MF5 FOR MENOPAUSAL SYMPTOMS

IATERION INC

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www.iaterion.com

THERE IS AN URGENT NEED TO SUPPORT WOMEN'S HEALTH

1

The Vast Majority of **Women Experience Menopause**

3

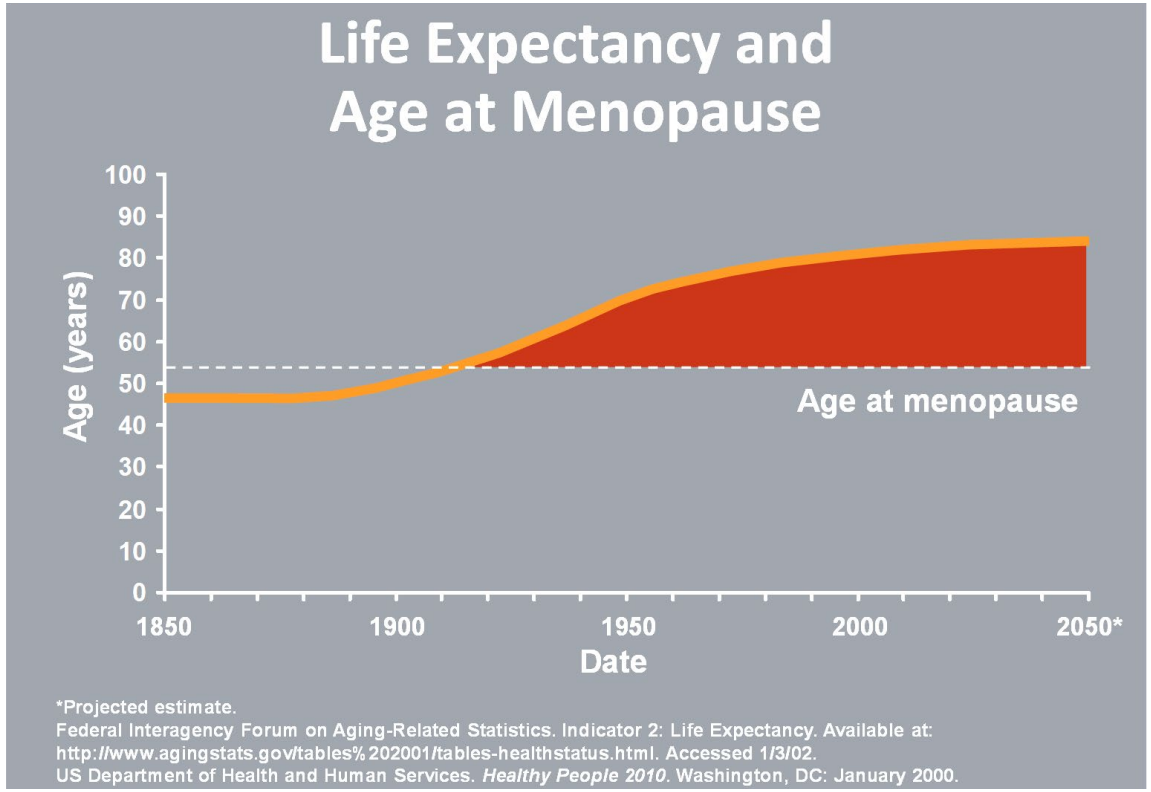
Currently there is **No Investment** in Women's Health

2

Current **Therapies are Not Safe**

MENOPAUSE WILL AFFECT EVERY WOMAN

Most women experience symptoms that disturb their quality of life and experience health issues both prior to and post menopause



Due to increased life expectancy, most women live 40% of their life in menopause

6,000 women in the US enter menopause daily

By 2025 that number will increase to 50 million in the US and 1.1 billion worldwide

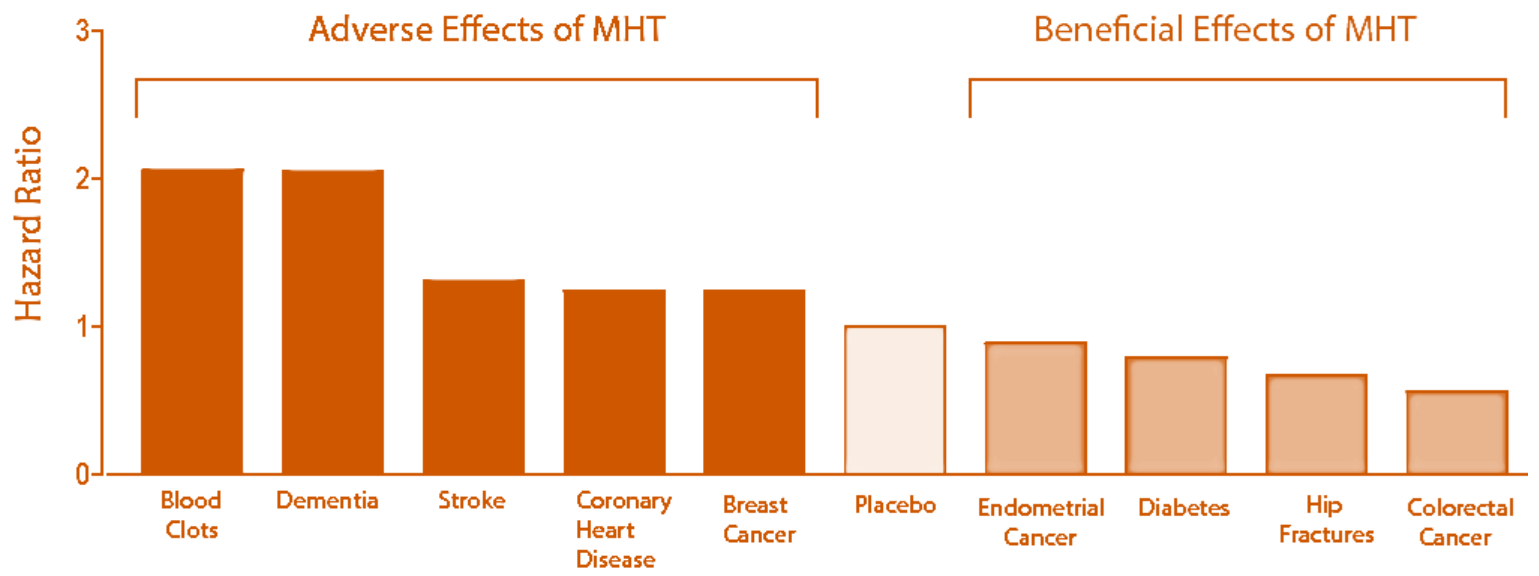
SYMPTOMS OF MENOPAUSE EFFECT WOMEN DAILY

Percent of women experiencing menopausal symptoms

EARLY STAGE SYMPTOMS	IMPACT	LATE STAGE CONDITIONS	IMPACT
Hot flashes/ Night Sweats	65-75%	Osteoporosis/ Fractures	43.1% of women over the age of 50 have low bone mass
Sleep Disturbance	65-75%	Type II Diabetes	19.4%
Mood Swings	64-70%	Cardiovascular disease	38% vs 4% in pre-menopause
Vaginal Atrophy/ Dryness	40-60%	Cancer	54% rate of breast cancer 73.5% die of breast cancer
Weight Gain/ Obesity	30-55%	Alzheimer's/ Dementia	65-70% of all Alzheimer's patients

CURRENT HORMONE THERAPIES PROVIDE MORE RISK THAN BENEFIT

MENOPAUSE HORMONE THERAPY (MHT)



Following the WHI results, FDA added 6 "black Box" warnings to MHT and allows MHT for short term use ONLY.

RESULTS

73% of women aged 40-65 are **NOT** currently treating their menopause symptoms

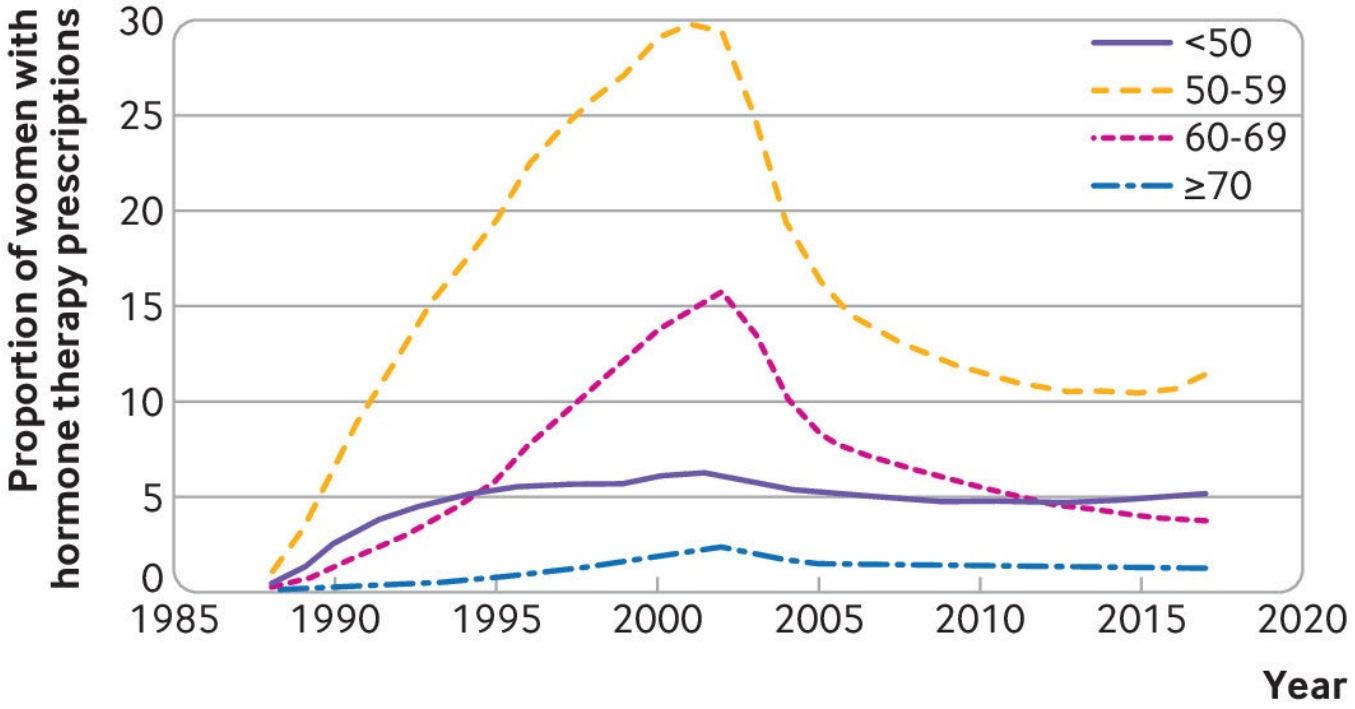
68% have **NOT** used OTC vaginal treatments

65% would **NOT** consider taking MHT

(Statista, 2022)

THE CURRENT HORMONE THERAPY MARKET IS FAILING WOMEN

There is a desperate need for an alternative treatment to address menopausal symptoms and mitigate downstream diseases



INSIGHTS

Sales of menopause hormone therapies dropped by 65% following the Women's Health Initiative (WHI) trials in 2002

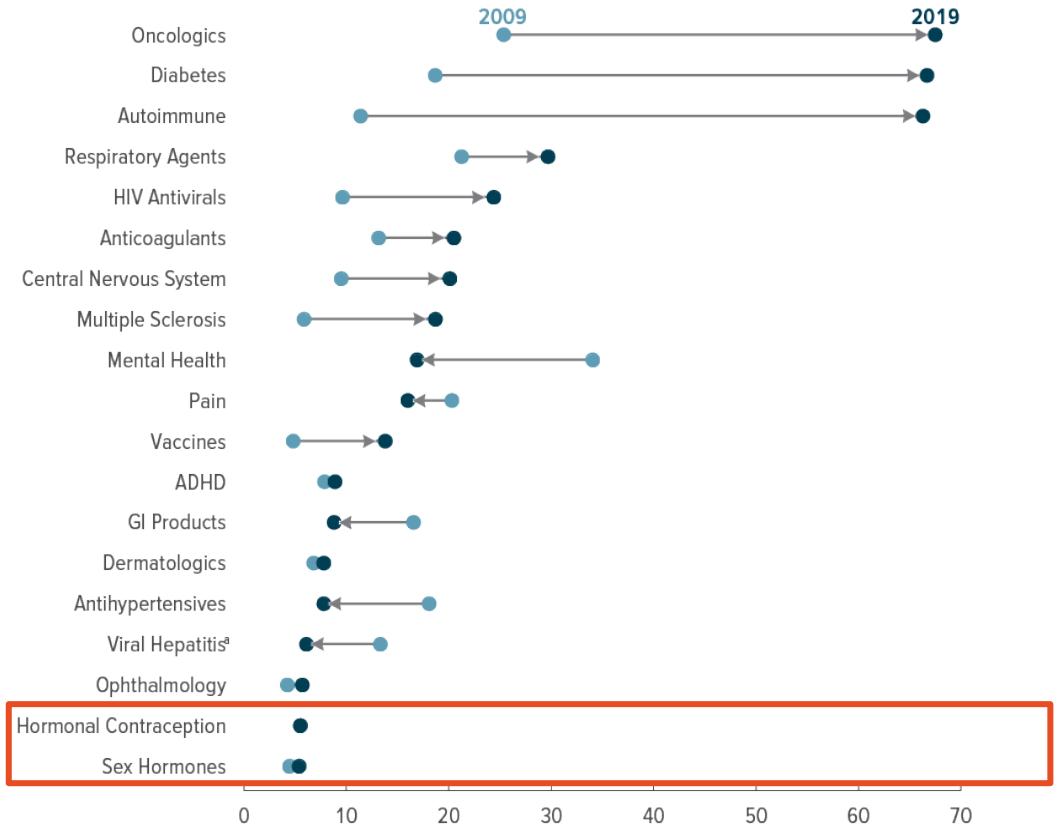
Hormone replacement therapy market is projected to hit $46.5 Bn by 2027, at a CAGR of 5.1%. The Menopausal segment is attributed to display the **fastest market growth by period**.

WOMEN'S HEALTH FUNDING

"Proving the return on investment is the hardest thing for most healthcare companies—providing it for women's health is even harder, even if we may have overcome the barrier of belief that women's health opportunities are significant"

Rock Health CEO Bill Evans. Aug 18, 2021

Total U.S. Retail Drug Spending by Therapeutic Class, 2009 and 2019



Congressional Budget Office, April 2021

MARKET INEFFICIENCIES

Despite media and political discussion concerning women's health there is no investment in women's health

There is not a single large or medium size pharma investing in women's health

There is no NIH study section dedicated to women's health

Most women's health products are on the market for >50 years

MF5: MENOPAUSAL HOT FLASHES

Based on Statistically significant Phase 2 results of Bionovo, Inc. botanical drug Menerba (MF101) under FDA IND	MF5 active chemical compounds were isolated	MH5 has a unique mechanism of action: Selective Estrogen Receptor β (ERβ) agonist
MH5 prevents breast and uterine cancer	MH5 does not increase the risk of clotting	MH5 may also prevent osteoporosis

"Although MF-101 appears to be a promising therapeutic, the herbal composition of the drug may be a disadvantage... If these isolates were demonstrated to be as effective and safe in clinical trials as preliminary data suggest regarding MF-101, these compounds could change the way clinicians treat menopause-associated symptoms"

Stovall DW, Pinkerton JV. Curr Opin Investig Drugs. 2009 Apr;10(4):365-71.PMID: 19337958 Review.

MF5 HISTORY- FROM TRADITIONAL CHINESE MEDICINE TO TARGETED DRUG

玉不琢，不成器。 – *Yù bù zhuó, bù chéng qì. "If a jade is not cut and polished, it can't be made into anything."*

1

MF101 originated from clinical practice treating women with a history of breast cancer experiencing hot flashes

2

It was conceived to treat menopausal symptoms without increasing breast cancer risk

3

After more than a decade of practice and over 1000 women treated a formula of 21 herbs was developed (Menopause Formula 101)

4

The formula was shown to be ERβ selective, resulting in no uterine hyperplasia and no breast cancer cell proliferation or tumor formation

5

The formula of 21 herbs was tested under FDA-IND, resulting in clinical efficacy and safety up to Phase 2B

6

20 of the 21 herbs showed ERβ selectivity (the 21st ingredient was used to enhance extraction of the compounds)

7

98 selective ERβ small molecules were isolated from the 20 active herbs

8

5 compounds with the highest specific ERβ activity and selectivity were chosen for further development in MF5

MF101 PHASE 2B RESULTS

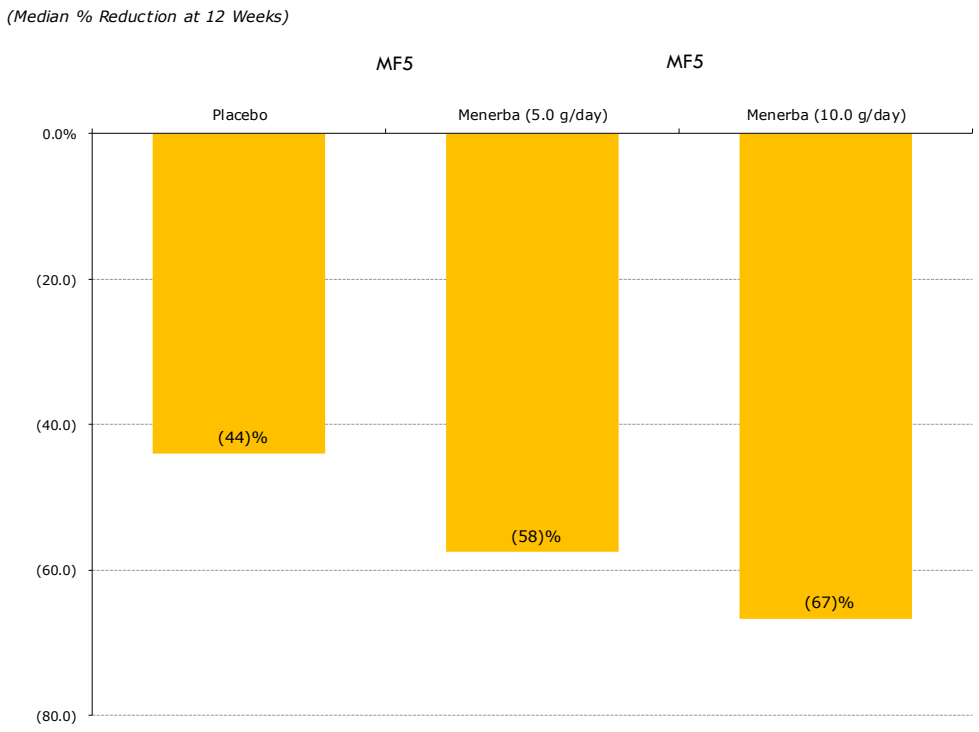
PRIMARY EFFICACY: HOT FLASHES

MF101 demonstrated statistically significant (p=0.04) reduction in hot flashes in the high dose group	62% absolute reduction in all hot flashes	Odds ratio of 60% reduction on MF101 vs. placebo was 2.4 (p=0.02)	At 12 weeks MF101 was 1.36/day moderate to severe hot flashes lower than placebo (p=0.04)	MF101 exhibits a clear dose response curve	Reduction in hot flashes is greater for the drug later in the study (week 4-12) in the treatment group vs placebo, confirming drug effect and not placebo effect

MF101 PHASE 2B RESULTS

SECONDARY EFFICACY: SLEEP DISORDER

MF101 demonstrated a significant reduction (67%) in nighttime awakenings, a common issue with hot flashes compared to placebo group



p-value (10.0g/day vs. Placebo)= 0.05

MF101 PHASE 2B RESULTS

SAFETY

No difference in the number of uterine bleeding episodes between treatment and placebo

No cases of endometrial hyperplasia

"Transient loose stools" was the only side effect (12.0% vs. 3.0% for placebo)

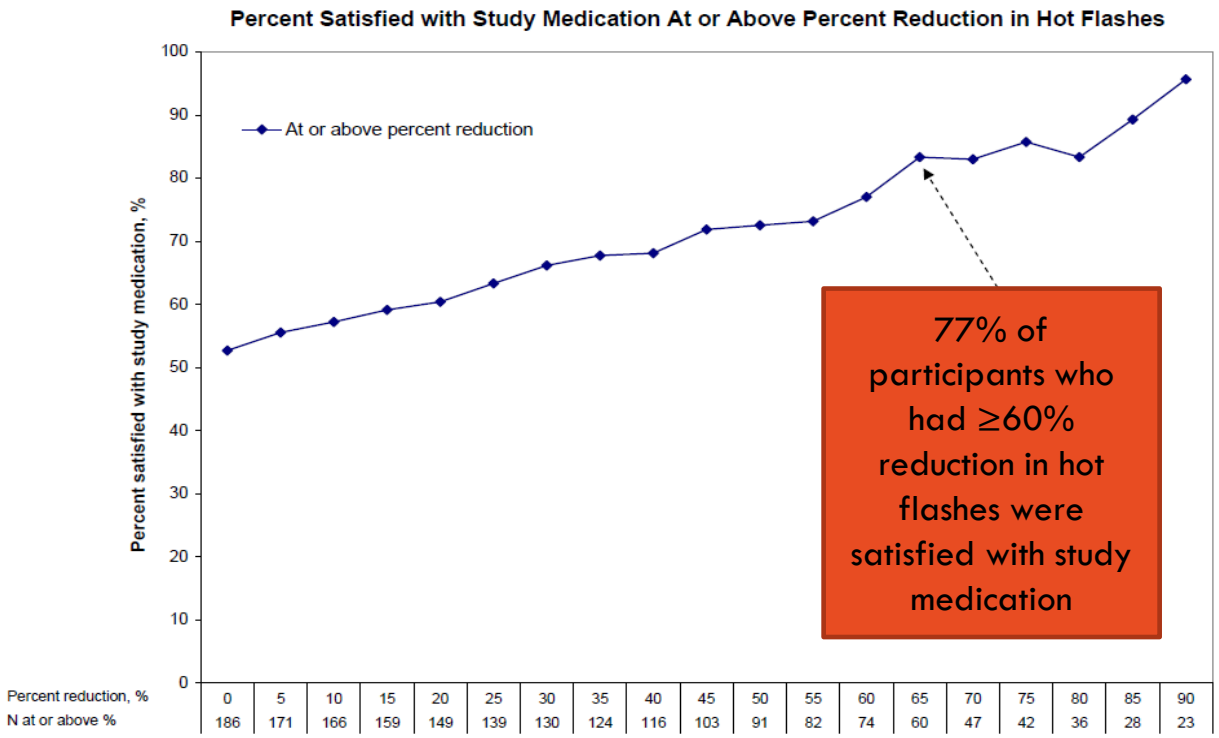
Benefit from reduced constipation on MF101 vs. placebo (1.3% vs. 4.0%)

Statistically significant reduction in weight (p=0.04) and BMI (p=0.05) on MF101 versus placebo (~10 Pounds)

91.0% of participants used greater than 75.0% of study medication during the 12-week period

Low drop out rate (2.0%)

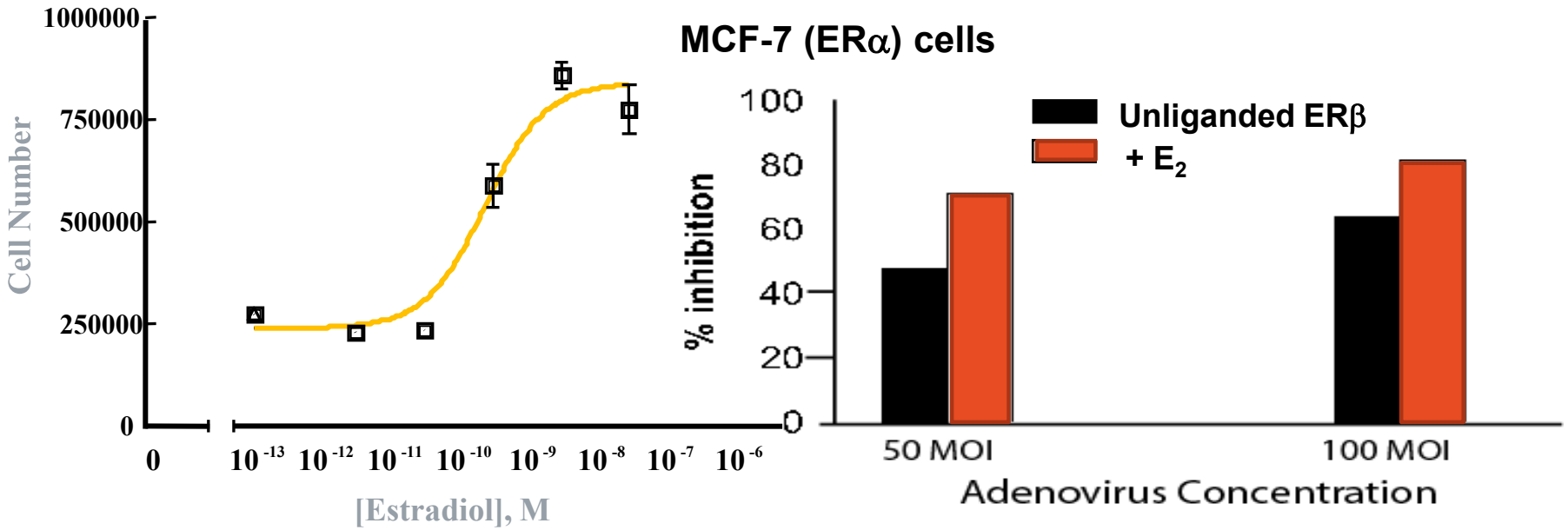
MF101 PHASE 2B FAVORED BY PATIENTS



Question at end of study (12 Weeks): Were you satisfied enough with the study medication that you would like to continue taking it for hot flashes?

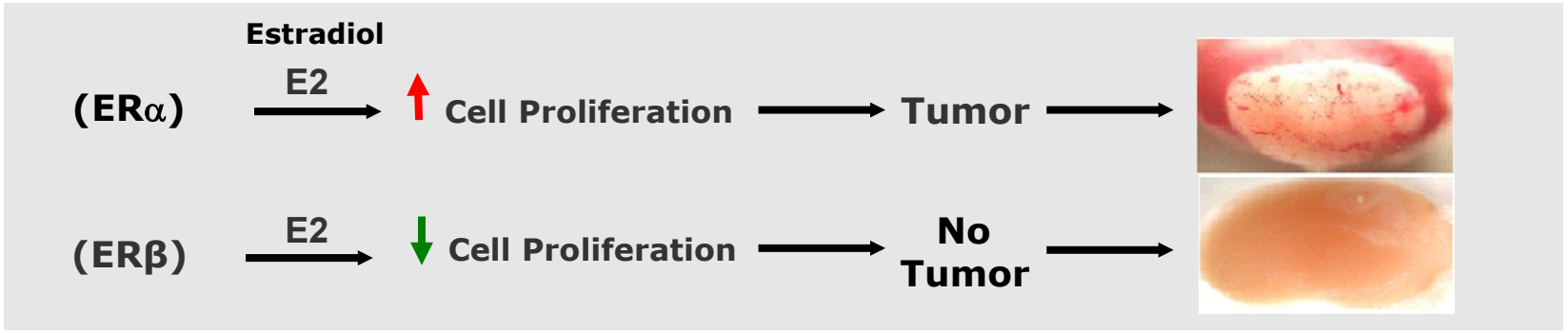
Phase 2B Efficacy	Odds Ratio (95% CI)	P value
With >50% Reduction in Hot Flashes at 12 weeks	2.3 (1.1- 4.7)	0.03
With >60% Reduction in Hot Flashes at 12 weeks	2.4 (1.1- 5.3)	0.02

MF101 IS A SELECTIVE ERβ MODULATOR



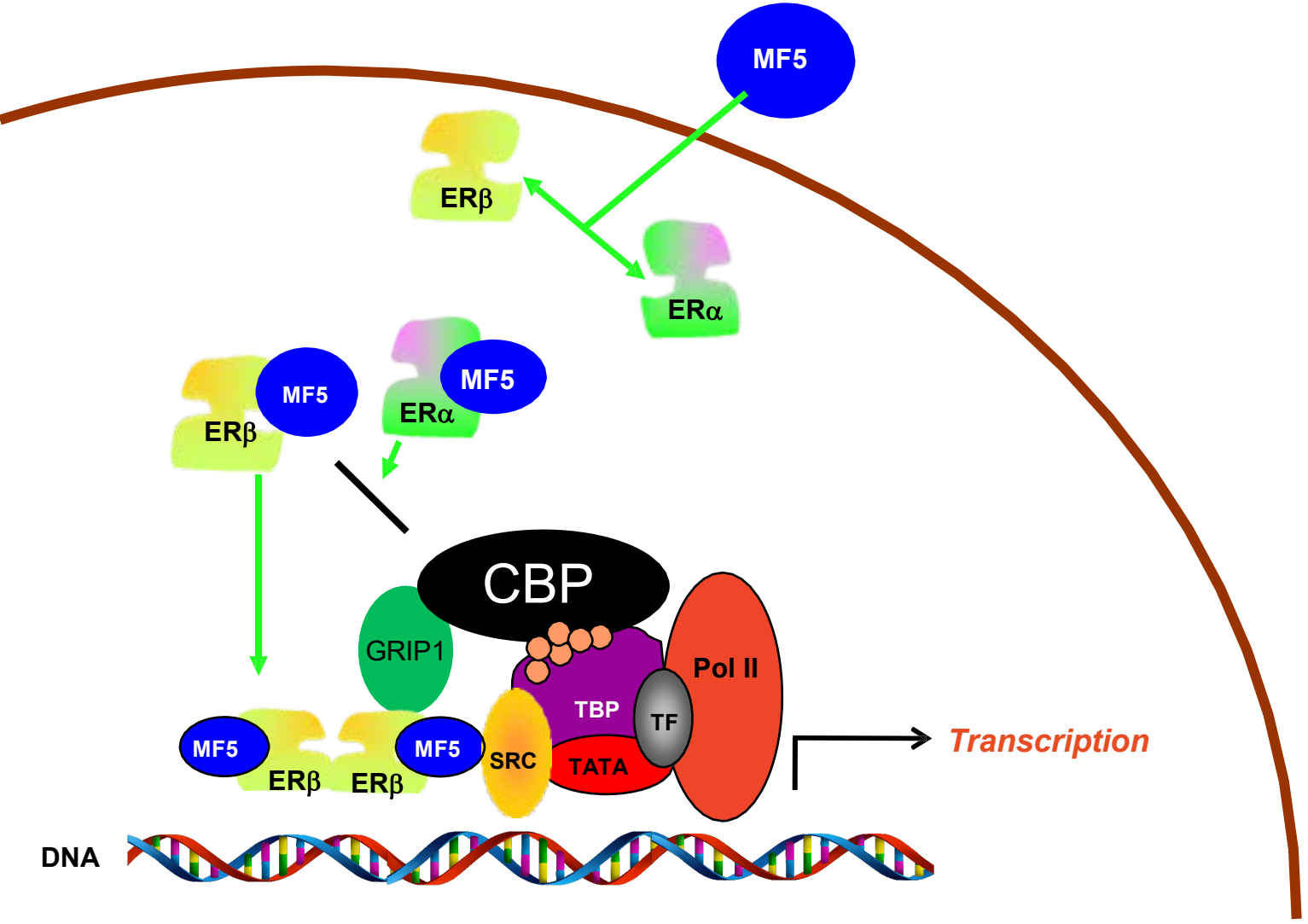
ERα mediates cell proliferation and tumor formation

ERβ inhibits breast cancer cells growth and tumor formation

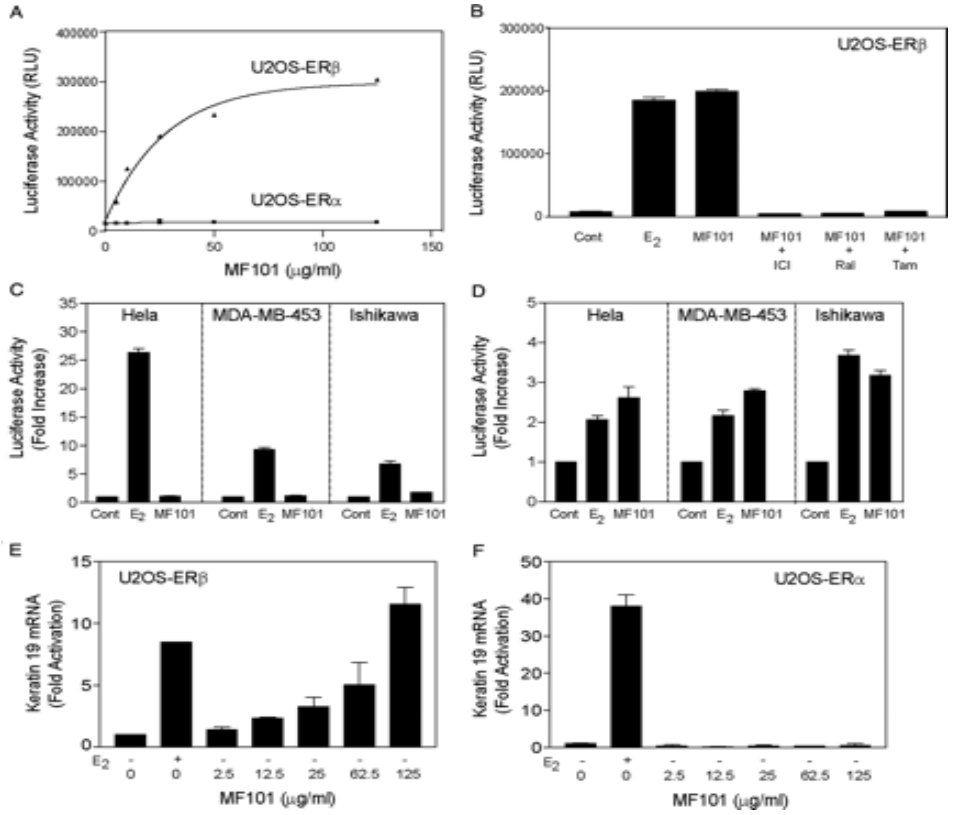


MF101 IS AN ESTROGEN RECEPTOR BETA (ERß) SELECTIVE MODULATOR

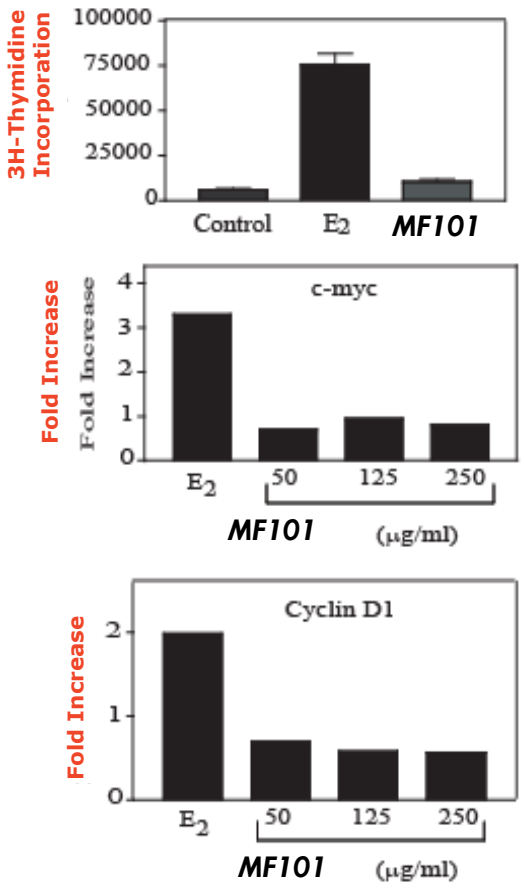
MF5 is comprised of active compounds from MF101

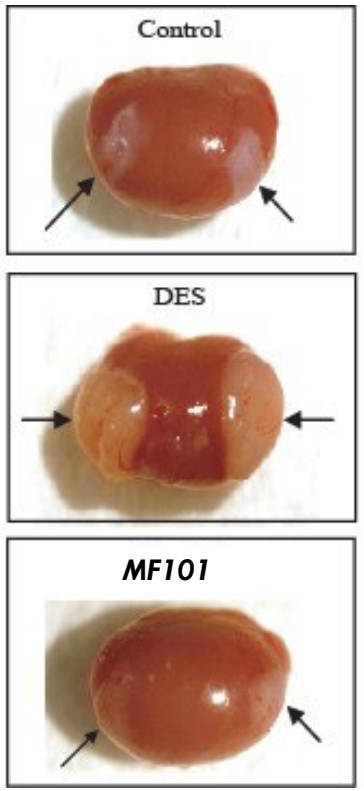


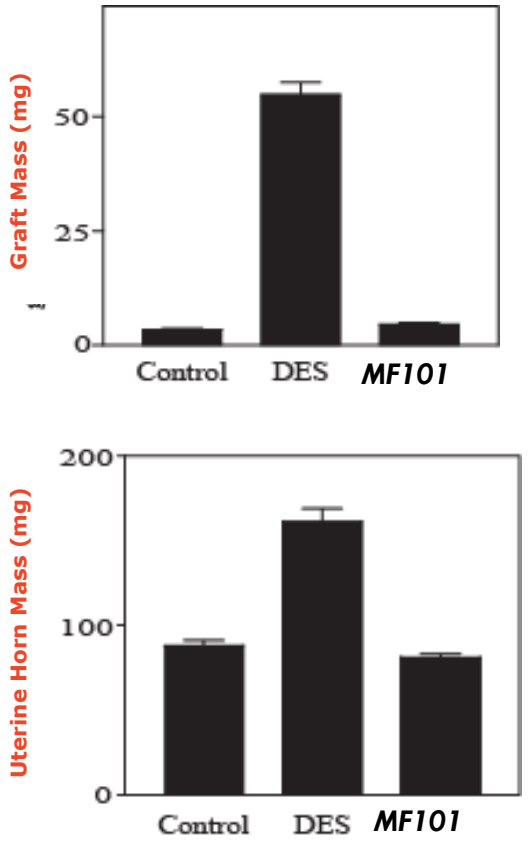
MF5 (MF101) SELECTIVELY ACTIVATES TRANSCRIPTION THROUGH ERß



MF101 DOES NOT STIMULATE CELL PROLIFERATION







IN CONTRAST TO ESTROGENS, MF101:

1. *Does not activate oncogenes related to estrogen mediated proliferation*
2. *Does not increase uterine proliferation*
3. *Prevents breast cancer tumor formation in animal models*

MARKET AND FDA PERSPECTIVE: LIKELIHOOD FOR SUCCESS

1

The FDA guidance requires inclusion criteria for vasomotor studies to treat postmenopausal women with over 50 moderate to severe hot flushes per week.

2

Placebo effect in hot flushes trials is very high (50%-60%)!. This makes FDA trials very challenging.

3

For example, Brisdelle™ (Paroxetine), a SSRI antidepressant was recently approved with efficacy -0.9 hot flush/day reduction over placebo (p=0.06)

4

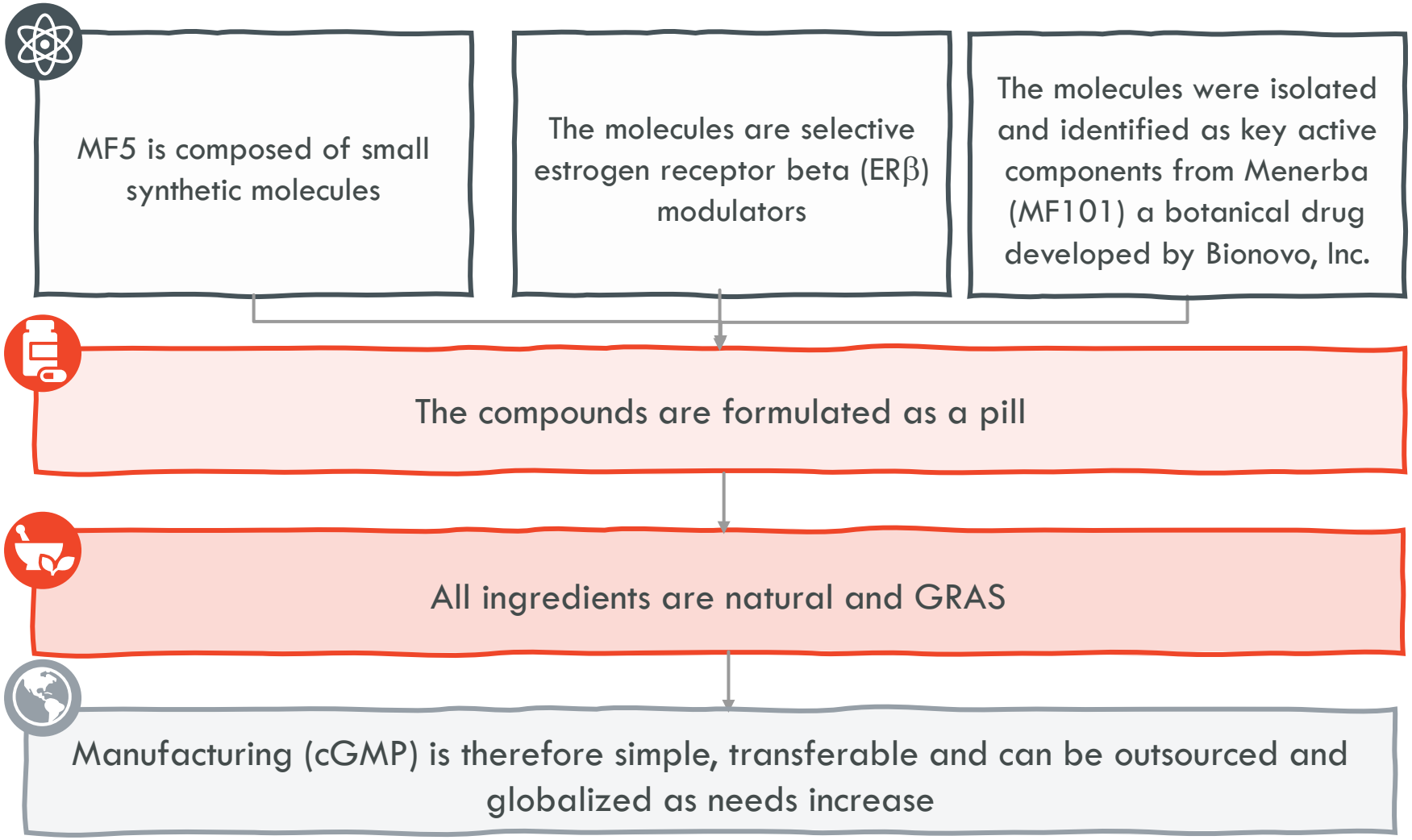
MF101 is already proven to be 50% more effective (-1.36 hot flush/day reduction) and much safer

REGULATORY PATHWAY TO MF5 DEVELOPMENT

- MF5 must follow the 2003 FDA Guidance for Estrogen and Estrogen/Progestin Drug Products
- Inclusion criteria for hot flashes >7 moderate to severe hot flashes per day (or >40 per week)
- Exclusion criteria: history of breast or uterine cancer
- Trial duration: 90 days of treatment with 30 days follow-up following treatment
- Expected efficacy of reduction of >2 moderate to severe hot flashes per day when compared to placebo
- Long term safety is measured by uterine bleeding episodes and increase in uterine double-wall increased thickness over placebo following 6 months of treatment (EMA requires one trial with standard MHT comparison)
- Two separate multi-center double blind placebo-controlled trials are required

1. Based on previous results the Phase 3 study size were 800 and 1200 women
2. Based on recent FDA approvals drugs were approved with far lower efficacy than >2 hot flashes/day reduction

MF5 CHEMISTRY AND MANUFACTURING OVERVIEW



SUMMERY OF THE DIFFERENCES BETWEEN MF101 AND MF5

DRUG	MF101	MF5
Development Rationale	Traditional Chinese Medicine/ Clinical Experience	Modern Molecular Biology MOA
Composition	21 herbs	5 pure compounds from MF101 herbs
Formulation/ Delivery	Oral-Crude extract in packet/ Sachet	Oral- Pill/ Capsule
Potential for Synthetic Analogs (NCEs)	No	Yes
Indications	Prevention of menopausal symptoms	Prevention of menopausal symptoms & Prevention of chronic menopausal conditions

INVESTMENT REQUIRED TO PROGRESS MF5 THROUGH TRIALS

Iaterion requests $18M to advance MF5 to the end of Phase 1 and 2

EXPENSE TYPE	COST
Synthesis and Scale-up	$0.5M
Final Formulation	$0.4M
Pre-Clinical Pharmacology	$1.6M
Animal Hot Flash Model	$0.5M
Toxicology	$2.5M
Phase 1/ 2 Clinical Trial	$8.0M
Regulatory	$0.5M
Legal (Corp and IP)	$1.0M
Corporate	$3.0M
Total	$18M

MILESTONES AND TIMELINE

MONTH 6:
LABORATORY STUDIES HOT FLASH MODEL

MONTH 9:
SYNTHESIS AND SCALE-UP

MONTH 12:
FORMULATION

MONTH 15:
TOXICOLOGY IND

MONTH 18:
INITIATE PHASE 1

MONTH 24:
INITIATE PHASE 2

MONTH 33:
FINALIZE PHASE 2

- Iaterion has synthetic path to all the compounds
- Laboratory confirmation studies will result in multiple publications
- Positive results from the hot flash model (mice or rats) will drive discussions with potential partners since only estrogens and progestogens work in the model
- Previous toxicology with Menerba (MF101) was clean with a wide therapeutic window; not expected to be different
- Phase 1 will be randomized placebo-controlled dose escalation (4 doses 30 postmenopausal women)
- Phase 2 will be randomized placebo controlled 120 days (90 treatment) study
- Positive Phase 2 results will most likely conclude in a licensing agreement

MF5 OPPORTUNITY SUMMARY

1

Iaterion's MF5 is the first and only clinically proven (with FDA Phase 2B study) to be safe and effective natural product for the treatment of menopausal women's symptoms

2

MF5 is likely superior to MHT because of its long-term safety

3

MF5 is superior to anti-depressants because of its safety, tolerability and long-term benefits

4

Women prefer natural products for Menopause, yet FDA approved

5

MF5 is likely to capture significant market share with proper marketing and continued clinical analysis (reduction in breast cancer risk, clotting events and stroke)

IP AND COLLABORATIONS

1

The company filed multiple provisional patents for its products

2

MF5 has 7 filings pending funding, including composition of matter and utility

3

The company is collaborating on the product science with multiple institutions

4

To date, all IPs are fully with the company

UCSF
University of California San Francisco

Stanford University

Berkeley
UNIVERSITY OF CALIFORNIA

UNIVERSITY OF MARYLAND

KU
THE UNIVERSITY OF KANSAS

SR
SOUTHERN RESEARCH

PERSONNEL

- Isaac Cohen, OMD, PhD- Chief Executive Officer
- Dale Leitman, MD, PhD- Chief Scientific Officer
- Klaus Kohl, PhD- Chief Technology Officer
- Lorin Johnson, PhD- BOD and SAB member. Founder Salix Pharmaceuticals
- Carlos Milla, MD- Acting Advisory Chief Medical Officer
- Uwe Christians, MD, PhD- Scientific Advisor for Clinical Pharmacology
- Mindy Goldman, MD- Scientific Advisor for Menopause
- Marcelle Cedars, MD- Scientific Advisor for Menopause
- Wally Wang, PhD- Scientific Advisor for Nuclear Receptors
- Chaoshen Yuan, MD, PhD- Senior Scientist
- Mark Rosenthal, MD- Scientific Advisor for Gerontology

CONCLUSION

IATERION

MULTI-PLATFORM	ROBUST PIPELINE	MARKET POTENCY	INVESTMENT
Iaterion developed multiple platforms for drug development utilizing multiple biological mechanisms	Iaterion has a robust pipeline of drugs for multiple indications	Iaterion's drugs can result in multibillion market potential	MF5 is seeking $18M to complete Phase 1/ 2 studies

info@iaterion.com

MENOPAUSE COMPETITIVE LANDSCAPE

- = Risk
+ = Benefit

Drug	Hot Flushes	Sleep Disturbance	Mood Swings	Breast Cancer	Uterine Cancer	Clotting	Alzheimer & Dementia	Weight Gain	Type 2 Diabetes
MHT*	+++	+++	+++	---	--- (1)	---	---	+++ (2)	+++ (2)
Anti- Depressants	++	+	+++	Zero Effect / -	Zero Effect	Zero Effect	Unknown	--	-
Botanical Supplements	Zero Effect	Zero Effect	Zero Effect	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
MF5	**+++**	**+++**	**+++**	**++ (3)**	**ZE**	**ZE**	**UNK**	**+++**	**++ (4)**

Notes:

(1) *Estrogen has to be opposed with progestins to prevent uterine cancer*

(2) *This benefit cannot be utilized for MHT because of the other long-term risks*

(3) *Mechanistically and in animal models Product M prevents breast cancer*

(4) *Mechanistically and in animal models* Product M *prevents Type 2 Diabetes*

**MHT: Menopause Hormone Therapy (Estrogen-based treatments)*

Menopause Market is estimated at ~$22B WW

1. MHT & Product M are useful for vaginal dryness and atrophy (VVA)
2. MHT & Product M are also useful for osteoporosis
3. **MHT cannot be utilized for neither condition due to its long-term risks**
4. Anti-Depressants and Botanical supplements have no effect on vaginal dryness and osteoporosis