

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT  
PURSUANT TO SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): November 18, 2014

**TherapeuticsMD, Inc.**

(Exact Name of Registrant as Specified in its Charter)

**Nevada**

(State or Other  
Jurisdiction of Incorporation)

**001-00100**

(Commission File Number)

**87-0233535**

(IRS Employer  
Identification No.)

6800 Broken Sound Parkway NW, Third Floor  
Boca Raton, FL 33487

(Address of Principal Executive Office) (Zip Code)

Registrant's telephone number, including area code: (561) 961-1900

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2 below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01. Regulation FD Disclosure.**

TherapeuticsMD, Inc. is furnishing as Exhibit 99.1 to this Current Report on Form 8-K an investor presentation which will be used, in whole or in part, and subject to modification, on November 18, 2014 and at subsequent meetings with investors or analysts.

The information in this Current Report on Form 8-K (including the exhibit) is being furnished pursuant to Item 7.01 of Form 8-K and shall not be deemed to be “filed” for the purpose of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor will any of such information or exhibits be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except as expressly set forth by specific reference in such filing.

**Item 9.01. Financial Statements and Exhibits.**

(d) *Exhibits.*

<u>Exhibit Number</u>	<u>Description</u>
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99.1	<a href="#">TherapeuticsMD, Inc. presentation dated November 2014.</a>
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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 18, 2014

THERAPEUTICSMD, INC.

By: /s/ Daniel A. Cartwright  
Name: Daniel A. Cartwright  
Title: Chief Financial Officer

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## EXHIBIT INDEX

Exhibit Number	Description
99.1	<a href="#">TherapeuticsMD, Inc. presentation dated November 2014.</a>



TherapeuticsMD®  
*Supporting Women's Health for Life*

# Investor Overview

NOVEMBER 2014



[www.TherapeuticsMD.com](http://www.TherapeuticsMD.com)

# Forward-Looking Statements

This presentation by TherapeuticsMD Inc. (referred to as “we” and “our”) may contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended.

Forward-looking statements may include, but are not limited to, statements relating to our objectives, plans and strategies as well as statements, other than historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future. These statements are often characterized by terminology such as “believe,” “hope,” “may,” “anticipate,” “should,” “intend,” “plan,” “will,” “expect,” “estimate,” “project,” “positioned,” “strategy,” and similar expressions and are based on assumptions and assessments made in light of our managerial experience and perception of historical trends, current conditions, expected future developments, and other factors we believe to be appropriate.

Forward-looking statements in this presentation are made as of the date of this presentation, and we undertake no duty to update or revise any such statements, whether as a result of new information, future events or otherwise. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties, many of which may be outside of our control. Important factors that could cause actual results, developments, and business decisions to differ materially from forward-looking statements are described in the sections titled “Risk Factors” in our filings with the Securities and Exchange Commission, including our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as well our current reports on Form 8-K, and include the following: our ability to maintain or increase sales of our products; our ability to develop and commercialize our hormone therapy drug candidates and obtain additional financing necessary therefor; the length, cost, and uncertain results of our clinical trials; potential adverse side effects or other safety risks that could preclude the approval of our hormone therapy drug candidates; our reliance on third parties to conduct our clinical trials, research and development and manufacturing; the availability of reimbursement from government authorities and health insurance companies for our products; the impact of product liability lawsuits; the influence of extensive and costly government regulation; the volatility of the trading price of our common stock; and the concentration of power in our stock ownership.

PDF copies of press releases and financial tables can be viewed and downloaded at our website:  
<http://www.therapeuticsmd.com/pressreleases.aspx>.



# A Promising Future

We are an **innovative women's health company** exclusively focused on developing and commercializing products for women throughout their life cycles.

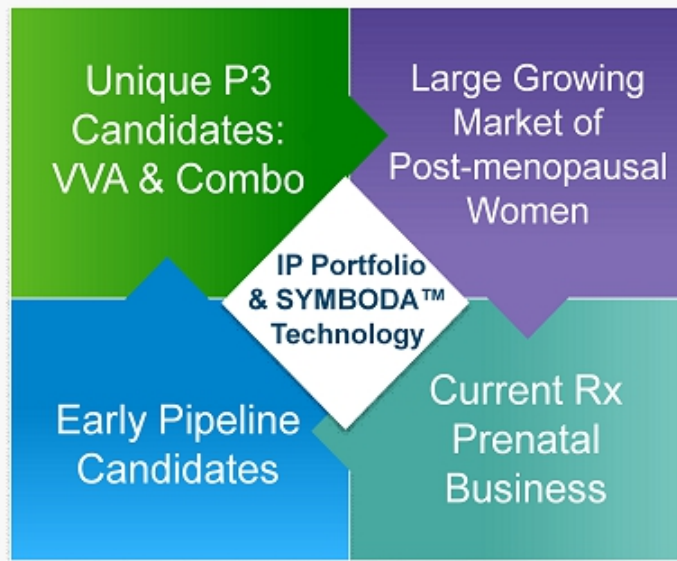


Our therapeutic portfolio of drug candidates is built on our SYMBODA™ technology platform, which enables new bio-identical hormone combinations, forms, and administration routes.

# Investment Rationale

- ❏ **Worldwide commercial rights for multiple hormone therapy products in Phase 3:**
  - ❏ Well-known chemical entities with established safety and efficacy thresholds
  - ❏ Expected FDA regulatory pathway: 505(b)(2)
  - ❏ Bio-identical market recently impacted by new Drug Quality and Security Act
- ❏ **Large, overlooked and growing markets** with unique competitive dynamics
- ❏ **Multiple earlier-stage candidates including transdermal applications**
- ❏ **U.S. commercial infrastructure** marketing prescription and OTC prenatal vitamins to Ob/Gyns and other women's health specialists
- ❏ **Experienced management team** with proven development and commercial success in women's health

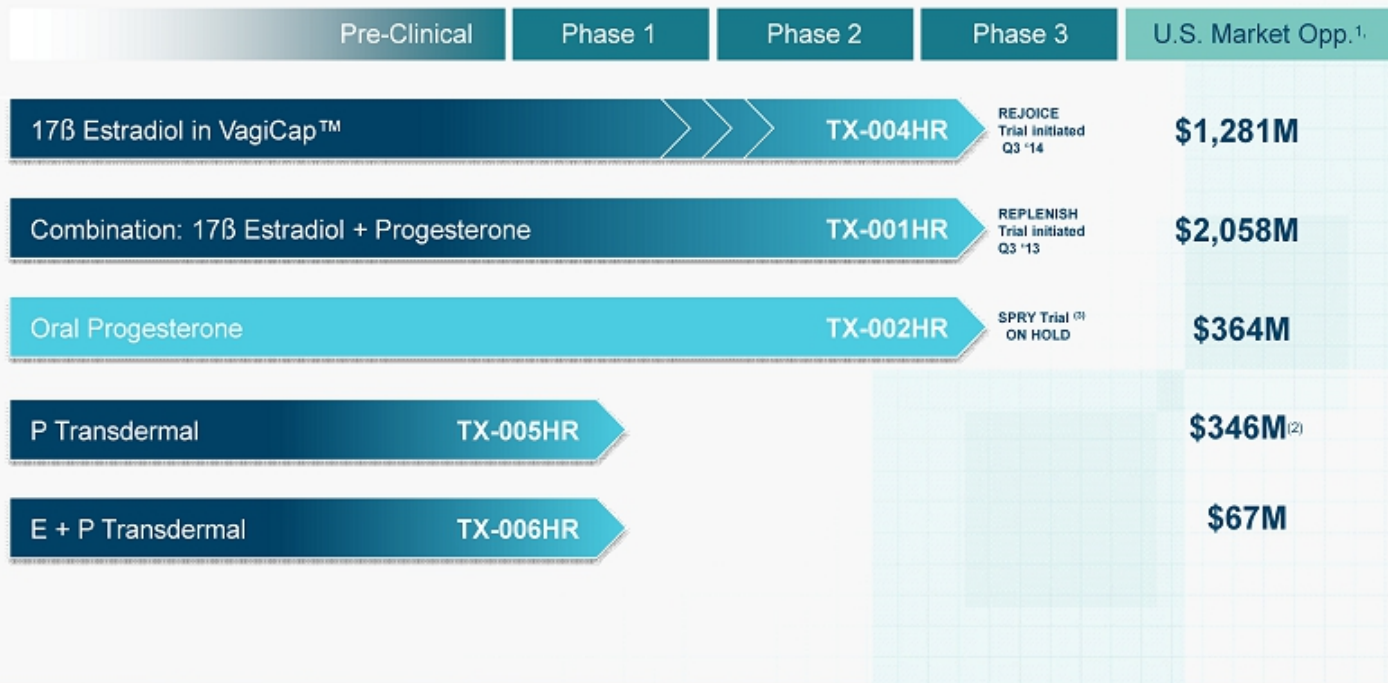
# TherapeuticsMD – Value Platform



*Experienced Women's Health Business & Clinical Team*



# Pipeline Targets Large Markets



1) PIVAST Prescription Monthly by Source Healthcare Analytics.  
 2) Estimated U.S. sales based on half-estradiol patch sales.  
 3) In July 2014, we temporarily suspended enrollment in the SPRY Trial and in October we temporarily stopped it in order to update the Phase 3 protocol based on discussions with the FDA. We intend to update the Phase 3 protocol to, among other things, target only those women with secondary amenorrhea due to polycystic ovarian syndrome and to amend the primary endpoint of the trial.

# SYMBODA™ Technology Enables Pipeline

- ❏ Converts estradiol and progesterone from solid / crystalline to a new liquid (solubilized) drug form:
  - ❏ Achieves FDA requirements of uniformity and stability
  - ❏ Improves functional effects (bioavailability, variability, food effect, lowest effective dose, side effects)
  - ❏ Enables new combinations, routes and dosages (creams, patches, etc.)
- ❏ Used in development of TX-001HR and TX-004HR
- ❏ Opportunity for IP protection

## Novel Formulations



**TX-004HR**  
**VVA Program**



**TherapeuticsMD<sup>®</sup>**  
*Supporting Women's Health for Life*



# Overview – Vulvar Vaginal Atrophy (VVA)

- ❏ Under-diagnosed condition characterized by thinning of vaginal tissue from decreased estrogen levels<sup>(1)</sup>
- ❏ Diagnosed in approximately 50% of postmenopausal women using measure of vaginal pH levels<sup>(1)</sup>
- ❏ Bothersome symptoms include: dryness, dyspareunia, itching, irritation, dysuria, bleeding with sexual activity

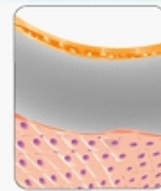
## Pre-Menopause

**Superficial cells:** >15%  
**Intermediate cells:** 80%  
**Parabasal cells:** < 5%



## Post-Menopause

**Superficial cells:** <5%  
**Intermediate cells:** 60%  
**Parabasal cells:** >10%



# VVA Market - Established and Growing

- US sales more than doubled since 2008
- Global market expected to be \$2.1 Billion in 2022<sup>(4)</sup>
- Currently no generic competition

Product	Compound	TRx (MAT 9/14) <sup>(1)</sup>	US Sales (\$M) <sup>(1) (2)</sup> (MAT 9/14)	WAC Price <sup>(3)</sup>
Premarin® Cream	Equine vaginal estrogen	1,767,810	\$448	\$220.02
Vagifem® Tablets	Vaginal Estradiol	1,945,711	\$378	\$222.12
Estrace® Cream	Vaginal Estradiol	1,738,856	\$324	\$174.25
Osphena® Tablets	Oral SERM	176,455	\$40	\$158.00
Estring®	Vaginal Estradiol Ring	336,803	\$88	\$244.52
<b>Total<sup>(3)</sup></b>		<b>5,965,635</b>	<b>\$1,281</b>	

(1) PHAST Prescription Monthly by Symphony Health Solutions

(2) Femring data was excluded due to VMS indication

(3) Medi-Span Price Rx Basic

(4) GlobalData July 2013 report GDHC54PIDR

# TX004-HR – Target Product Profile



## Target Goals

Lower Systemic Exposure

Phase 1 data suggest lower systemic absorption

Faster Onset of Action

Demonstrated activity at 14 days in P2

New Lower Effective Dose

Broad range of doses being evaluated in P3, including 4 mcg

Improved User Experience

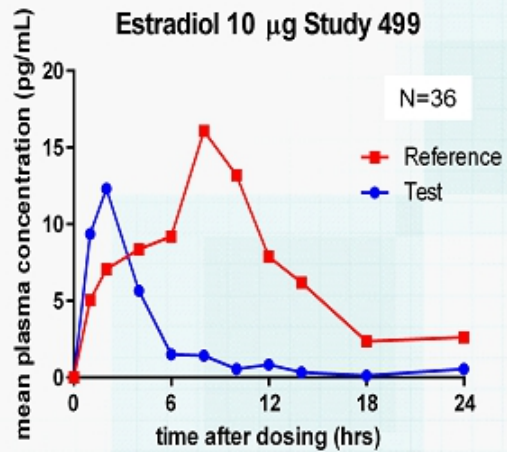
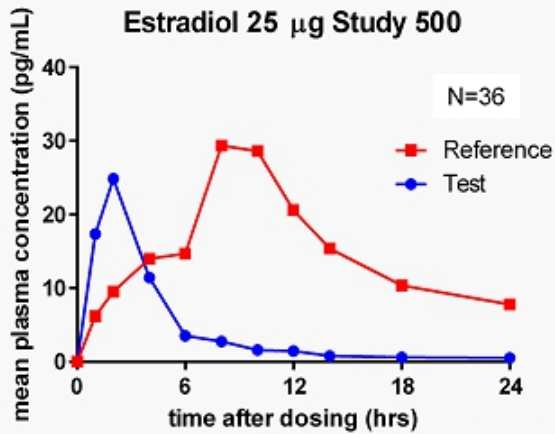
Preliminary patient satisfaction (e.g., no applicator, quick dissolution, no burning)

*VagiCap Target Product Profile evaluated in ongoing Phase 3 Rejoice Trial*

# VagiCap™ vs. Vagifem® – Phase 1 PK Study

## Key Findings

- Tmax ~2 hours with VagiCap and ~8 hours with Vagifem
- Systemic absorption AUC (0-24 hours) is 2- to 3-fold lower with VagiCap relative to Vagifem





# TX-004HR – Promising P2 Data

## Approved Treatments: Pivotal Clinical Data (Week 12)\*

	Maturation Index (Mean)		Change in pH (Mean)	
	Active	Placebo	Active	Placebo
Premarin® Vaginal Cream (0.3 mg) n=36	27.90	3.00	-1.60	-0.40
Vagifem® (10 ug) n=36	11.10	NA	NA	NA

## TX-004HR: Phase 2 Pilot Data (Day 14)

	Maturation Index (Mean)		Change in pH (Mean)	
	TX-004HR	Placebo	TX-004HR	Placebo
VagiCap™ 10 ug n=50	44.48	7.08	-0.92	-0.40

\*Data from product prescribing information. For reference only. Comparative efficacy cannot be demonstrated without head-to-head clinical studies.

# TX-004HR Positive Phase 2 Results



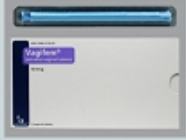


## Double Blind, Controlled Phase 2 Study

- 48 post-menopausal women with VVA
- Randomized 1:1 to 10 $\mu$ g
- Self-administered 1x daily for 2-week period
- Same endpoints measured in Phase 3 (2 vs 12 weeks)

## TX-004HR Compared to Placebo

- Decrease in parabasal cells ( $p < 0.0001$ )
- Increase in superficial cells ( $p = 0.0002$ )
- Decrease in vaginal pH ( $p = 0.0002$ )
- Reduction in atrophic effects on epithelial integrity and vaginal secretions
- Positive trend in reduction of most bothersome symptoms

# TX-004HR – Potential Competitive Profile

Product Characteristic*	Vagifem	Premarin	Estrace
<b>Design</b>			
<b>Burning</b>		✓	
<b>Discharge</b>	✓	✓	✓
<b>Cream</b>		✓	✓
<b>Quick Dissolution</b>			
<b>Applicator</b>	✓	✓	✓
<b>Placement Issues</b>	✓		



## TX-004HR Profile Goals

- Eliminate burning sensation
- Not a cream
- Improve ease of use/placement
- Quick dissolution
- Digital insertion/No applicator
- Deliver elegant patient experience

OPERA Survey (n=178); TXV-1301 Survey (n=49)

\*Perceived product characteristics reported by health care professionals and patients in separate surveys. Not based on head-to-head clinical comparisons or validated instruments.

# Phase 3 – TX-004HR Vaginal Estradiol



	Q3 '14	Q4 '14	Q1 '15	Q2 '15	Q3 '15	Q4 '15	Q1 '16	Q2 '16	Q3 '16	Q4 '16
TX-004HR Estradiol VVA VagiCap	P3 Protocol			Enrolmt Cmpltd	Data Read					
						NDA and PDUFA				
		Phase 3 Study								

- 📌 **Trial: 12 weeks**
- 📌 **Sites: ~100**
- 📌 **Subjects: ~700<sup>1</sup>**
  - 3 active arms: 4 mcg, 10 mcg, 25 mcg (~175 per arm)
  - 175 placebo
- 📌 **Co-Primary Endpoints**
  - Cell change
  - Lowering of pH
  - Reducing Dyspareunia as most bothersome symptom



1) The FDA has to date noted that in order to approve a drug based on a single trial, the trial would need to show statistical significance of at least a .01 level, and that a trial that is merely statistically positive may not provide sufficient evidence to support an NDA filing or approval of a drug candidate.



# TX-001HR Combination Program



**TherapeuticsMD<sup>®</sup>**  
*Supporting Women's Health for Life*




# Indication Overview

- Menopause is defined as the final menstrual period and is typically confirmed after an otherwise healthy woman has not had a period for 12 consecutive months
- Hot flashes are due to lower Estrogen levels
- Estrogen is given to reduce hot flashes
- Estrogen causes the uterus to thicken (hyperplasia)
- Progesterone is given to prevent thickening in women with an intact uterus

# HT Market Size – Two Markets

Compounded Product	Progestin	US Sales Cash Pay	Company
Estradiol + Progesterone	Untested Bioidentical	\$1,500 mm <sup>(3)</sup>	Various Compounding Pharmacies Not FDA approved

*Significant Market with No FDA approved bioidentical product*

FDA Approved Product	Progestin	U.S. Sales (est.)	Company
<b>17β Estradiol + NETA / DSP</b> Activella / FemHRT / Angeliq)	<b>Non-bioidentical</b>	\$ 42 mm <sup>(1)(2)</sup>	
Generic 17β + Progestins	<b>Non-bioidentical</b>	\$ 216 mm <sup>(1)(2)</sup>	
<b>Premarin + MPA</b> (Prempro / Premphase)	<b>Non-bioidentical</b>	\$ 336 mm <sup>(1)(2)</sup>	
<b>Total FDA Approved Oral Combination Sales</b>		<b>\$ 594 mm</b>	
<b>Total Combination Market Sales</b>		<b>\$ 2,094MM</b>	

Notes:

- (1) PHAST by Symphony Health Solutions
- (2) Based on last twelve months sales through September 30, 2014
- (3) "Women's Use and Knowledge of Custom Compounded Bioidentical Hormones" Santoro, N. and Pinkerton, J NAMS poster 2014.

# Compounding Market Dynamics

- Compounding prescriber<sup>(1)</sup> base:

- 66% Wellness practitioners
- 33% OB/GYNs

- Growing cash pay market

- \$46 average cost per unit

- An estimated 1M-2.5M women in the US use BHRT



(1)-Pharmacy Survey conducted by Rose Research on behalf of inThought Research and the International Journal of Pharmaceutical Compounding



# Drug Quality and Security Act (DQSA)

- ❏ Spurred by public health scares, DQSA establishes clear FDA oversight of compounding pharmacies
- ❏ Prohibits compounding of essential copies of an FDA- approved and marketed drug except in limited circumstances such as drug shortages
- ❏ Recent FDA enforcement actions related to essential copies
- ❏ DQSA anticipated to have significant impact on market post-approval of first combination drug
- ❏ TXMD would look to distribute through compounding pharmacies once approved



# TX-001HR – Differentiated Target Product Profile

## Goals for Replenish Trial

Meet Patient Demand for Bio-identicals

Potential for FDA approved natural estradiol plus natural progesterone combination pill

New Lower Effective Dose

Broad range of doses being evaluated in P3, one of which would be a new lower effective dose

Labeling Differentiation

Bio-identical terminology as both hormones similar to those produced by the ovary

Leverage Data on Natural Progesterone

Inclusion of PEPI and E3N data via label negotiation

# Rationale for Natural Progesterone vs. Synthetic Progestins

Side Effect <sup>(1)</sup>	Bio-identical Natural Progesterone	Non-bioidentical Progestins (MPA, NETA, drospirinone)
<b>Breast cancer</b>	Neutral in breast cancer (E3N-EPIC study)	Increased risk
<b>Cardiovascular</b>	More favorable profile (PEPI trial)	Increased risk of MI, stroke, VTE
<b>Lipid profile</b>	More favorable profile (PEPI trial)	Less favorable effects on lipid profile (cholesterol, LDL, triglycerides)
<b>Glucose / insulin</b>	Improved carbohydrate metabolism (PEPI trial)	Deterioration of glucose tolerance or hyperinsulemia or both
<b>Sleep / mood</b>	Improved sleep efficiency <sup>(2)</sup>	No benefit on sleep properties

(1) Alone or in combination with estrogen.

(2) Caufriez, Anne, Rachel Leproult, Mireille L'Hermite-Bale´riau, Myriam Kerkhofs, and Georges Copinschi. "Progesterone Prevents Sleep Disturbances and Modulates GH, TSH, and Melatonin Secretion in Postmenopausal Women." *J Clin Endocrinol Metab* 95.4 (2011): 614-23.

# TX 001-HR (Estrogen/Progesterone) Phase 3 Study - REPLENISH

2013E		2014E				2015E				2016E				2017E			
Q3 '13	Q4 '13	Q1 '14	Q2 '14	Q3 '14	Q4 '14	Q1 '15	Q2 '15	Q3 '15	Q4 '15	Q1 '16	Q2 '16	Q3 '16	Q4 '16	Q1 '17	Q2 '17	Q3 '17	Q4 '17



NDA and PDUFA

Phase 3 Vasomotor and Endometrial Protection Study

## ☒ Designed to enroll 1,750 subjects at ~ US 100 sites

### ☒ Four active arms (N=400/ arm)

- Estradiol 1mg/Progesterone 100mg
- Estradiol 0.5 mg/Progesterone 100mg
- Estradiol 0.5 mg/Progesterone 50 mg
- Estradiol 0.25 mg/Progesterone 50 mg

### ☒ Placebo arm (N=150)

## ☒ 12-month study with 12 week VMS substudy Endpoints:

- ☒ Vasomotor Substudy: number and severity of hot flashes (4 week and 12 wks)
- ☒ Endometrial safety: incidence of endometrial hyperplasia (12 months)



# Transdermal Programs

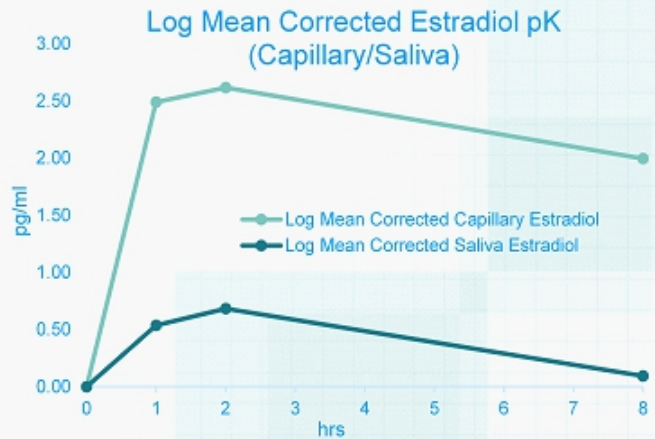
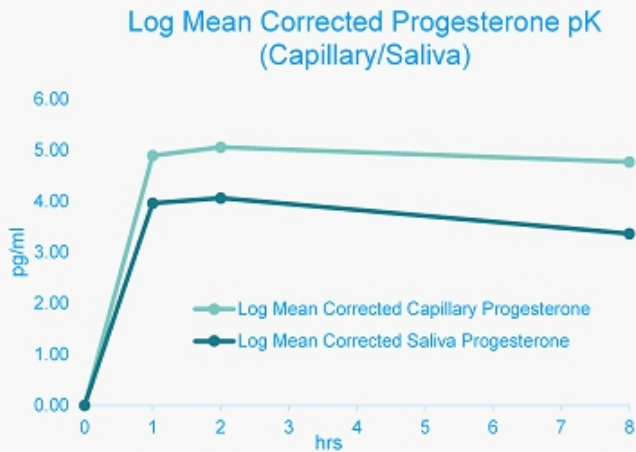


# Why Transdermal?

- Transdermal delivery perceived safer due to a lower first pass effect
- No FDA-approved transdermal progesterone
- New TXMD PK data suggest leveraging solubilized progesterone, show elevated and sustained transdermal levels
- Leveraging this technology creates an opportunity for new progesterone IP, products and novel dosage forms







# E+P Topical PK Results

## New Formulation PK Data Suggest Sustained 8 hr Duration



- Levels in the saliva and capillary samples are higher than in the serum where it was not detectable
- This is consistent with the published article from Du and Stanczyk 2013.<sup>1</sup>

# Transdermal Market Opportunity

Product (Combination E+P)	TRx <sup>(1)(2)</sup>	U.S. Sales (est.) <sup>(1)(2)</sup>	Company
Estradiol/Levonorgestrel (Climara Pro)	129,755	\$ 22.5 M	 Bayer
Estradiol/Norethindrone Acet (CombiPatch)	408,598	\$ 44.0 M	 NOVEN PHARMACEUTICALS, INC.
<b>Total Combination Transdermal Sales</b>	<b>538,353</b>	<b>\$ 66.5 M</b>	
Product (Estradiol Only)	TRx <sup>(1)(2)</sup>	U.S. Sales (est.) <sup>(1)(2)</sup>	Company
Estradiol (Patch, Gel, Spray) (Alora, Climara, Estraderm, Menostar, Vivelle, Vivell-Dot, Minivelle; Divigel, Elestrin, Estrogel; Evamist)	5,762,725	\$ 692 M	 Bayer  Watson  NOVARTIS  ASCEND PHARMACEUTICALS  MEDA  UPsher-Knowlton
<b>Total Estradiol Transdermal Sales</b>	<b>5,762,725</b>	<b>\$ 692 M</b>	

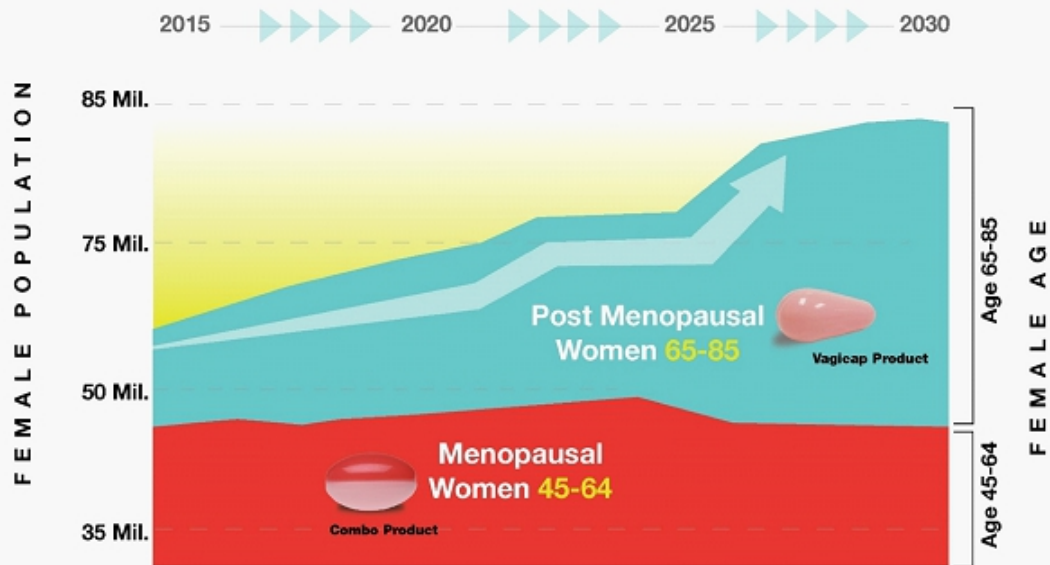
Notes:

(1) PHAST by Symphony Health Solutions

(2) Based on last twelve months sales through September 30, 2014

# Growing Opportunity for Hormone Therapy

## US Population



US Census 2010



# Intellectual Property Update

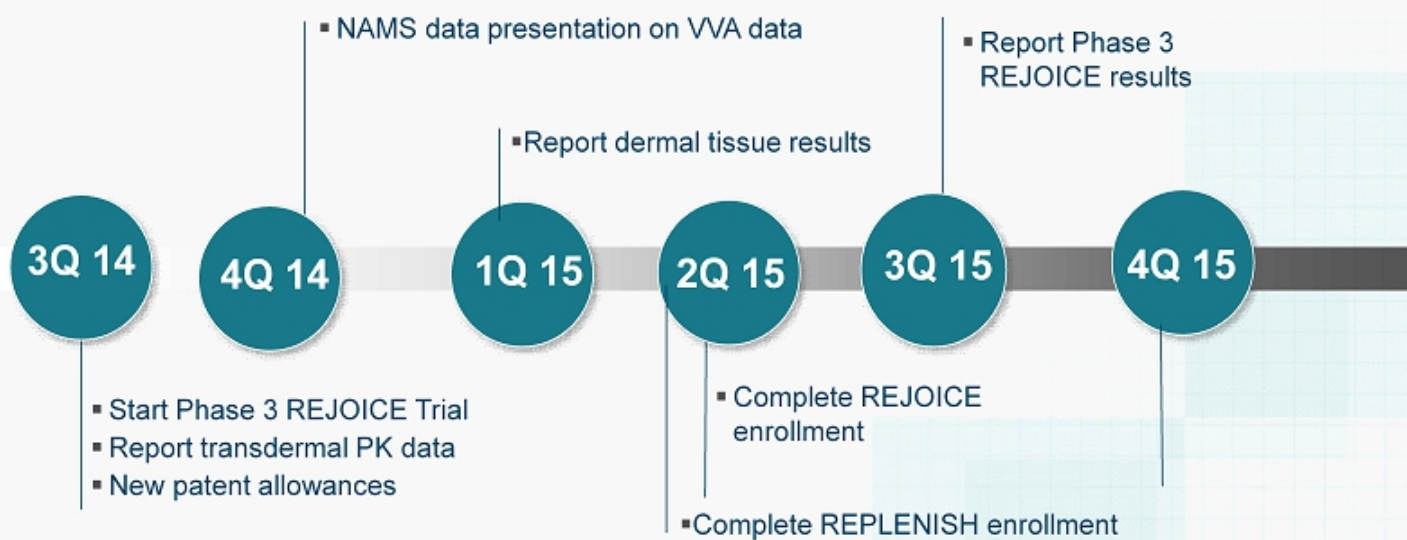


# Growing Patent Portfolio

	Filed	Provisional	Non-Provisional	Issued
U.S.	37	13	24	4
Ex-U.S.	21			

- Two new patents issued; one on method of treating menopausal symptoms which strengthens competitive barriers to entry and builds on layered coverage strategies
- Others issued:
  - Field spanning estradiol and progesterone pharmaceutical compositions (SYMBODA™)
  - OPERA reporting and analysis software patent
- Layered patent strategies
  - Field spanning pharmaceutical compositions by family of estradiol and progesterone alone and in combination
  - Siloed strategy for each product

# Key Milestones





# TXMD: Financial Snapshot

Listing Exchange	NYSE MKT
Shares outstanding	156 million (as of Nov 4, 2014)
Cash	\$67 million (as of Sept 30, 2014)
Debt	\$ 0 million

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*Supporting Women's Health for Life*

**Thank You**

[www.TherapeuticsMD.com](http://www.TherapeuticsMD.com)

**TX-004HR – VVA Program  
- Appendix -**



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# TX-004HR Positive Phase 2 Study



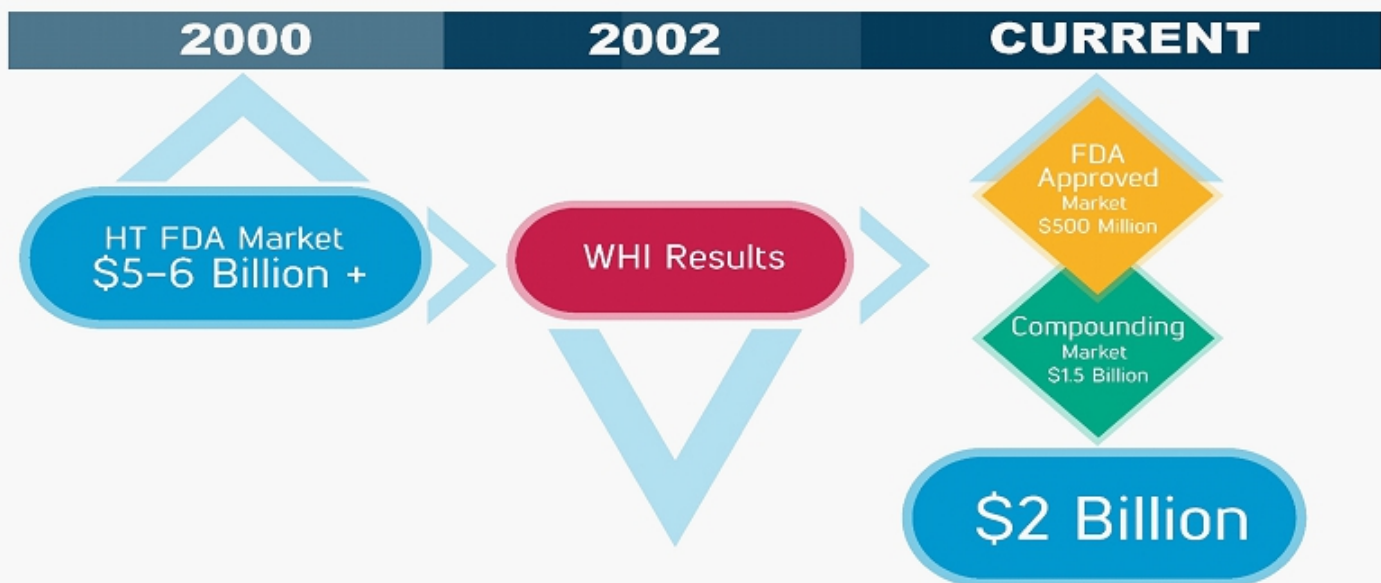
- ❏ **48 postmenopausal women with symptoms of VVA**
- ❏ **Randomized 1:1 to 10µg dose of TX-004HR or placebo**
  - ❏ Self-administered 1x daily for 2-week period
- ❏ **Endpoints (2 weeks) based on Phase 3 (12 weeks) study design criteria**
- ❏ **As compared to placebo, women treated with TX-004HR showed:**
  - ❏ Statistically significant decreases in parabasal cells ( $p < 0.0001$ )
  - ❏ Statistically significant increases in superficial cells ( $p = 0.0002$ )
  - ❏ Statistically significant decreases in vaginal pH ( $p = 0.0002$ )
  - ❏ Significant reduction in the atrophic effects on epithelial integrity and vaginal secretions
  - ❏ Not powered for most bothersome symptom (positive trends)



## TX-001HR Combination Program - Appendix -



# Evolution of Hormone Therapy Market

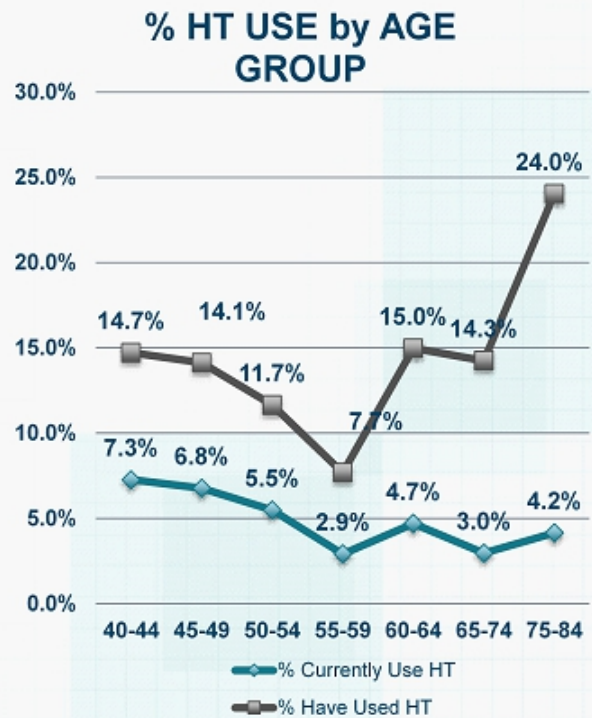


(1) PHAST Prescription Monthly by Source Healthcare Analytics. Inflation Adjusted Number\*

(2) Estimates per: Dr. Loyd Allen Jr., Editor-in-Chief, the *International Journal of Pharmaceutical Compounding*; Tom Murry, Executive Director of the Pharmaceutical Compounding Accreditation Board; and Wulf Utian, Consultant on Gynecology and Women's Health at The Cleveland Clinic and Executive Director Emeritus and Honorary Founding President of The North American Menopause Society ("NAMS").

# Hormone Therapy Use Is Increasing<sup>1,2</sup>

- Post-WHI, expert consensus: HT before 60 has a favorable benefit/risk profile<sup>3</sup>
- Women using FDA-approved and compounded HT increasing:
  - Estimated 30% of use is compounded
  - Natural or “Bio-identicals” preferred
- 83% of women believe hormone therapy helps treat their symptoms
- More younger women asking for HT



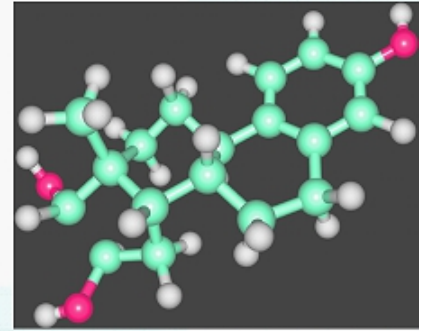
39

1. harris INTERACTIVE (July 2013 N: 1,100 women age 45 to 60 with 801 currently going through or have gone through menopause)
2. Rose Research Survey (April 2014 N:17,897 women age 40 to 80 with 2,044 using or have used HT)
3. 2013 BMS statement, 2012 NAMS statement, 2013 IMS statement

TherapeuticsMD®

# Current Demand For Natural Hormones

- ❏ Women actively requesting “bio-identical” hormone therapy (HT) containing natural estradiol and natural progesterone
- ❏ Compounded drugs are not approved by FDA, including requirements for safety, efficacy, or manufacturing quality
- ❏ Emerging evidence of the advantages of natural hormones over synthetics





# Current Evidence Shows Potential Advantages of Natural Estradiol

**“CEEs (Premarin) were associated with a higher incidence of venous thrombosis and myocardial infarction than estradiol”<sup>1</sup>**

— *Journal of the American Medical Association*,  
September 2013

**“Oral estradiol may be associated with a lower risk of stroke ... compared with conventional-dose oral CEE”<sup>2</sup>**

— *Menopause*,  
September 2013

(1) Smith *et al.* Lower Risk of Cardiovascular Events in Postmenopausal Women Taking Oral Estradiol Compared with Oral Conjugated Equine Estrogens (CEE)

(2) Shufelt *et al.* Hormone Therapy Dose, Formulation, Route of Delivery, and Risk of Cardiovascular Events in Women: Findings from the Women's Health Initiative Observational Study

# Dose Rationale: TX-001HR (Estradiol/Progesterone)

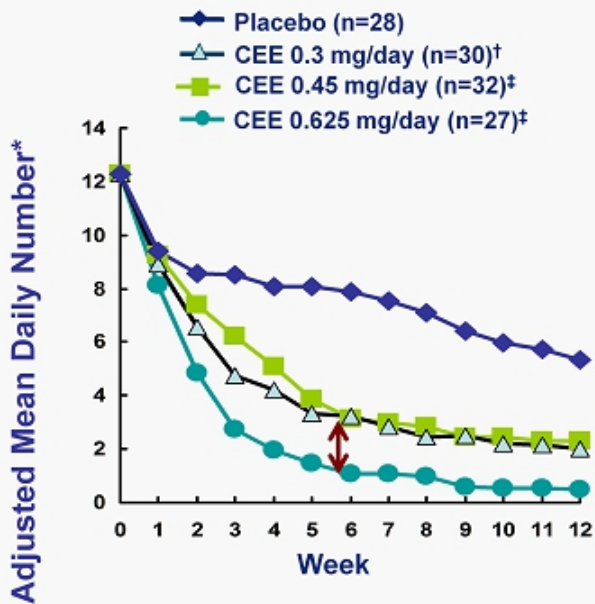
🔍 **Objective:** to provide the first FDA approved natural estradiol/progesterone (combination) product with lowest effective doses

🔍 **Dose selection:** Four estradiol/progesterone combinations being evaluated based upon:

- Known effective doses of estradiol
  - 1mg and 0.5 mg have established efficacy for the treatment of VMS
  - Estradiol 0.25 mg alone has not been shown to be effective; however, progesterone has been shown to have an additive effect, thus the combination of E/P may provide lowest effective dose
- To deliver a low dose of progesterone that provides endometrial safety with the lowest side effect profile (50 mg and 100 mg)
- To provide multiple doses for tapering and adjustment based on patient therapeutic response

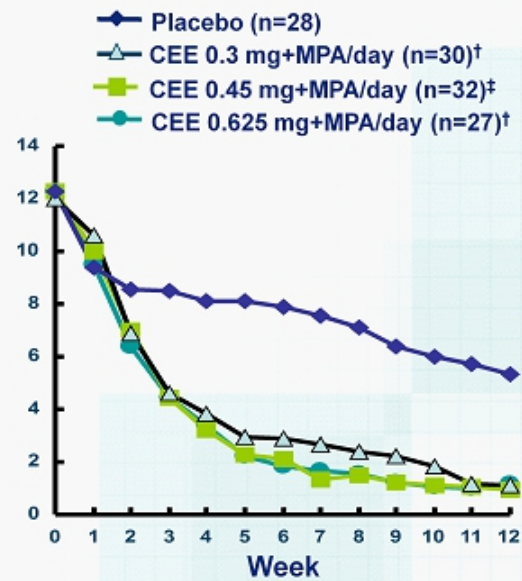
# Women's HOPE Study Hot Flashes

## Number of hot flashes (CEE-Alone)



Range of hot flashes at baseline=11.3-13.8.  
 \*Adjusted for baseline.  
 †P<0.05 by week 3 compared with placebo.  
 ‡P<0.05 by week 2 compared with placebo.

## Number of hot flashes (CEE+MPA)



Range of number of hot flashes at baseline=11.3-13.8.  
 \*Adjusted for baseline.  
 †P<0.05 by week 3 compared with placebo.  
 ‡P<0.05 by week 2 compared with placebo.

# Low Dose Approvals

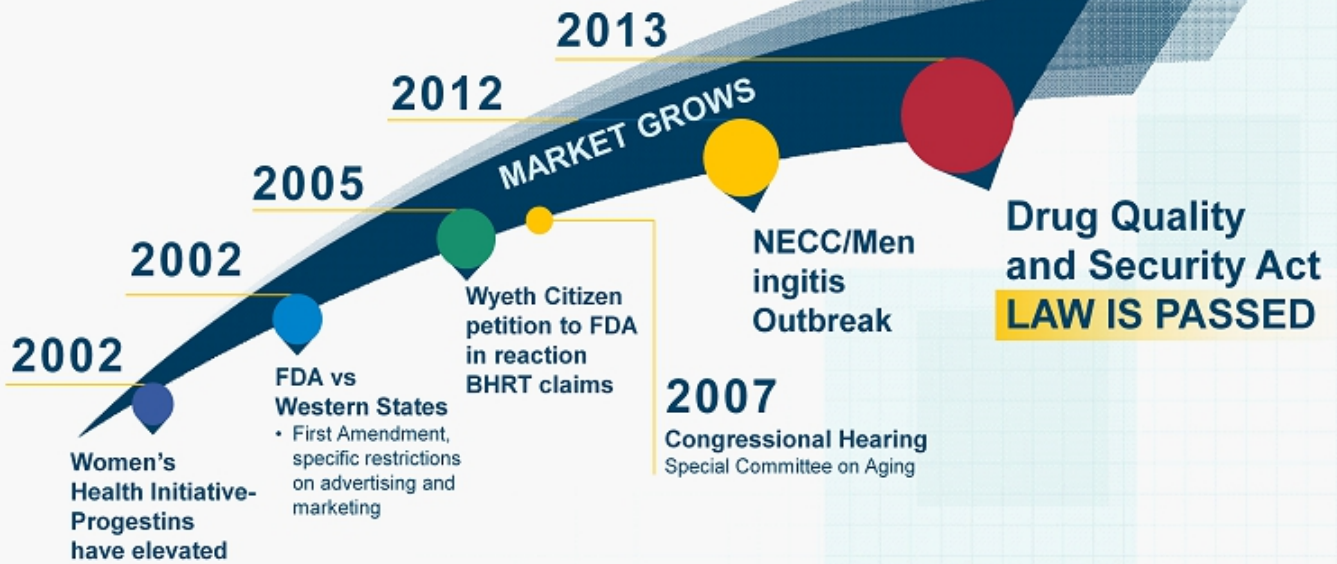
Activella – mean # HFlashes	Placebo	E2/NETA .25/.1	E2/NETA .5/.1	E2/NETA 1/.5	E2/NETA 2/1
Baseline	72	74.4	73.4	69.6	70.1
Week 4 (vs Pbo)	39.7	37.1 (p=0.397)	32.5 (p=0.122)	22.9 (p=0.005)	16.4 (p=0.000)
Week 8	32.1	26.9 (p=0.163)	18.5 (p=0.004)	14.6 (p=0.002)	7.5 (p=0.000)
Week 12	29.7	25.6 (p=0.242)	16.0 (p=0.007)	9.1 (p=0.000)	5.6 (p=0.000)

FemHRT – mean # HFlashes	Placebo	NETA/EE .5/2.5	NETA/EE 1/5µg	NETA/EE 1/10
Baseline	85.2	85.8	79.4	91.8
Week 4 (extrapl)	46	38	25	19
Week 12	39.4	18.9 (p=0.00)	13.4 (p=0.00)	9.8 (p=0.00)



# History of Compounding

## Market Shift to Bio-identical Hormone Replacement (BHRT)



# The Total Menopause Hormone Market

## COMPOUNDING SEGMENTS<sup>(2)(3)</sup>



American Academy of Anti-Aging Medicine (A4M) – [www.a4m.com](http://www.a4m.com)  
 World Society of Anti-Aging Medicine (WSOAM)  
[www.wosaam.ws](http://www.wosaam.ws)

➔ **24,000 Specialists  
in United States**

## TOTAL E+P HORMONE MARKET<sup>(1)(2)</sup>



- Both traditional medicine and so-called anti-aging/wellness are targeting the same biologic processes in women — menopause.

(1) PhAST Prescription Monthly by Source Healthcare Analytics.  
 (2) \$50 notes per Dr. Lloyd Allen Jr., Editor in Chief, International Journal of Pharmaceutical Compounding; Tom Murry, Executive Director of the Pharmaceutical Compounding Accreditation Board; and Mark Utter, Consultant on Gynecology and Women's Health at The Cleveland Clinic and Executive Director Emeritus and Honorary Founding President of The North American Menopause Society ("NAMS").  
 (3) Symphony Health Report

# ~2 Million Women are Using Compounded HT

## Estimate from Pharmacies

**2.3 million women**  
use compounded HT

## Estimate from Physicians

**2.5 million women**  
use compounded  
HT

## Estimate from Patients

**2.1 million women**  
use compounded HT



- Women using FDA-approved HT has increased slowly from 4.5 million in 2005 to **5.0 million in 2014**.
- Women using compounded HT has increased dramatically from less than 500,000 in 2005 to **2.1 million – 2.5 million in 2014**.

1. Rose Research Survey: (April 2014) N:17,897 women age 40 to 80 with 2,044 using or have used HRT
2. harris INTERACTIVE: (July 2013) N: 1,100 women age 45 to 60 with 801 currently going through or have gone through menopause
3. Rose Research data: Ongoing survey of 400 physicians actively prescribing HT
4. Ob/Gyn Surveys: OPERA Survey (N=178); TXV-1301 Survey (N=49)
5. Pharmacy Phone Survey: 4 (N=200) Compounding Pharmacies per state

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