

# **Sermonix Pharmaceuticals**

## **Non-Confidential Company Presentation**

October 2020

# A de-risked clinical stage oncology company enrolling phase 2 study of lasofoxifene monotherapy and initiating combination study, with near term value creation in targeted mutation driven metastatic breast cancer

- **Breast cancer is the most common malignancy in women worldwide**
  - 60,000 patients in U.S. diagnosed each year with metastatic breast cancer
- **All patients currently progress** and are subject to toxic chemotherapy, substantial morbidity, mortality
  - Up to **40% develop ESR1 mutations after first line therapy<sup>(1)</sup>** confer resistance to current therapies, are prone to metastasize, and have worse prognosis
- **Sermonix Pharmaceuticals** is developing the SERM **lasofoxifene**—with newly discovered **class-leading activity in ESR1 mutations, metastases, and novel late-expiring IP**—as the **precision medicine of choice** in Estrogen Receptor positive (**ER+**) **metastatic breast cancer (mBC)** **ESR1 mutations** to delay disease progression and improve quality of life in area of unmet medical need
- **Lasofoxifene** can be **first-to-market, best-in-class**
  - **De-risked, capital efficient program with \$34M raised to date**, built upon previous large phase I-III non-oncology program. **Over 10,000 postmenopausal women dosed; well-characterized safety and tolerability profile**
  - Full FDA agreement on Phase 2 ELAINE study; IND opened Dec-18, fast-track designation granted; **potential breakthrough designation with phase 2 data**
  - ELAINE 2 combination CDK4/6i study collaboration with Lilly initiated Q3 2020
- **\$35M Series B planned Q4 2020/Q1 2021 to fund company through 2023 for EOP2 meeting, potential accelerated approval, CDx and manufacturing scale up, Phase 3 or PMA planning**
  - **Primary market research confirms \$800+ million peak annual U.S. sales potential for first indication**
    - – Global rights, with >\$2B upside potential for broadening to combinations, earlier lines of therapy

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# Management Team

## Seasoned Team with Proven Track Record of Success



**David Portman, MD** Founder and Chief Executive Officer

- Lasofoxifene PhII & III principal investigator
- 140+ clinical trials at own women's health clinical research center (CCWHR) as CEO
- Experience in all aspects of drug development, approval process and commercialization



**Barry Komm, PhD** Chief Scientific Officer

- Headed Pfizer's bazedoxifene SERM program
- 25 years at Wyeth in SERMs & SERDs; led TSEC program (Duavee)



**Elizabeth Attias, ScD** Chief Strategy and Development Officer

- Track record in SERMs market development, strategic market entry, commercialization and brand optimization for Parke-Davis



**Lawrence R. Hoffman CPA, Esq.,** Chief Financial Officer

- Track record of creating shareholder value in specialty pharma companies
- Former clinical research services CFO

**Miriam Portman, MD** Chief Operating Officer

- COO at CCWHR for 18 years
- Track record in clinical research, FDA dealings, budgets, contracts, pt. recruitment, marketing

**Paul Plourde, MD** VP, Onc. Clinical Development

- Headed AZ's US PhII/III/IIIb trials as Onc. VP
- 25 years developing endocrine therapies incl. fulvestrant, tamoxifen & anastrozole

**Simon Jenkins, PhD** VP, Operations

- 30 years experience in drug development
- Led the global regulatory development programs for bazedoxifene and CE/bazedoxifene (Duavee)

**Anthony Wild, PhD** Non-executive Chairman

- Long-standing investor (e.g. BOWS, Sprout, Slate, MedPointe and Sermonix) with track record of successful exits
- Former President of Warner-Lambert's Global Pharmaceutical Sector, and management roles at Schering Plough



# Experienced Board of Directors

## Sermonix is Supported by a Strong Experienced Board of Directors.



**Anthony Wild, PhD** Non-executive Chairman

- Long-standing investor in a series of healthcare start-ups with track records of successful exits
- Previously Chairman and CEO of MedPointe Pharmaceuticals
- Past chairman of Innocoll plc and of Sprout Pharmaceuticals Inc.
- Former President of Parke-Davis (Warner-Lambert's Pharmaceutical Sector)
- Various management and executive roles with Schering-Plough in 6 different countries



**Michael A. Friedman, MD**

- Currently a director of Intuitive Surgical
- Former director at Celgene Corporation
- Past roles include CEO and chair holder at City of Hope cancer treatment and research center; and acting FDA commissioner
- Authored more than 150 papers and chapters
- Board-certified in Int. Medicine and Med. Onc.



**Thomas Pfsterer**

- Direct Investments activities of the Hans-Peter Wild Family Office
- Previously, investment banking division Morgan Stanley AG in Frankfurt, Germany, focus on M and A and capital market transactions in health care

**Richard U. De Schutter**

- Long-standing investor in several private healthcare start-ups
- Past CEO and President of DuPont Pharmaceuticals; and Chief Administration Officer of Monsanto Inc.; as well as Chairman, CEO and president of G.D. Searle Pharmaceuticals & Co., and chief administration officer of Pharmacia
- Roles as director including of Incyte, Sprout, Smith & Nephew, Ecolab, and ING Americas



**Stephen Rubino, PhD**

- Chief Business Officer of Celyad SA
- Wide range of commercial, strategy, BD&L and IR experience from leadership roles at Novartis and Schering-Plough
- Board director at ILKOS Therapeutics



**David Portman, MD** Chief Executive Officer

- Sermonix Founder
- Lasofoxifene PhII & III principal investigator
- 140+ clinical trials at women's health clinical research center (CCWHR) as CEO
- Experience in all aspects of drug development, approval process and commercialization



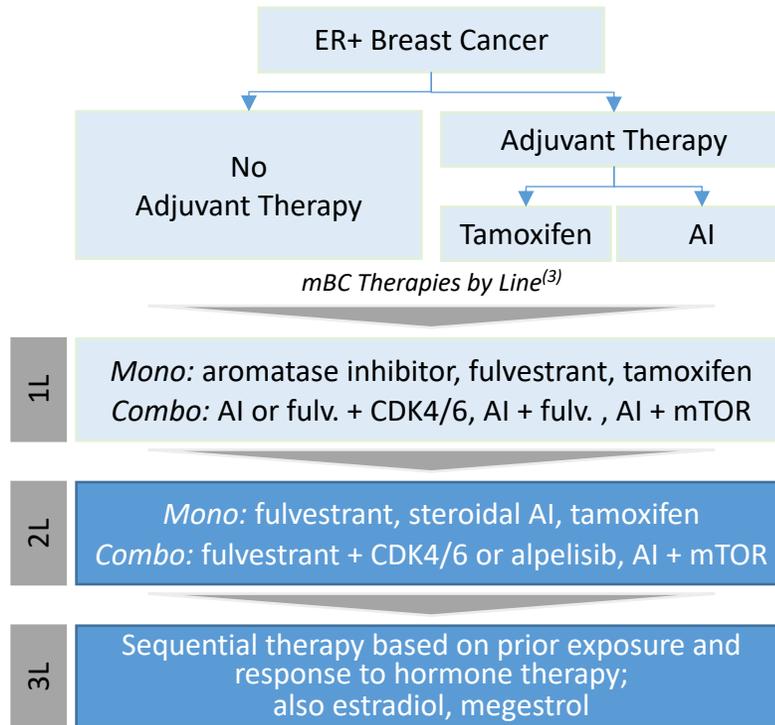
# Why ESR1 Mutated Breast Cancer Matters: Significant Unmet Need

- Constitutively active ESR1 mutations present in up to 40% of patients who progress on prior endocrine therapy in the metastatic setting<sup>1</sup>
- Patients with BC with ESR1 mutations particularly D538G and Y537S<sup>2</sup> have shorter PFS, overall survival and are more prone to metastasize
- Injectable Fulvestrant, current gold standard<sup>3</sup> is:
  - Limited by poor pharmaceutical properties; potency in ESR1 mutations reduced compared to WT; frequent acquisition of ESR1 mutations on treatment<sup>4</sup>; potentially less effective in visceral, particularly liver, metastases<sup>6,7</sup>
  - PlasmaMATCH demonstrated fulvestrant PFS of only 2.2 mos in ESR1 mutations<sup>8</sup>
- New solutions beyond fulvestrant are needed
  - Lasofoxifene has demonstrated proof-of-principle efficacy in vitro activity in ESR1 mutated breast cancer cell lines and greater in vivo inhibition of tumor growth and visceral metastases compared to fulvestrant both alone and in combination with CDK 4/6 inhibitors

# Unmet Need: Physicians express only moderate satisfaction, with none highly satisfied, with the existing mBC armamentarium for patients with an ESR1 mutation<sup>(1)</sup>

**Primary market research confirms significant opportunity in 2L/3L mBC for effective, well tolerated endocrine therapy to prolong PFS and delay chemotherapy without toxic impact.**

## Simplified ASCO Guidelines<sup>(2)</sup>



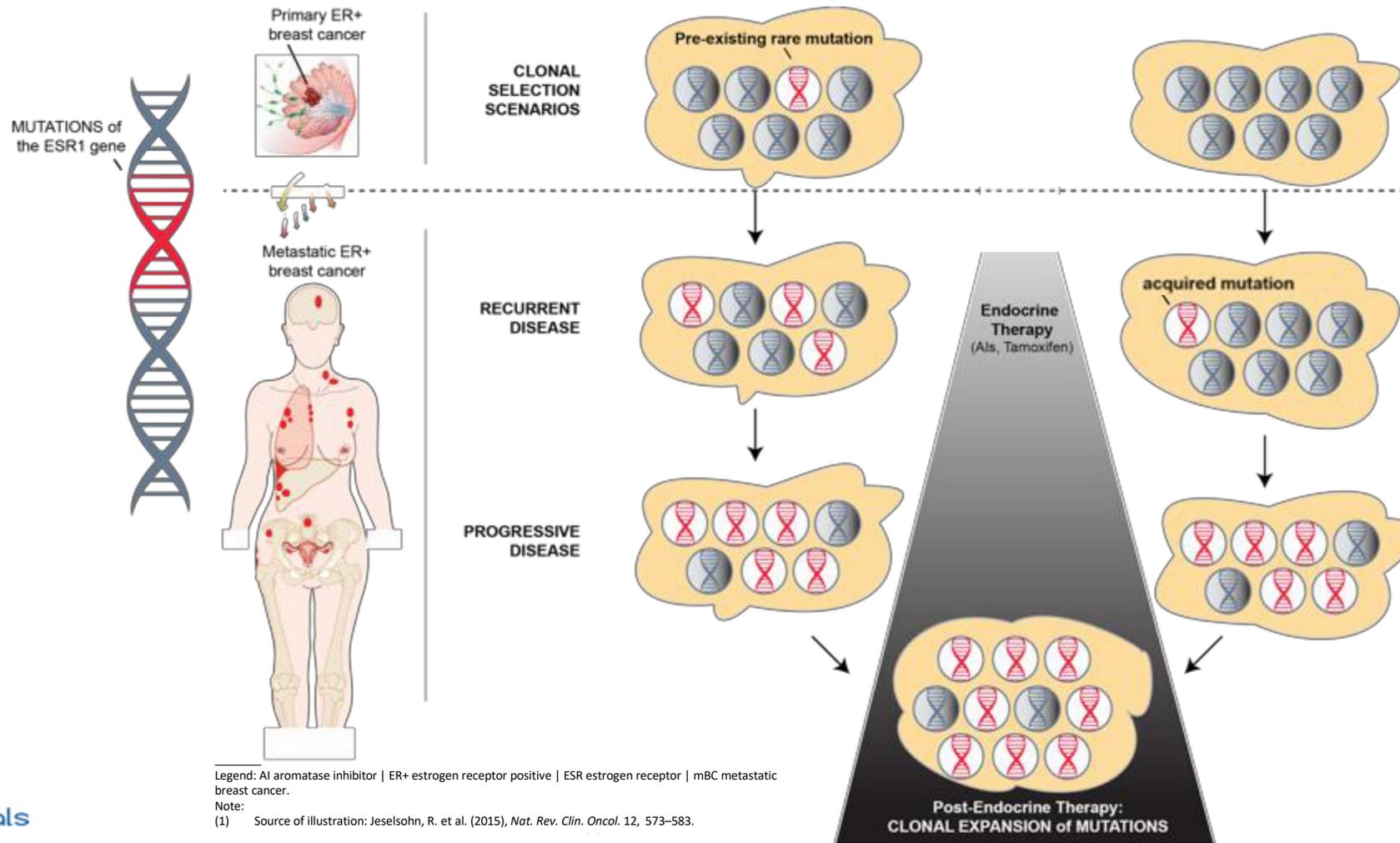
- **MBC remains a fatal disease, unmet need**
- Existing 1L treatments allow years of living with the disease before developing resistance/ progression of the disease
  - Bone loss and VVA common with current and future SERDs
- ~65% patients receive AI in 1L<sup>(4)</sup>
- Up to 40%<sup>(5)</sup> of mBC patients develop ESR1 mutations causing resistance; **>16,000 addressable U.S. patients annually**
- **Existing 2L options have significant efficacy, tolerability, compliance and administration/ bioavailability issues**
  - Strong need for new, effective, well tolerated endocrine therapy in the 2L and 3L setting that prolongs progression-free survival and delays chemotherapy after progression on AI/ in acquired resistance

Legend: 1L first line | 2L second line | 3L third line | AI aromatase inhibitor | ASCO American Society of Clinical Oncology | CDK cyclin-dependent kinase | fulv. Fulvestrant | mBC metastatic breast cancer | mTOR mechanistic target of rapamycin | PFS progression-free survival | SERM/SERD selective estrogen receptor modulator/downregulator | VVA vulvo-vaginal atrophy.

Notes:  
 (1) BioVid proprietary market analysis.  
 (2) <http://www.asco.org/guidelines/advancedendocrinebreast>  
 (3) Practitioner's choice will depend on cascade of prior therapies the given patient has been exposed to.  
 (4) Source: comprehensive proprietary market research fieldwork project.  
 (5) Source: Jeselsohn, R. et al. *Nat. Rev. Clin. Oncol* 2015.

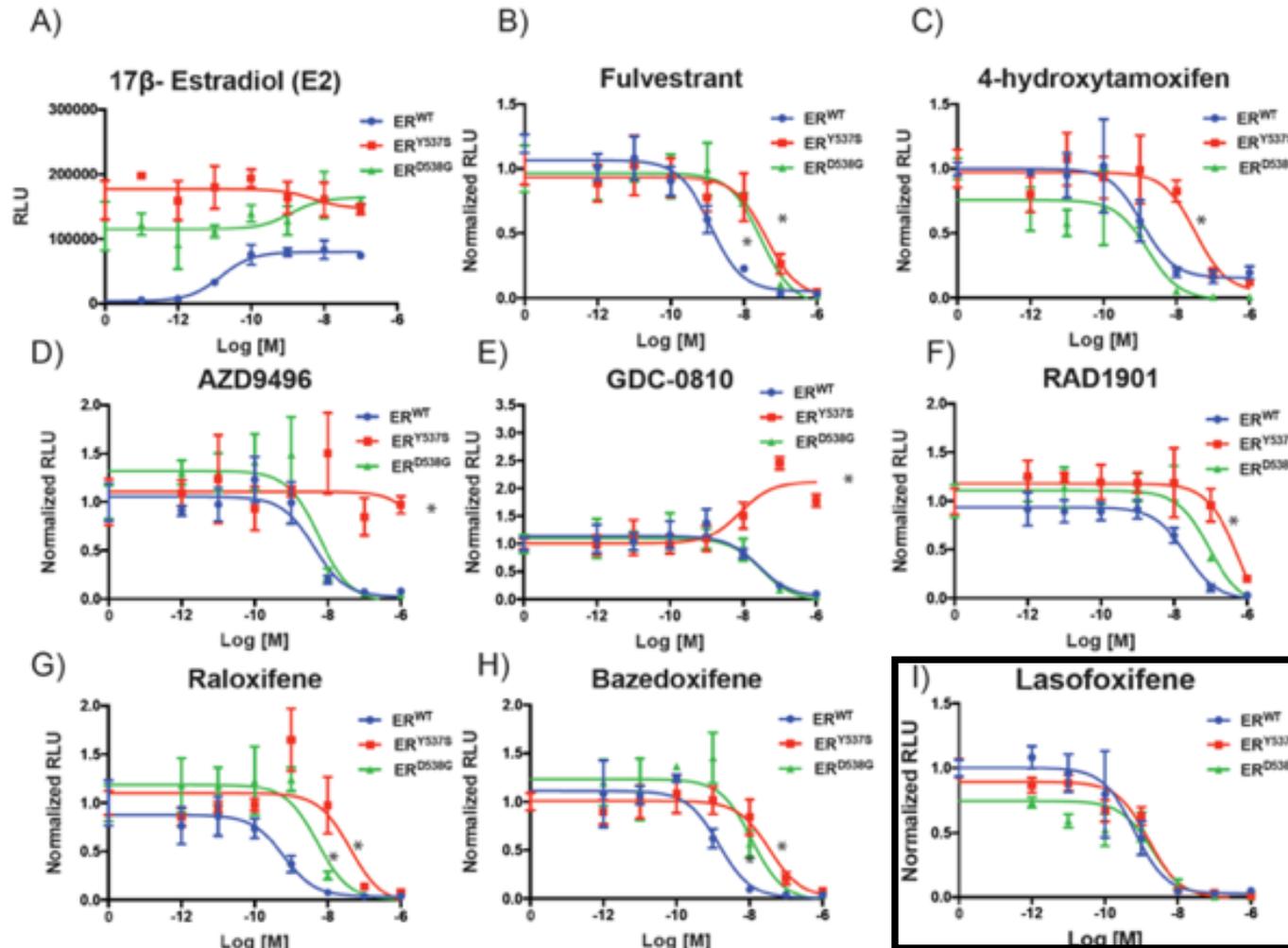
# A Growing Problem: Widespread aromatase inhibitor (AI) use and selective pressure increases the incidence of endocrine resistant ESR1 mutations and the problem that lasofoxifene can solve

AI use in the metastatic setting leads to acquired resistance and patients no longer respond optimally to current endocrine therapies; ESR1 mutations seen in up to 40% of mBC patients.



# In Vitro Duke University: Lasofoxifene maintains its potency against mutant-only reporter assay model while other SERMs/SERDs do not

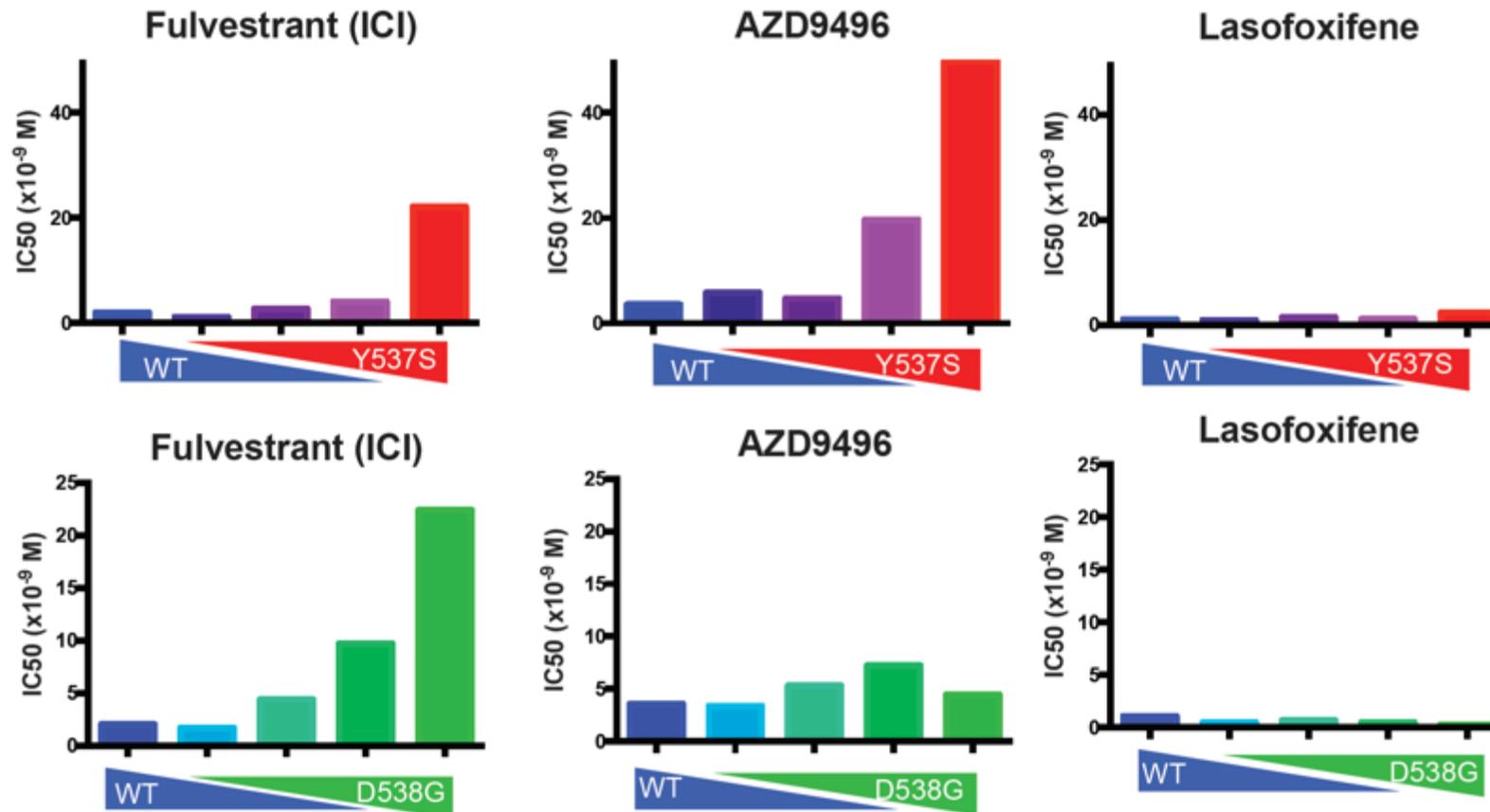
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# Lasofoxifene antagonist efficacy remains robust as the level of ESR1 mutant expression increases

Potency of SERDs fulvestrant and AZD9496 reduced in cells expressing ER<sup>Y537S</sup> or ER<sup>D538G</sup> alone

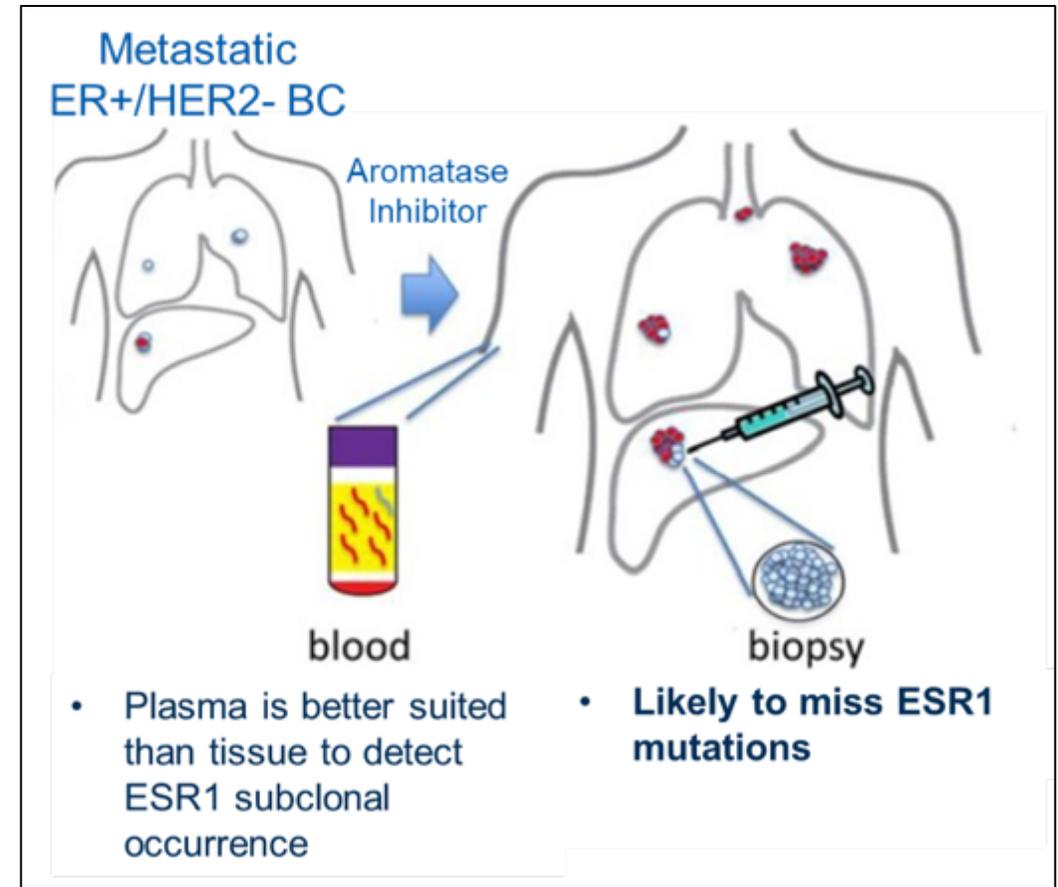
SKBR3 cells transfected with an estrogen responsive reporter gene in the presence of different WT to mutant ER (Y537S or D538G) construct ratios with IC50s of each dose-response curve plotted.



# Wave of the Future in ESR1 Plasma Mutations: A Sensitive Liquid Biopsy Can Identify Patients with an ESR1 Mutation

## A Precision Medicine Approach with Companion Diagnostic Commands High Patient Value.

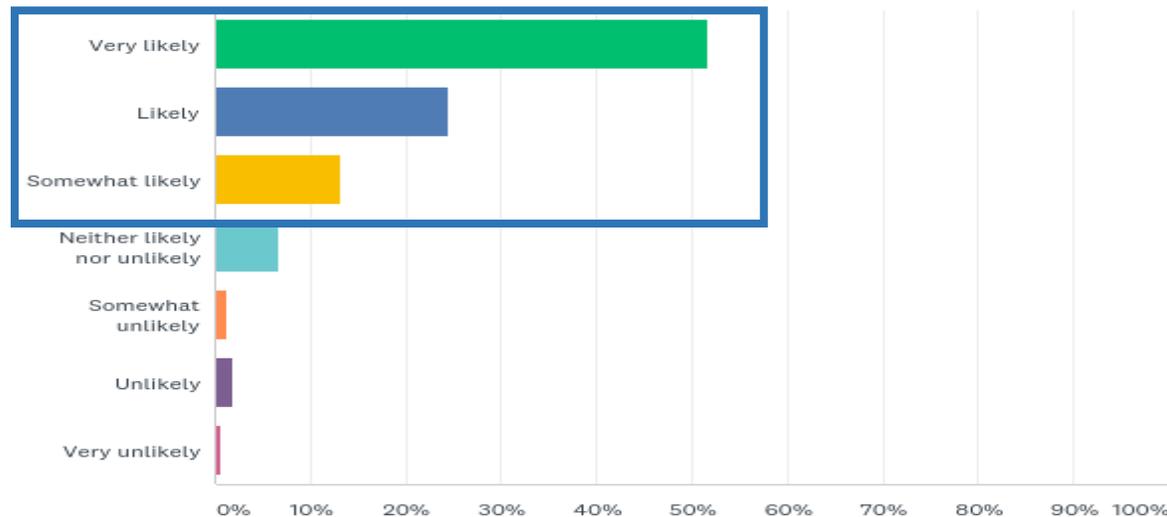
- Approximately 1/3 of patients develop ESR1 mutations during endocrine therapy in advanced disease<sup>1,2</sup>
- 7% 1L patients present with detectable ESR1 mutations after adjuvant AI therapy alone<sup>3,4</sup>
- ESR1 mutations show a high degree of variability across tumor sites in an individual patient
- A tissue biopsy is challenging in a patient with advancing disease and may not accurately identify a patient's ESR1 status
- Liquid biopsies have demonstrated great potential for ESR1 mutation detection
- Sermonix is validating a highly sensitive companion liquid biopsy for ESR1 mutations in the ELAINE study



# Liquid Biopsy Testing for ESR1 Mutation has Great Appeal to Patients

**Patients expressed their lack in information regarding ESR1 mutations and how interested they would be in knowing how it can improve their quality of life by tailoring their breast cancer treatments.**

- 96% of patients surveyed were not familiar with ESR1 mutations in the breast cancer setting and its impact on progression
- Patients were informed that there is a biomarker blood test available to identify the ESR1 mutation and there is potential to have a more tailored treatment if this test was taken and tested positive for ESR1 mutation
- 90% of patients said they would be very likely or likely to ask their provider about getting tested for ESR1 mutation



**152**  
Total  
Patients/Patient  
Advocates  
Surveyed

# Targeted and Easily Identifiable Patient Population: U.S. 2025 Endocrine-eligible Stage IV ER+/HER2- Breast Cancer Population with Detectable ESR1 Mutations

Total Stage IV Breast Cancer Patients	118,631
% Post-Menopausal	79%
% HR+/HER2- (Luminal A)*	72%
Total Stage IV Post-Menopausal HR+HER2- Patients	62,302 40,830 of which are newly diagnosed / progressed = inherently 1L a start of year

- ❑ 30-40% develop ESR1 mutations after 1L endocrine-containing treatment regimens in the metastatic setting
  - ❑ 12,000-16,000 2L and 3L lasofoxifene eligible patients/per year
  - ❑ Duration of treatment 7-14 months (in mono- and combination therapy)
- ❑ 5-10% may develop ESR1 mutations after adjuvant AI<sup>1,2</sup>
  - ❑ Up to 10,000 1L patients eligible for lasofoxifene in the 1L setting
  - ❑ Opportunity to move into adjuvant space as early detection becomes the norm
  - ❑ Duration of treatment >18 months (in earlier setting and in combination in 1L)

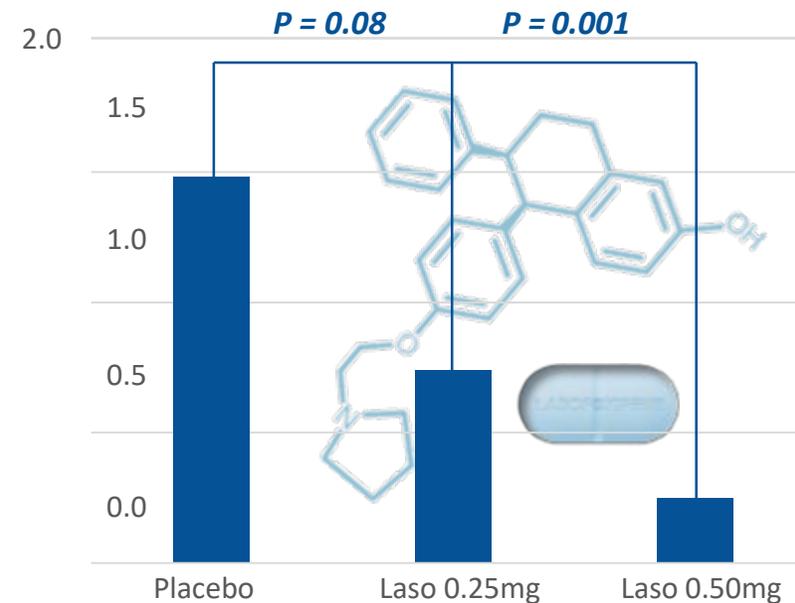
**\*Does not include premenopausal women on ovarian suppression**

# Lasofloxifene Heritage: Pre-existing pre-clinical and clinical program, efficacy and safety data provides Sermonix with strong foundation

## Lasofloxifene's estrogen receptor activity in osteoporosis<sup>1</sup>, demonstrated a significant decrease in breast cancer incidence.

Safety		Efficacy	
	Over 40,000 patient years of experience		Over 8,500 patient 5yr PEARL osteoporosis trial
Safety database		Efficacy observation	
<b>6</b>	Phase III trials	<b>-83%</b>	ER+ BC
<b>11</b>	Phase II trials	<b>-42%</b>	Vertebral fractures
<b>23</b>	Phase I trials	<b>-24%</b>	Non-vertebral fractures
<b>5 years</b>	PEARL trial (>8,500 women)	<b>No increase</b>	Endometrial cancer
<b>&gt;10,000</b>	Patients on lasofloxifene		

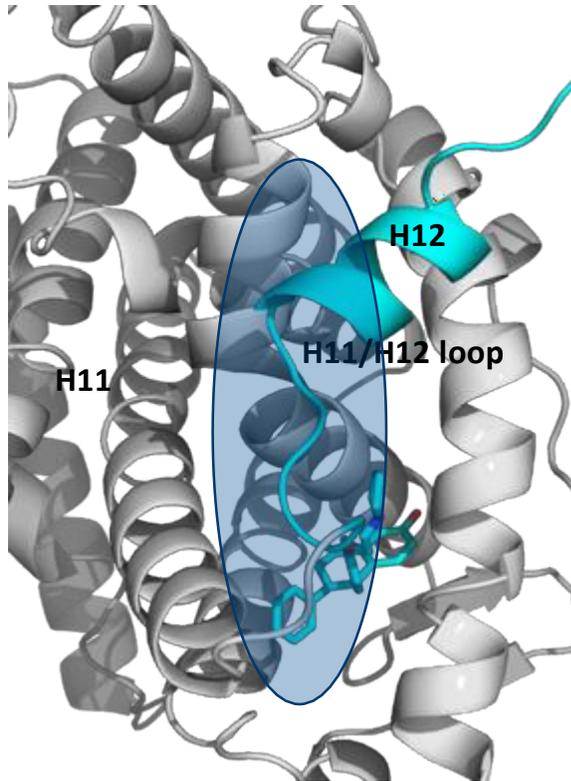
### Breast Cancer Incidence Rate (per 1,000 pt years)<sup>1</sup>



- EMA approved lasofloxifene for osteoporosis in 2009; never launched
- FDA differed—with non-approval for osteoporosis
- Lasofloxifene risk/ benefit ratio highly favorable in terminal cancer patients

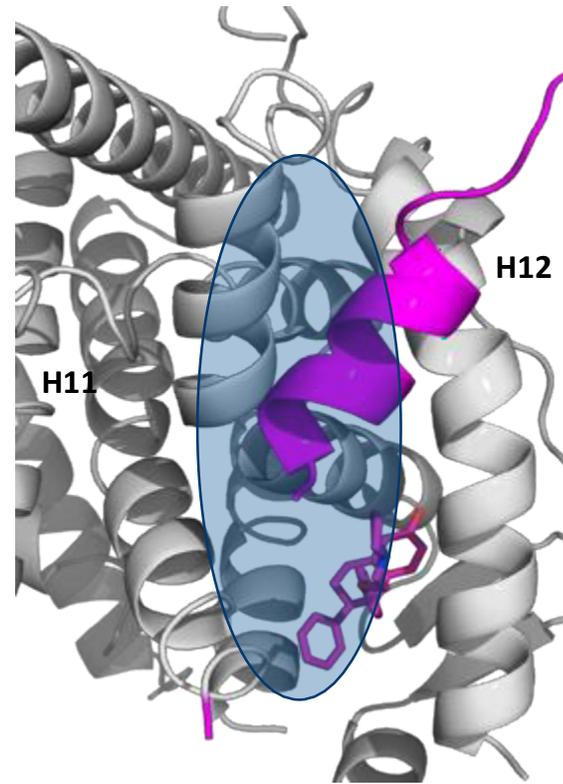
# Newly Discovered Mechanism of Action: Lasofoxifene binding and potency retained even in constitutively active ESR1 mutated receptors

WT-Lasofoxifene



- Lasofoxifene does not disrupt the loop between H11 and H12  
– Similar to other SERMs e.g. 4-OHT, RAL

Y537S-Lasofoxifene<sup>1</sup>



- For Y537S ER LBD, this loop is absent
- When occupied by OHT or RAL, the H11/H12 loop in the Y537S ER LBD structure is only partially disordered

✓ Lasofoxifene has higher potency in mutant ER, along with more favorable pharmaceutical properties such as excellent volume of distribution, long half-life and bioavailability compared to fulvestrant

✓ Lasofoxifene distorts agonist structure of Y537S ER LBD

✓ No receptor degradation necessary

✓ Potential mechanistic explanation for lasofoxifene's efficacy in ESR1 mutations

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# Well-Characterized Lasofoxifene: Competitive Lens on Fulvestrant and Oral SERDs in Development

## Advantages of oral lasofoxifene compared to injected fulvestrant and SERDs in development.

### Fulvestrant

- Current branded endocrine therapy gold standard after aromatase inhibitor use
- US\$1 billion in global annual sales
- ✗ Two painful gluteal injections, in office monthly; Inconvenient
- ✗ Poor PK and unable to dose adequately
  - ✗ Limited efficacy in ESR1 mutations given low bioavailability

### Selective ER Degraders (SERDs) in development

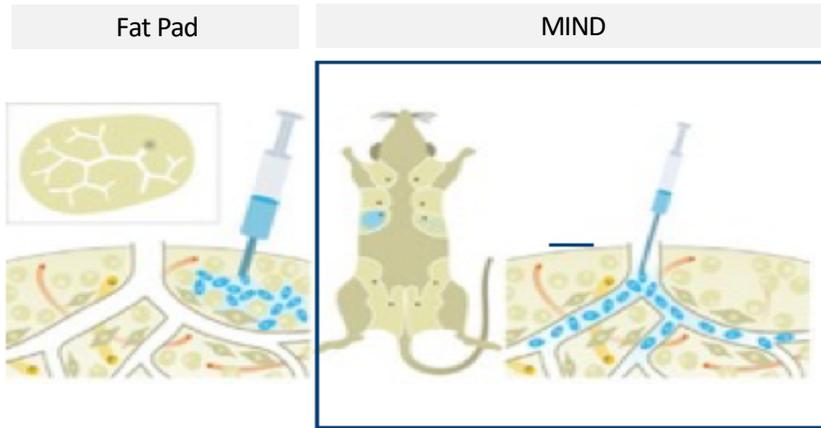
- New SERDs will need to prove differentiation from fulvestrant
- ✗ ER degradation is not the functional driver of transcriptional inhibition (from Clara Metcalfe, Genentech Inc, SABCS 2018)
- ✗ Earlier in development than lasofoxifene
- ✗ Still unproven efficacy, safety, tolerability
- ✗ Negative on- and off-target effects of investigational SERDs particularly GI; adverse impact on bone and genitourinary

### Lasofoxifene

- ✓ **Preclinical superiority in common ESR1 mutations and metastases; unique conformational changes**
- ✓ **Higher binding affinity; greater bioavailability**
- ✓ **Oral option; tolerable at high doses**
- ✓ **Bone and urogenital protective effect**
  - ✓ **Potential benefit to cancer skeletal related events & metastases**
- ✓ **Targeted therapy; Liquid biopsy and companion diagnostic**

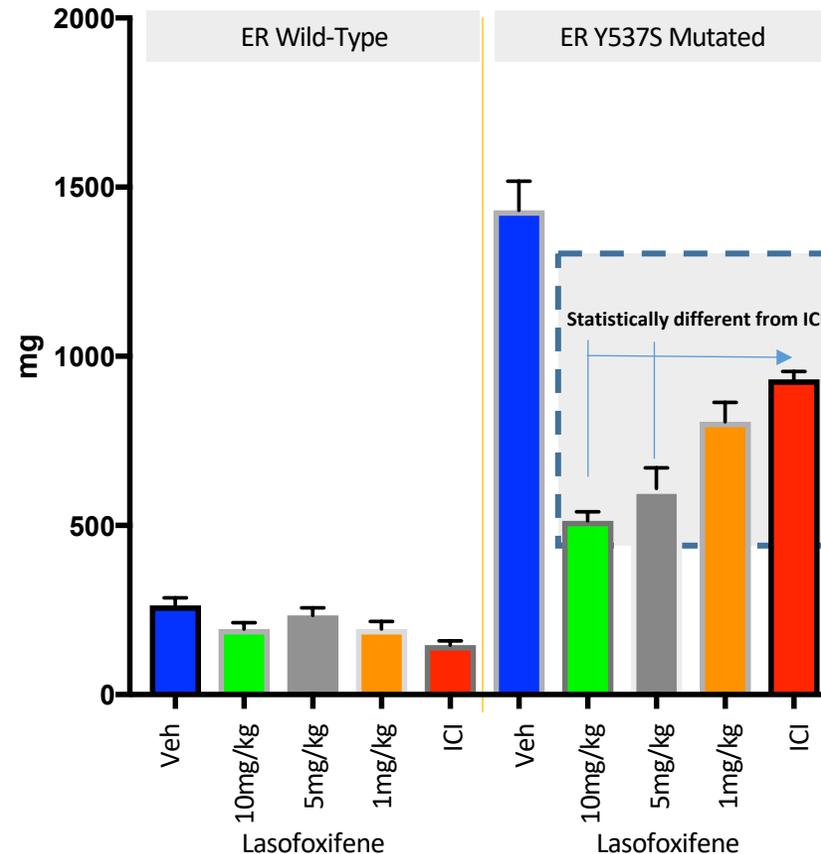
# Positive Fulvestrant Comparison: In vitro data in ESR1 mutations translates to in vivo with lasofoxifene demonstrating superiority to fulvestrant in inhibiting primary tumor growth

## Lasofoxifene demonstrates superiority in vivo to fulvestrant (ICI) in inhibiting tumor growth in a Mouse Intraductal (MIND) model.



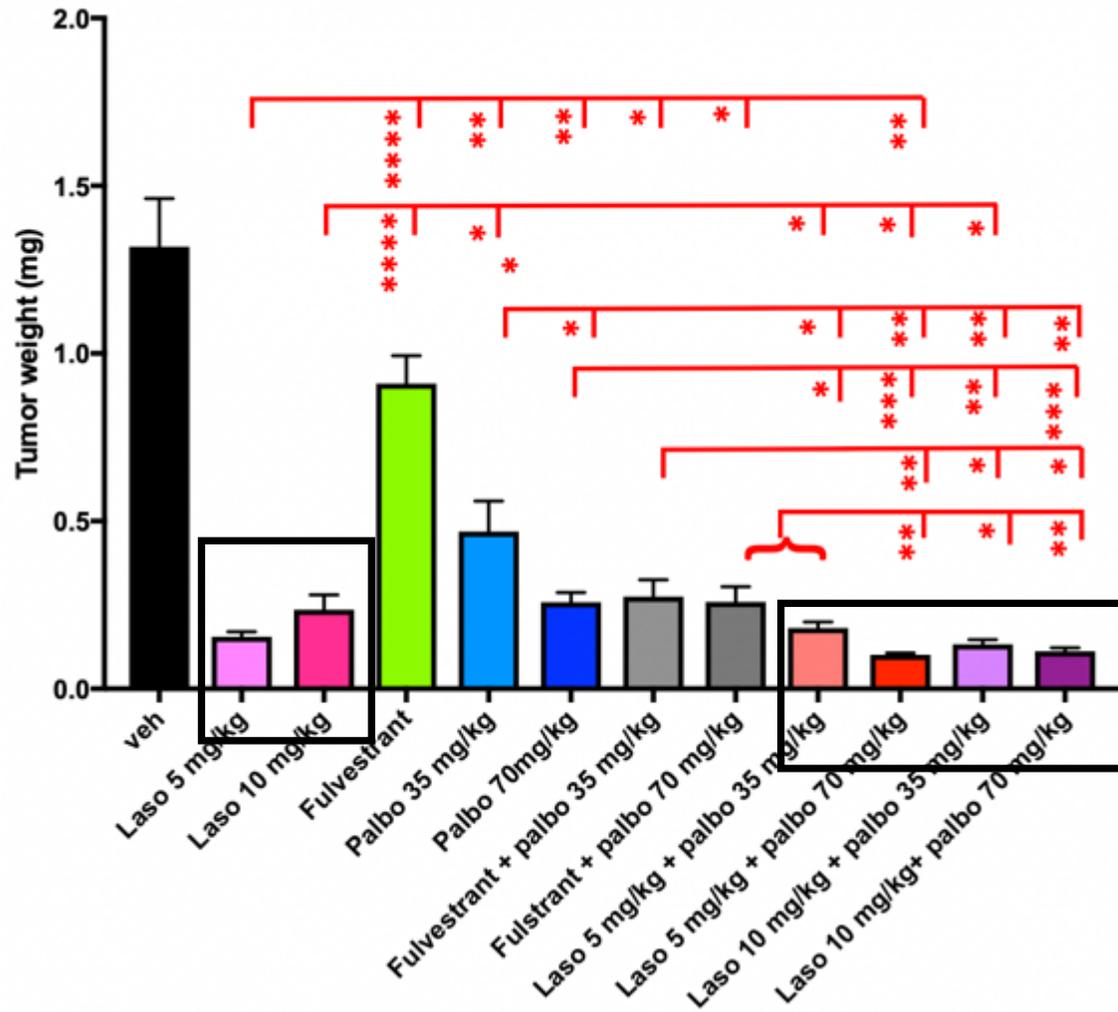
- WT/Y537S tumor cells injected directly into mammary ducts through nipple, invade and then metastasize
- Tumors mimic original luminal A Breast Cancer<sup>2</sup>

### Primary Tumor Weights



- Laso and fulvestrant similar efficacy in wild type
- In a treatment resistant model when ER has a Y537S mutation, lasofoxifene demonstrates dose dependent inhibition of tumor growth with statistical superiority to fulvestrant

# Synergistic and Additive Effect: Lasofoxifene + Palbociclib improved efficacy signals differentiation from Fulvestrant

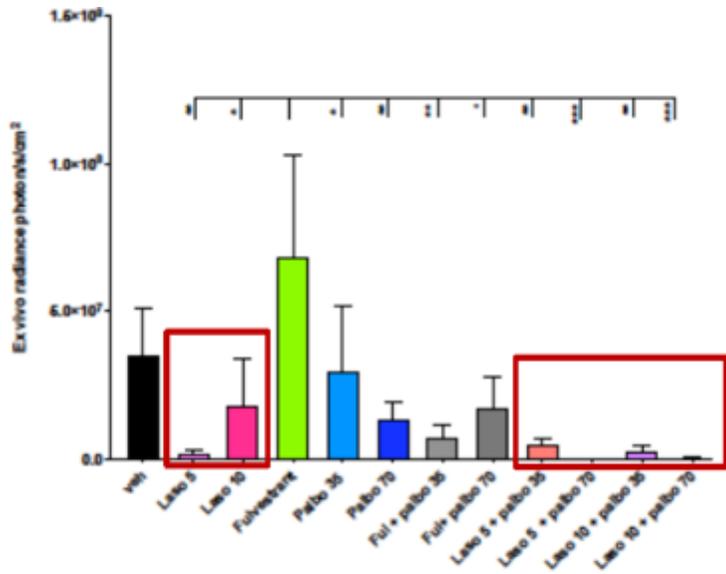


- Lasofoxifene at 5 and 10mg/kg superior to high dose fulvestrant
- Both doses of laso significantly different from palbo (35 mg/kg)
- Synergy seen with fulvestrant + palbo is driven by palbo, and not as effective as laso alone
- Synergy observed with laso + palbo; efficacy improvement may be driven predominantly by laso
- Both laso and palbo effects are improved ~50% when combined

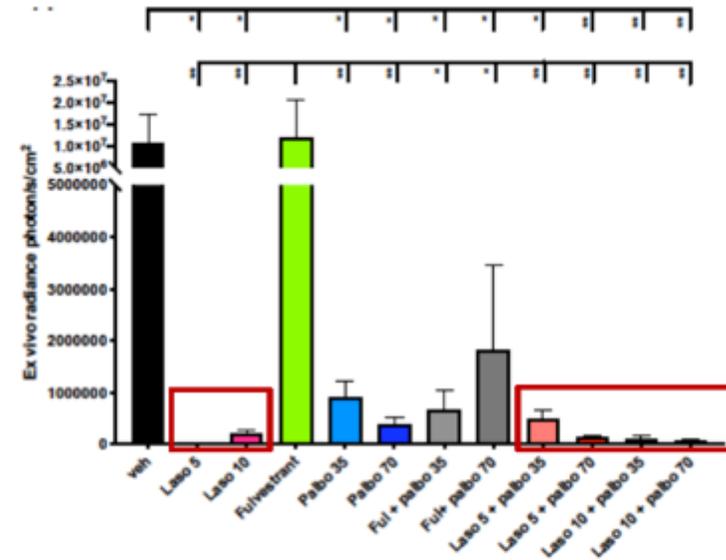
- Veh vs Fulvestrant  $P < 0.05$ , Veh vs everybody else  $p < 0.0001$
- Fulvestrant vs P35  $p < 0.01$ , fulvestrant vs everybody else  $p < 0.0001$

# Lasofoxifene inhibits liver, lung, bone brain metastases and is superior to fulvestrant<sup>1</sup>

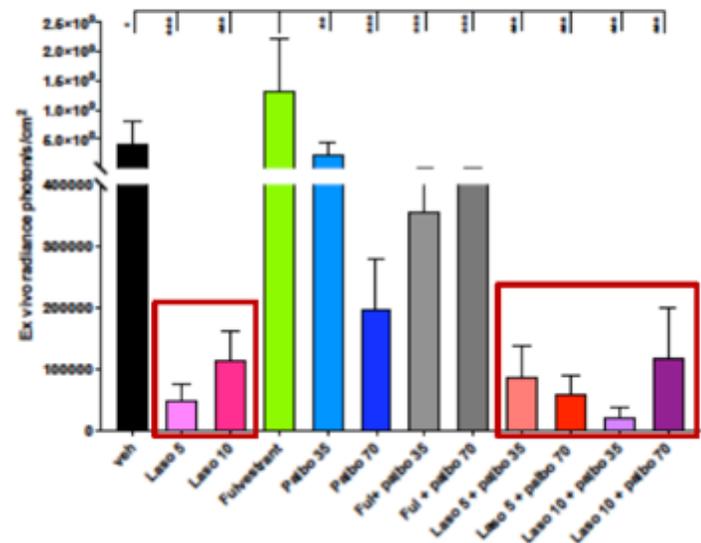
Lung



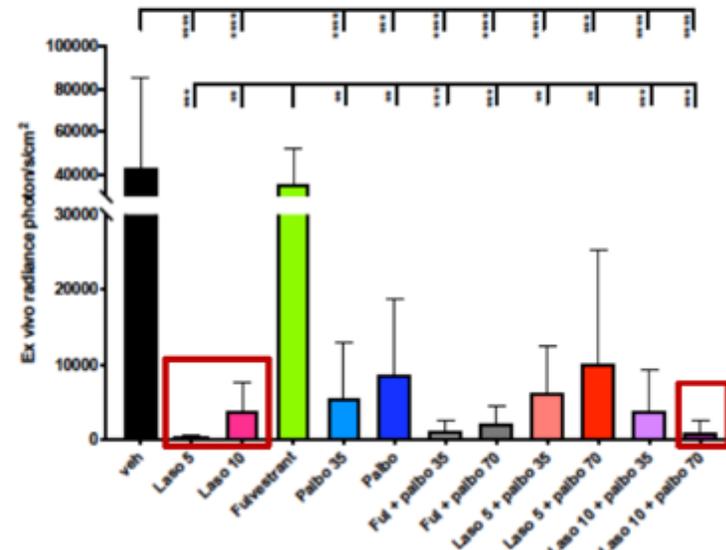
Bone



Liver



Brain



- Lasofoxifene alone statistically reduces liver metastases, while fulvestrant demonstrates little to no effect
- Combining lasofoxifene with palbociclib does not improve the outcome on metastases suggesting the effect seen is a lasofoxifene independent effect
- Clearly, the fulvestrant + palbociclib effect on metastases is being driven by palbociclib
  - Implied clinically with PARSIFAL results showing parity between AI/Palbo and fulvestrant/Palbo<sup>2</sup>

# Data Support Fast-Track Evaluation of Lasofoxifene alone and in Combination with CDK 4/6 Inhibitors for the Treatment of Breast Cancers with ESR1 Mutations

- Outstanding pharmaceutical characteristics of lasofoxifene separate it from almost all currently available and in development hormonal therapies for the treatment of metastatic breast cancer
- Lasofoxifene avidly binds and inactivates both wild type and mutated estrogen receptors (constitutively active)
- Lasofoxifene demonstrates a dose dependent inhibition of breast cancer (bearing ESR1 mutations) growth and metastasis superior to fulvestrant
- Lasofoxifene combined with palbociclib demonstrates synergistic efficacy supporting the use of a CDK4/6 inhibitor with lasofoxifene in clinical evaluation
- Lasofoxifene offers an enhanced tolerability profile

**Robust preclinical studies enabled late-expiring issued IP and informed the design of the ELAINE 1 and ELAINE 2 clinical studies**

# SERMONIX PHASE 2 PROGRAMS

ELAINE 1: Recruiting at sites across the U.S. with recently added sites in Canada and Israel

ELAINE 2: Lasofoxifene/Abemaciclib Lilly collaboration launched across the U.S.

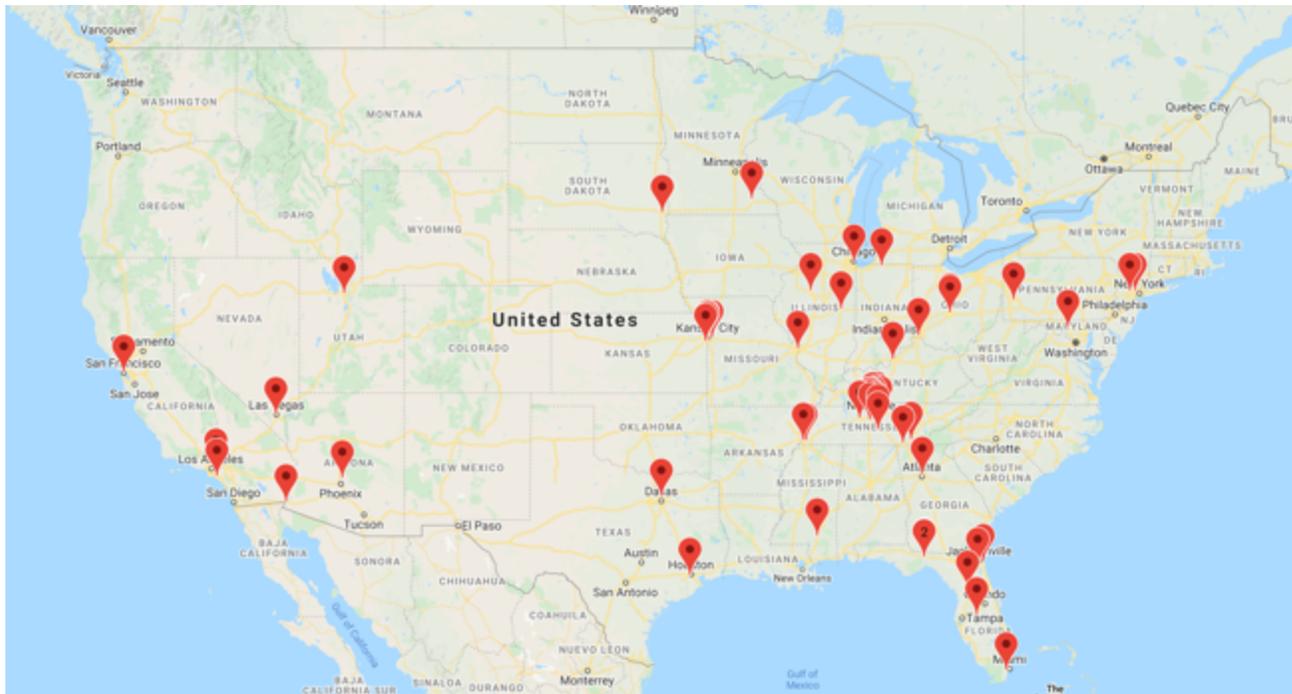


Exactis Innovation   
National Centre of Excellence in Personalized Medicine

MD Anderson  
~~Cancer Center~~



**TEMPUS**



ELAINE U.S. study sites



- ELAINE 1: Lead site Mayo Clinic
  - First patient in: September 2019
  - Recently initiated collaboration with Exactis and Personalize My Treatment (PMT) in Canada and will be pre-identify patients with ESR1 mutations at 7 Cancer Centers of Excellence in Ontario, Quebec, Nova Scotia, and New Brunswick for enrollment
  - Israel sites include renowned Sheba and Hadassah Medical Centers
- ELAINE 2: Lead site: MD Anderson
  - Sermonix in collaboration with TEMPUS is identifying patients at point of care and will be rapidly activating up to 12 U.S. sites
  - First patient in: October 2020
- Both trials targeting complete enrollment for mid-2021 and top-line data late 2021/early 2022

# FDA Fast Tracked Currently Enrolling Phase 2 Evaluation of LasofoxifeNe in ESR1 Mutations Relative to Fulvestrant after Progression on AI and CDK 4/6i, First Patient Dosed Q3 2019, Top-line data Q4 2021

## Objective to demonstrate efficacy in ESR1 mutation-positive, endocrine therapy-relapsing 2L patients.

### Design



- **Open, 1:1 randomized, multi-center, two-arm study**
- **5.0mg daily oral lasofoxifene or fulvestrant 500 mg IM q month**
- 5.0mg lasofoxifene dose chosen for maximum efficacy in acquired endocrine resistance; FDA agreement obtained
- **Stratified by visceral/non-visceral disease, and ESR1 Y537S status**

### Endpoints

- **Primary: progression free survival (PFS)**
- *Secondary:* clinical benefit rate (CBR) defined as percentage of all patients with complete or partial response and stable disease for  $\geq 24$  weeks, safety
- *Further:* objective response rate (ORR), duration and time to response, overall survival (OS), ESR mutations, QoL, pharmacokinetics

### Patients

- **100 in total (50:50)**
- Postmenopausal women and Premenopausal women on ovarian suppression ECOG 0 or 1
- **ESR1 mutation present on ct-DNA liquid biopsy** confirmed and having progressed on first or second hormonal treatment incl. AI mono, AI+CDK4/6

### Data Readout

- Interim data readouts throughout this open label study; top-line data expected Q4 2021
- **Robust data in ESR1 mutations could enable breakthrough designation and accelerated approval**

- Lead Study Site: MD Anderson



- Open label, multicenter, single arm safety study evaluating the safety and tolerability of the lasofoxifene and abemaciclib combination for the treatment of postmenopausal women with locally advanced or metastatic ER+/HER2- breast cancer and who have disease progression on first and/or 2<sup>nd</sup> lines of hormonal treatment for metastatic disease with ESR1 mutations
- 24 subjects at 6-10 sites
- Progression may have occurred on no more than two of the following treatments for metastatic breast cancer:
  - Aromatase inhibitor (AI) and/or fulvestrant either as monotherapy or in combination with any commercially approved CDK 4/6 inhibitor (CDKi)
  - And/or the combination of fulvestrant and alpelisib; and/or tamoxifen; and/or the combination of exemestane/everolimus
- Topline Data early 2022

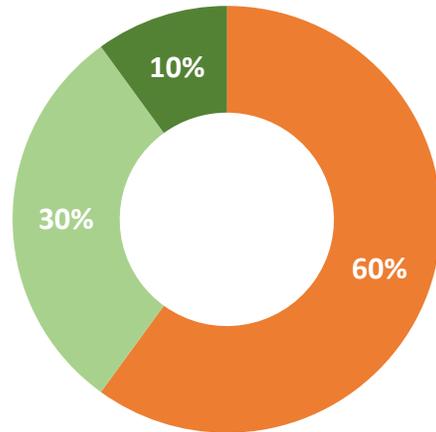
# Lasofoxifene ESR1 Development Strategy: Precision Medicine Target Product Profile Vetted in Pricing and Payer Market Research

Lasofoxifene's unique target product profile in the acquired endocrine resistance setting and presence of ESR1 mutations.

Indication	LASOFOXIFENE is an estrogen agonist/antagonist indicated for the treatment of postmenopausal women, and premenopausal women on ovarian suppression, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after a combination aromatase inhibitor and CDK 4/6 inhibitor.	
Efficacy	Primary Endpoint (PFS)	Product Laso Superiority to Fulvestrant: 7 months (Laso) vs. 4 months (F)
	Secondary Endpoints (ORR, CBR, OS)	<b>ORR:</b> 25% (Laso) vs. 15% (F) <b>Clinical Benefit Rate (CBR):</b> 50% vs. 35% <b>OS:</b> Data not mature at time of analysis
Safety	Endometrial safety: <ul style="list-style-type: none"> <li>No increase in endometrial cancer</li> <li>Benign endometrial changes</li> <li>No increase in endometrial hyperplasia</li> </ul>	<b>Most common AEs (Grade 1-2):</b> <ul style="list-style-type: none"> <li>Hot flashes 12.3%</li> <li>Vaginal discharge 5.5%</li> <li>Muscle spasm 14.8%</li> <li>Deep vein thrombosis 1%</li> </ul>
	<b>Most severe AEs (Grade 3-4):</b> <ul style="list-style-type: none"> <li>Hot flashes 1.1%</li> <li>Vaginal discharge 0.9%</li> <li>Muscle spasm 0.9%</li> <li>Deep vein thrombosis 1%</li> </ul>	Grade 3 + 4 AE equivalence to fulvestrant  *SERM class box warning for VTEs
Convenience	Once-daily pill suitable for out-patient administration (potent and orally bioavailable), no DDIs, taken with or without food	
Dosing	5mg PO QD with or without food	
Companion Diagnostic	FDA approved liquid biopsy, Next Generation Sequencing (NGS) test for presence of common ESR1 mutations; Medicare Part B reimbursable	
Pricing	US\$10,000 per month (with precision approach and companion diagnostic; parity with targeted therapies)	

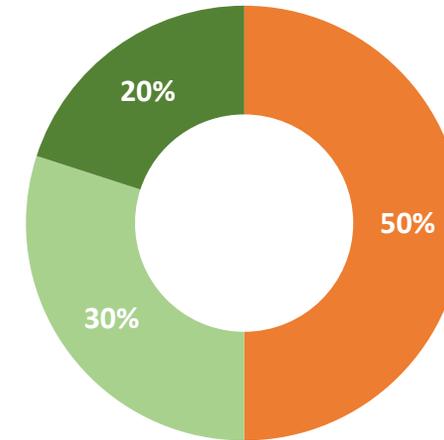
# The majority of MDs expect LASO monotherapy to shift 2<sup>nd</sup> and 3<sup>rd</sup>-line treatment landscape

### Anticipated Impact for LASO use in 2<sup>nd</sup> Line



Poised after an AI+CDK 4/6 failure to displace Fulvestrant monotherapy or an mTOR combo in 2<sup>nd</sup>-line

### Anticipated Impact for LASO use in 3<sup>rd</sup> Line



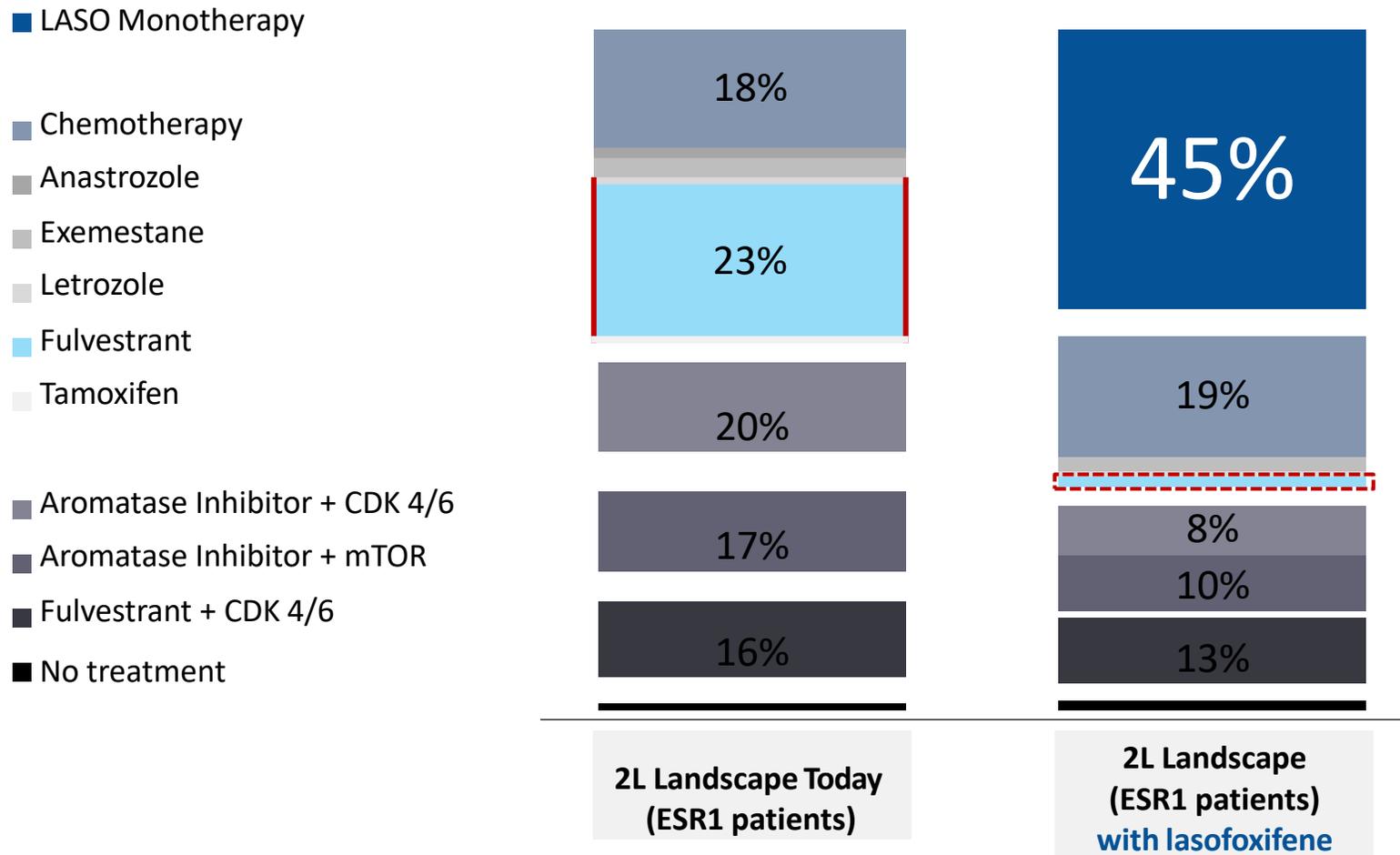
Valued for providing the option to delay chemotherapy and/or to offer a less toxic option for more fragile patients in 3<sup>rd</sup>-line

- No Practical Impact
- Incremental change
- Significant Change
- Paradigm Shift

Assuming superiority to Fulvestrant, physicians see a meaningful role for LASO monotherapy in 2<sup>nd</sup> and 3<sup>rd</sup>-line

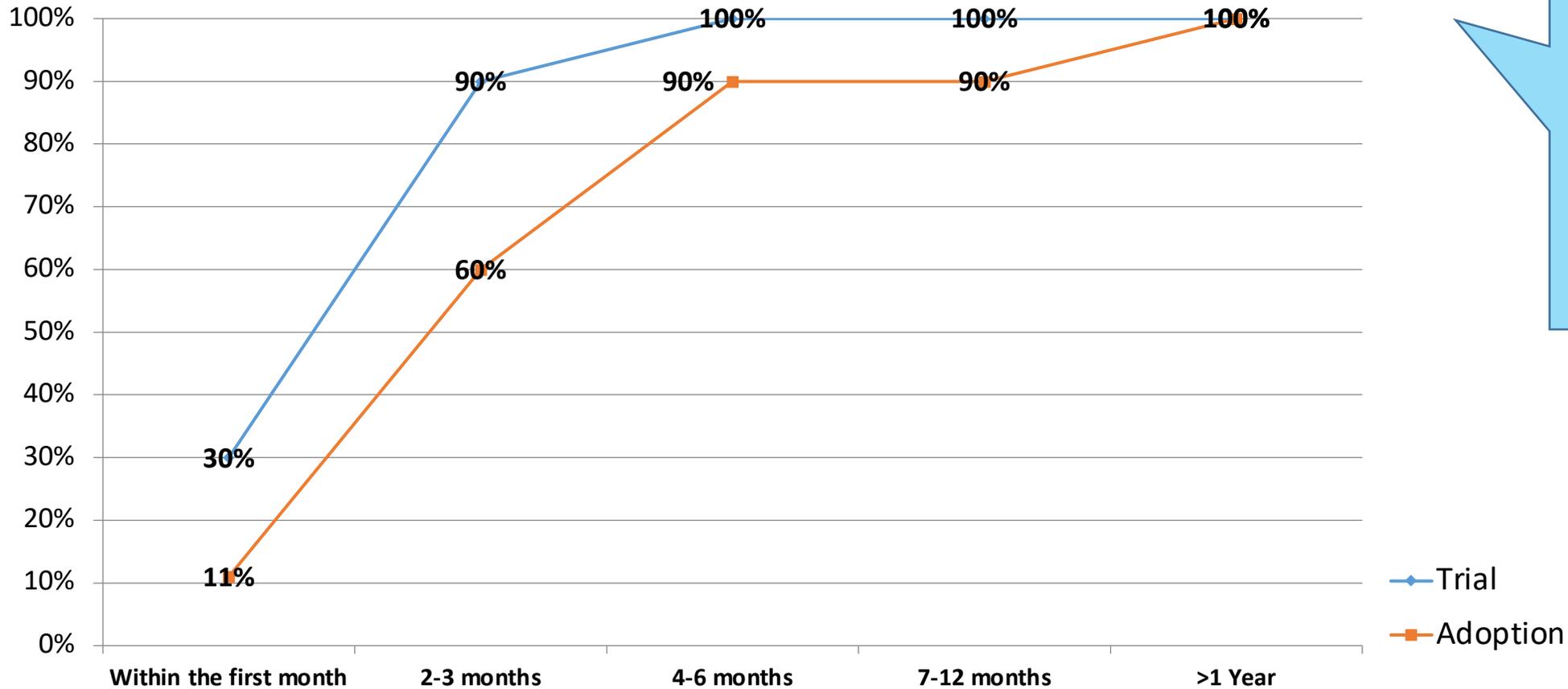
# Lasofoxifene Monotherapy – Shift away from Fulvestrant even with targeted therapy price point

**Market Research Suggests Lasofoxifene Monotherapy Will Be Used in 45% of Second Line Patients With ESR1 Mutation, replacing Fulvestrant and AIs.**



# SERM Comfort and Appeal: Majority of MDs see few obstacles and will adopt lasofoxifene monotherapy within 3 months of launch

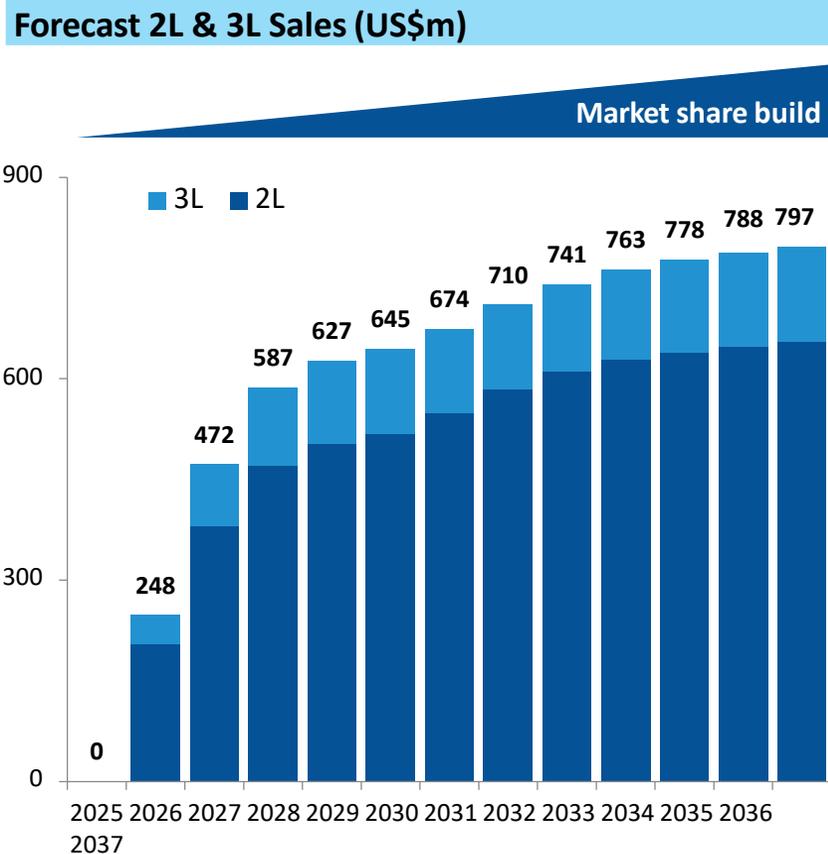
**Trial & Adoption of Lasofoxifene Monotherapy**  
*In 2<sup>nd</sup> & 3<sup>rd</sup> Line ESR1+ Patients*



*“A targeted SERM with better efficacy and tolerability is what we need in our armamentarium.”*

# US\$800M Peak Sales Projection confirmed by Primary Market Research

Significant potential can be accessed by label-broadening Phase 2 combination trials.



- Potential for US\$1+ billion peak sales at end of exclusivity period
  - Chart shows US 2L & 3L monotherapy alone; based on proprietary primary market analysis in 60 high-prescribing medical oncologists
  - Treatment duration: 2L 14 months, 3L 7 months
- Price target of US\$10,000/month
  - Payer access and formulary acceptance with companion dx; known class with fast to prescribing within 1-3 months
  - Cumulative sales of ~US\$7.8 billion
- “Low hanging fruit” for further revenue potential from use in various combinations
  - Substantiated by a series of Ph II-III trials for compendium submission
  - Payer research confirms coverage and access in mono and combination based on publications and NCCN guidelines

Source: BioVid proprietary market analysis.

# Late-expiring intellectual property maximizes value creation and life-cycle management

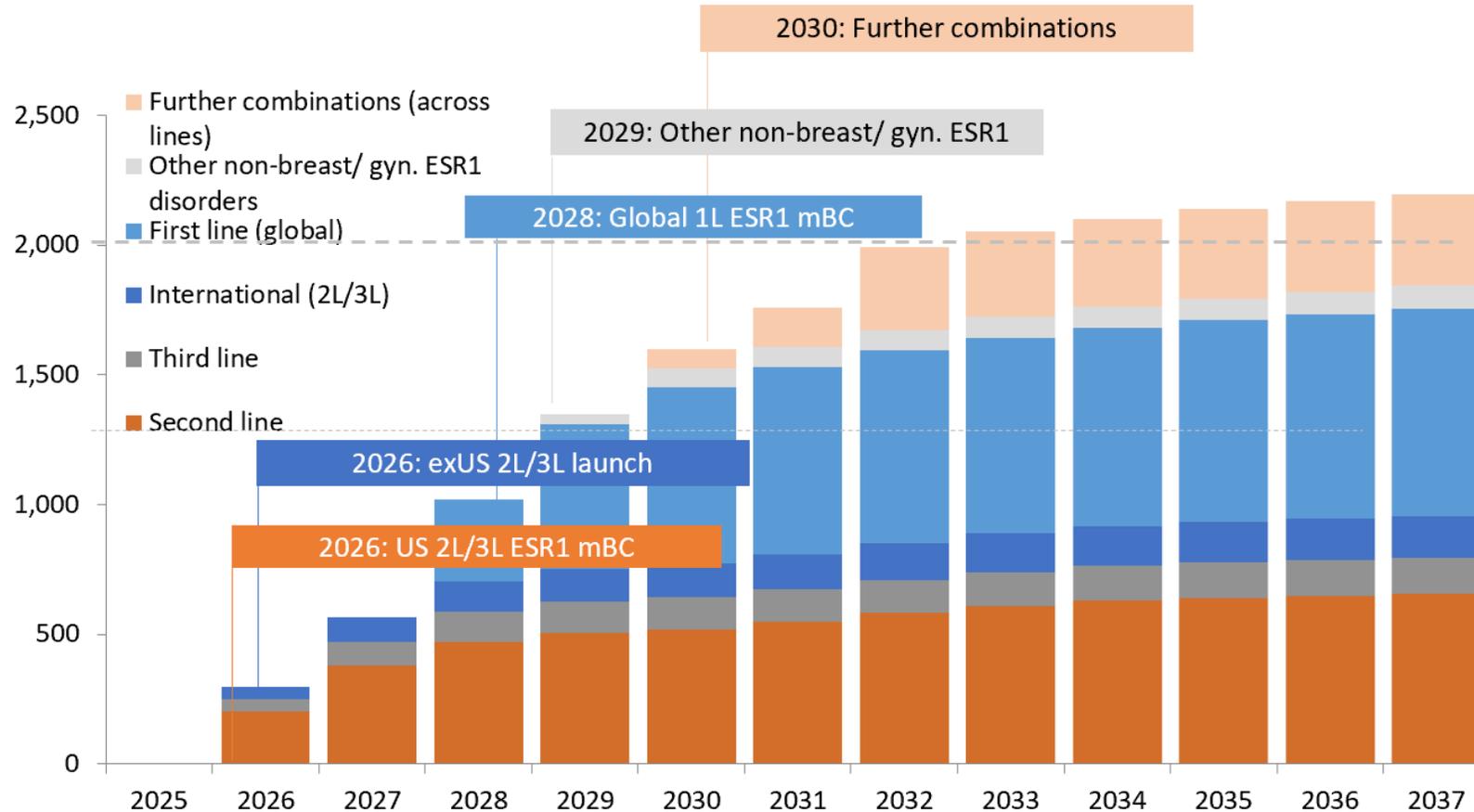
## Sermonix has strong, multi-faceted and late-expiring IP protection for lasofoxifene.

- Sermonix holds exclusive global license to oral lasofoxifene from Ligand
  - All rights Pfizer previously held in lasofoxifene were fully returned to originator Ligand Pharmaceuticals (LGND)
- Sermonix holds exclusive global license to new non-obvious and enabled IP from Duke University on use of lasofoxifene in acquired endocrine resistance with ESR1 mutations
  - Provides exclusivity and protection through 2037 at the earliest
  - **Strongly protect exclusivity for labeled indications for cancers with ESR1 mutations**
  - **Final U.S. office action Jan-19: claims allowed**
  - **Favorable EPO action**
  - **Sermonix response to Chinese Patent Office action Aug 3, 2020**
- Regulatory exclusivity
  - NCE status in US, Japan, China; potential new data exclusivity in the EU

# Building the Brand: Unique ESR1 Platform Substantiates Full Opportunity

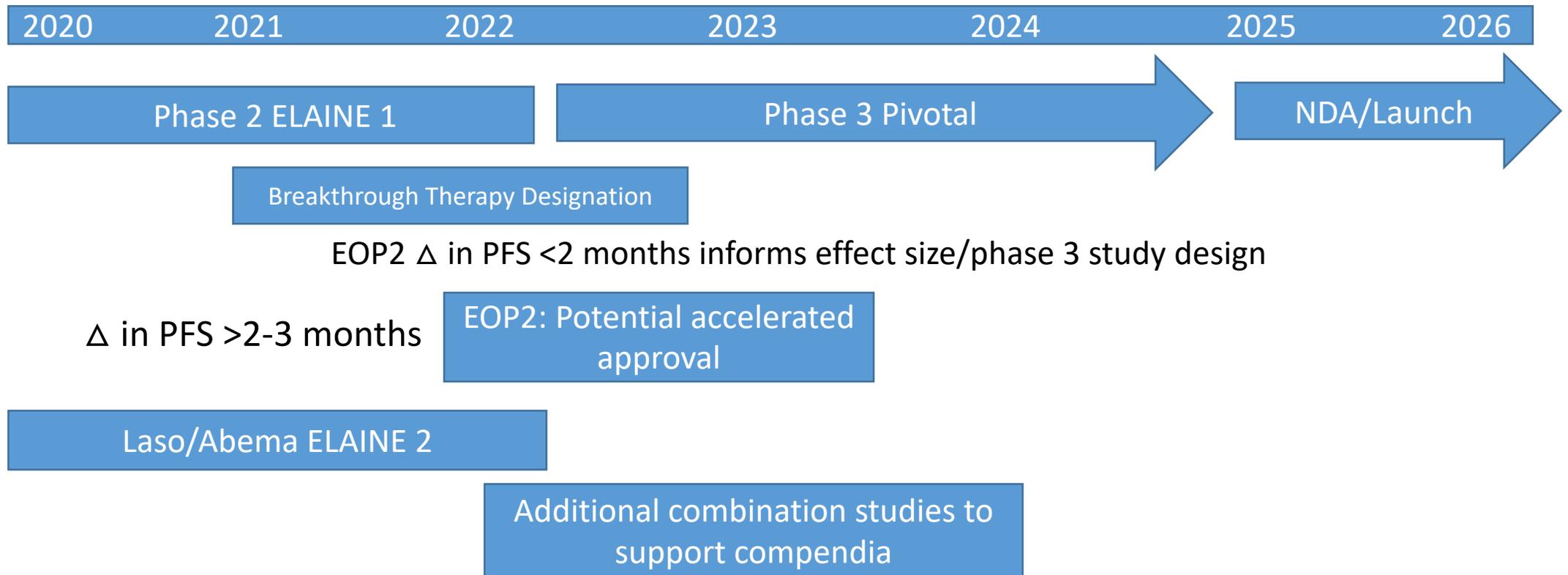
Potential for a >\$2bn blockbuster.

Illustrative Launches & Total Sales (US\$m)



# Initial launch and clinical development plan with longer term value creation

LASOFOXIFENE is an estrogen agonist/antagonist indicated for the treatment of postmenopausal women, and premenopausal women on ovarian suppression, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, ESR1-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after a combination aromatase inhibitor and CDK 4/6 inhibitor.



# Use of Series B proceeds to fund company through 2023 for potential accelerated approval, CDx and manufacturing scale up, Phase 3 planning

In US\$	2020				2021				2022				2023				Total
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
Manufacturing	49k	208k	360k	351k	310k	350k	350k	350k	550k	550k	550k	550k	1,000k	1,000k	1,000k	50k	7,579k
CMC																	4,729k
Clinical Trials	649k	1,197k	1,648k	1,723k	2,753k	2,753k	2,604k	3,396k	3,644k	3,644k	3,519k	3,519k	850k	850k	850k	850k	34,325k
ELAINE 1																	13,460k
ELAINE 2																	7,364k
Japan PK																	1,000k
CDRH/CDX																	7,100k
NDA/Registration Study Prep																	5,400k
Commercialization	40k	25k	123k	123k	150k	150k	150k	150k	500k	500k	500k	500k	-	-	-	-	2,912k
Preclinical	75k	75k	75k	75k	100k	100k	100k	100k	-	-	-	-	-	-	-	-	700k
Management/Operations	476k	453k	460k	750k	530k	480k	480k	460k	520k	520k	520k	520k	520k	520k	520k	520k	8,249k
Quarterly Total:	1,289k	1,958k	2,666k	3,022k	3,844k	3,833k	3,684k	4,456k	5,214k	5,089k	5,089k	5,089k	2,370k	2,370k	2,370k	1,420k	
Annual Total:	8,935k				15,817k				20,482k				8,530k				
Grand Total:																	53,765k

Q1-21:  
LPFV  
ELAINE  
1 and 2

ELAINE  
Top Line  
Data

2022:  
EOP2 Breakthru Designation



# Sermonix Investment and Partnering Opportunity

**Lasofoxifene – a unique de-risked program as a targeted therapy for ESR1 mutated metastatic breast cancer with significant opportunity for near term value creation and ROI.**

- ✓ Widely de-risked best-in-class endocrine agent
- ✓ Unique activity against ESR1 mutations; \$800M peak annual U.S. sales potential in first labelled indication with significant >\$2B peak sales upside from global and label buildout
- ✓ Potential for mono- and combination therapy across treatment lines; Lilly collaboration
- ✓ Exclusive license to newly generated late-expiring IP with protection through 2037
- ✓ Short pathway to value creation given FDA-accepted and fast-tracked phase II enrolling study; large existing preclinical, clinical program; extensive safety database; activity signal by Q4 2020; topline data Q4 2021 – potential for breakthrough designation
- ✓ Established platform for strategic acquirer with investments across phase II, CMC, CDx & commercial
- ✓ Seasoned investor base with track record of identifying high-value investments