48 mo)

5 mg QD lasofoxifene
+ 150 mg BID abemaciclib
N ≈ 300

500 mg monthly fulvestrant (IM)
+ 150 mg BID abemaciclib
N ≈ 300

Study Outcomes

Primary Endpoint

- Progression-free survival

Key Secondary Endpoints

- Objective response rate, overall survival

Other Secondary Endpoints

- Clinical benefit rate, duration of response, time to response, time to cytotoxic chemotherapy, quality of life, and safety

Study Milestones

- ***FPI:*** *1Q2024 (recruiting)*
- ***LPI:*** *Expected 2H2026*
- ***Topline:*** *Expected 2H2027*

ELAINE-3 aims to demonstrate the potential of lasofoxifene as a new standard-of-care for ESR1-driven post-CDK4/6i metastatic breast cancer

Adapted from Goetz et. al, *Future Oncology, 2025.*

ELAINE-3 is on track to complete enrollment in 2H2026

OVER 50% ENROLLED – EXPECTED TO READOUT IN 2H2027

- Global study with >200 sites Europe, North America, and APAC (including China)
- Study is being executed by Medpace, a full-service global CRO with extensive experience running large, successful breast cancer trials
- Primary endpoint is determined by an independent review of centralized scans using industry standard RECIST criteria
- Primary readout conducted when 285 patients have been determined as meeting the RECIST criteria for progression

Lasofoxifene was generally well-tolerated and had a differentiated impact on women's quality of life over standard of care in early trials

- Lasofoxifene is a SERM that primarily reduces estrogen signaling in breast tissue sparing healthy signaling in other tissues such as bone and urogenital
- Participants in the ELAINE-1 trial participated in self-assessed urogenital symptom surveys[1]
- Lasofoxifene treatment tended to **reduce** incidence of VAS/VuAS symptoms
  - Fulvestrant, the SoC comparator tended to increase symptoms

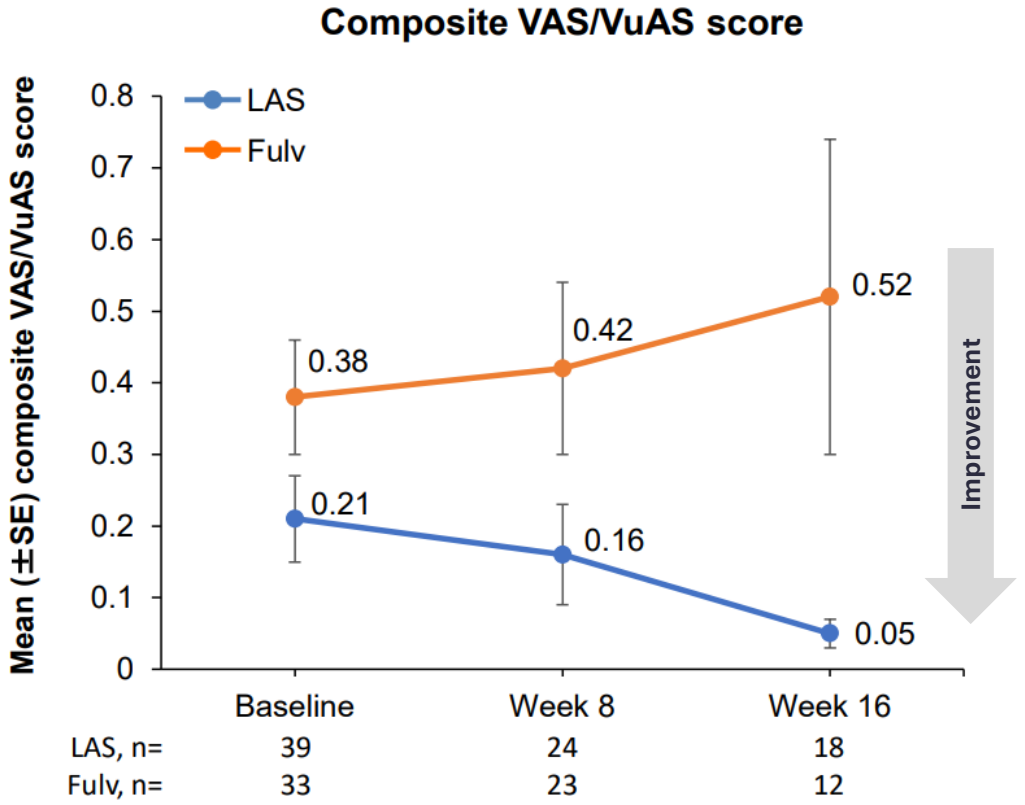


Figure: *Self-assessed urogenital symptoms (composite VAS/VuAS) for lasofoxifene vs fulvestrant.*

"Lasofoxifene is reported to promote vaginal and sexual health benefits [...] **this could have broad implications for both the survival and quality of life for women** in the metastatic and early-stage adjuvant settings." [2]

MD, the iSPY-2 EOP study's principal investigator

VAS, vaginal assessment scale; VuAS, vulvar assessment scale

Sources: 1. Goldfarb et al. *ISSWSH Annual Meeting 2023 (Poster)*; 2. Sermonix Conf Presentation (Slide #82).

Lasofoxifene exhibits added clinical benefits over other endocrine therapies important to breast cancer patients and clinicians

- The effects of lasofoxifene have been extensively investigated in several clinical studies
  - Increased bone density and reduced vertebral and non-vertebral fractures[1,2]
  - Reduced LDL and coronary heart disease events [2,3,4]
  - Improved symptoms of vaginal atrophy in two Phase 3 studies[5]

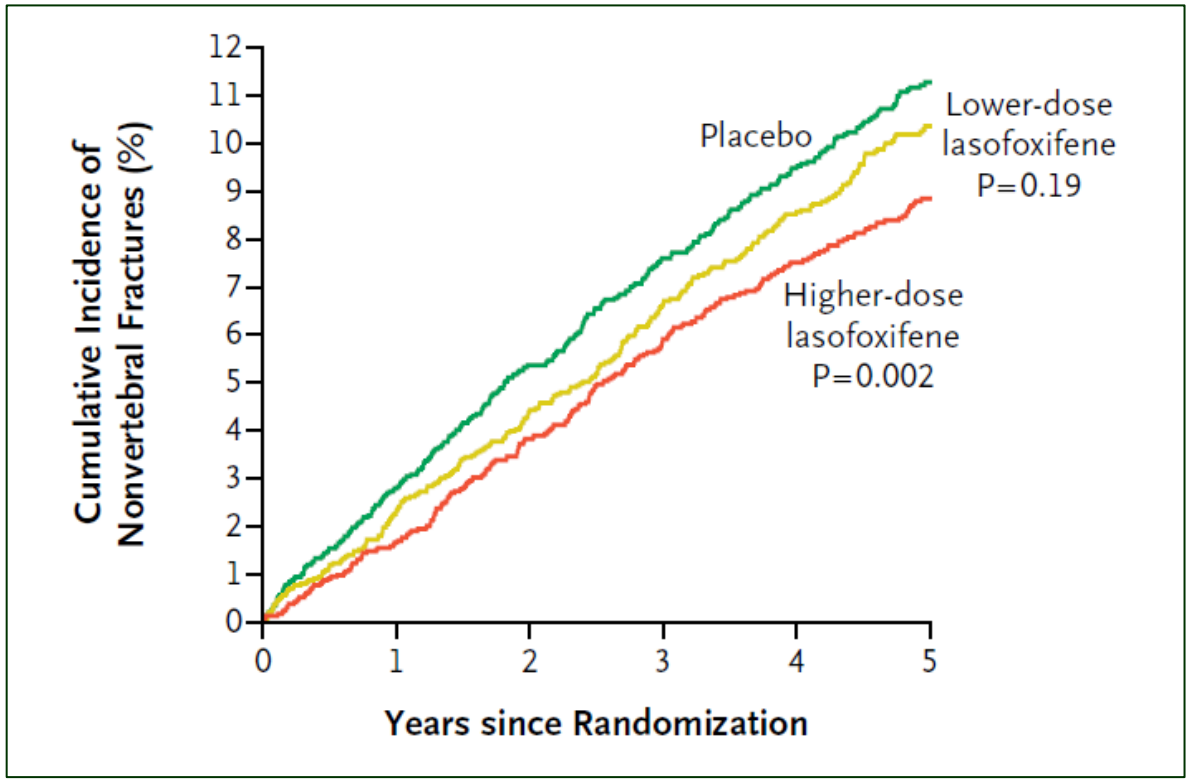


Figure: *Cumulative incidence of nonvertebral fractures showing placebo, lasofoxifene 0.25 mg (low dose), lasofoxifene 5 mg (high dose)*

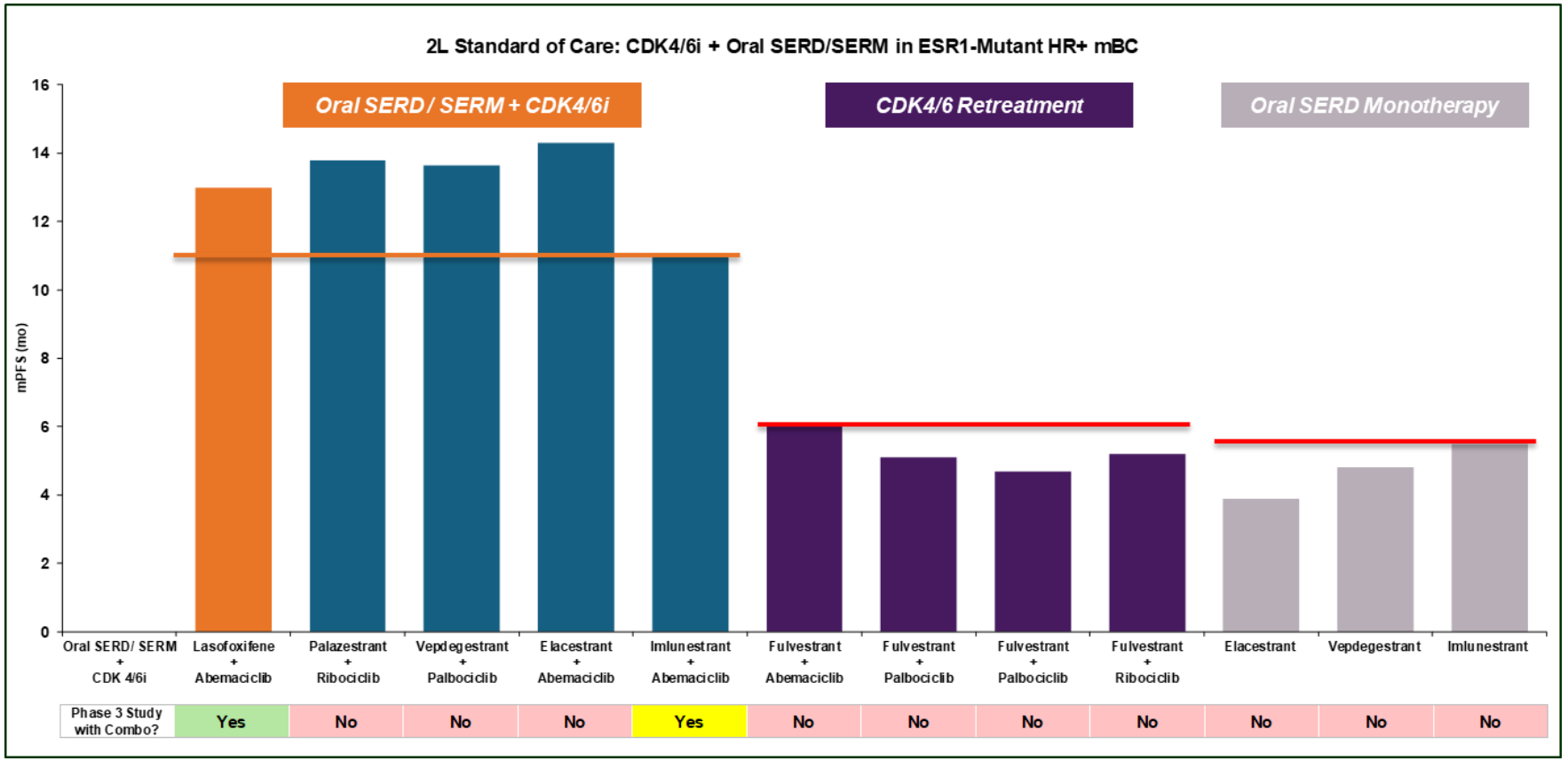
No head-to-head trials have been conducted comparing combination lasofoxifene therapy to other endocrine therapies

Sources: 1. McClung et al. *American Society of Bone and Mineral Res Annual Meeting 2015 (Poster)*;
2. Cummings et al. *NEJM 2010*; 3. Lewiecki et al., *Ther Clin Risk Manag. 2009*; 4. Ensrud et al *Circulation AHA Journal, 2010*; 5. Kagan et al., *Menopause 2024*

ELAINE-3 is a registrational Phase 3 program

BUILT ON ESTABLISHED BIOLOGY, PRIOR CLINICAL SIGNAL, AND ESTABLISHED STANDARD-OF-CARE BENCHMARKS

- ✓ **Clear, validated comparator:** Fulv + abema is a well-established 2L SoC in mESR1 mBC, enabling a clear and interpretable superiority test
- ✓ **Promising prior efficacy signal:** ~13 mo PFS exceeds historical benchmarks
- ✓ **Mechanistically differentiated backbone:** SERM profile enables mESR1 suppression with favorable tolerability and potential for added clinical benefit
- ✓ **Aligned with emerging treatment paradigm:** Oral SERD/SERM + CDK4/6i combinations increasingly defining the post-CDK4/6 treatment landscape



Comparisons are based on independently published study results. No head-to-head trials have been conducted comparing lasofoxifene combination regimens to SoC combination regimens. Therefore, such data may not be directly comparable due to differences in trial protocols, dosing regimens, and patient populations. Accordingly, these cross-trial comparisons should not be relied on. Sources – Laso+abema: Damodaran et. al, *Annals of Oncology 2023;* Palazestrant + Ribo: Olema oncology, *ESMO 2025*; Vepdegestrant + Palbociclib: Arvinas and Pfizer, *ESMO 2024*; Elacestrant + abema: Rugo et al, *SABCS 2025*; Imlunestrant + abema: Jhaveri et al *NEMJ 2024*; Fulvestrant + abema: Kalinsky et al, *JCO 2024*; Fulvestrant + Palbociclib (2): Mayer et al, *JCO 2024*; Fulvestrant + Ribociclib: Kalinsky et al, *JCO 2023*; Elacestrant monotherapy: Bidard et al, *JCO 2022*; Vepdegestrant monotherapy: Campone et al *NEJM 2025;* Imlunestrant monotherapy: Jhaveri et al *NEMJ 2024*

LeonaBio

Competitive advantages of Laso combo in 2L/3L ESR1-mutant BC

Lasofoxifene profile:

- ✓ Differentiated MOA
- ✓ Competitive efficacy profile
- ✓ Strong safety and tolerability profile
- ✓ Exhibits QoL & clinical benefits over SERDs
- ✓ Large pivotal Phase 3 (n ≈ 600) underway in all post-CDK4/6i ESR1 mutations to support potential registration
- ✓ FDA-recommended combination comparator as opposed to monotherapy in EMBER-3

	Imlunestrant + Abema[1,2]	Lasofoxifene + Abema[3,4]
Administration	Oral, 400 mg daily tablet, must be taken fasting	Oral, 5 mg daily tablet, no food effect
MOA	SERD (ER degradation)	**SERM** (ER modulation; tissue selectivity)
Efficacy	EMBER-3, mESR1 population, 60-75% prior CDK4/6i: PFS 11.1 mo (n=67) ORR 39% (n= 54)	ELAINE-3, mESR1 population, 100% prior CDK4/6i: **PFS ~13 mo** (n=29) **ORR 56%** (n=29)
Safety & Tolerability	• Dose reductions: 42% • Grade 3 diarrhea: 9% • Anemia: 46%	• **Dose reductions: 21%** • **Grade 3 diarrhea: 0%** • **Anemia: 28%**
QoL & Clinical Benefits	• None	• **Improved urogenital symptoms (ELAINE-1)** • **Potential bone density and lipids health benefits (PEARL, CORAL, OPAL studies)**

Ongoing Phase 3 registrational trial (ELAINE-3) will directly evaluate lasofoxifene + abema vs fulvestrant + abema (SoC) and potentially establish lasofoxifene as endocrine backbone 2L/3L SOC

ER, estrogen receptor; SERD, selective estrogen receptor degrader; SERM, selective estrogen receptor modulator; ESR1 (gene), estrogen receptor 1; ORR, objective response rate; QoL, Quality of life; PFS, progression-free survival. Comparisons are based on independently published study results. No head-to-head trials have been conducted comparing combination lasofoxifene therapy to other combinations presented in this slide. Therefore, such data may not be directly comparable due to differences in trial protocols, dosing regimens, and patient populations. Accordingly, these cross-trial comparisons should not be relied on. Sources: 1. Jhaveri et al, *NEJM 2025*; 2. Jhaveri et al *SABCS presentation 2025*; 3. Goldfarb et al. *ISSWSH Annual Meeting 2023 (Poster)*; 4. Damodaran et. al, *Annals of Oncology 2023*.

Endocrine backbone choice drives long-term risk and differentiation

LASOFOXIFENE + ABEMACICLIB vs. SERD + CDK4/6I REGIMENS

Safety and tolerability

- While cross trial comparisons should be interpreted with caution, lasofoxifene exhibits a favorable safety and tolerability profile, specifically with regards to dose reduction and serious AEs, and additional QoL benefits
  - No stacking with abemaciclib for diarrhea

Combination treatment strategy drives long-term risk

- Regimens rely on chronic CDK4/6 inhibition, which defines the dominant toxicity burden
- Endocrine backbone choice therefore determines **safety risk, tolerability, combinability and long-term adherence**

Chronic exposure considerations

- Oral SERDs are entering longer-duration use across lines and combinations
- While short-term safety is reassuring, SERD chronic toxicity profiles are still maturing, and longer-term use may impact ER in healthy tissues (e.g. bone, vagina)
- SERMs bring decades of human exposure and predictable long-term safety characteristics

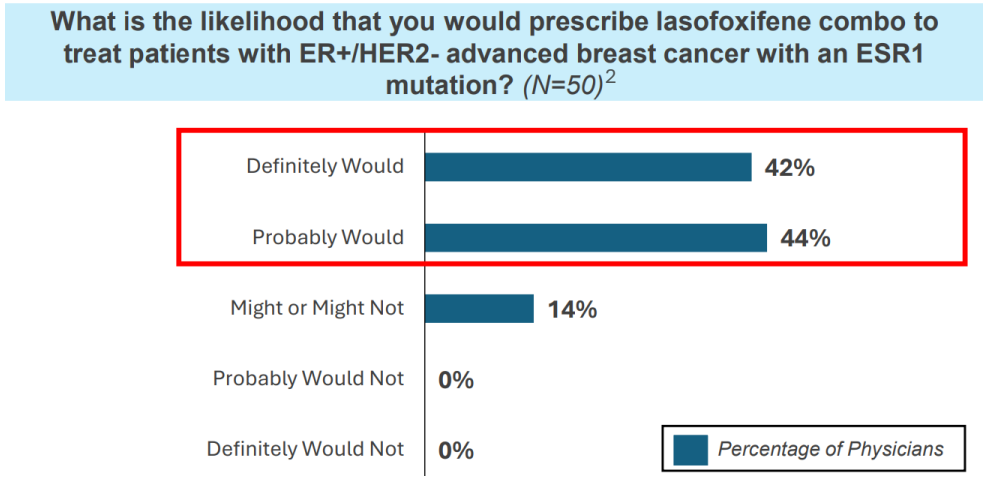
Lasofoxifene has the potential to deliver durable efficacy, minimize long-term safety risks, and provide QoL and clinical benefits that may position it as the next backbone endocrine therapy

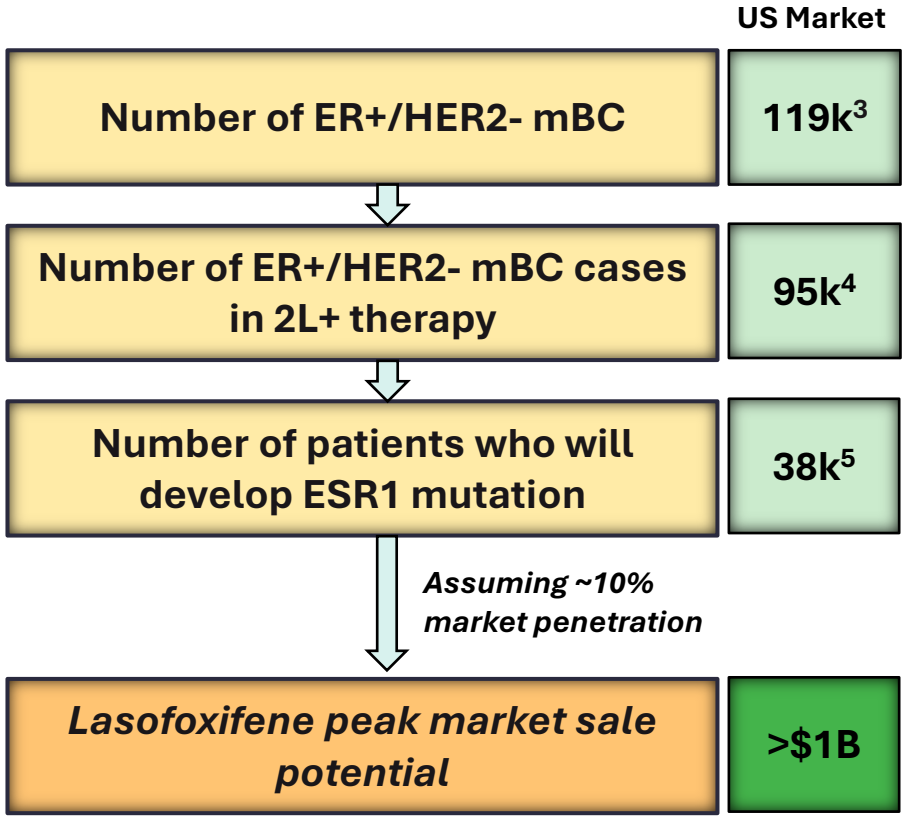
LeonaBio

Comparisons are based on independently published study results. No head-to-head trials have been conducted comparing combination lasofoxifene therapy to other combinations presented in this slide. Therefore, such data may not be directly comparable due to differences in trial protocols, dosing regimens, and patient populations. Accordingly, these cross-trial comparisons should not be relied on.

Lasofoxifene's targeted activity in mutant ESR1 presents a billion-dollar precision oncology opportunity in 2L/3L ER+ mBC

- **Global breast cancer market:** $55B (2027)[1]
- **Expected payer acceptance:** Fulvestrant, elacestrant precedents
- **Favorable outlook:** Physician enthusiasm and QoL advantages may help increase adherence and compliance





Sources: 1. Fortune Business Insights. *Retrieved from https://www.fortunebusinessinsights.com/industry-reports/breast-cancer-therapeutics-market-100163*; 2. LifeSci 1Q2023 Quantitative Survey, Sermonix; 3. Calculated from Komen MBC prevalence (~170k) × NCI ER+/HER2− share (~70%), Komen: *Retrieved from https://www.komen.org/breast-cancer/facts-statistics/breast-cancer-statistics*, NCI: *Retrieved from https://seer.cancer.gov/statfacts/html/breast-subtypes.html*; 4. Calculated based on 80% transition to 2L+ (Almekinders et al. *Breast Cancer Res Treat 2025*); 5. Calculated based on 40% ESR1 mutation incidence (Venetis et al. *Cancer Treat Rev 2023*).

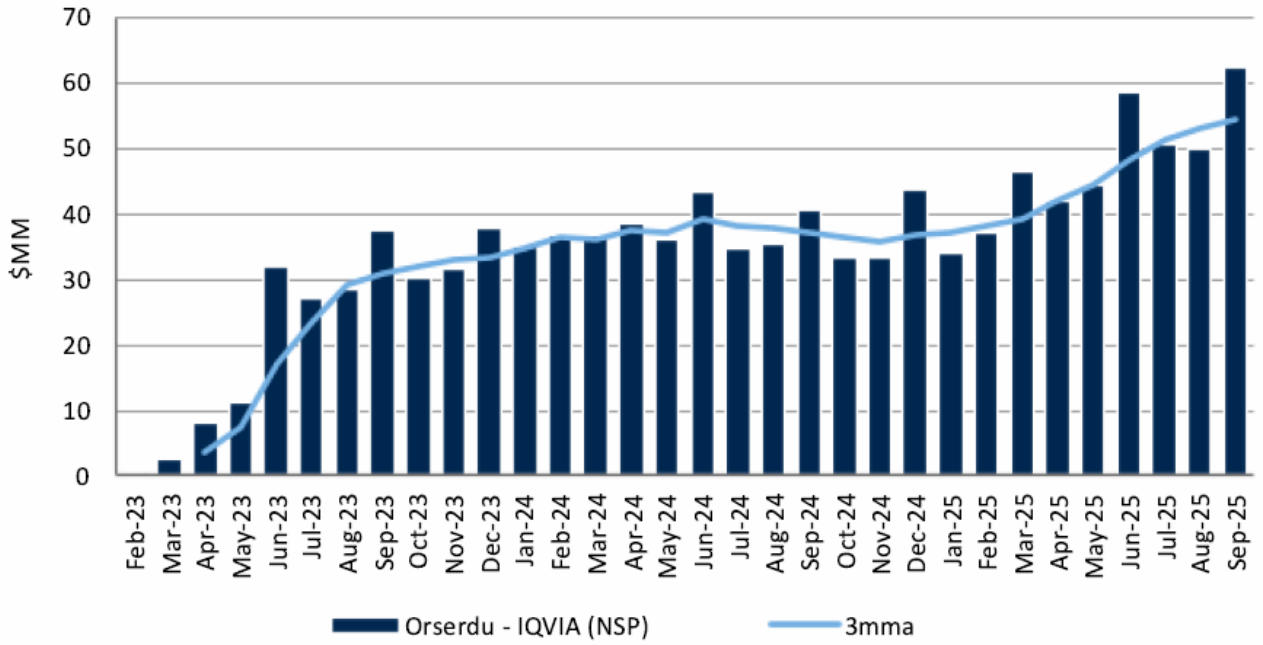
Orserdu sales illustrate the commercial opportunity for lasofoxifene's precision oncology opportunity in 2L/3L ER+ mBC

- **Orserdu (elacestrant) achieved rapid commercial uptake**, validating ESR1 mutation as a commercially viable biomarker
- **Commercial success** was achieved despite modest clinical efficacy with PFS of ~4 months and low ORR in post-CDK4/6 setting[2]
- **Adoption occurred despite notable tolerability challenges**, including GI adverse events and lipid abnormalities, underscoring strong physician willingness to use targeted endocrine agents in ESR1-mutant disease

Lasofoxifene has the potential to meaningfully expand this validated market, with:

- ✓ Superior efficacy signals including prolonged PFS
- ✓ Improved tolerability, QoL profile, and exhibits added clinical benefits
- ✓ Combination-ready positioning aligned with evolving treatment paradigm

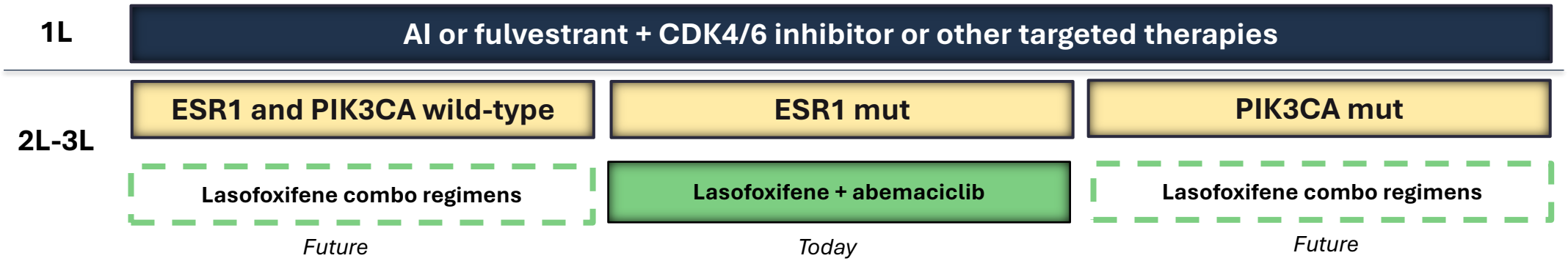
Orserdu sales[1]



Sources: 1. IQVIA, *RBC Capital Markets*; 2. Bidard et al, *J Clin Oncol 2022*

Lasofoxifene has the potential to be a backbone endocrine candidate with expansion potential beyond ESR1 mutant disease

DRIVEN BY COMBINABILITY, TOLERABILITY, AND DIFFERENTIATED CLINICAL BENEFIT



<u>If lasofoxifene demonstrates superiority vs fulvestrant</u>, we believe it has the potential to:

- Replace fulvestrant as the preferred endocrine partner in CDK4/6-based regimens
- Expand beyond ESR1-mutant disease into broader post-CDK4/6 populations with other targeted therapies
- Opportunity to move into earlier lines including the adjuvant setting, and serve as a more tolerable and combinable endocrine backbone

LeonaBio

Treatment landscape schematic is illustrative and not intended to be comprehensive

Lasofoxifene: Ongoing registrational Phase 3 trial with readout in 2027

A DIFFERENTIATED THERAPY DESIGNED TO OVERCOME RESISTANCE, IMPROVE QOL, AND ESTABLISH A NEW STANDARD OF CARE IN ER+ ESR1-MUTANT BREAST CANCER

- Oral administration
- Large unmet need
- Superior PFS from Ph2
- Favorable safety profile and generally well-tolerated
- Exhibits improved QoL and clinical benefits
- Expansion potential as endocrine partner of choice

LeonaBio

ATH-1105 for the potential treatment of ALS

Small molecule positive modulator of HGF

Slowing neurodegeneration in ALS is a critical unmet need

Burden of ALS

ALS is a devasting neurodegenerative disease in which people progressively lose muscle control

- 225,000 people globally affected by ALS[1] with ~33,000 of those cases in the US[2]
- Average life expectancy is 2-5 years post-diagnosis[3]
- Every 90 minutes someone is diagnosed with ALS[4]
- Estimated annual out-of-pocket cost for care is $250,000[5]

Treatment Limitations[6]

- There is no cure for ALS and few effective treatment options
- Approved therapies only modestly slow progression and improve survival
- No current ALS drugs significantly protect motor neurons from the complex pathology and progressive degeneration

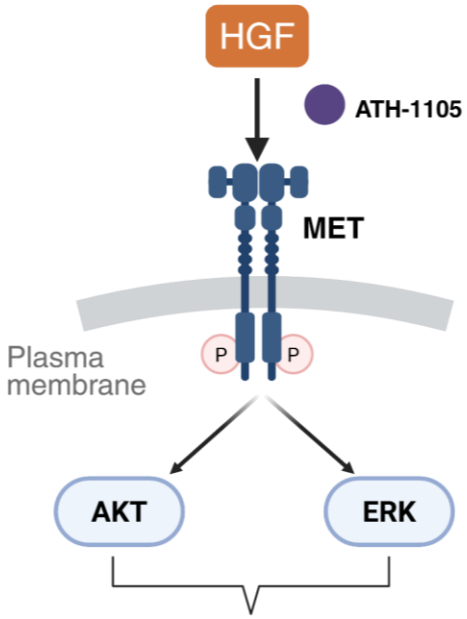
Significant Unmet Need

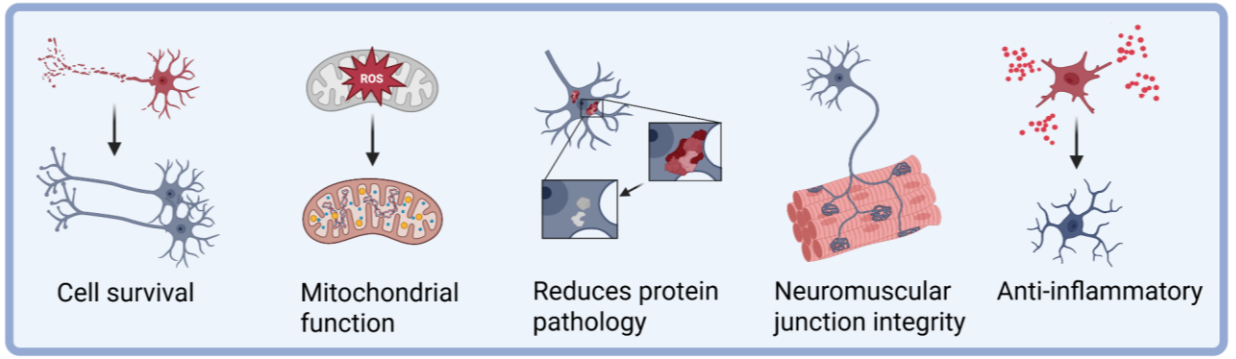
There is an urgent need for therapies that meaningfully slow neurodegeneration, preserve motor function, improve quality of life, and prolong survival

Sources: 1. Packard Center. *Retrieved from https://packardcenter.org/answer-als-partners-to-launch-the-end-als-challenge-digital-competition*; 2. CDC. *Retrieved from https://www.cdc.gov/als/php/abstracts-publications-reports/prevalence-2022-2030.html*; 3. ALS United. *Retrieved from https://alsunitedchicago.org/als-life-expectancy-by-age/*; 4. ALS Association. *Retrieved from https://www.als.org/understanding-als*; 5. ALS Association. *Retrieved from https://www.als.org/advocacy/federal-public-policy-priorities*; 6. ALS Association. *Retrieved from https://www.als.org/navigating-als/living-with-als/therapies-care.*

ATH-1105: A CNS-penetrant positive modulator of HGF as a potential treatment for ALS

- ATH-1105 enhances activity of HGF, a critical neurotrophic factor in the nervous system
- Activation of HGF signaling through MET (HGF receptor) on the surface of neurons and glia initiates processes that counteract neurodegeneration
- Strong rationale from literature to support HGF modulation in ALS
  - Improves motor function, preserves motor neurons, and delays disease progression[1,2,3]
- ATH-1105 has demonstrated robust effects in preclinical models of ALS[4]



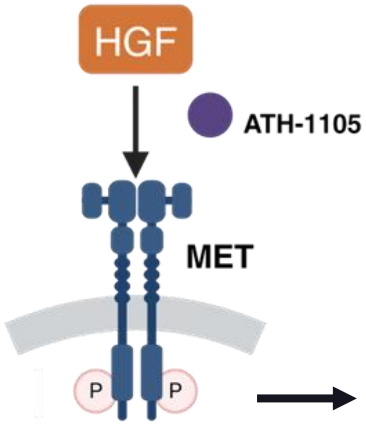


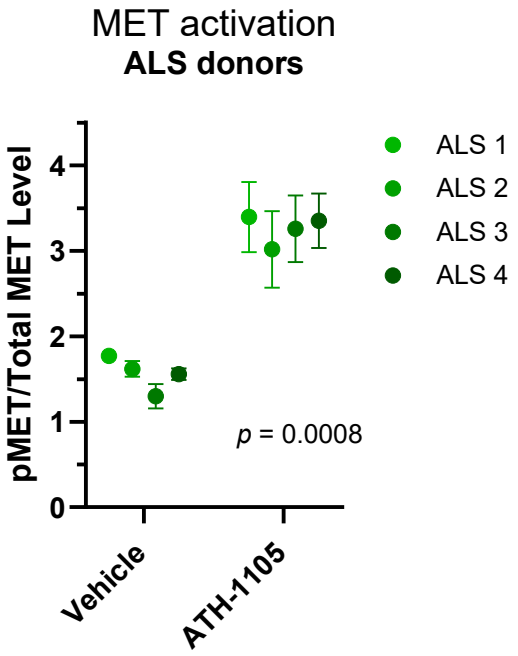
HGF, hepatocyte growth factor

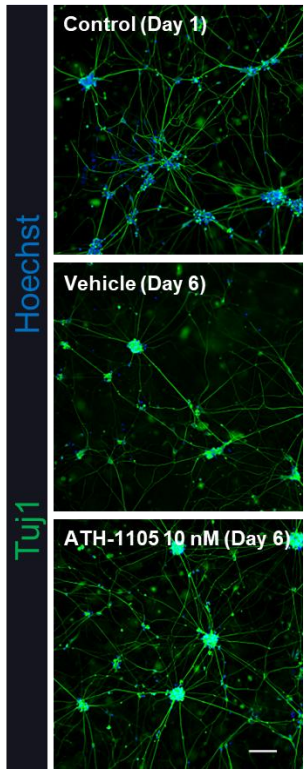
Sources: 1. Ishigaki et al., *J Neuropathol Exp Neurol 2007*; 2. Lee et al., *Acta Neuropathol Commun 2019*; 3. Vallarola et al., *Int J Mol Sci 2020*; 4. Berthiaume et al., *Front. Neurosci 2024*.

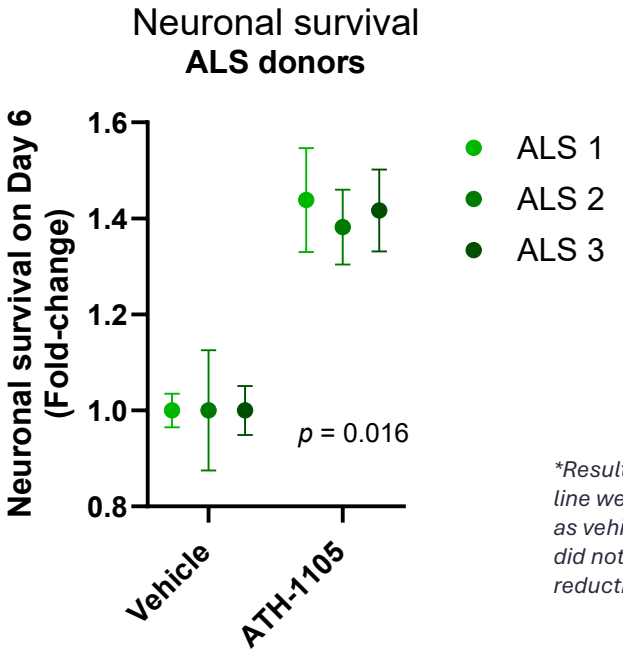
ATH-1105 enhanced MET activation and survival in ALS-patient derived motor neurons

CELLS DERIVED FROM FOUR PEOPLE WITH SPORADIC ALS









**Results from ALS 4 cell line were uninterpretable as vehicle-treated group did not exhibit a significant reduction in survival.*

ALS patient-derived motor neurons treated with ATH-1105 exhibited an increase in MET activation (pMET) resulting in improved neuronal survival confirming neuroprotective activity in ALS relevant tissue

MET activation: Data presented as mean ± SEM. Statistical significance was determined via paired t-test comparing MET activation (pMET/Total MET) in motor neurons treated with vehicle or ATH-1105 10 nM for 24 hours ; n = 2-3 technical replicates from each donor. Neuronal survival: Representative image highlighting effect of ATH-1105 on ALS patient-derived motor neurons (ALS 1) in culture. Neuronal survival (number of Tuji1+ neurons) was measured as surviving neurons on Day 6 divided by number of neurons on Day 1 (control expressed as 100%). Scale bar = 100 µm. Data expressed as fold-change between vehicle and ATH-1105 and presented as mean ± SEM. Statistical significance was determined via paired t-test comparing vehicle (containing HGF 0.05 ng/ml) with ATH-1105 10 nM; n = 3-6 technical replicates from each donor . Select doses shown.

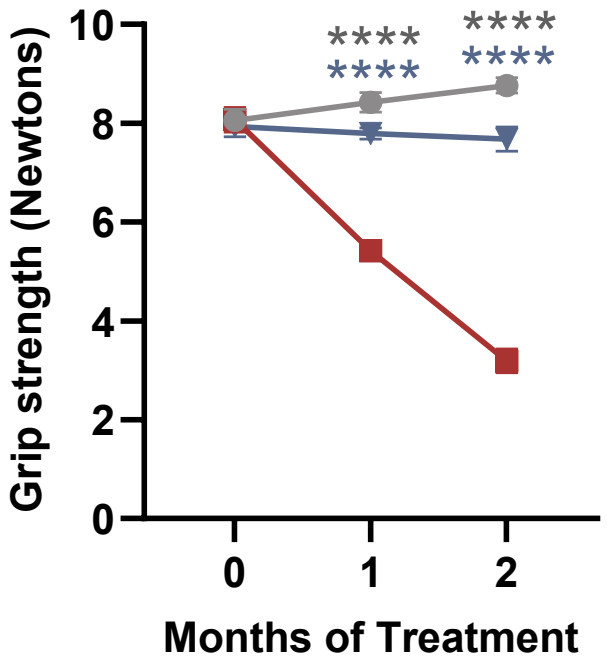
Source: Reda et al. *ALS Drug Development Summit 2025 (Poster)*.

LeonaBio

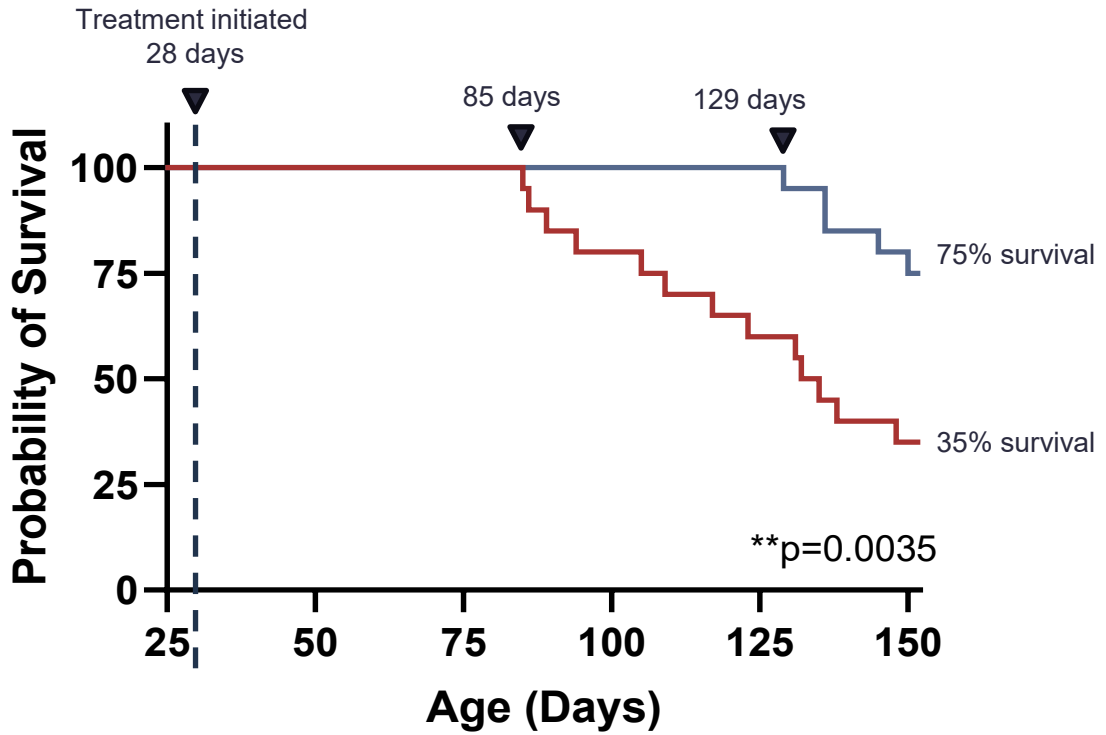
ATH-1105 preserved motor function and prolonged survival in preclinical model of ALS

PRP-TDP43^{A315T} TRANSGENIC MOUSE MODEL OF ALS

Motor Function



Survival



WT + vehicle ALS + vehicle ALS + ATH-1105 20 mg/kg

Motor Function: Data presented as mean ± SEM. Statistics applied: 2-way ANOVA with the Dunnett's test versus ALS + vehicle. ****p < 0.0001. n=10 mice per group

Survival: Data presented as Kaplan-Meier survival curves. Statistics applied: Log-rank (Mantel-Cox) test, n=20 mice per group at start. Treatment initiated at 28 days old.

Source: Berthiaume et al., *Front. Neurosci 2024*.

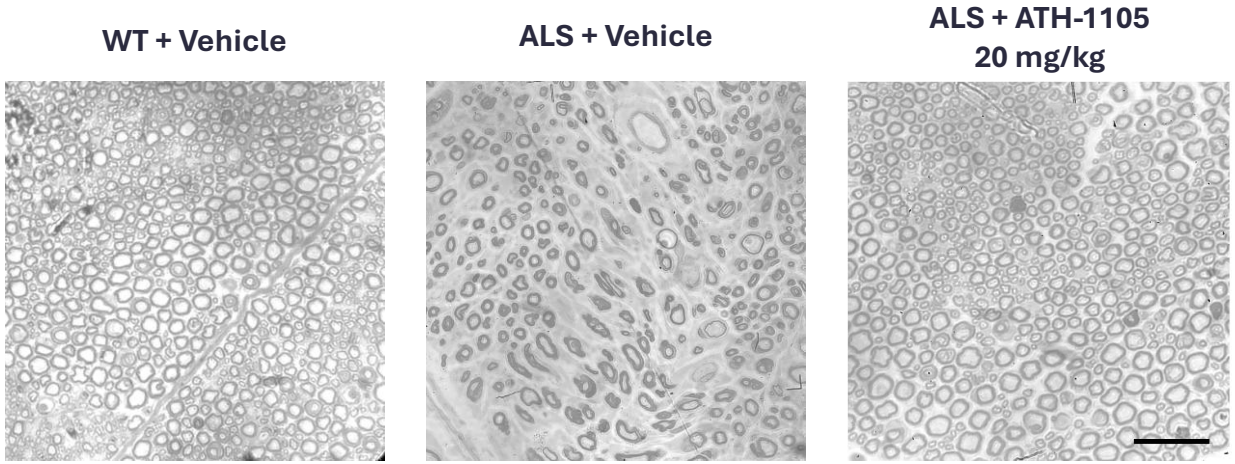
ATH-1105 protected against degeneration and demyelination of large motor axons in ALS mice

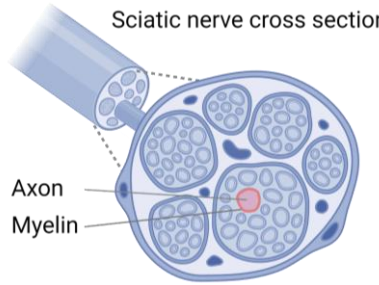
PRP-TDP43^{A315T} TRANSGENIC MOUSE MODEL OF ALS

Sciatic nerve histopathology

In ALS mice (center), axons in the sciatic nerve are smaller, fewer, and more poorly myelinated → Neurodegeneration

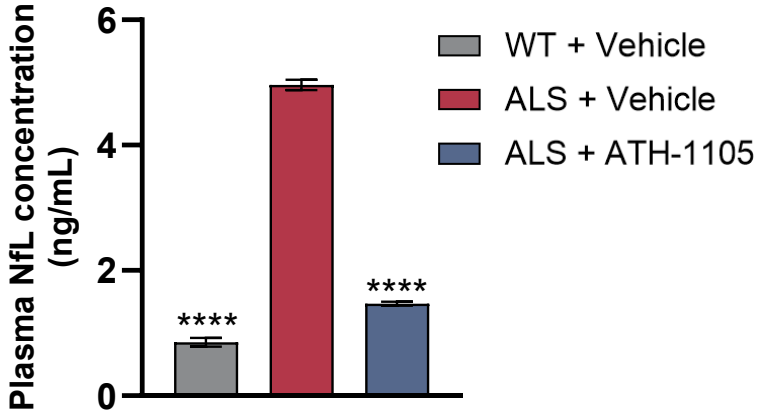
ATH-1105 (right) normalizes axon morphology

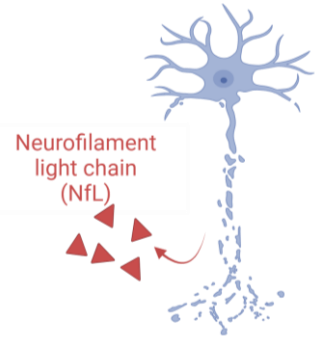




NfL in plasma

In ALS mice, ATH-1105 reduces NfL, a robust marker of neurodegeneration





NfL release from degenerating neurons is a translatable biomarker of ALS

Two months of treatment, Prp-TDP43A315T transgenic mice, "ALS" or "ALS mice." WT = wild type (healthy control). Sciatic nerve sections stained with toluene blue to highlight axon structure. Scale bar = 10 µm. Data presented as mean ± SEM. Statistics applied: One-way ANOVA with Dunnett's multiple comparisons test ; ****p<0.0001 vs ALS + vehicle. n=10 mice/group

Source: Berthiaume et al., *Front. Neurosci 2024*.

LeonaBio

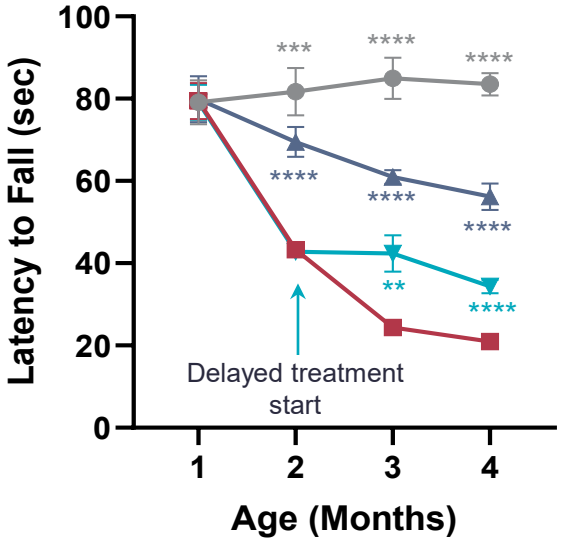
Disease progression was attenuated in ALS mice following early or delayed treatment initiation with ATH-1105

PRP-TDP43^{A315T} TRANSGENIC MOUSE MODEL OF ALS

WT + Vehicle
ALS + Vehicle
ALS + ATH-1105 20 mg/kg (Early)
ALS + ATH-1105 20 mg/kg (Delayed)

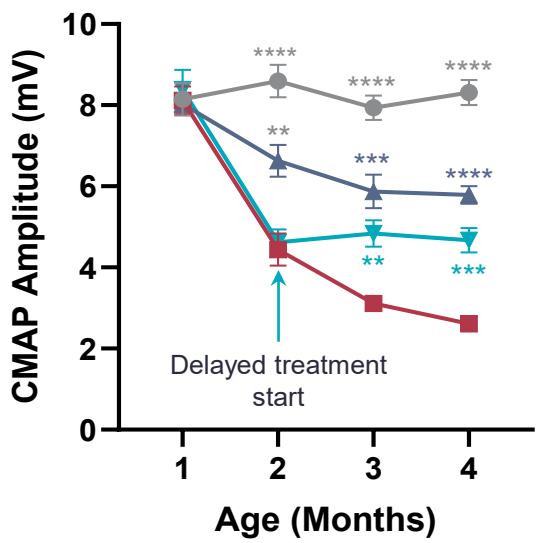
Motor function

Rotarod



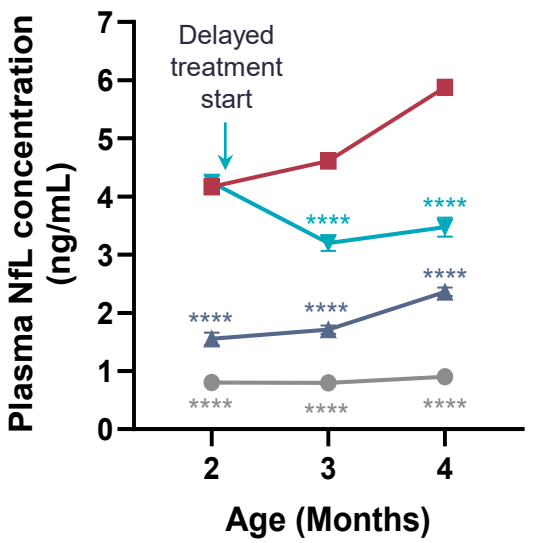
Nerve function

Compound muscle action potential amplitude



Neurodegeneration

Plasma NfL



Delayed intervention with ATH-1105 resulted in a slowing of further disease progression from time of treatment onset

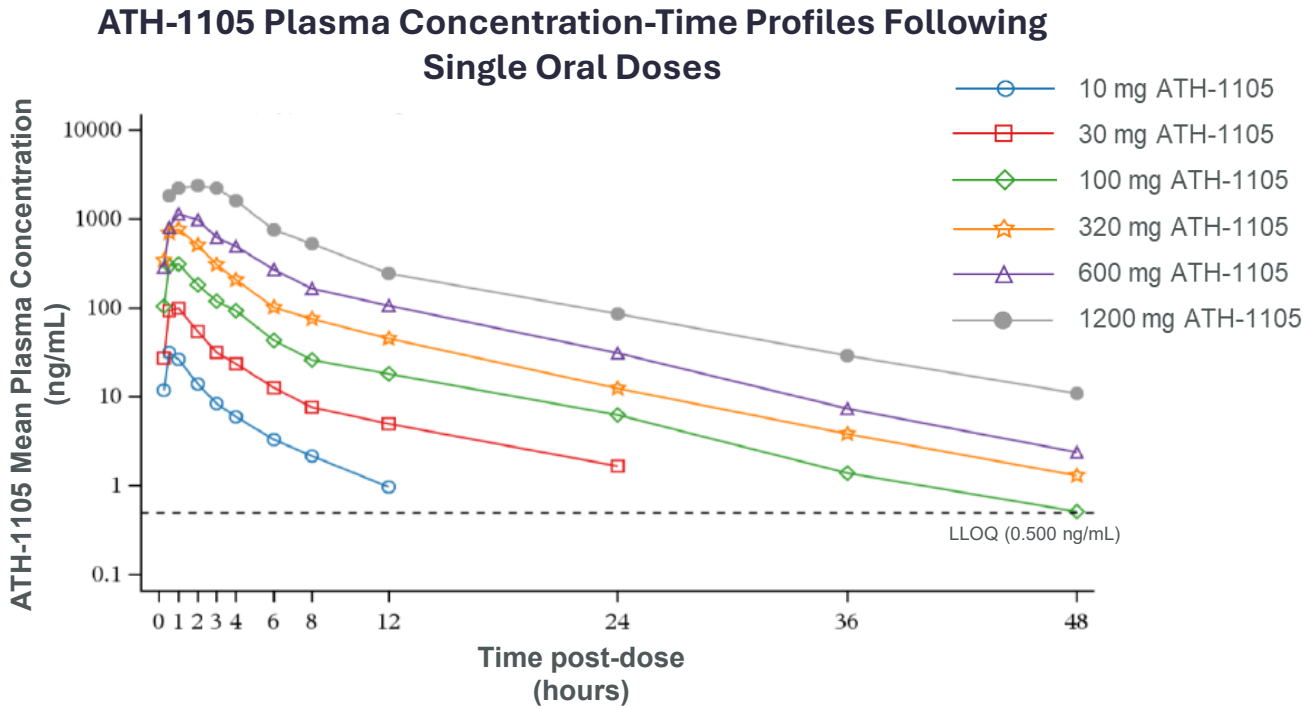
A reduction in plasma NfL levels observed once delayed ATH-1105 treatment begins

Data presented as mean ± SEM. Statistics applied: 2-way ANOVA with the Dunnett's test versus ALS + vehicle. **p < 0.01; ***p < 0.001; ****p < 0.0001.
n=10 mice per group
Source: Berthiaume et al., *Front. Neurosci 2024.*

Phase 1 results support continued development of ATH-1105 for the treatment of ALS

COMPLETED PHASE 1 SINGLE AND MULTIPLE DOSE STUDIES IN HEALTHY VOLUNTEERS

- All doses studied were generally well tolerated with no dose-limiting adverse events
  - All adverse events were mild
  - There were no serious adverse events
  - No trends suggestive of a safety signal
- Favorable PK profile
  - Dose linearity
  - Rapid absorption; consistent elimination
  - No accumulation after repeat doses for 10 days
  - Good CNS penetration reaching target exposures that were effective in preclinical studies



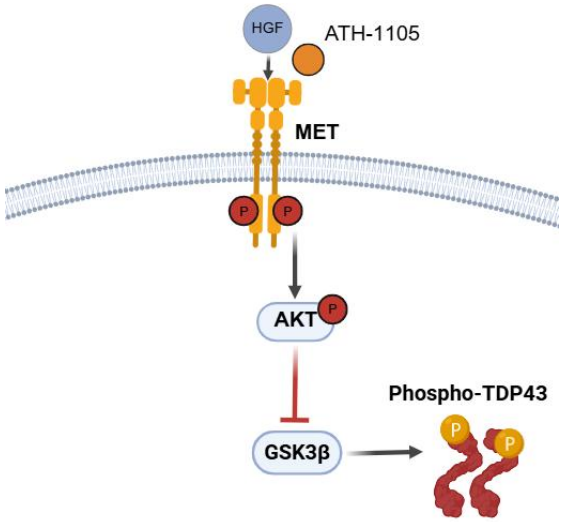
- Encouraging exploratory findings in a potential target engagement biomarker from plasma samples

Source: Ooi et al. *NEALS Annual Meeting 2025 (Poster).*

Biomarker results indicated a biological effect of ATH-1105 in humans and suggest potential to improve protein pathology in ALS

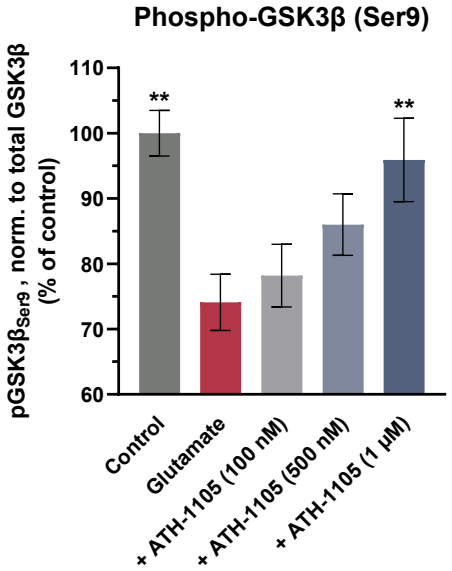
EXPLORATORY ANALYSIS OF NEURONAL-DERIVED EXOSOMES (NDE) IN THE PLASMA FROM PHASE 1 STUDIES

Mechanism



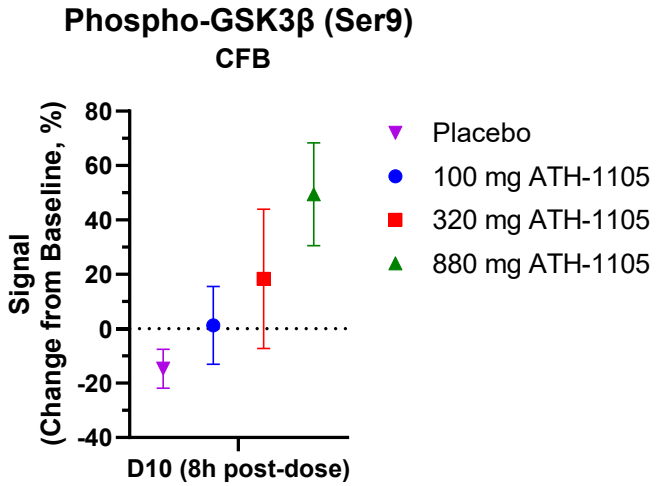
Preclinical data supports mechanism

In vitro (spinal motor neurons)



Exploratory biomarker analysis suggests translation of effects on **GSK3β**

NDEs in human plasma



HGF/MET→AKT is known to phosphorylate **GSK3β** at Ser9 inhibiting its activity and ability to promote protein pathology (**pTDP-43**)

ATH-1105 treatment inhibited **GSK3β** activity in vitro (increased phosphorylation at Ser 9) shown above, and reduced **phospho-TDP-43** in the Prp-TDP43 mouse model of ALS

ATH-1105 treatment led to increased expression of **phospho-GSK3β** (inactive form), a potential biomarker of target engagement that may be relevant for TDP-43 pathology

In vitro data: **p<0.01 vs. glutamate alone. One-way ANOVA with Fisher's multiple comparison post-test; n = 3-4 biological replicates.

NDE: Data expressed as percent change from baseline (Day 1 Pre-dose). Mean ± SEM. Mixed effects model analysis with Dunnett's multiple comparison test vs placebo at 8h-post dose; n = 5-6 subjects per treatment group

LeonaBio

ATH-1105 is ready for a Phase 2 study in people living with ALS

- Planning underway for a Phase 2 proof-of concept study to explore functional measures, biomarkers, and safety in people living with ALS

- Design considerations:
  - ≥ 6 months treatment duration
  - Biomarkers, including plasma NfL and NDEs
  - Functional measures
    - ALSFRS-R
    - Vital capacity
    - Grip strength

- Aim is to explore safety and preliminary efficacy to inform a potentially pivotal clinical trial

LeonaBio

ATH-1105 is a Phase 2 ready asset for the treatment of ALS

A NOVEL THERAPY DESIGNED TO ADDRESS THE COMPLEX PATHOLOGY AND MITIGATE NEURODEGENERATION IN ALS

- Oral administration
- Neuroprotective*
- Reduces plasma NfL*
- Favorable safety profile and generally well-tolerated
- Biomarker signals in Phase 1
- Expansion potential

LeonaBio

*in preclinical models

Transforming our future

Advancing 2 programs that have the potential to deliver life-changing therapies in breast cancer and ALS

Compelling clinical development programs in areas of profound need

Multibillion-dollar market opportunities

Key clinical readouts within 2 years

LeonaBio

PIPE financing up to $236 million

- Financing up to $236M supports lasofoxifene development program through topline data with sufficient capital runway into 2028
- $90M upfront priced at a greater than 50% premium to our December 17, 2025 closing price of $6.35/share
- If exercised, warrants provide up to additional $146M for further support

Expected key inflection points within ~2 years

✓ **Lasofoxifene**

- Phase 3 registrational study ongoing with >50% enrolled

Topline results expected in 2H2027

✓ **ATH-1105**

- Phase 2 POC study in ALS planned to start in 2H2026

Topline results expected 2027

LeonaBio

Thank You

