

# Investor Day

March 1, 2017



TherapeuticsMD<sup>®</sup>

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TherapeuticsMD.com

# Introduction

**Robert Finizio**  
Chief Executive Officer

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# Forward-Looking Statements

This presentation by TherapeuticsMD, Inc. (referred to as “we” and “our”) may contain forward-looking statements. 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 as 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, protect and defend our intellectual property; our ability to develop and commercialize our hormone therapy drug candidates and obtain additional financing necessary therefore; whether the company will be able to prepare a new drug application for its TX-001HR product candidate and, if prepared, whether the FDA will accept and approve the application; whether the FDA will approve the company’s new drug application for its TX-004HR product candidate and whether any such approval will occur by the PDUFA date; 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.

TX-004HR, TX-001HR, TX-005HR, and TX-006HR are investigational drugs and are not approved by the FDA. This non-promotional presentation is intended for investor audiences only.

*PDF copies of press releases and financial tables can be viewed and downloaded at our website:  
[www.therapeuticsmd.com/pressreleases.aspx](http://www.therapeuticsmd.com/pressreleases.aspx).*

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# Today's Agenda

**8:30-8:40 a.m.**

**Introduction**

**8:40-10:00 a.m.**

**TX-004HR**

- Disease & VVA Market Overview - Brian Bernick, M.D.
- Labeling & Regulatory Background - Lisa Rarick, M.D.; Sheryl Kingsberg, Ph.D.
- Payer Overview – Joseph Auci; Tony Lanzone, inVentiv
- Launch Strategy – Dawn Halkuff

**9:30-10:00 a.m.**

**Q&A Panel**

**10:00-10:10 a.m.**

**Break**

**10:10-11:00 a.m.**

**TX-001HR**

- Disease Overview – Brian Bernick, M.D.
- Replenish Trial & Clinical Data – Sebastian Mirkin, M.D.
- Quantifying the Market Opportunity – Robert Finizio
- Launch Strategies & Case Studies – Joseph Auci
- Compounding Regulatory Dynamics – David Miller, R.Ph.
- Compounding Pharmacy Economics – Rich Moon, Principal of PVPCN

**11:00-11:30 a.m.**

**Q&A Panel**

**11:30 a.m.**

**Closing Remarks**

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# TherapeuticsMD<sup>®</sup> (TXMD)

**Innovative women's health company** exclusively focused on developing and commercializing products for women throughout their life cycles



Drug candidate portfolio is built on **SYMBODA™** technology for the solubilization of bio-identical female hormones

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# Business Transformation



## May 2008

vitaMedMD founded in Boca Raton, Florida

## April 2013

TherapeuticsMD (TXMD) listed and traded on the NYSE MKT

## December 2015

Released positive top-line results from the Phase 3 Rejoice Trial for TX-004HR

## December 2016

Released positive top-line results from the Phase 3 Replenish Trial for TX-001HR

## December 2012

Successful Phase 1 PK study of TX-001HR showing bioequivalence to Estrace and Prometrium



## October 2013

Released positive results from the Phase 1 clinical study for TX-004HR



## September 2016

NDA filing for TX-004HR accepted for review by the FDA



# Two Late Stage Women's Health Assets With Large Total Addressable Market Opportunities

	TX-004HR	TX-001HR
		
<b>Proposed Indication</b>	Moderate to severe dyspareunia, a symptom of VVA, due to menopause	Moderate to severe hot flashes due to menopause
<b>Condition Description</b>	VVA due to Menopause	Menopause
<b>Active Ingredients</b>	Bio-Identical 17 $\beta$ -Estradiol	Bio-Identical 17 $\beta$ -Estradiol + Bio-Identical Progesterone
<b>Form</b>	Vaginal softgel capsule	Oral softgel capsule
<b>Key Value Proposition</b>	Easy to use, negligible systemic exposure, designed to support long-term use	Potential first and only bio-identical FDA-approved combination product
<b>Affected US Population</b>	32 million women <sup>1,2</sup>	36 million women <sup>3</sup>
<b>US TAM Opportunity</b>	>\$20B <sup>5</sup>	>\$25B <sup>4,5</sup>
<b>Status</b>	NDA submitted July 7, 2016 PDUFA target action date: May 7, 2017	Positive Phase 3 topline data NDA submission expected 3Q17

1) The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society.

*Menopause.* 2013;20(9):888–902.

2) Gass ML, Cochrane BB, Larson JC, et al. Patterns and predictors of sexual activity among women in the hormone therapy trials of the Women's Health Initiative.

*Menopause.* 2011;18(11):1160–1171.

3) Derived from U.S. Census data

4) Based on pre-WHI annual scripts of FDA-approved HT products

5) Based on market pricing of current FDA-approved HT products

# Seasoned Management Team with a Proven Track Record of Commercial Execution

Tommy Thompson



Chairman of the Board

- Former U.S. Secretary of Health and Human Services (2001-2005)
- Holds multiple board memberships, including Centene and United Therapeutics
- 40-year public health career

Angus Russell



Board Member

- Former Chief Executive Officer and Chief Financial Officer of Shire PLC
- Former Vice President of Corporate Finance at AstraZeneca
- Holds multiple board memberships, including Chairman of Revance Therapeutics

J. Martin Carroll



Board Member

- Former President and Chief Executive Officer of Boehringer Ingelheim (U.S.)
- Former EVP of Customer Marketing and Sales of U.S. Human Health at Merck
- Holds multiple board memberships, including Catalent

Robert Finizio  
CEO,  
Co-Founder,  
and Director



- Co-founded vitaMedMD in 2008
- Co-founded CareFusion (Sold to Cardinal Health in 2006)
- 22 years of experience in early stage healthcare company development

Brian Bernick, MD  
Chief Clinical  
Officer,  
Co-Founder



- Co-founded vitaMedMD in 2008
- 25 years of experience in healthcare/women's health
- Past OBGYN Department Chair - Boca Raton Regional Hospital
- Past ACOG Committee Member
- OBGYN - trained University of Pennsylvania

Sebastian Mirkin, M.D.



Chief Medical Officer

- Former Clinical Lead of Women's Health at Pfizer
- 15+ years of experience developing women's health products
- Reproductive endocrinologist & infertility specialist

John Milligan



President

- Co-founded CareFusion
- Held executive sales and operation management positions at McKesson, Cardinal and Omnicell
- 20+ years of operations experience

Dan Cartwright



Chief Financial Officer

- Former CFO of American Wireless, Telegeography, and WEB Corp
- Participated in American Wireless/Arush Entertainment merger
- Former KPMG and PricewaterhouseCoopers accountant

Julia Amadio



Chief Product Officer

- 25+ years of women's health pharmaceutical experience
- Product development leader for J&J, Wyeth, Aventis, and others
- Worked on development of Prempro®, Premphase®, and Estalis®

Jason Spitz



VP, Marketing

- 25+ years of pharmaceutical marketing, sales, and operations experience
- Led commercialization of anti-estrogens/estradiol, breast cancer, and ovarian cancer drugs

Dawn Halkuff



Chief Commercial Officer

- 20+ years of commercial and marketing experience
- SVP of the Pfizer Consumer Healthcare Wellness Organization
- Commercial lead for sales and marketing of the Pfizer Women's Health Division
- Head of Global Innovation at Weight Watchers International

Yulii Bogatyrenko  
Executive VP,  
Corporate  
Development



- 20+ years of experience in biopharma and consumer businesses
- SVP of BD at Paratek Pharmaceuticals
- VP and GM at Teva Pharmaceuticals
- Senior women's health positions at Bayer and Pfizer

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**TX-004HR**  
Vulvar and  
Vaginal Atrophy (VVA)  
Program



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# VVA Overview

**Brian Bernick, M.D.**  
Chief Clinical Officer

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# Vulvar and Vaginal Atrophy (VVA)

- **Chronic** and **progressive** condition characterized by thinning of vaginal tissue from decreased estrogen levels
- Diagnosed in approximately 50% of postmenopausal women<sup>1</sup>
- Primary symptom = dyspareunia (painful intercourse)
- Secondary symptoms include: vaginal dryness, itching, irritation, bleeding with sexual activity, dysuria, urgency, frequency, recurrent UTIs, and incontinence
- Current treatments include: prescription creams, tablets, and rings in addition to over-the-counter lubricants

## Healthy Vaginal Tissue

Superficial cells: >15%

Intermediate cells: 80%

Parabasal cells: < 5%

pH: < 5



## Atrophic Vaginal Tissue

<5%

60%

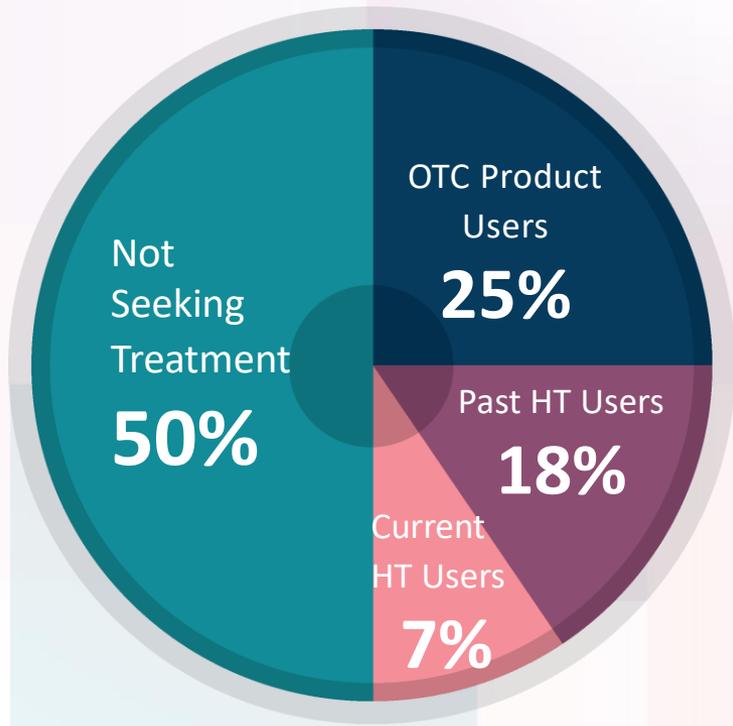
>30%

> 5



1) Kingsberg, Sheryl A., et al. "Vulvar and Vaginal Atrophy in Postmenopausal Women: Findings from the REVIVE (REAL Women's Views of Treatment Options for Menopausal Vaginal Changes) Survey." International Society for Sexual Medicine 2013, no. 10, 1790-1799.

# Current US VVA Market Overview



**>\$20B Branded Total US Market Opportunity<sup>5</sup>**

## 32M Women with VVA Symptoms<sup>1,2</sup>

*~50%, or ~16M seek treatment for VVA<sup>4</sup>*

- **Only 7%, or ~2.3M women**, are currently being treated today with Rx hormone therapy (HT)<sup>3</sup>
  - Long-term safety concerns<sup>6</sup>
  - Efficacy<sup>6</sup>
  - Messiness<sup>6</sup>
  - Need for applicator<sup>6</sup>
- **18%, or ~5.7M women**, are **past HT users** and were unsatisfied/unsuccessful with past treatments<sup>4</sup>
- **25%, or ~8M women**, are **users of OTC products\*** such as lubricants that do not treat the underlying pathological cause of VVA nor halt or reverse symptoms<sup>4</sup>

*~50%, or ~16M women do not seek treatment for VVA<sup>4</sup>*

- Lack of awareness that VVA is a treatable condition
- Estrogen exposure concerns

1) The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. *Menopause*. 2013;20(9):888–902.

2) Gass ML, Cochrane BB, Larson JC, et al. Patterns and predictors of sexual activity among women in the hormone therapy trials of the Women's Health Initiative. *Menopause*. 2011;18(11):1160–1171.

3) IMS Health Plan Claims (April 2008-Mar 2011).

4) TherapeuticsMD "EMPOWER" Survey, 2016

5) Based on current FDA-approved market pricing

6) Wysocki, S et al, Management of Vaginal Atrophy: Implications from the REVIVE Survey. *Clinical Medicine Insights: Reproductive Health* 2014;8 23-30 doi:10.4137/CMRH.S1449

\* Not treated with an FDA approved Rx product. OTC products do not effectively treat the underlying pathological causes of VVA and therefore do not halt or reverse the progression of this condition.

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# Current FDA-Approved VVA Products

Products	Estrace Cream®	Premarin Cream®	Vagifem®	Estring®	Osphena®	Intrarosa®
						
						
TRx Dollars 2016 <sup>1</sup>	\$511,035,880	\$505,351,340	\$502,715,665 <sup>a</sup>	\$105,040,703	\$72,755,311	Approved 11/2016
Method of Admin	Vaginal Cream	Vaginal Cream	Vaginal Tablet	Ring	Oral Tablet	Vaginal Insert
Application	Reusable Vaginal Applicator	Reusable Vaginal Applicator	Vaginal Applicator	90-day Ring	Oral Daily SERM	Vaginal Applicator
Active Ingredient	100 mcg Estradiol	625 mcg/g Conjugated Equine Estrogens	10 mcg Estradiol	2,000 mcg Estradiol	60,000 mcg Ospemifene	6,500 mcg Prasterone
Average Maintenance Dose	100 mcg 2x/week	312.5 mcg 2x/week	10 mcg 2x/week	7.5 mcg daily	60,000 mcg daily	6,500 mcg daily
Onset of Action* Dyspareunia	Approval Without Dyspareunia and Dryness data	Week 4+	Week 8	Approval Without Dyspareunia and Dryness data	Week 12	Week 6
Onset of Action* Dryness		Not Demonstrated			Not Demonstrated	Week 12

\*Onset of Action = First efficacy observation

**Based on Product Prescribing Information  
Not Head-to-Head Comparative Studies**

1. Symphony Health Solutions PHAST Data powered by IDV; Annual 2016  
a. 2016 Vagifem and Yuvaferm (authorized generic of Vagifem)

Vagifem [package label] <http://www.novo-pi.com/vagifem.pdf>

Premarin Vaginal Cream [package label] <http://labeling.pfizer.com/showlabeling.aspx?id=132>

Estrace Vaginal Cream [package label] [http://pi.actavis.com/data\\_stream.asp?product\\_group=1880&p=pi&language=E](http://pi.actavis.com/data_stream.asp?product_group=1880&p=pi&language=E)

Osphena [package label] [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/203505s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203505s000lbl.pdf)

Intrarosa [package label] [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/208470s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208470s000lbl.pdf)

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# 2016 VVA Market Overview and Metrics

Product	TRx Count <sup>1</sup>	TRx Count % Share <sup>1</sup>	TRx Dollars <sup>1</sup>	TRx Dollars % Share <sup>1</sup>	Patient Count <sup>2</sup>	Patient Count % Share <sup>2</sup>
Estrace <sup>®</sup>	1,603,209	32%	\$511,035,880	30%	868,052	39%
Premarin <sup>®</sup>	1,363,725	28%	\$505,351,340	30%	750,185	34%
Vagifem <sup>®</sup>	1,280,708	26%	\$452,289,452	27%	330,045	15%
Yuvaferm <sup>®</sup> (Vagifem AG)	148,701	3%	\$50,426,213	3%	103,142	5%
Estring <sup>®</sup>	276,151	6%	105,040,703	6%	97,960	4%
Osphena <sup>®</sup>	271,824	5%	72,755,311	4%	68,868	3%
<b>Grand Total</b>	<b>4,944,318</b>	<b>100%</b>	<b>\$1,696,898,899</b>	<b>100%</b>	<b>2,218,252</b>	<b>100%</b>

1) Symphony Health Solutions PHAST Data powered by IDV; Annual 2016

2) IMS SDI's Total Patient Tracker; Annual 2016

# Compliance and Fills Per Year Drives Top-Line Revenue

## Current VVA Market

### Vaginal Creams:

Average:  
1.5 Fills Per Year<sup>2</sup>



Estrace



Premarin

### Reasons Women Stop

Messiness<sup>1</sup>

Reusable Applicator<sup>1</sup>

Long-term Safety<sup>1</sup>

Dose Preparation by User Required<sup>3</sup>

### Vaginal Tablets:

Average:  
3.5 Fills Per Year<sup>2</sup>



Vagifem

### Reasons Women Stop

Efficacy<sup>1</sup>

Applicator<sup>1</sup>

Long-term Safety<sup>1</sup>

Systemic Absorption<sup>1</sup>

Product	TRx Dollars	Patient Count	Patient Share
Estrace	\$511,035,880	868,052	39%
Premarin	\$505,351,340	750,185	34%
Vagifem/Yuvaferm	\$502,715,665	433,187	20%

- Higher average fills per year enable Vagifem/Yuvaferm to generate equal revenue as Premarin and Estrace with significantly less patients on therapy

1) Wyszocki, S et al, Management of Vaginal Atrophy: Implications from the REVIVE Survey. *Clinical Medicine Insights: Reproductive Health* 2014;8 23-30 doi:10.4137/CMRH.S14498

2) Total Rx/Patient Count

3) The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. *Menopause*. 2013;20(9):888-902.

# TX-004HR: Product Candidate Profile



- First vaginal estrogen (4 mcg and 10 mcg) with negligible systemic exposure
- Strong efficacy data on both dyspareunia and vaginal dryness with a 2-week onset of action
- Small, digitally inserted, rapidly dissolving softgel capsule without the need for an applicator
- Fraction of the dose (4 mcg, 10 mcg and 25 mcg) of many existing products (Premarin and Estrace)
- No patient education required for dose preparation or applicators
- Mechanism of action and dosing that is familiar and comfortable
- Proposed dose packaging to optimize compliance and convenience
- Strong patent estate with patent expirations starting 2032
- **FDA PDUFA target action date of May 7, 2017**

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# Co-Primary and Key Secondary Efficacy Endpoints

	4 mcg	10 mcg	25 mcg
Superficial Cells	<0.0001	<0.0001	<0.0001
Parabasal Cells	<0.0001	<0.0001	<0.0001
Vaginal pH	<0.0001	<0.0001	<0.0001
Severity of Dyspareunia	0.0149	<0.0001	<0.0001
Severity of Vaginal Dryness	0.0014	<0.0001	<0.0001

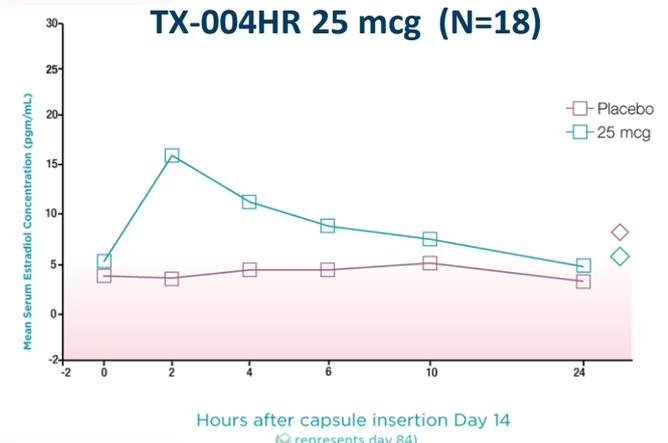
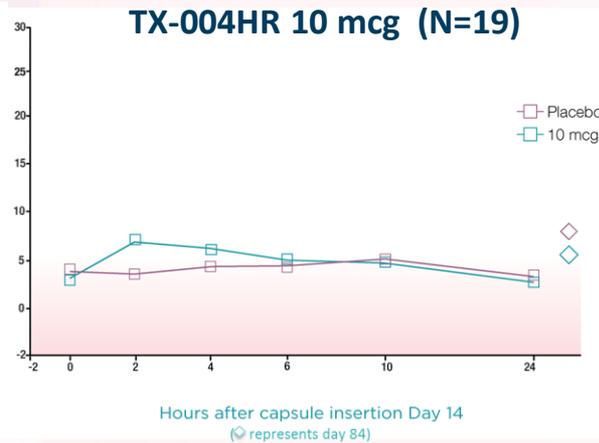
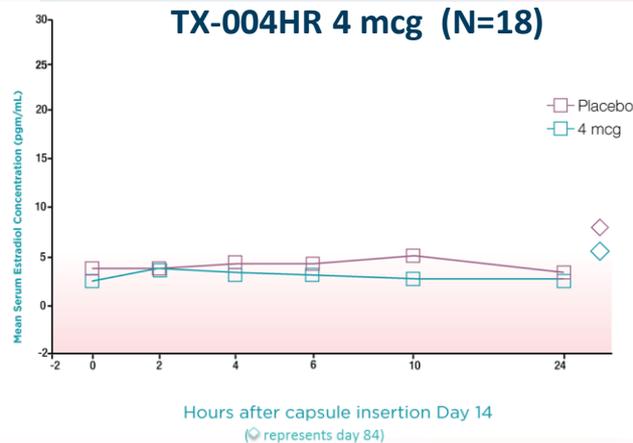
MMRM P-value vs placebo LS = Least Squares

## Arithmetic Mean Estradiol Serum Concentrations – Unadjusted

TX-004HR 4 mcg (N=18)

TX-004HR 10 mcg (N=19)

TX-004HR 25 mcg (N=18)



	AUC <sub>0-24</sub> (pg.h/mL)	C <sub>avg(0-24)</sub> (pg/mL)		AUC <sub>0-24</sub> (pg.h/mL)	C <sub>avg(0-24)</sub> (pg/mL)		AUC <sub>0-24</sub> (pg.h/mL)	C <sub>avg(0-24)</sub> (pg/mL)
<b>4 mcg</b>	87.22 (42.77)	3.634 (1.78)	<b>10 mcg</b>	110.14 (54.57)	4.58 (2.27)	<b>25 mcg</b>	171.56 (80.13)	7.14 (3.33)
<b>Placebo (pl)</b>	104.16 (66.38)	4.34 (2.76)	<b>Placebo (PI)</b>	104.16 (66.38)	4.34 (2.76)	<b>Placebo (PI)</b>	104.16 (66.38)	4.34 (2.76)
<b>P-value vs PI</b>	0.3829	0.3829	<b>P-value vs PI</b>	0.7724	0.7724	<b>P-value vs. PI</b>	0.0108	0.0108

# TX-004HR Qualitative Attributes



## Ease of Use

	4 mcg (N=191)	10 mcg (N=191)	25 mcg (N=190)	Placebo (N=192)
Easy to Use	171 (89.5%)	172 (90.1%)	175 (92.1%)	164 (85.4%)

## Patient Satisfaction

	4 mcg (N=191)	10 mcg (N=191)	25 mcg (N=190)	Placebo (N=192)
Very Satisfied	74 (38.7%)	84 (44.0%)	83 (43.7%)	41 (21.4%)
Satisfied	57 (29.8%)	55 (28.8%)	62 (32.6%)	68 (35.4%)
Unsure	23 (12.0%)	28 (14.7%)	21 (11.1%)	39 (20.3%)
Dissatisfied	19 (9.9%)	9 (4.7%)	12 (6.3%)	20 (10.4%)
Very Dissatisfied	8 (4.2%)	5 (2.6%)	6 (3.2%)	17 (8.9%)

## Preferred vs Competition

	4 mcg (N=119)	10 mcg (N=113)	25 mcg (N=128)
TX-004HR preferred over previously used VVA therapies	73.9%	67.3%	74.2%
P-value vs. Placebo	0.0010	0.0212	0.0003

# Labeling & Regulatory Background

**Lisa Rarick, M.D.**

## **Board Certified OB/GYN**

### **FDA Medical Officer 1988-2003**

- CDER, Division Director, Division of Reproductive and Urologic Products from its creation (1995-1999)
- Office of the Commissioner, Office of Women's Health (2002-2003)

### **2003-Present**

- Independent consultant to pharmaceutical industry

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# TX-004HR Potential Label Discussions

Current Product Labels (based generally on Premarin Vaginal Cream label)	Base Case	Upside case
<p><b>BOXED WARNINGS</b>                      Estrogen-Alone Therapy Boxed Warning                      Estrogen Plus Progestin Therapy Boxed Warning</p>	<p><b>BOXED WARNINGS</b>                      Class labeling</p>	<p><b>BOXED WARNINGS</b>                      Removal of Boxed Warning related to Estrogen Alone Therapy                      – Modified language in the “Warnings and Precautions” Section                      Removal of Boxed Warning related to Estrogen Plus Progestin Therapy                      – Removal throughout the label</p>
<p><b>Section 1 INDICATIONS AND USAGE</b>                      Treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause</p>	<p><b>Section 1 INDICATIONS AND USAGE</b>                      “TX-004HR is a muco-adhesive vaginal softgel capsule indicated for the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause”</p>	<p><b>Section 1 INDICATIONS AND USAGE</b>                      “TX-004HR is a muco-adhesive vaginal softgel capsule indicated for the treatment of moderate to severe dyspareunia <u>and vaginal dryness</u>, symptoms of vulvar and vaginal atrophy, due to menopause”</p>
<p><b>Section 2 DOSAGE AND ADMINISTRATION</b>                      Generally, when estrogen is prescribed for a postmenopausal woman with a uterus, a progestin should also be considered to reduce the risk of endometrial cancer</p> <p>Use of estrogen-alone, or in combination with a progestin, should be with the lowest effective dose and for the shortest duration</p>	<p><b>Section 2 DOSAGE AND ADMINISTRATION</b>                      Class labeling</p>	<p><b>Section 2 DOSAGE AND ADMINISTRATION</b>                      Removal of progestin use for endometrial protection</p> <p>Removal of shortest duration concept</p>

# TX-004HR Potential Label Discussions

Current Product Labels (based generally on Premarin Vaginal Cream label)	Base Case	Upside case
<p><b>Section 3 DOSAGE FORMS AND STRENGTHS</b></p>	<p><b>Section 3 DOSAGE FORMS AND STRENGTHS</b> TX-004HR is a small, light pink, tear-shaped, mucoadhesive, softgel capsule containing solubilized estradiol</p>	<p><b>Section 3 DOSAGE FORMS AND STRENGTHS</b> TX-004HR is a small, light pink, tear-shaped, <u>rapidly dissolving</u>, mucoadhesive, softgel capsule containing solubilized estradiol</p>
<p><b>Section 4 CONTRAINDICATIONS</b></p>	<p><b>Section 4 CONTRAINDICATIONS</b> Class labeling</p>	<p><b>Section 4 CONTRAINDICATIONS</b> Removal of contraindication of history of breast cancer Removal of contraindication of history of DVT and PE</p>
<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> <b>5.1 Risks from Systemic Absorption</b> Systemic absorption occurs with the use of X</p>	<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> The use of TX-004HR resulted in negligible to very low systemic absorption of estradiol</p>	<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> The use of TX-004HR resulted in <u>negligible systemic absorption</u> of estradiol</p>
<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> The warnings, precautions, and adverse reactions associated with the use of systemic estrogen-alone therapy should be taken into account</p> <p>Warnings and precautions of Estrogen alone</p> <p>Warning and precautions of Estrogen Plus Progestins</p>	<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> Class labeling</p>	<p><b>Section 5 WARNINGS AND PRECAUTIONS</b> Although TX-004HR use does not result in the level of systemic exposure associated with (place holder for individual warning) increased risk, long-term safety studies with TX-004HR are not available.”</p> <p>Modified language in Estrogen Alone “Warnings and Precautions”</p> <p>Elimination of Warnings and Precautions related to Estrogen Plus Progestin Therapy</p>

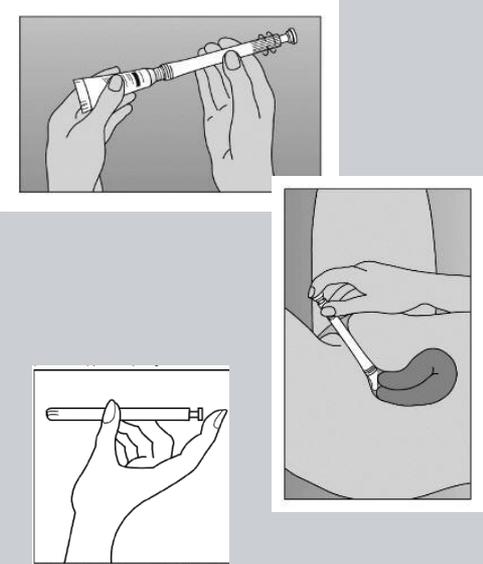
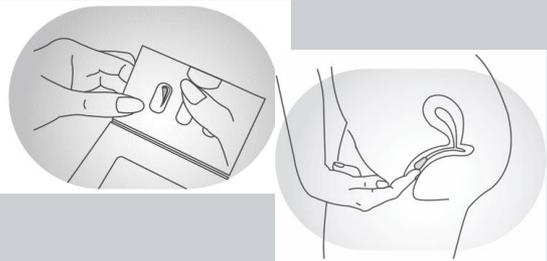
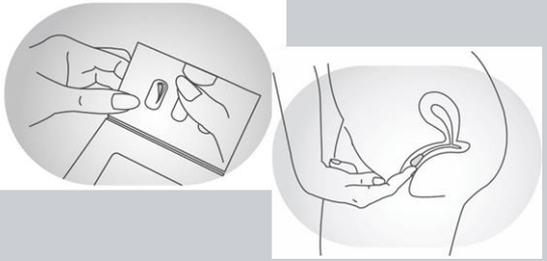
# TX-004HR Potential Label Discussions

Current Product Labels (based generally on Premarin Vaginal Cream label)	Base Case	Upside Case
<p><b>Section 6 ADVERSE REACTIONS</b></p> <ul style="list-style-type: none"> <li>- Dysuria</li> <li>- Leukorrhea</li> <li>- Vaginal discharge</li> <li>- UTI</li> <li>- Urinary Frequency</li> <li>- Vasodilatation</li> <li>- Breast pain</li> </ul>	<p><b>Section 6 ADVERSE REACTIONS</b> Information from the clinical trials included here</p>	<p><b>Section 6 ADVERSE REACTIONS</b> Specifically state that the active group had fewer reported adverse reactions than placebo in all categories except for headache</p>
<p><b>Section 8 USE IN SPECIFIC POPULATIONS</b> <b>8.5 Geriatric Use</b> WHI Studies information on stroke, breast cancer and dementia in women in greater than 65 years of age</p>	<p><b>Section 8 USE IN SPECIFIC POPULATIONS</b> <b>8.5 Geriatric Use</b> Class labeling</p>	<p><b>Section 8 USE IN SPECIFIC POPULATIONS</b> <b>8.5 Geriatric Use</b> Removal of information related to stroke, breast cancer and dementia in women greater than 65 years of age</p>
<p><b>Section 11 DESCRIPTION</b> Each gram of PREMARIN (conjugated estrogens) Vaginal Cream contains 0.625 mg conjugated estrogens, USP in a nonliquefying base containing cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate, benzyl alcohol, sodium lauryl sulfate, glycerin, and mineral oil</p>	<p><b>Section 11 DESCRIPTION</b> TX-004HR (estradiol vaginal softgel capsules) are <b>small</b>, light pink, tear-shaped, softgel capsules containing solubilized <b>estradiol</b></p> <p>TX-004HR softgel capsules are used intravaginally. When the softgel capsule comes in contact with the vaginal mucosa, the softgel capsule dissolves and the estradiol is released into the vagina</p>	<p><b>Section 11 DESCRIPTION</b> TX-004HR (estradiol vaginal softgel capsules) are <b>small</b>, light pink, tear-shaped, softgel capsules containing solubilized <b>estradiol</b></p> <p>TX-004HR softgel capsules are used intravaginally. When the softgel capsule comes in contact with the vaginal mucosa, the softgel capsule dissolves <b>rapidly</b> and the estradiol is released into the vagina</p>

# TX-004HR Potential Label Discussions

Current Product Labels (based generally on Premarin Vaginal Cream label)	Base Case	Upside Case
<p><b>Section 12 CLINICAL PHARMACOLOGY</b> <b>12.3 Pharmacokinetics Absorption</b></p>	<p><b>Section 12 CLINICAL PHARMACOLOGY</b> <b>12.3 Pharmacokinetics Absorption</b> In a multicenter, double-blind placebo-controlled study of 764 postmenopausal women randomized to placebo or 4, 10 and 25 mcg of TX-004HR, a subset of 72 subjects participated in a pharmacokinetics substudy. Estradiol, free estrone, and conjugated estrone concentrations were measured in plasma on Day 1 and Day 14, and Day 84 (approximately four days after the last dose). Key pharmacokinetic parameters are presented in Tables 1 to 3. There were no statistical differences between 4 mcg and 10 mcg and placebo at Days 1 and 14. At both Day 1 and Day 14, the 25 mcg dose was statistically significantly higher than placebo. The use of TX-004HR resulted in negligible to very low systemic absorption of estradiol.</p>	<p><b>Section 12 CLINICAL PHARMACOLOGY</b> <b>12.3 Pharmacokinetics Absorption</b> In a multicenter, double-blind placebo-controlled study of 764 postmenopausal women randomized to placebo or 4, 10 and 25 mcg of TX-004HR, a subset of 72 subjects participated in a pharmacokinetics substudy. Estradiol, free estrone, and conjugated estrone concentrations were measured in plasma on Day 1 and Day 14, and Day 84 (approximately four days after the last dose). Key pharmacokinetic parameters are presented in Tables 1 to 3. There were no statistical differences between 4 mcg and 10 mcg and placebo at Days 1 and 14. At both Day 1 and Day 14, the 25 mcg dose was statistically significantly higher than placebo. The use of TX-004HR resulted in <b><u>negligible systemic absorption</u></b> of estradiol.</p>
<p><b>Section 14 CLINICAL STUDIES</b> Co-primary endpoints with p values</p>	<p><b>Section 14 CLINICAL STUDIES</b> Co-primary endpoints with p values</p>	<p><b>Section 14 CLINICAL STUDIES</b> Onset of action at week 2 Vaginal dryness efficacy</p>
<p><b>Section 14.2 &amp; 14.3 Women’s Health Initiative Studies</b></p>	<p><b>Section 14.2 &amp; 14.3 Women’s Health Initiative Studies</b> Class labeling</p>	<p><b>Section 14.2 &amp; 14.3 Women’s Health Initiative Studies</b> Modified language for Estrogen Alone studies Removal Estrogen Plus Progestin studies</p>

# TX-004HR Potential Label Discussions

Current Product Labels (based generally on Premarin Vaginal Cream label)	Base Case	Upside Case
<p data-bbox="137 361 546 386">Section 17 PATIENT COUNSELING</p> 	<p data-bbox="678 361 1087 386">Section 17 PATIENT COUNSELING</p> 	<p data-bbox="1257 361 1667 386">Section 17 PATIENT COUNSELING</p> 

# Labeling & Regulatory Background

**Sheryl Kingsberg, Ph.D**

## Chief, Behavioral Medicine at University Hospitals Case Medical Center

- Specializes in sexual medicine, female sexual disorders, menopause, pregnancy, postpartum, psychological aspects of infertility
- Principal investigator for clinical trials of sexual dysfunction treatments
- Associate Editor for Sexual Medicine Reviews and editorial board of Menopause
- President-Elect of NAMS

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# Continued Activism Against VVA Black Box Warnings

## History of Activism

FDA “boxed warnings” workshop provided an opportunity for FDA to obtain input related to prescribing information of lower-dose estrogen alone products<sup>1</sup>

ACOG Committee Opinion supporting use of vaginal estrogen in women with a history of estrogen-dependent breast cancer as data showed no increased risk<sup>2</sup>

Citizen Petition, spearheaded by NAMS, formally filed with the FDA for modification of black box warnings

Women’s Congressional Caucus writes letter to the FDA addressing concerns of existing black box warnings of VVA products

November 2015

March 2016

May 2016

October 2016

### Citizen’s Petition Supporters:

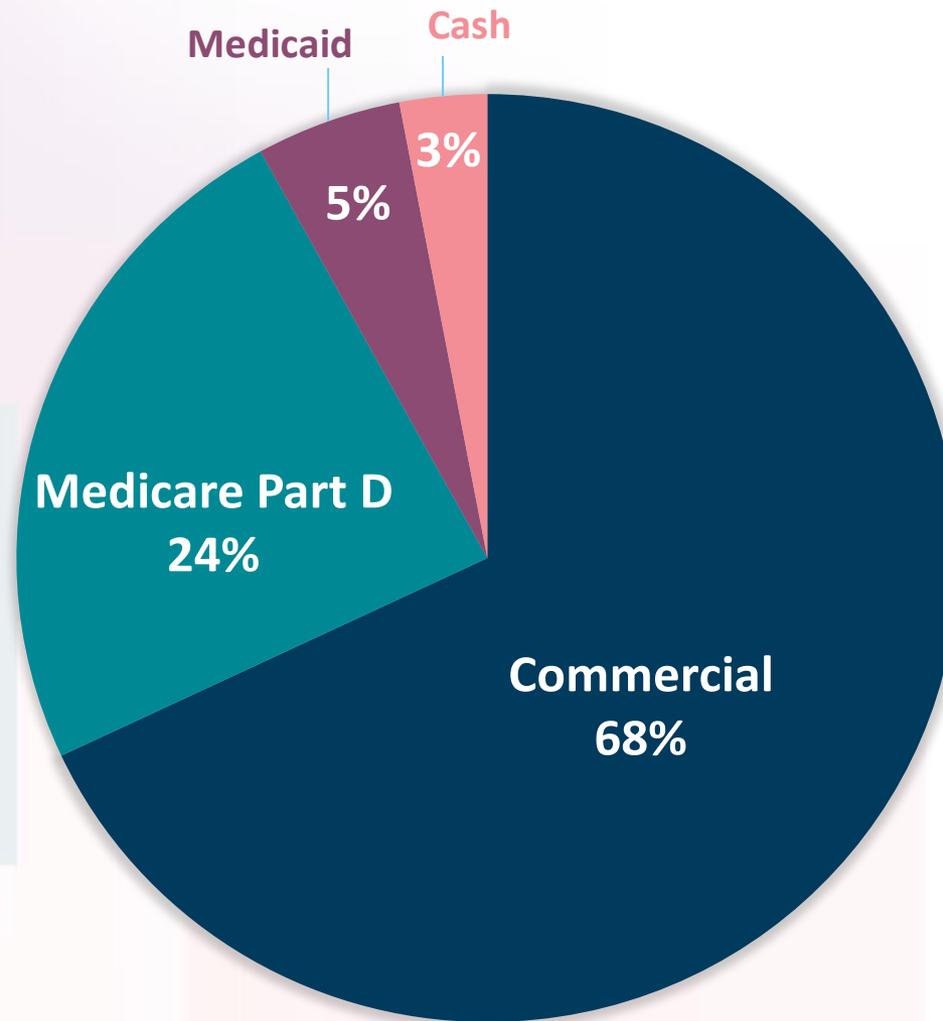


1) Scientific Workshop on Labeling “Lower” Dose Estrogen-Alone Products for Symptoms of Vulvar and Vaginal Atrophy (VVA) <http://www.fda.gov/Drugs/NewsEvents/ucm459690.htm>  
 2) ACOG Supports the Use of Estrogen for Breast Cancer Survivors <http://www.acog.org/About-ACOG/News-Room/News-Releases/2016/ACOG-Supports-the-Use-of-Estrogen-for-BreastCancer-Survivors>

# Payer Overview

**Joseph Auci**  
VP, Managed Care,  
Distribution, and Policy

# Payer Breakdown of FDA-Approved VVA Products



# Payers are Continuing to Provide Choice

## 80% of Payers Prefer 2+ Products

VVA Category		Estrace Cream	Estring	Osphena	Premarin Cream	Vagifem
Payers	Lives	Univ. Status	Univ. Status	Univ. Status	Univ. Status	Univ. Status
Express Scripts PBM	28,411,137	Preferred	Covered	Covered	Preferred	Preferred
CVS Caremark RX	25,490,409	Preferred	Covered	Preferred	Preferred	Preferred
UnitedHealth Group, Inc.	15,606,808	Covered	Preferred	Covered	Covered	Preferred
Anthem, Inc.	14,307,637	Preferred	Preferred	Covered	Preferred	Covered
OptumRx	9,508,973	Covered	Covered	Covered	Preferred	Covered
Aetna, Inc.	9,265,194	Covered	Covered	Covered	Preferred	Covered
Department of Defense - TRICARE	7,004,961	Preferred	Preferred	Preferred	Preferred	Preferred
Kaiser Foundation Health Plans, Inc.	6,610,331	Preferred	Preferred	Not Covered	Preferred	Not Covered
CIGNA Health Plans, Inc.	6,375,734	Covered	Preferred	Covered	Preferred	Covered
Blue Cross Blue Shield Association Corporatic	5,442,846	Preferred	Covered	Covered	Preferred	Preferred
Health Care Service Corporation	5,135,711	Preferred	Covered	Covered	Covered	Preferred
Department of Veterans Affairs (VHA)	4,803,818	Covered	Covered	Covered	Preferred	Covered
Humana, Inc.	2,325,564	Covered	Covered	Not Covered	Covered	Covered
Blue Cross Blue Shield of Michigan	2,317,410	Covered	Preferred	Covered	Preferred	Preferred
Indian Health Service (IHS)	2,201,809	Covered	Covered	Covered	Preferred	Covered
Blue Shield of California	1,894,377	Preferred	Preferred	Covered	Preferred	Preferred
Prime Therapeutics	1,885,924	Preferred	Covered	Covered	Covered	Preferred
Blue Cross and Blue Shield of Florida, Inc.	1,861,938	Covered	Covered	Covered	Preferred	Preferred
Highmark, Inc.	1,781,021	Covered	Preferred	Covered	Preferred	Covered
CareFirst, Inc.	1,530,652	Preferred	Covered	Preferred	Preferred	Preferred

# Why are Payers Providing Open Access?

## Several reasons:

- Overall low cost category compared to other therapeutic areas
- Importance of providing choice for women
- Lack of innovation in the VVA category
- Prior authorization to drug cost ratio is not favorable
  - **Cost of a prior authorization runs between \$80-\$140 per patient per year depending on payer**

# Pathway to Obtaining Broad Coverage

- TherapeuticsMD has seasoned managed care professionals on team with significant payer relationships
- Building out managed care team with inVentiv to help staff appropriately for launch
- Performed ad boards and significant payer research pre-launch
- Established relationships and planned meetings with largest plans pre-PDUFA

**Reception to TherapeuticsMD and our products has been very favorable**

# Payer Overview

**Tony Lanzone**

## **Managing Director, inVentiv Health Consulting**

- 25 years of consulting in pharmaceutical/life sciences industry; member of Pricing and Market Access Practice
- Former director of Healthcare Informatics at Premier, a hospital GPO; provided consulting and market research
- Formerly in Ernst & Young's healthcare practice
- Commercial roles at Bristol-Myers Squibb

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# Primary Research

## VVA Management

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VVA products are considered to be a very low budget impact category, and as such, the utilization management techniques are minimal, with no PA/SE for most commercial payers.

- Hormone Replacement Therapy (HRT) in general and Vulvar and Vaginal Atrophy (VVA) specifically are not actively managed by payers due to very low budget impact
  - This category is not on payers' radar and can be classified as "top 100" in terms of the financial impact
  - Payers typically don't differentiate deeper than the HRT category – few payers appreciated the nuance of VVA or the specific sub-indications
  - Tiering is the most common utilization management method used by payers, with no Prior Authorization (PA) and Step Edit (SE) techniques for most of the drugs in this category
  - Most of the legacy drugs have been on formulary for a very long time, and payers sometimes don't remember why or when drugs like Premarin or Estrace ended up on Tier 2
- New drugs are usually reviewed through standard P&T committee process, and may not have a coverage decision until 3-6 months post-launch
- There is a perception that in this category very little can be done to show clinical differentiation for a new product

*"We don't manage this category at all, nothing here, not tight management."*

-Pharmacy Director, National Payer

Research conducted in September-October 2016, sample included 20 national and regional payers, including two PBMs, representing ~157MM lives

# Primary Research

## Product X (TX-004HR) Initial Reaction

Reaction to Product X was positive, and respondents are quick to pick up the features of Product X that stand out: elegance, low dose, absence of applicator and local administration.

### ***Unaided mentions of high differentiation features include:***

- Absence of applicator
- Route of administration and “elegance” of formulation (locally administered estradiol in dissolving softgel capsule)
- Low dose of estrogen (aligned with guidelines)
- Various doses that may allow to titrate
- Statistically significant safety data
- Absence of BBW is mostly viewed as a “nice to have” feature, with some payers focusing more on real world evidence than just FDA label

### ***Product features that did not resonate with payers include:***

- Another form of estradiol, not a new formulation
- No head-to-head comparison with other drugs that would assume clinical differentiation, although many realize that it would not be typical or necessary in this category

*“Advantage is that it is the only product with the smallest dose. It does not need applicator. It is soft gel – another difference. Indications are not really that important to us. We don’t manage them by indication.”*

-Pharmacy Director,  
National Payer

*“Good feature – dissolution. Less messy, low dose, simple estrogen. Level of effectiveness is something that is going to come up. Disadvantages – this is still an estrogen, general approach to treating. Nothing new here, we would be interested in cost of the product...”*

-Pharmacy Director,  
National Payer

Research conducted in September-October 2016, sample included 20 national and regional payers, including two PBMs, representing ~157MM lives

# TX-004HR Launch Strategy\*

**Dawn Halkuff**  
Chief Commercial Officer

- Former SVP of the Pfizer Consumer Healthcare Wellness Organization
- Former Marketing and Sales Lead of the Pfizer Women's Health Division
- Former Head of Global Innovation at Weight Watchers International
- 20+ years of commercial experience across pharmaceuticals, consumer packaged goods, and services
- Majority of career spent in Women's Health

\*Assuming approval

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# Experience Aligns to VVA Market Needs

Important Touch  
Point of VVA Market

## Kimberly Clark – Marketing Feminine Protection

- Private subject; Innovation through user experience



## Weight Watchers - Global Innovation

- Drive urgency to take care of an ongoing and worsening issue



## Pfizer Women's Health – Marketing/Sales of Premarin Franchise

- Hormone therapy opportunities and challenges



## Pfizer Consumer Products - Head of Wellness

- Drive innovation on both scientific advances and patient desire



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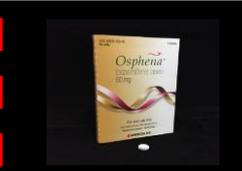
# Local Estrogen Therapy Current Standard of Care

Local estrogen therapy currently represents over 95% market share in the VVA market

- Current standard of care per medical society guidelines
- OB/GYNs comfortable with safety and efficacy profile – low education hurdle

However, there has been zero innovation for local estrogen products since 1999



Products	Estrace Cream®	Premarin Cream®	Vagifem®	Estring®	Osphena®	Intrarosa®
						
						
TRx Dollars 2016 <sup>1</sup>	\$511,035,880	\$505,351,340	\$502,715,665 <sup>a</sup>	\$105,040,703	\$72,755,311	Approved 11/2016
Active Ingredient	100 mcg Estradiol	625 mcg/g Conjugated Equine Estrogens	10 mcg Estradiol	2,000 mcg Estradiol	60,000 mcg Ospemifene	6,500 mcg Prasterone
Year Approved	1984	1978	1999	1996	2013	2016

1. Symphony Health Solutions PHAST Data powered by IDV; Annual 2016

a. 2016 Vagifem and Yuvaferm (authorized generic of Vagifem)

Vagifem [package label] <http://www.novo-pi.com/vagifem.pdf>

Premarin Vaginal Cream [package label] <http://labeling.pfizer.com/showlabeling.aspx?id=132>

Estrace Vaginal Cream [package label] [http://pi.actavis.com/data\\_stream.asp?product\\_group=1880&p=pi&language=E](http://pi.actavis.com/data_stream.asp?product_group=1880&p=pi&language=E)

Osphena [package label] [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2013/203505s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/203505s000lbl.pdf)

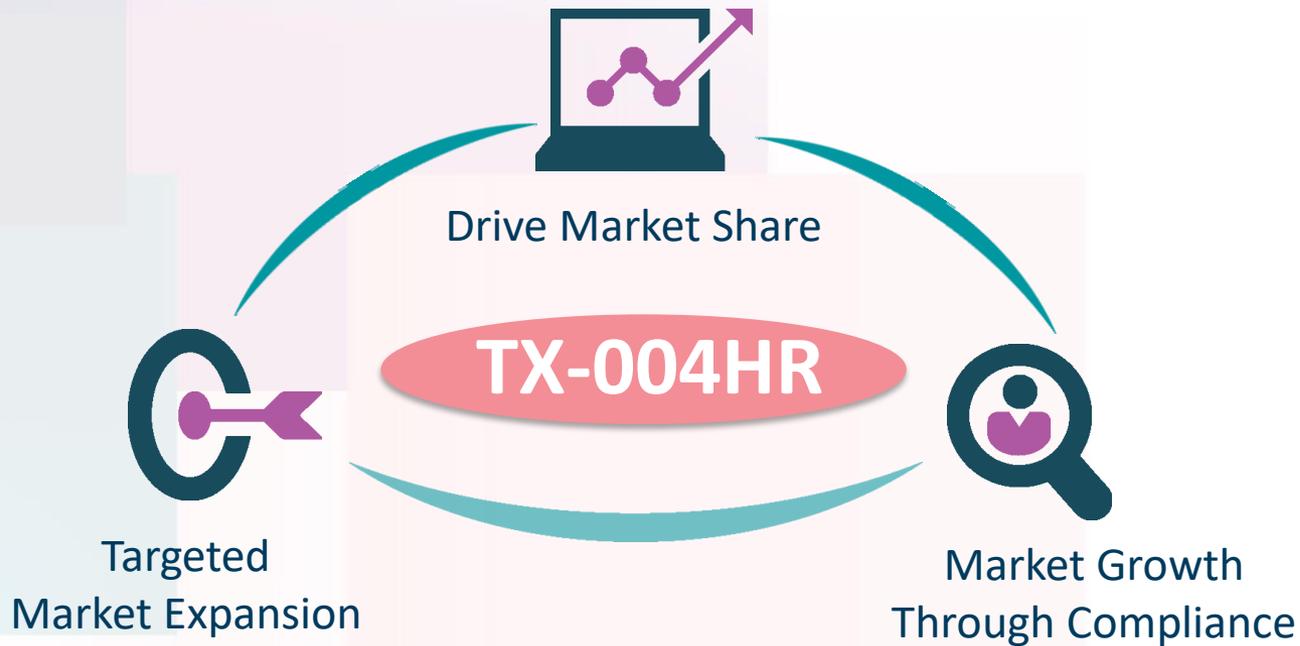
Intrarosa [package label] [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2016/208470s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208470s000lbl.pdf)

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# Focus on Three Main Fundamental Levers to Drive TX-004HR Launch



# Aligned Healthcare Providers (HCPs) and Patient Strategies Drive Fundamental Levers of Growth

## Drive Market Share

Differentiate TX-004HR as new treatment option that redefines relief

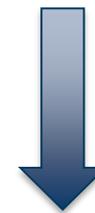


## Targeted Market Expansion

Elevate importance of VVA by demonstrating true impact of disease



## Market Growth Through Compliance



Build a differentiated national care model for successful diagnosis, treatment, and management of symptoms of VVA caused by menopause

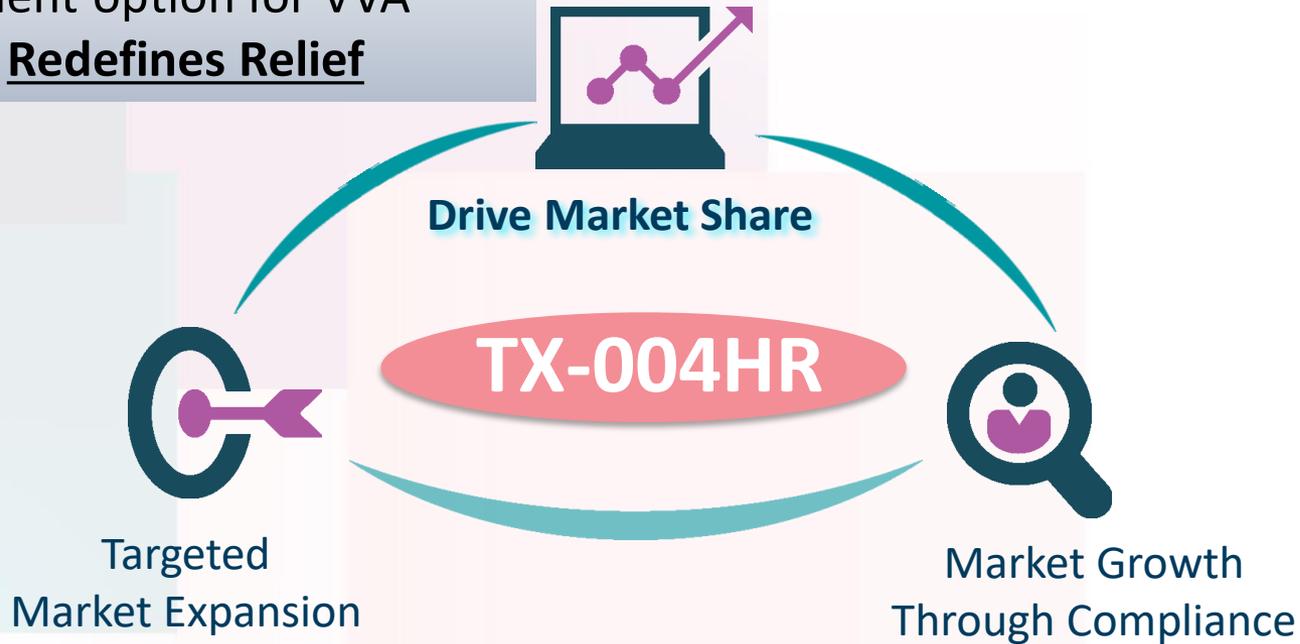
## Commercial Execution

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# Drive Market Share

Differentiate TX-004HR as new treatment option for VVA that **Redefines Relief**



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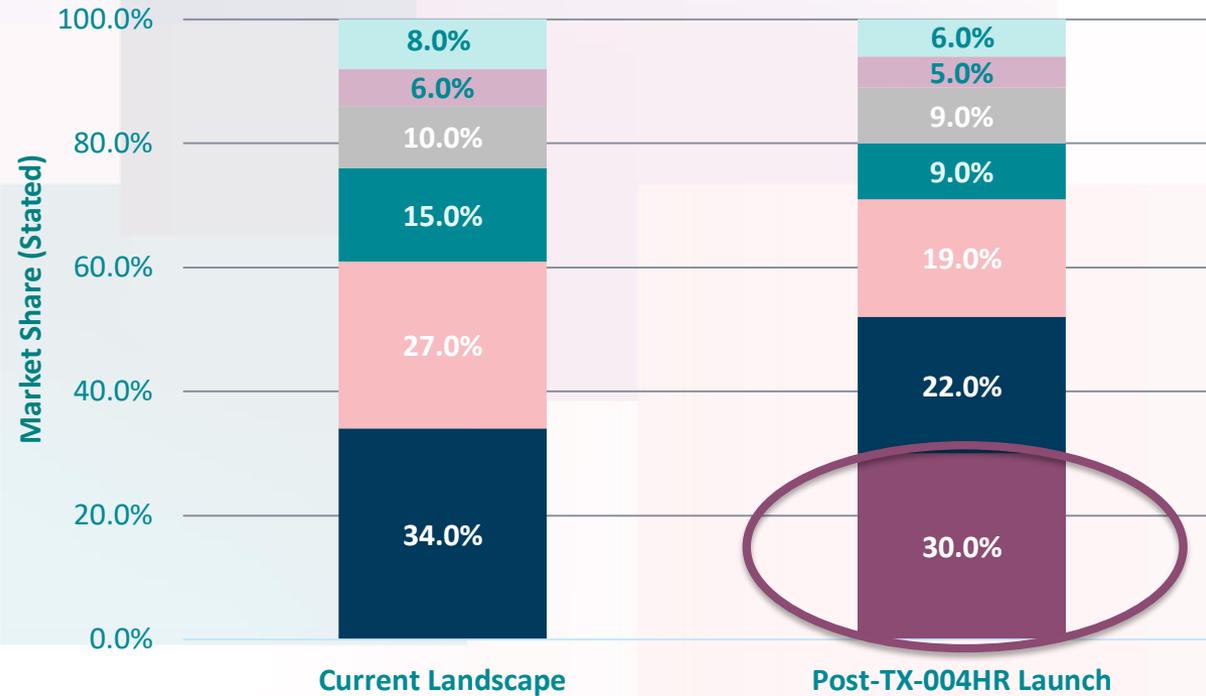
# Efficacy, Safety, and Positive User Experience Redefines Relief

	Perceived Shortcomings	TX-004HR Solution		
Efficacy	<ul style="list-style-type: none"> <li>▪ 1 in 4 women achieve limited relief<sup>1</sup></li> <li>▪ Delayed onset of efficacy<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>▪ Early efficacy observed at week 2</li> <li>▪ Efficacy for vaginal dryness</li> </ul>		
Safety/ Side Effects	<ul style="list-style-type: none"> <li>▪ Hormone exposure concerns<sup>1</sup></li> <li>▪ Messiness<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>▪ Negligible systemic exposure</li> <li>▪ No messiness</li> </ul>		
Convenience	<ul style="list-style-type: none"> <li>▪ Products difficult to use<sup>1</sup></li> <li>▪ Inadequate instructions on use<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>▪ No applicator; any time of day use</li> <li>▪ Simple dose pack; easy instructions</li> </ul>		
Patients Choose TX-004HR	Rejoice Trial Survey Results	4 mcg (N=119)	10 mcg (N=113)	25 mcg (N=128)
	TX-004HR preferred over previously used VVA therapies	73.9%	67.3%	74.2%

1) Wysocki, S et al, Management of Vaginal Atrophy: Implications from the REVIVE Survey. *Clinical Medicine Insights: Reproductive Health* 2014;8:23-30 doi:10.4137/CMRH.S14498  
REJOICE Trial Results

# HCPs Estimate Giving TX-004HR 30% Market Share

*HCP Stated Preference Share*  
 (Adjusted Percent of Prescriptions, n = 400 HCPs)



- Large share gains from 3 largest competitors
- Set attainable 3-5 year company launch goals

■ TX-004HR 
 ■ Premarin Cream 
 ■ Estrace Cream 
 ■ Vagifem 
 ■ Osphena 
 ■ Estring 
 ■ Other

# Market Share Comes From High Writing HCPs

## Target HCPs Representing 80% of Active Prescribing Volume in Market

- Sales force targets – 8,000 practices = 22,000 HCPs
- Group practice focus vs. individual HCP to maximize impact
  - Efficient launch plan to maximize sales force ROI
- Experienced women's health representatives
- Integrated multi-channel marketing (MCM) campaign to complement sales force and extend reach to lower-decile HCPs

# Our Approach: Detailed HCP Strategy

## What needs are we addressing?

### Simplify the Prescribing Experience

- Simplify the conversation
- Simplify the product experience – how to use, product support for patients



## What are our core tactics?

### What We Are Doing Today

- Preparing the sales force: learning from HCPs the main barriers of diagnosing and treating VVA
- Unbranded communications of the true impact on their patients

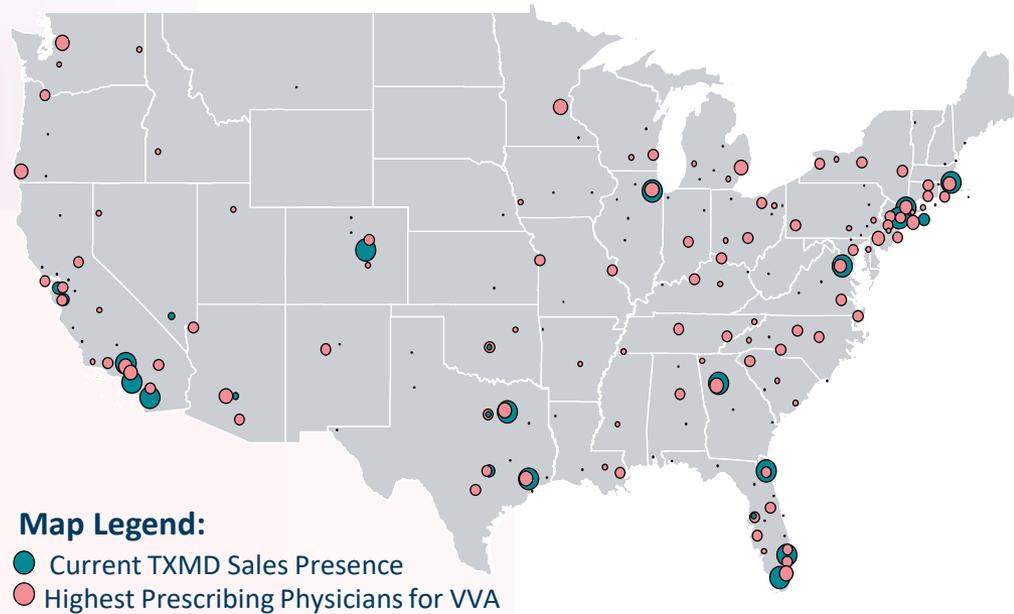
### Post Launch

- Branded clinical presentations to pull through “Redefining Relief” (sales force, peer-to-peer programs)
- Education, reimbursement and compliance programs via national support model

# Foundation Already Built for a Strong Launch

## TXMD Sales Force Currently in OB/GYN Offices

- 40% overlap with current prenatal vitamins business
- Currently calling on VVA targets with market condition campaign
- Planned sales force of 100 in place prior to launch
- Partnership with inVentiv, leading contract sales organization
- Operational and analytic systems



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# Targeted Market Expansion



Elevate the importance of VVA by demonstrating **true impact** of disease

# Significant Untapped Opportunity in the VVA Market

**~2.3M (7%)  
Rx Treated<sup>1</sup>**

**~29.7M (93%)  
Untreated Women**

- Past HT users = ~5.7M<sup>2</sup>
- OTC users = ~8M<sup>2</sup>
- Not seeking treatment = ~16M<sup>2</sup>

1) IMS Health Plan Claims (April 2008-Mar 2011)

2) TherapeuticsMD "EMPOWER" Survey, 2016

# Main Barriers to Expansion: Education and Motivation

## Women's Reality

- 42% believe VVA is natural part of aging
- 67% never spoke to doctor about the condition

## Plan to Address

- Help women self-identify
- Prepare women to have a conversation

**Educate and Motivate By Helping Women Understand the True Impact of VVA**

# Educate and Motivate Women Through True Impact

**OUCH!**

Sex last Night was more than a little Uncomfortable

THERE MIGHT BE SOMETHING MORE GOING ON

Pain is your body's way of telling you something is wrong

Every itch, burn, and pain has a meaning. It's your body's signal to the brain that something is wrong, and that pain—even in the vagina—deserves attention. If you are feeling pain during sex, and you are past menopause, you may have a progressive medical condition called VVA that lubricants alone can't fix. Fortunately, there are treatments available that can treat the underlying condition and relieve your pain.

So listen to your body's signals and talk to your doctor today. Or visit [ListenToYourBody.com](http://ListenToYourBody.com).

*"I dread going to bed. I'm so guilt-ridden. He doesn't deserve this..."*

*"He doesn't want to hurt me. He knows it's not the same..."*

*"We're still young. We want to be young. You just feel so old, dried-up..."*

# Our Approach: Detailed Patient Strategy

What needs are we addressing?	What are our core tactics?
<p data-bbox="131 365 890 411"><b>Women's Understanding and Comfort</b></p> <ul data-bbox="131 482 1012 862" style="list-style-type: none"><li data-bbox="131 482 857 582">▪ Educate her on the condition and provide tools to help self-identify</li><li data-bbox="131 654 1012 753">▪ Help her acknowledge the true impact to drive urgency</li><li data-bbox="131 825 568 862">▪ Make it affordable</li></ul>	<p data-bbox="1074 365 1711 411"><b>What We Are Doing Pre-Launch</b></p> <ul data-bbox="1074 482 1750 639" style="list-style-type: none"><li data-bbox="1074 482 1750 639">▪ Unbranded communications to educate on true impact – live, print, and digital</li></ul> <p data-bbox="1074 711 1315 748"><b>Post Launch</b></p> <ul data-bbox="1074 825 1785 1090" style="list-style-type: none"><li data-bbox="1074 825 1702 925">▪ Branded print, digital, and in office brochures</li><li data-bbox="1074 996 1785 1090">▪ Education and support programs via national care model</li></ul>

# Other Opportunities To Expand the Market

## Relevant Suffering Populations: Oncology\*

- Currently 3M breast cancer survivors on Aromatase Inhibitors
- Most of these patients suffer from severe VVA due to lack of estrogen production

### TX-004HR designed to overcome hurdles oncologists have with HT:

- Potential lowest effective doses
- Negligible systemic exposure

## Expanding the Mainstream Market: Primary Care Physicians (PCPs)

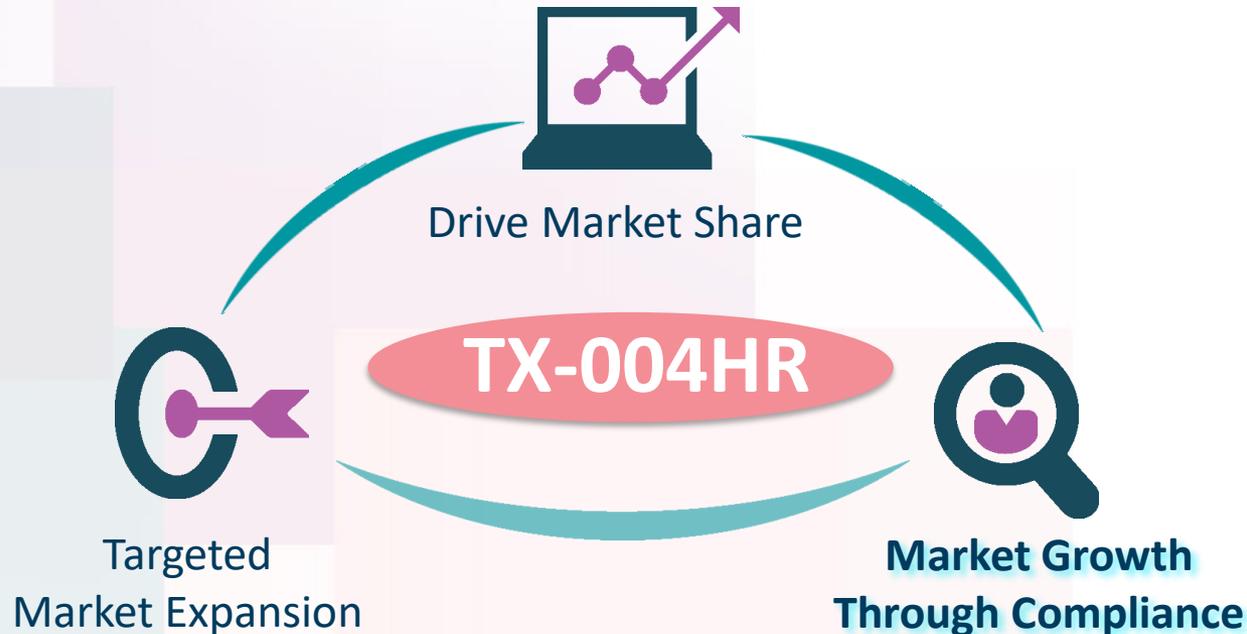
- PCPs currently write about 10-15% of the prescriptions for local estrogen therapy
- Menopausal women visit their PCP more frequently than their OB/GYN

### TX-004HR designed to overcome hurdles PCPs have with HT:

- Easy to prescribe packaging
- Negligible systemic exposure

\*Current FDA-approved product labels include a contraindication for known, suspected, or history of breast cancer; TX-004HR upside case label assumptions include removal of this contraindication

# Market Growth Through Compliance



Build a differentiated **national care model** for successful diagnosis, treatment, and management of symptoms of VVA caused by menopause

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# Current VVA Market Average Compliance and Fills Per Year

## Vaginal Creams



Average:  
1.5 Fills Per Year<sup>2</sup>



## Vaginal Tablets



Average:  
3.5 Fills Per Year<sup>2</sup>

### Reasons Women Stop

Messiness<sup>1</sup>

Reusable applicator<sup>1</sup>

Long-term safety<sup>1</sup>

Dose preparation  
required by user<sup>3</sup>

### Reasons Women Stop

Efficacy<sup>1</sup>

Applicator<sup>1</sup>

Long-term safety<sup>1</sup>

Systemic absorption<sup>1</sup>

Slight, incremental changes have led to increased fills per year for vaginal tablets

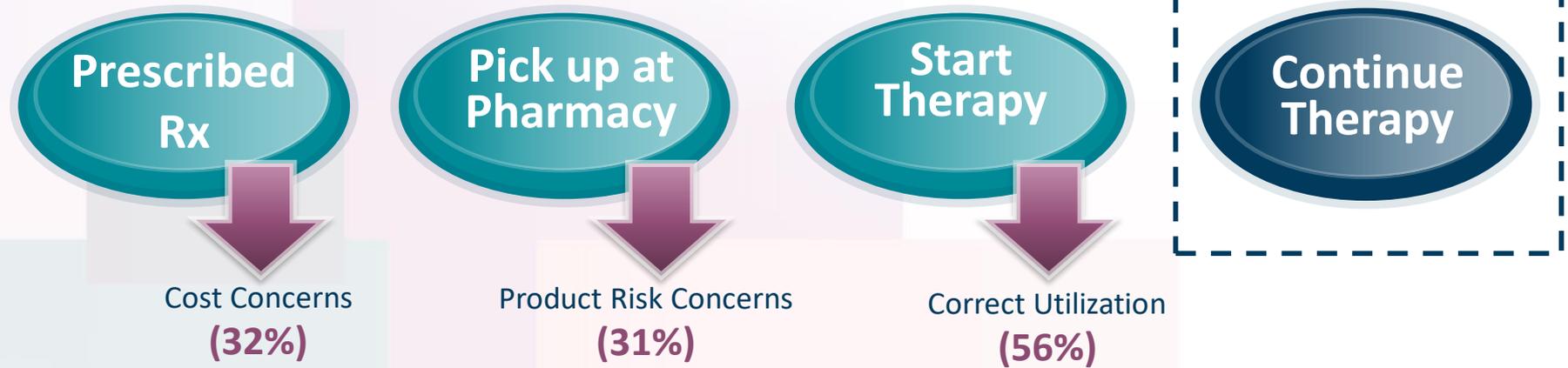
- Disposable applicator
- Pre-packaged doses
- Monthly dosing regimen

1) Wysocki, S et al, Management of Vaginal Atrophy: Implications from the REVIVE Survey. *Clinical Medicine Insights: Reproductive Health* 2014;8 23-30 doi:10.4137/CMRH.S14498

2) Total Rx/Patient Count

3) The North American Menopause Society. Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. *Menopause*. 2013;20(9):888-902.

# Opportunity to Further Increase Compliance with Focus on Patient Journey Drop Off Points



## National Care Model

### Patient Care

- Financial
- Condition and product education
- Follow on communications

### Proven Results in Prenatal Business

- 70% of patients utilize services

### Compliance in Prenatal Business

- 8 months vs category average of 2 months



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# Increased Compliance and Fills Per Year Drives TX-004HR Net Revenue at Year 5 of Launch

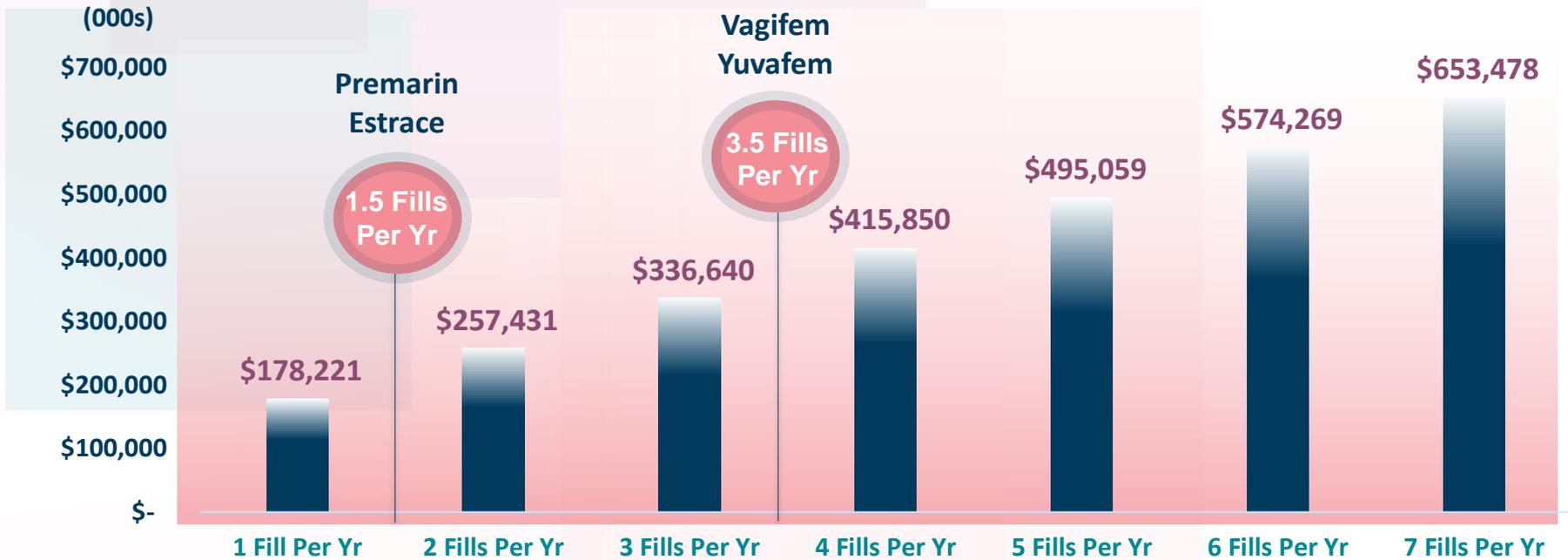
Year 5 Assumptions	
Total VVA Patients on HT <sup>1</sup>	2,218,252
TX-004HR Market Share	30%
TX-004HR Patients	665,000
WAC of Loading Dose	\$ 382.86
WAC of Maintenance Dose	\$ 170.16
Average Rebate per Rx	30%



Zero market growth



Parity pricing - Vagifem  
Zero price increases



1) IMS SDI's Total Patient Tracker; Annual 2016

# TX-004HR Launch Timeline

## January - April (Pre-Approval)

- Sales force preparedness
- Payer pipeline discussions
- Launch planning
- Unbranded HCP campaign

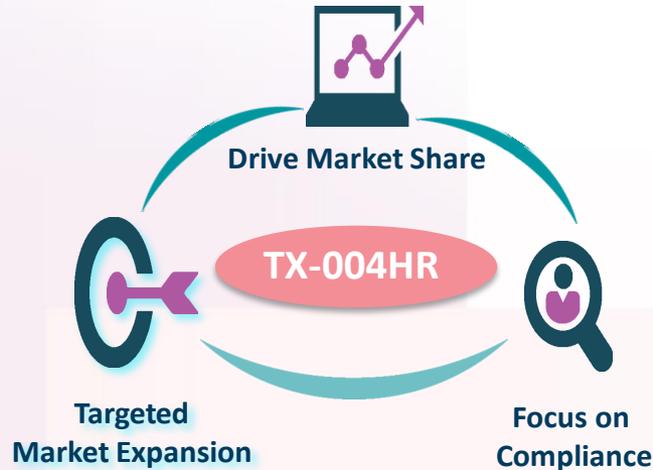
## May - September (FDA-Approval)

- **PDUFA date - May 7<sup>th</sup>**
- Continued build out of the sales force
- Continued payer outreach to secure broad coverage
- Unbranded patient campaign

## 4Q 2017 (Launch)

- Branded launch
  - Patient
  - HCP campaign
  - Speaker programs
  - MCM/digital
  - Patient and HCP tools
  - Public relations
- Establish national care model
  - Samples
  - Patient programs
  - Reimbursement programs

# Conclusion



**TherapeuticsMD<sup>®</sup>**  
*For Her. For Life.*

TX-004HR designed for clinical success and improved user experience

Focus on 3 fundamental levers for continued growth and strong execution

Commitment to women's health drives goodwill and brand loyalty

**TherapeuticsMD<sup>®</sup>**  
*For Her. For Life.*

# Q&A

## *Panel*

**Steven Goldstein, M.D.**

**Robert Gregory, R.Ph.**

**Dawn Halkuff**

**Sheryl Kingsberg, Ph.D.**

**Lisa Rarick, M.D.**

**Rob Reid**

**James Simon, M.D.**

# TX-001HR

Combination

Estrogen + Progesterone

(E+P) Program



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# Menopause & VMS Overview

**Brian Bernick, M.D.**  
Chief Clinical Officer

TherapeuticsMD®

*For Her. For Life.*

# Menopause Overview

- **Menopause represents the natural life-stage transition when women stop having periods as the production of Estrogen (E) and Progesterone (P) decreases**
  - Average age of menopause 51 years<sup>1</sup>
  - Women may spend, on average, more than one-third of their lives in a hypoestrogenic state
- **May result in physical and emotional symptoms<sup>1</sup>**
  - Symptoms include vasomotor symptoms (hot flashes, night sweats), mood changes and vaginal dryness
  - Prolonged lack of estrogen can affect the bones, cardiovascular system, and increases risks for osteoporosis
- **Long history of Estrogen (E) and Progesterone (P) use**
  - Estrogen and progesterone have been used for over 50 years as treatment
  - Estrogen to reduce symptoms and other long-term conditions
  - Progesterone to prevent thickening of the uterine wall<sup>2</sup>
    - Increased risk for endometrial hyperplasia/endometrial cancer if estrogen unopposed<sup>2</sup>

1) National Institutes of Health, National Institute on Aging, <https://www.nia.nih.gov/health/publication/menopause>, last accessed November 3, 2015.

2) International Journal on Women's Health, <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3897322/>

# TX-001HR Product Development Rationale

- **2002 Women's Health Initiative (WHI) study showed that *synthetic* hormones increased the risk of breast cancer, stroke, heart attack and blood clots** (all FDA-approved combination hormonal products contain a synthetic Progestin and not a bio-identical Progesterone)
- **Post WHI, women and healthcare providers shifted to Bio-Identical Hormone Therapy (BHRT) containing bio-identical estradiol and bio-identical progesterone as an alternative despite being *unapproved* drugs that are *not covered by insurance***
  - 90M+ scripts of synthetic hormone therapy prescribed annually before 2002, declining to ~10M in 2015<sup>1</sup>
    - Today, patients have the choice between three second best therapies:
      - FDA-approved, **synthetic** combination hormones
      - FDA-approved, **separate** bio-identical hormone products
      - Unapproved, **compounded** bio-identical hormones that have not been proven safe and effective, or covered by insurance
- **Compounding filled the need for BHRT**
  - 30M scripts (3M women) of Compounded Bio-identical Hormone Therapy (CBHRT) prescribed annually in the U.S. currently<sup>2,3</sup>
- **No FDA-approved BHRT combination product of estradiol + bio-identical progesterone**
- **TX-001HR would become the first and only FDA-approved bio-identical combination product to fill this unmet need**



1) Symphony Health Solutions PHAST Data powered by IDV; Annual 2015  
2) The reported number of annual custom compounded hormone therapy prescription of oral and transdermal estradiol and progesterones taken combined and in combination (26MM to 33MM)  
3) Pinkerton, J.V. 2015. Menopause, Vol.22, No.9, pp 0-11.

# Medical Societies Discourage Prescribing of Compounded Bio-Identical Hormones

## ACOG and ASRM Committee Opinion states compounded hormones may pose additional risks compared to FDA-approved products<sup>1</sup>

- Lack of efficacy and safety data
- Lack of Good Manufacturing Practices (GMP)
- Variable purity
- Variable content uniformity
- Variable potency (under/over dose)
- Lack of stability
- Unopposed E / Ineffective P leads to increased risk of endometrial hyperplasia / cancer

ENDOCRINE SOCIETY 100 YEARS OF PROMOVING SCIENCE TO HEALTH

1916-2016

COMPOUNDED BIOIDENTICAL HORMONES IN ENDOCRINOLOGY PRACTICE: AN ENDOCRINE SOCIETY SCIENTIFIC STATEMENT

CONCLUSION: The widespread availability of FDA-approved bioidentical hormones produced in monitored facilities demonstrates a high quality of safety and efficacy in trials; **therefore, there is no rationale for the routine prescribing of unregulated, untested, and potentially harmful custom-compounded bioidentical HTs. Clinicians are encouraged to prescribe FDA-approved hormone products according to labeling indications and to avoid custom-compounded hormones.**

COMMITTEE OPINION  
November 2012 • August 2014 (Reaffirmed 2014) Replaces No. 387, November 2007 and No. 322, November 2005

Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee

Compounded Bioidentical Menopausal Hormone Therapy

ABSTRACT: Although improvement in symptoms, efficacy, and safety of compounded hormones, has not been demonstrated, the use of compounded hormones is increasing. The use of compounded hormones is discouraged because of the lack of efficacy and safety data.

NAMS Survey  
Use of compounded hormone therapy in the United States: report of The North American Menopause Society

Objective: A national survey was conducted to determine the extent of use of compounded hormone therapy (CHT) in the United States. The survey included 1,372 women aged 40 to 64 years who were postmenopausal in the United States. The survey included 1,372 women aged 40 to 64 years who were postmenopausal in the United States. The survey included 1,372 women aged 40 to 64 years who were postmenopausal in the United States.



1) Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee, Number 532, August 2012 (Reaffirmed 2014, Replaces No. 387, November 2007 and No. 322, November 2005).

# TX-001HR – Potential Best in Class Therapy

	<b>TX-001HR</b> (If Approved) 
Bio-Identical	✓
Single Dose Combination	✓
VMS Efficacy Data	✓
Endometrial Cancer Safety Data	✓
FDA-Approved	✓ <sup>1</sup>
Third-Party Reimbursement	✓ <sup>2</sup>

## Potential first and only:

- 1) Bio-identical combination estradiol & progesterone
- 2) FDA-approved

## Dosing and Delivery

- Once-a-day single oral softgel capsule

## Addresses Unmet Medical Need

- First and only combination of bio-identical estradiol and bio-identical progesterone product candidate
- Single combination dose option
- Positive Phase 3 Replenish Trial safety and efficacy results
- Potential FDA-approval with insurance coverage

**Benefits to women, healthcare providers, and pharmacies**

1) NDA to be submitted  
2) Reimbursement anticipated if FDA-approved

# TX-001HR Could Fulfill Therapeutic Gap For All Participants

## Patients

- Meet demand for bio-identical hormone therapy with an FDA approved product that is proven safe and effective
- Reduce of out-of-pocket costs via insurance coverage
- Convenience of one combination product

## Healthcare Providers

- First and only FDA-approved bio-identical combination hormone therapy
- Clinically validated dose regimens
- Eliminate risks of compounded hormone therapy
- Meet patient demands and reduce patient out-of-pocket costs via insurance coverage
- Follow medical standards of care and society guidelines while reducing liability

## Pharmacies

- Meet patient and physician demand for bio-identical hormone therapy
- Significantly improve net margin per script with third-party reimbursement
- Lower legal and regulatory costs and risk

## FDA/Regulatory Bodies

- Reduce need for compounded hormone products
- Full enforcement of regulations regarding compounded hormones
- Reduce false claims and misleading advertising statements about compounded HT products

# Replenish Trial Results

**Sebastian Mirkin, M.D.**  
Chief Medical Officer

TherapeuticsMD<sup>®</sup>

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# Replenish Trial Overview

A Phase 3, Double-Blind, Placebo-Controlled, Randomized, Multicenter Study to Evaluate the Safety and Efficacy of Estradiol in Combination with Progesterone in Postmenopausal Women with an Intact Uterus

# Current FDA Guidance for VMS Drug Products\*

- **Co-primary efficacy endpoints (12 week VMS Efficacy Population)**
  - Mean change from baseline to Weeks 4 and 12 in the frequency and severity of moderate and severe vasomotor symptoms versus placebo
- **Primary safety endpoint (12 month Endometrial Safety Population)**
  - Incidence rate of endometrial hyperplasia at 12 months (to demonstrate a hyperplasia rate that is  $\leq 1\%$  with an upper bound of the one-sided 95% confidence interval for that rate does not exceed 4%)

## Study Analysis

- **Clinically meaningful and statistically significant reduction within 4 weeks of initiation of treatment and maintained throughout 12 weeks of treatment**

## Study Considerations

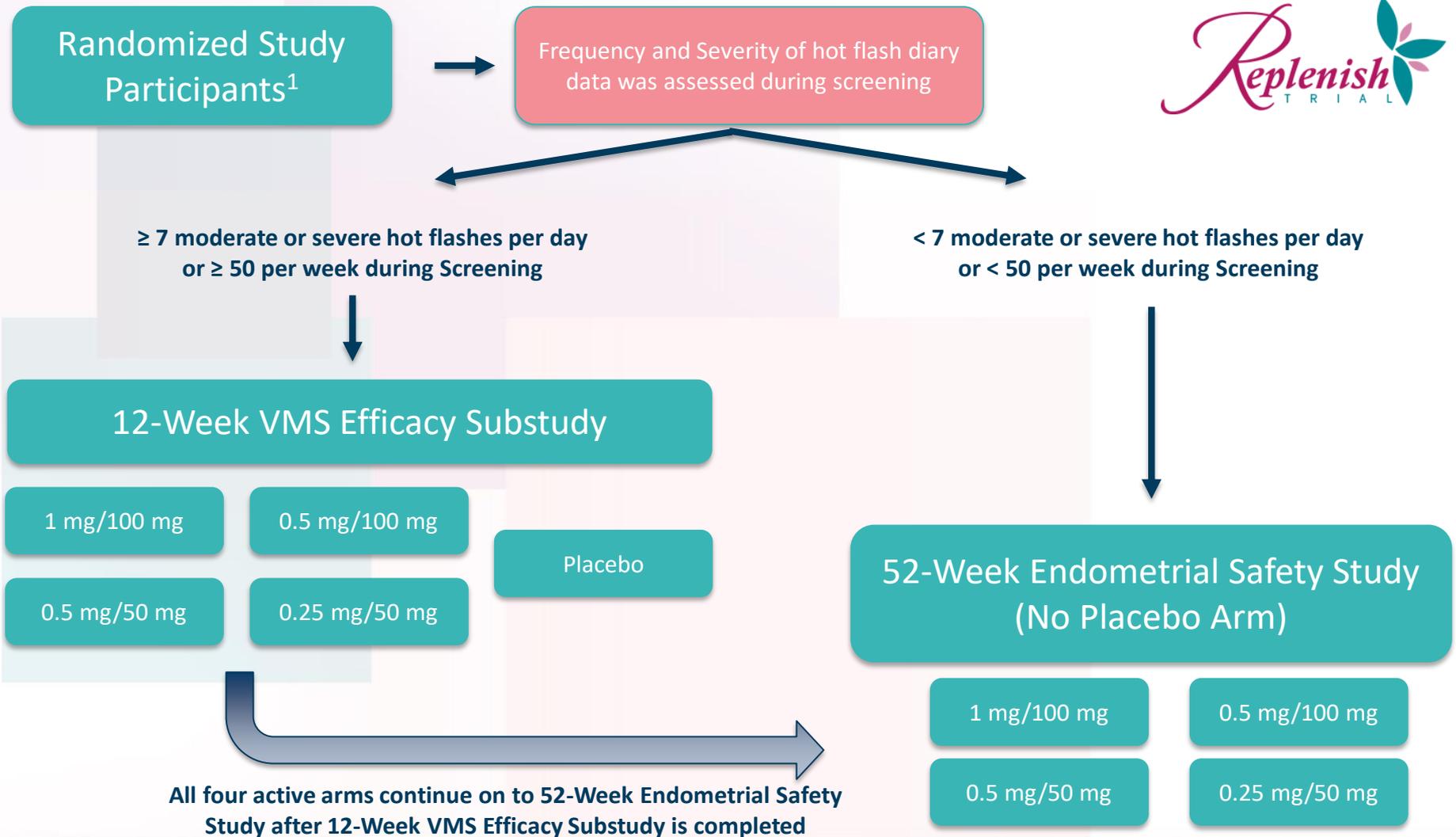
- **Single, 12-month study to demonstrate endometrial protection**

## Single Pivotal Phase 3 trial required unless:

- **The drug to be studied is considered a new molecular entity**
- **The drug to be studied poses unique safety concerns**

\* 2003 FDA Draft Guidance for Industry Estrogen and Estrogen/Progestin Drug Products to Treat Vasomotor Symptoms and Vulvar and Vaginal Atrophy Symptoms – Recommendations for Clinical Evaluation  
<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm071643.pdf>

# Replenish Trial Study Design - Flow Chart



1. Healthy postmenopausal women aged 40 to 65 years with an intact uterus who were seeking relief from vasomotor symptoms (VMS) and who met all inclusion/exclusion criteria were eligible for 12 months of study treatment.

# Replenish Trial Co-Primary Endpoints

Primary Efficacy Endpoints: Mean Change in Frequency and Severity of Hot Flashes Per Week Versus Placebo at Weeks 4 and 12, VMS-mITT Population					
Estradiol/Progesterone	1 mg/100 mg (n = 141)	0.5 mg/100 mg (n = 149)	0.5 mg/50 mg (n = 147)	0.25 mg/50 mg (n = 154)	Placebo (n = 135)
Frequency					
Week 4 P-value versus placebo	<0.001	0.013	0.141	0.001	-
Week 12 P-value versus placebo	<0.001	<0.001	0.002	<0.001	-
Severity					
Week 4 P-value versus placebo	0.031	0.005	0.401	0.1	-
Week 12 P-value versus placebo	<0.001	<0.001	0.018	0.096	-
Primary Safety Endpoint: Incidence of Consensus Endometrial Hyperplasia or Malignancy up to 12 months, Endometrial Safety Population <sup>‡</sup>					
Endometrial Hyperplasia	0% (0/280)	0% (0/303)	0% (0/306)	0% (0/274)	0% (0/92)

MITT = Modified intent to treat

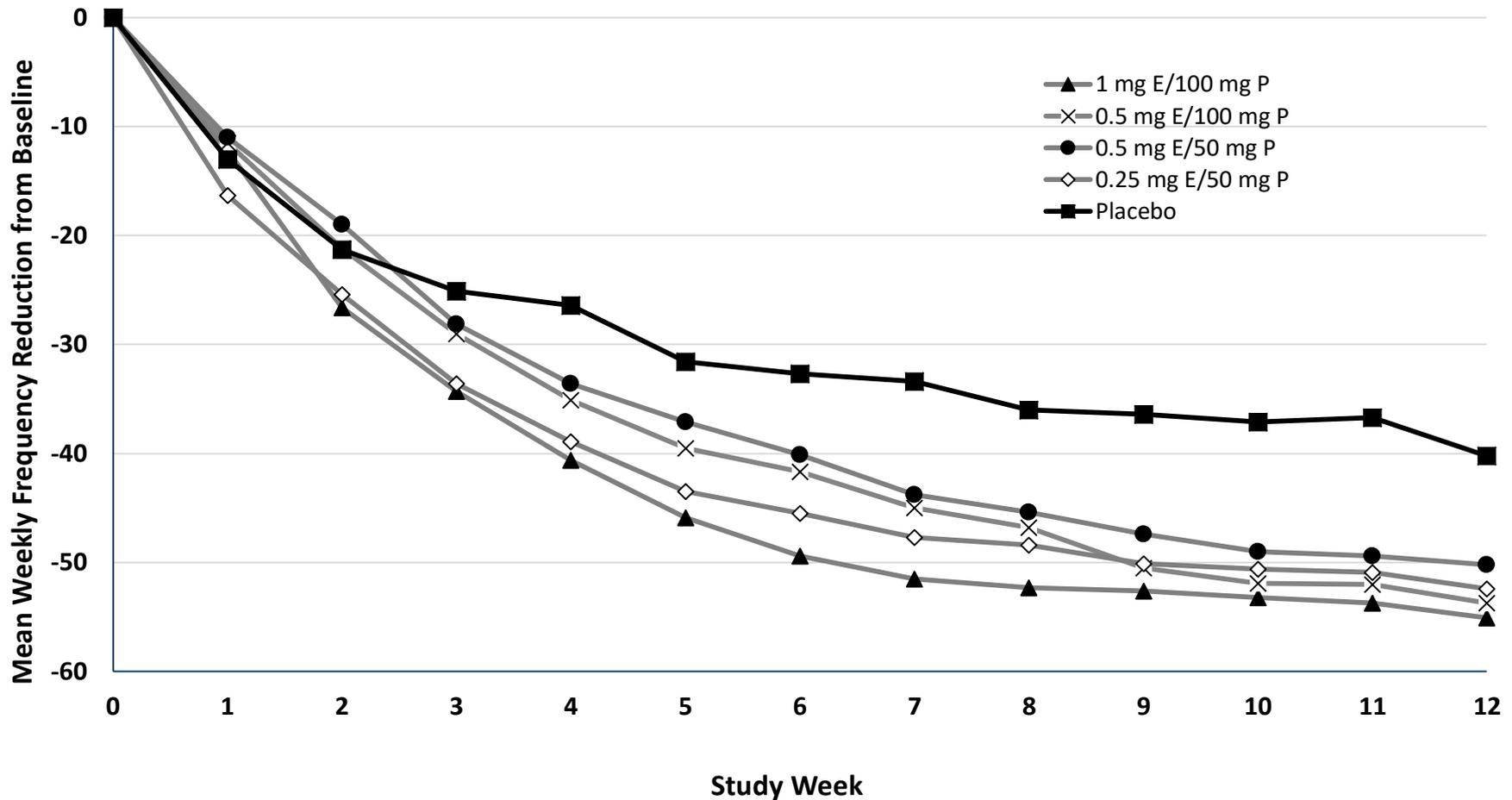
<sup>‡</sup>Per FDA, consensus hyperplasia refers to the concurrence of two of the three pathologists be accepted as the final diagnosis

P-value < 0.05 meets FDA guidance and supports evidence of efficacy

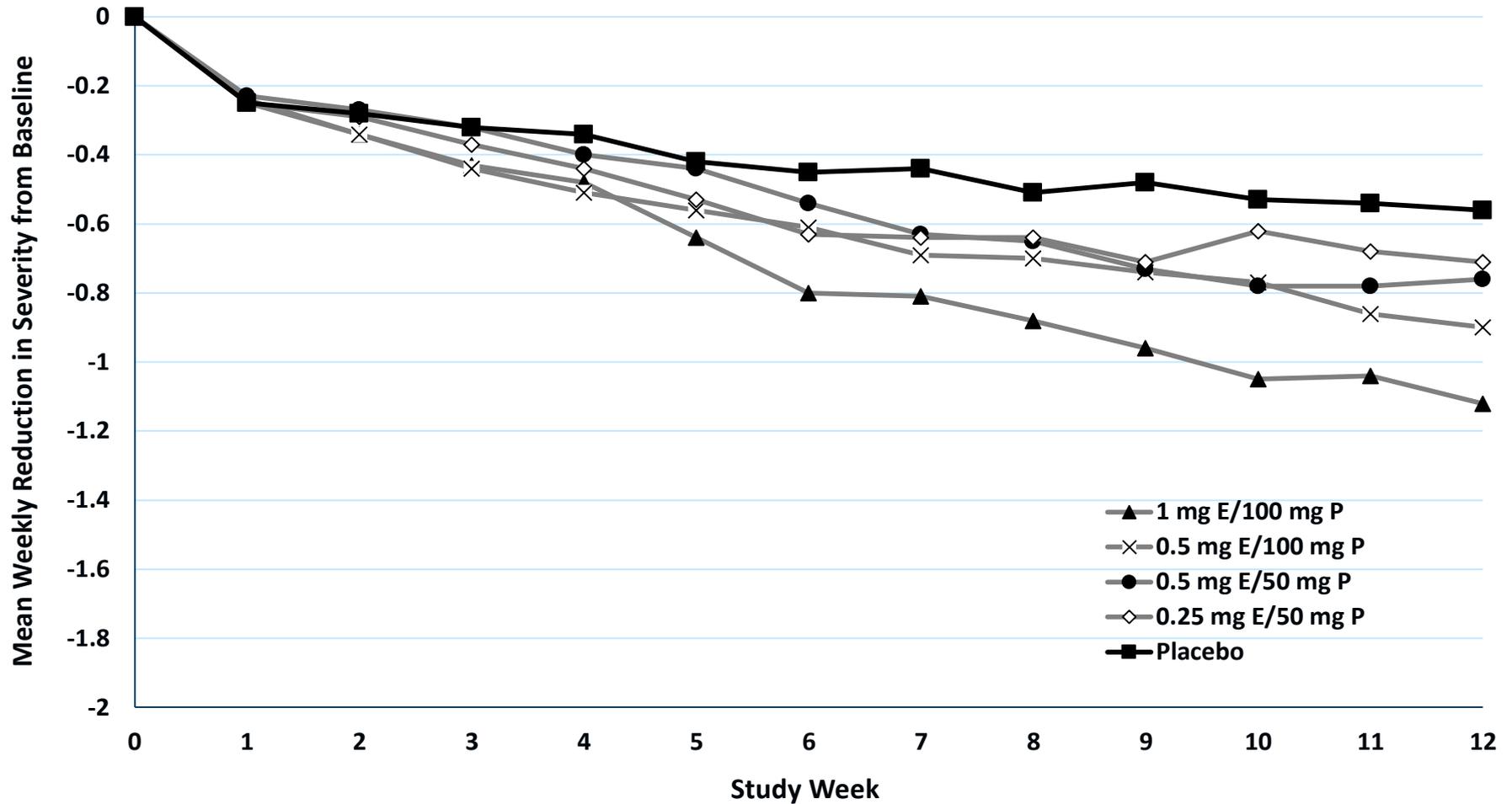
## Primary Efficacy Analysis pre-specified with the FDA in the clinical protocol and Statistical Analysis Plan (SAP)

- P-value < 0.05 meets FDA guidance and supports evidence of efficacy

# Mean Change from Baseline in Weekly Frequency of Moderate to Severe Hot Flashes for Weeks 1 to 12



# Mean Change from Baseline in Weekly Severity of Moderate to Severe Hot Flashes for Weeks 1 to 12



# Quantifying the Market Opportunity

**Robert Finizio**  
Chief Executive Officer

TherapeuticsMD®

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# Multi-Billion Dollar Total Substitutable Market Opportunity

	<b>TX-001HR</b> (if approved) 		
	<b>FDA-Approved</b>		<b>Compounded Combination Bio-Identical E+P</b>
	<b>Separate Bio-Identical E &amp; P Pills</b> 	<b>Combination Synthetic E+P<sup>1</sup></b> 	
<b>TRx US:</b>	~3.5 million <sup>2</sup>	~3 million <sup>2</sup>	12 – 18 million
<b>TX-001HR Potential Market</b>	\$700M-\$875M <sup>3</sup>	\$600M-\$750M <sup>3</sup>	\$2.4B-\$4.5B <sup>3</sup>
<b>TX-001HR Total Substitutable Market Opportunity</b>	<b>\$3.7B – \$6.1B</b>		

**If approved, TX-001HR can provide a single pill solution for women and physicians who:**

- 1) Demand an FDA-approved bio-identical combination hormone product
- 2) Do not trust compounded hormones

1) Includes the following drugs: Activella®, FemHRT®, Angeliq®, Generic 17β + Progestins, Prempro®, Premphase®, Duavee®, Brisdelle®

2) Symphony Health Solutions PHAST Data powered by IDV; 12 months as of December 31 2015

3) Assume WAC pricing between \$200-250

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# TXMD has the Most Comprehensive Body of Research Available

## Quantifying the Compounded BHRT Space

	Date	Purpose	Size
<b>Consumer Survey</b> Harris Interactive	July 2013	15 question Internet Survey to identify % of women going or having been through menopause and quantify symptoms and treatments utilized especially HRT	1,100 women age 45 to 60 with 801 completed survey
<b>Consumer Survey</b> Rose Research	April 2014	30 question Internet Survey to identify % of women using or who have used HRT and quantify (FDA approved vs Compounded) along with 40 detailed chats	17,825 women age 40 and over with 2,044 reporting use of HRT completing full survey
<b>Physician Survey</b> Rose Research	July 2014	20 question Internet Survey to identify prescribing patterns and volume of HRT for different groups of physicians (PCP, OBGYN, GYN & Wellness/Anti-aging) & reaction to our E+P drug candidate	762 physicians of which 440 qualified as prescribing HRT to women
<b>Pharmacy Survey</b> Rose Research	Dec. 2014	31 question Internet Survey to benchmark compounding metrics of community and compounding pharmacies including quantity, type and form of HRT	500+ community and compounding pharmacists (excluded national chain and hospital)
<b>Consumer Survey</b> Rose Research	July 2016	43 multi-part question survey to analyze the patient decision and use experience of women using these products to support product adoption and switch assumptions and to identify key drivers that promote adoption/switch	2,474 women (1,894 FDA approved users and 556 compounded users)
<b>Physician Survey</b> Rose Research	July 2016	21 multi-part question survey designed to analyze the physician treatment decision and prescribing preferences related to these products to support product adoption and switch assumptions and to identify key drivers that promote adoption/switch	600 HCPs (300 OBGYN & 300 PCP)
<b>Pharmacy Survey</b> Health Research & Analytics (an affiliate of Pharmacy Times)	Aug. 2016	52 multi-part question survey to compare trends in business of compounders since 2014 and to confirm size of compounding market specifically focusing on compounded estradiol and progesterone products	191 pharmacies: Focus on pharmacies that have at least 20% of business coming from compounding services (75% of responders)
<b>Big Three Consulting Firm</b>	Oct. 2016	Retained top-tier consulting firm to provide an independent opinion on the size of the E+P addressable compounding market	Includes additional physician survey data
<b>BIO-IGNITE</b>	Nov. 2016	Physical outreach to compounding pharmacy networks as well as independent pharmacies to quantify E+P scripts flowing through pharmacies that have interest in TXMD partnership	To date, >662 pharmacies: 2M E+P scripts

# Methodologies to Quantify Compounded E+P Segments

Simple Extrapolation	Addressable %	Top-Tier Consultant Validation	BIO-IGNITE™
<ul style="list-style-type: none"><li>• Simple extrapolation from survey data applying average reported addressable prescriptions to universe of pharmacies that compound</li><li>• Independent community pharmacies that compound = 14,500</li><li>• Compounding focused pharmacies = 3,500</li></ul>	<ul style="list-style-type: none"><li>• Quantify overall compounded hormone therapy market within compounding pharmacies</li><li>• Apply percentage addressable E+P prescriptions to overall CBHRT market</li></ul>	<ul style="list-style-type: none"><li>• Segment pharmacies by size using prescription volume</li><li>• Calculate average metrics based on category given dispersion in pharmacy size and business</li><li>• Apply average metrics by category</li><li>• Independent community pharmacies that compound = 14,500</li><li>• Compounding focused pharmacies = 3,500</li></ul>	<ul style="list-style-type: none"><li>• Outreach to individual compounding pharmacies and compounding pharmacy networks that are interested in working with TXMD</li><li>• As an indication of interest, pharmacies provide E+P addressable prescriptions their pharmacies fill today</li></ul>
<b>~14M E+P Prescriptions</b>	<b>~12M E+P Prescriptions</b>	<b>~12M E+P Prescriptions</b>	<b>&gt;12M E+P Prescriptions</b>

# Learnings from Our Research:

## Problems Using Physician and Consumer Data to Quantify BHRT Market Size

### • Physician Survey Data:

- 67% of prescribers of compounded BHRT believe it is FDA-approved
- Difficult to capture the population of compounded BHRT prescribers:
  - Prescribers are dispersed across specialties: OBGYN, PCP, and Wellness/Integrative
  - 3% of prescribers account for over 40% of compounded prescription volume
  - Internet panels of physicians are weighted toward high FDA-approved prescribers which under-represents prescribers of compounded products

### • Consumer Survey Data:

- 78% of patients believe their compounded products are FDA-approved
  - Example: Compounded products and FDA-approved products look very similar when they receive it from pharmacy
  - Physicians and pharmacists do not refer to products as compounded or FDA-approved
- Distinguishing feature of consumer data is over half of menopausal women get their HRT prescription filled at an independent community pharmacy vs. chain or retail pharmacy

**Pharmacies are only group with clear understanding of what is being dispensed**

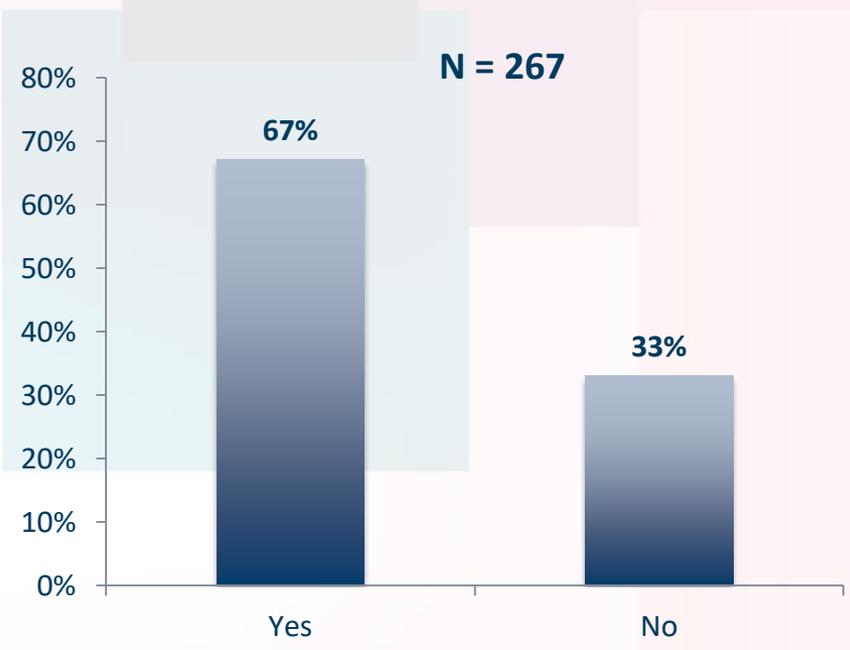
# Compounded BHRT Market is Difficult to Extrapolate Using Physician Data

## 3 Primary Reasons

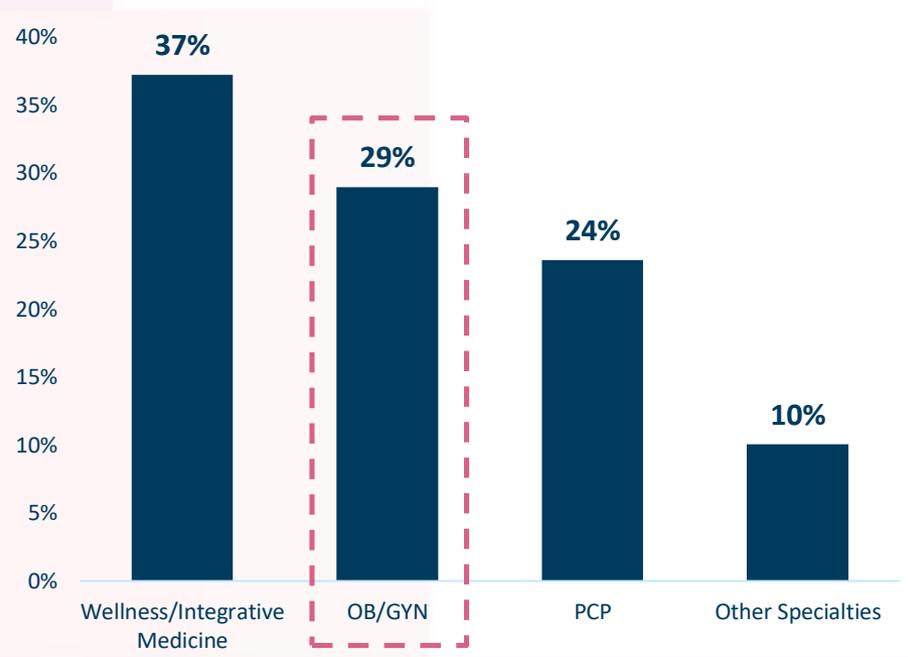
**1** 67% of physicians who prescribe compounded BHRT falsely believe that these are FDA approved

**2** Prescribers are dispersed among 4 specialties with many high volume writers outside of OB/GYNs

Are prescription compounded hormone replacement therapy products made by the compounding pharmacy FDA-approved?



Weighted average based on script volume

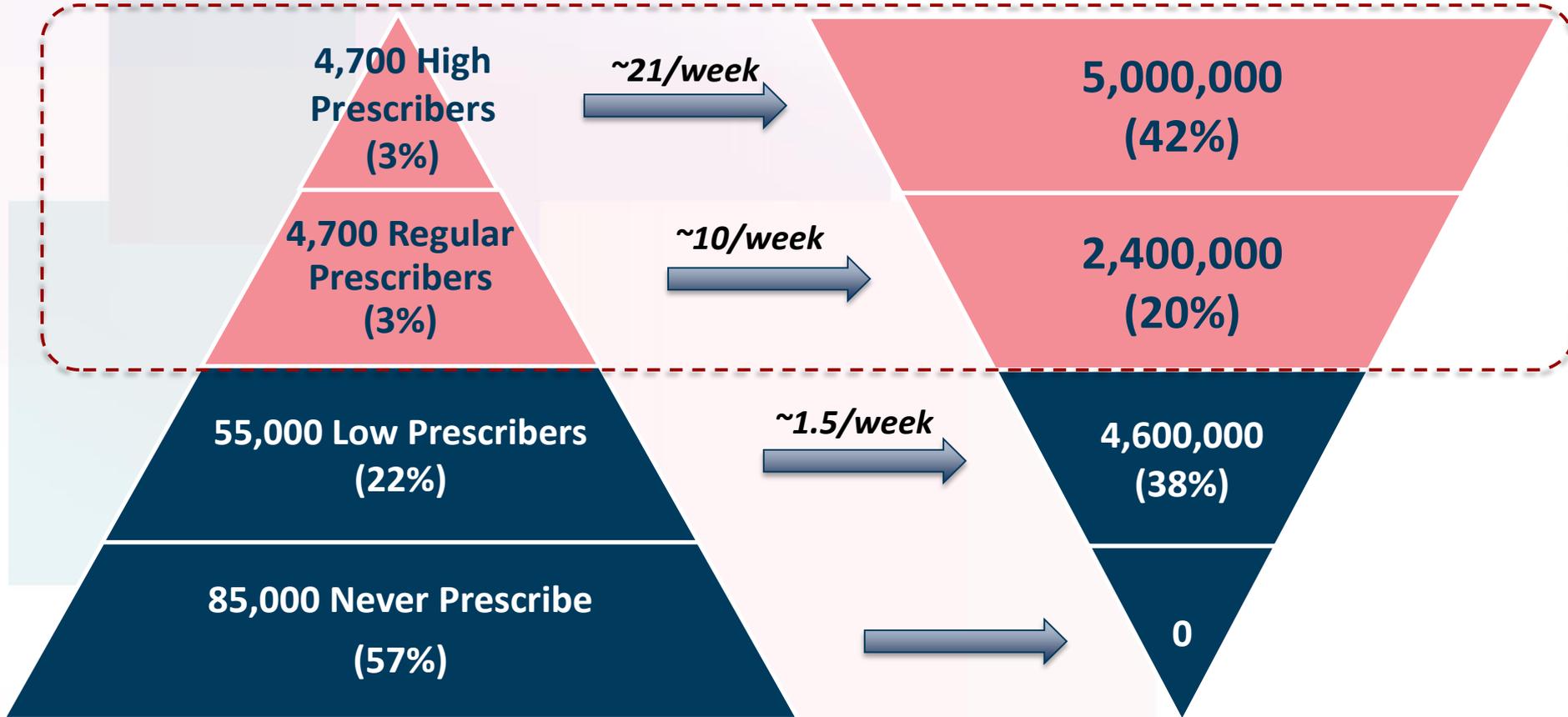


3

# Small Number of Physicians Account for Large Percentage of the Compounded BHRT Market

150,000 Total Eligible Physicians<sup>1</sup>  
(Includes OB/GYNs, PCPs, and Anti-Aging)

~12M Annual Compounded Bio-Identical E+P  
Prescriptions Breakout by Volume



1) SK&A Nationwide Physician Specialty Report – June 2015

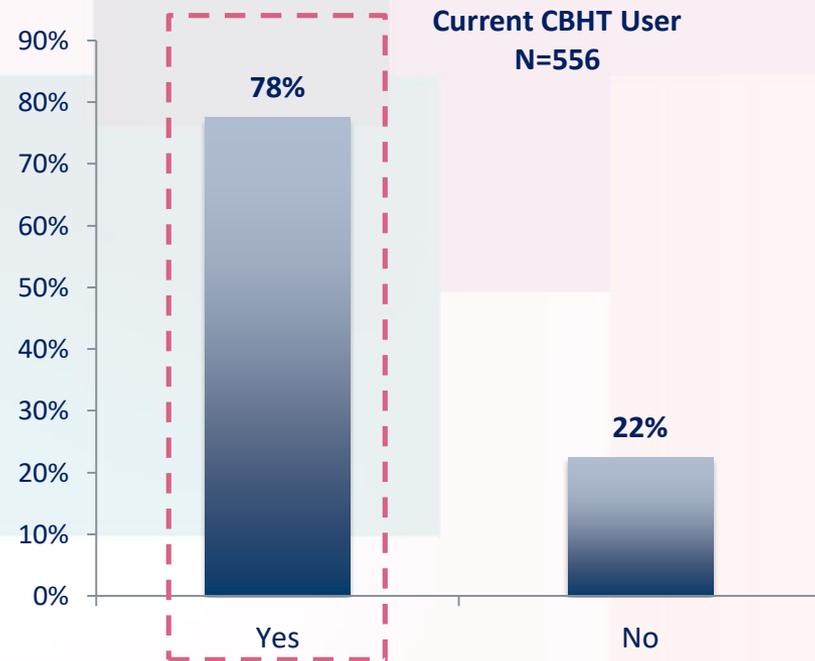
# Compounded BHRT Market is Difficult to Extrapolate Using Consumer Data

## 2 Primary Reasons

1

78% of compounded BHRT patients falsely believe that their prescription is FDA-approved

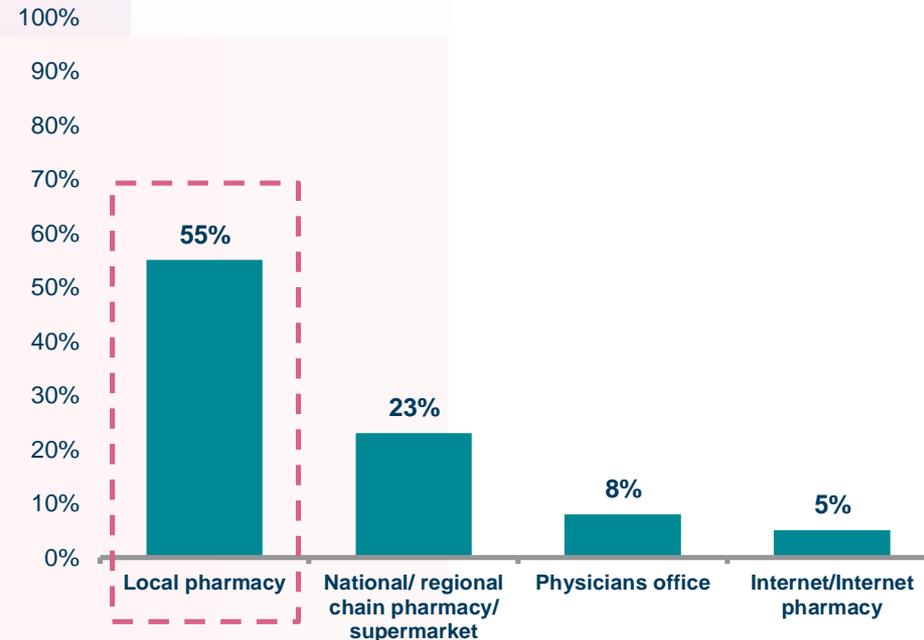
Do you believe that the product made specifically for you by your compounding pharmacy is FDA-approved?



2

More than half of menopausal women purchased their hormone therapy at a "local pharmacy"

Where was your therapy obtained?



# Methodologies to Quantify Compounded E+P Segments

## Simple Extrapolation

- Simple extrapolation from survey data applying average reported addressable prescriptions to universe of pharmacies who compound
- Independent community pharmacies that compound = 14,500
- Compounding focused pharmacies = 3,000

**~14mm  
E+P Prescriptions**

## Addressable %

- Quantify overall compounded hormone therapy market within compounding pharmacies
- Apply percentage addressable E+P prescriptions to overall CBHRT market

**~12mm  
E+P Prescriptions**

## McKinsey Approach

- Segment pharmacies by size using prescription volume
- Calculate average metrics based on category given dispersion in pharmacy size and business
- Apply average metrics by category

**~12mm  
E+P Prescriptions**

## BIO-IGNITE™

- Outreach to individual compounding pharmacies and compounding pharmacy networks that are interested in working with TXMD
- As an indication of interest, pharmacies provide E+P addressable prescriptions their pharmacies fill today

**>12mm  
E+P Prescriptions**

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# FDA-Approved Separate Bio-Identical E & P Substitutable Market Opportunity

- Healthcare providers not comfortable with compounding will often prescribe two separate FDA-approved bio-identical products to treat menopausal symptoms



Product Use by Age	AGES 41-50	AGES 51-60	AGES 61-70	AGES 71+	TRx Totals
<u>Progesterone*</u>	528,325	1,326,618	1,060,666	678,775	3,594,384 <sup>1</sup>
<u>Estradiol</u>	2,677,210	5,494,846	2,826,636	1,083,726	12,082,418 <sup>1</sup>

\*Menopausal use of progesterone directly substitutable to TX-001HR

**~3.5M Potential Prescriptions for TX-001HR (if approved)**  
**Market Opportunity = \$700M-875M<sup>2</sup>**

- This regimen carries **significant risk** of endometrial hyperplasia/cancer if the patient is non-compliant with regular progesterone use
  - Side effects of progesterone including nausea and somnolence can lead to a patient not taking the progesterone
  - Results in two separate co-pays for the patient

1) Symphony Health Solutions PHAST Data powered by IDV; 12 months as of December 31 2015

2) Assume WAC pricing between \$200-250

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# FDA-Approved Combination Synthetic E+P Substitutable Market Opportunity

TX-001HR

## FDA-Approved Combination Synthetic E+P Prescriptions by Age

**PREMPHASE**



*Prempro*<sup>®</sup>

AGES 31-40	AGES 41-50	AGES 51-60	AGES 61-70	AGES 71+	Unknown Ages	TRx Totals
52,575	372,968	1,712,852	759,634	151,821	68,672	<b>3,118,522<sup>1</sup></b>

**~3M Potential Prescriptions for TX-001HR (if approved)  
Market Opportunity = \$600M-750M<sup>2</sup>**

1) Symphony Health Solutions PHAST Data powered by IDV; 12 months as of December 31 2015  
Includes the following drugs: Activella<sup>®</sup>, FemHRT<sup>®</sup>, Angeliq<sup>®</sup>, Generic 17β + Progestins, Prempro<sup>®</sup>, Premphase<sup>®</sup>, Duavee<sup>®</sup>, Bristelle<sup>®</sup>  
2) Assume WAC pricing between \$200-\$250

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# Conclusions

- **Total E+P market size of \$3.7B - \$6.1B**
  - 12 – 18 million compounded E+P scripts
  - 6.5 million FDA-approved E+P scripts
- **Large, readily convertible compounded E+P market**
  - Meaningful economic incentives for compounding pharmacies to convert patients to TX-001HR
  - Regulatory incentives provide meaningful tailwinds
  - Compounding pharmacy partnerships enables rapid adoption

# Launch Strategies & Case Studies

**Joseph Auci**  
VP, Managed Care,  
Distribution, and Policy

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# Understanding the Traditional Retail Pharmacy

## Transactional Relationship

Patient feels sick



Patient visits Physician



Physician writes Rx



Patient picks up Rx  
from Pharmacy

Traditional Retail Pharmacies  
% of Business (by Prescription Units)

FDA-Approved Products  
~100%

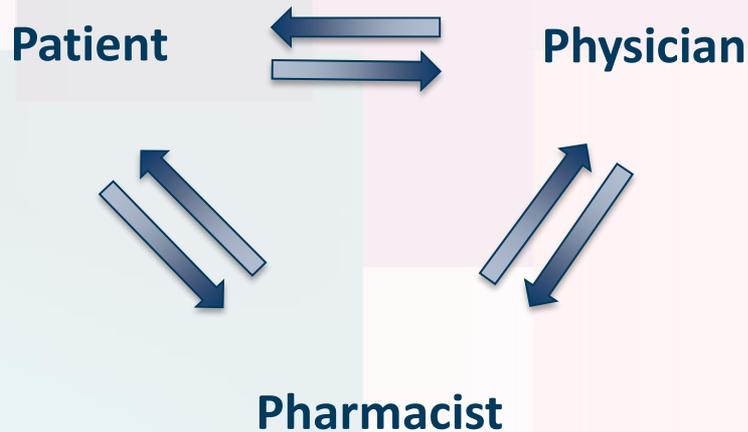
CVS, Walgreens, Duane Reade, ...

TherapeuticsMD®

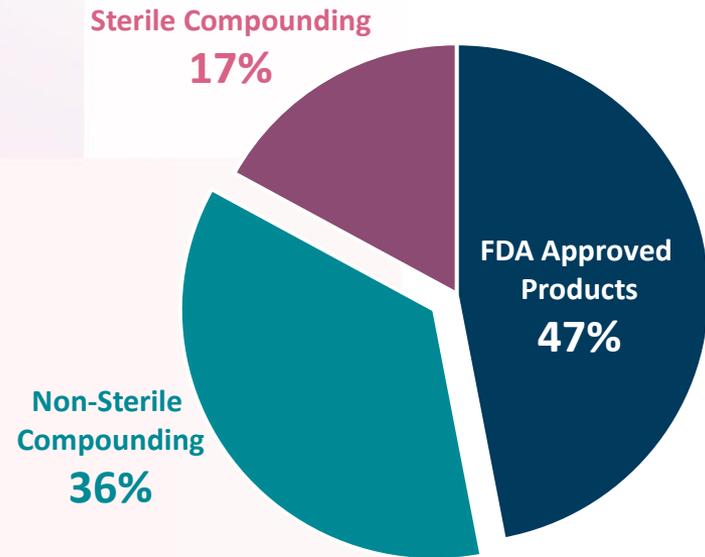
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# Understanding the Compounding Pharmacy

## Collaborative Relationship



## Compounding Pharmacies % of Business (by Prescription Units)

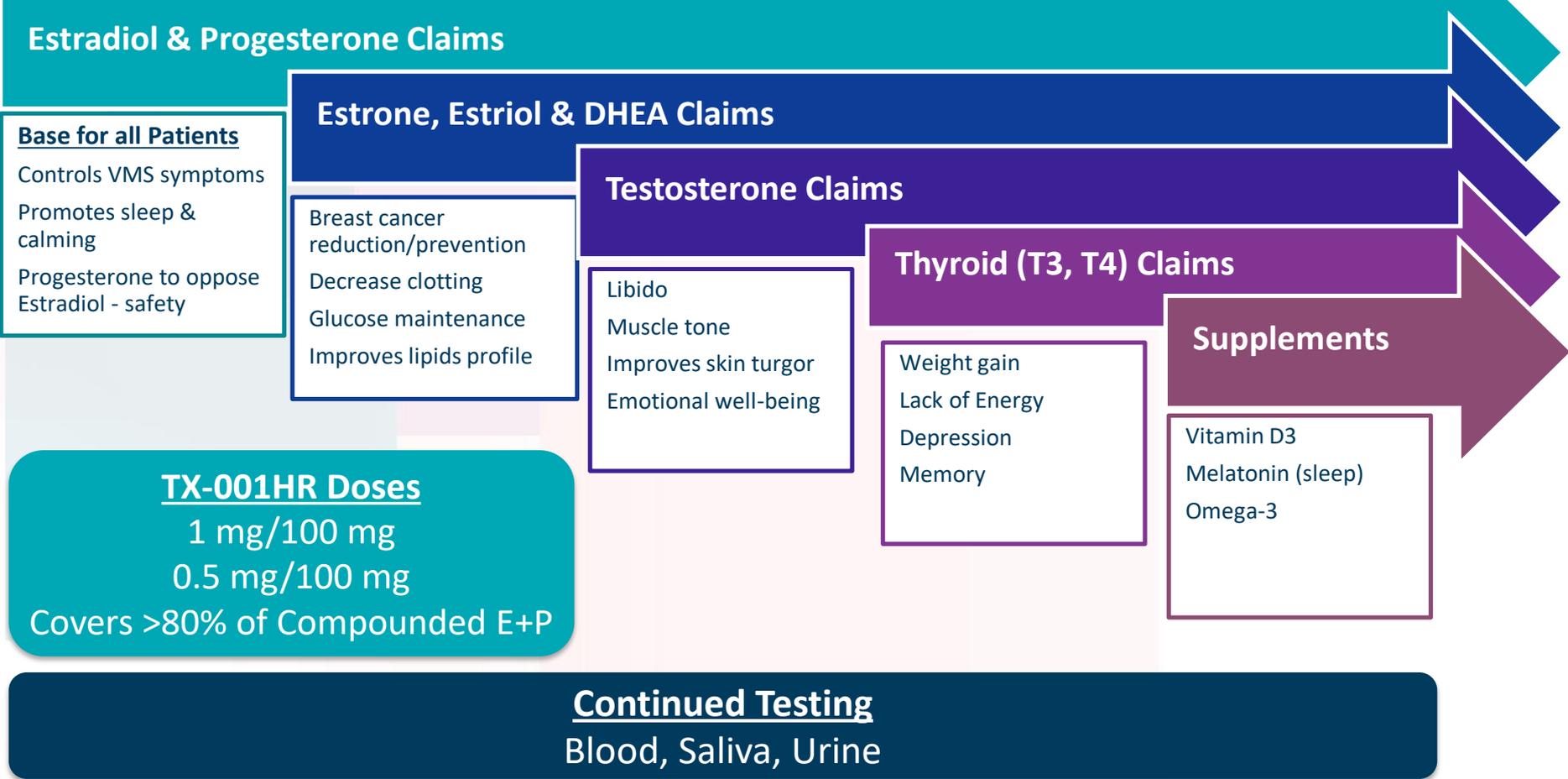


N = 3,000-3,500 Compounding Focused Pharmacies<sup>1,2,3</sup>

(1) 2013 National Community Pharmacists Association Digest: Financial Benchmarks (Sponsored by Cardinal Health)  
(2) NCPA Community Pharmacy Compounding Survey (November 2012)  
(3) NPI Database: using taxonomy codes

# Compounding Pharmacy Menopausal Treatment Paradigm

Customization is adding therapy...not tweaking dosages



# BIO-IGNITE™

## Compounding Pharmacy Partnership Strategy

**BIO-IGNITE™** is an outreach program to quantify the number of compounded bio-identical estradiol and progesterone prescriptions currently dispensed by the 3,000-3,500 high-volume compounding pharmacies, and qualify their interests in distributing our hormone product candidates, if approved.

### Phase 1:

Understand and identify the high volume pharmacies and prescribers that have developed a specialty focus around women's menopausal health

### Phase 2:

Work with these specialists to transition patients from unapproved compounded therapies to an FDA-approved treatment

# Compounded E+P Conversion Strategy

## Objective

- Collaborate to expand utilization of BHRT for menopausal women
- Convert the majority of compounded preparations for E+P to TX-001HR

## Tactics

- **Create a cooperative network**
  - Establish relationships with top BHRT compounding pharmacies to execute Rx transitions to approved product
  - Concentrate on high BHRT compounding geographies (e.g., CA, FL, NY, VA, TX and others)
- **Utilize typical pharmacy programs**
  - Programs for patient education and outreach
  - Programs to improve compliance and persistency
  - Patient adherence programs
  - Pharmacy Medical Therapy Management (MTM) programs
- **VitaCare™ Referral Approach**
  - Link VitaCare customer service hub to cooperative compounding network pharmacies to improve the patient care and experience

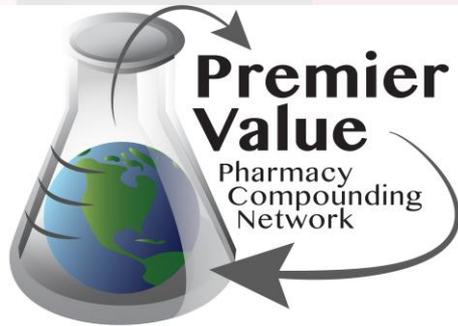
# BIO-IGNITE Progress and Results

## Partnerships with Large Pharmacy Network and Individual Pharmacies

Pharmacy Network and Individual Pharmacy Partners

# of Pharmacies

Combination Bio-Identical E+P Scripts



>300 Pharmacies In Network

~1,500,000 prescriptions annually

TXMD Outreach to Individual Pharmacies

362 Pharmacies with Prescription Data

~500,000 prescriptions annually

# TXMD Is Not Re-Inventing The Wheel

- **Makena<sup>®</sup> Case Study**
- **Androgel<sup>®</sup> Case Study**

*Case studies are for example only and not indicate of how other products, including TX-004HR, may perform.*

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# Makena<sup>®</sup> Case Study: History

- **Makena<sup>®</sup> approved and launched in February 2011 by KV Pharmaceutical**
  - Planned to limit distribution and rely on FDA enforcement
- **FDA and CMS guidance on 3-31-2011 stated that there will be no government enforcement of making “essential” copies of a commercially available product**
  - DQSA had not yet been implemented
- Payers and state Medicaid plans publicly stated that only compounded product will be covered
  - Backlash on pricing was immediate and significant
- In response to significant pricing criticism, on April 1, 2011, KV reduced price from \$1,500 per injection to \$690 per injection
- Sales struggled and company began taking legal action against the FDA and numerous states (GA, AL, SC, TX & IL)
- **June 2012 - FDA submitted a “weak” statement recommending providers use Makena<sup>®</sup> over compounded product but no legal action**
  - KV Pharmaceutical subsequently won its lawsuit in GA and negotiated contracts with IL, SC, and TX
  - The company began signing additional contracts with payers in 2012 but sales did not significantly grow

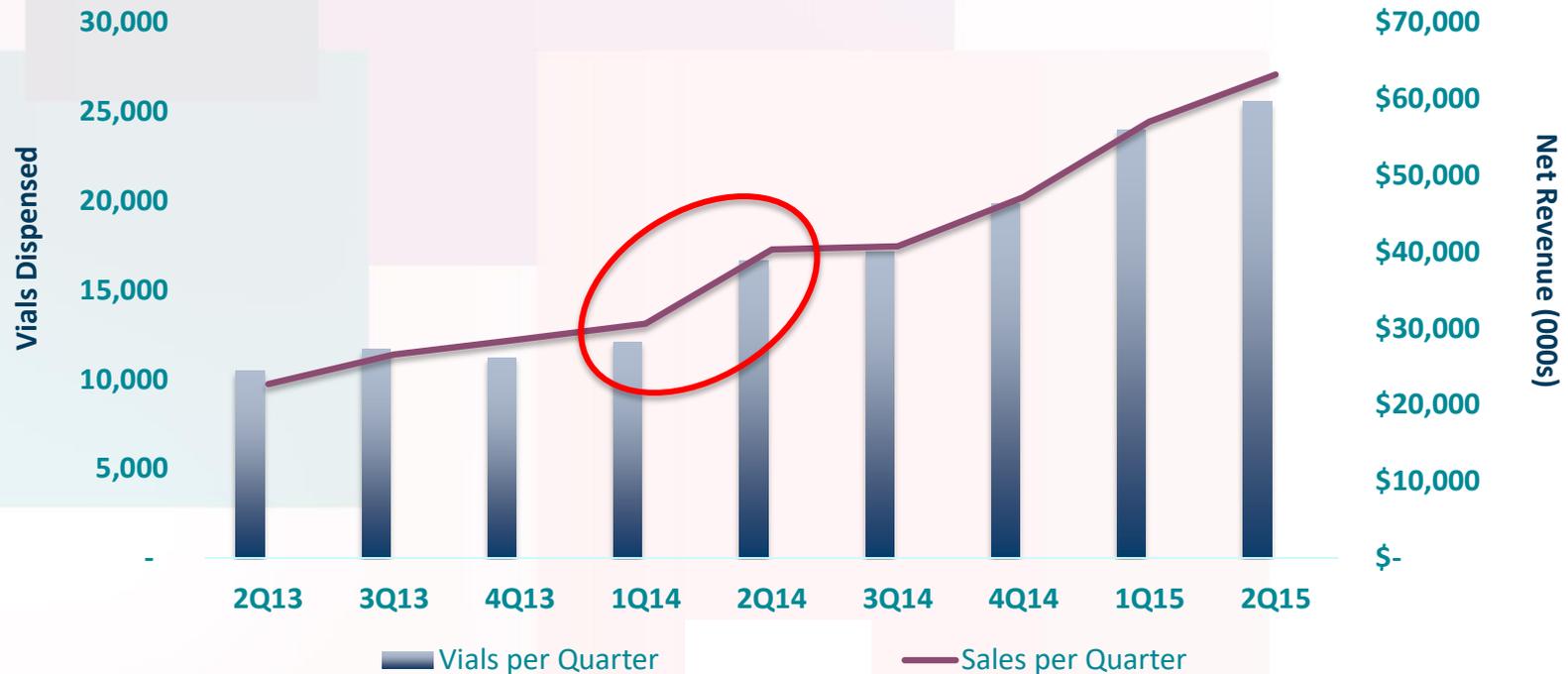
# Makena<sup>®</sup> Case Study: History

- **KV Pharmaceutical entered bankruptcy in August 2012 with less than 3% market share**
  - “Overall, the FDA’s public stance on compounding 17P and failure to take enforcement action against compounding pharmacies combined with CMS reimbursement policies invited numerous compounders back into the market and resulted in substantial sales of compounded alternatives to Makena<sup>®</sup> and effective loss of the Company’s orphan drug marketing exclusivity for the affected period of time. Moreover, limited reimbursement for Makena<sup>®</sup> under various State Medicaid programs had a severe negative impact on Makena<sup>®</sup> sales and the Company’s overall business prior to the Petition Date”
- **September 2012 – New England Compounding Center meningitis breakout occurred**
- Most payers and physicians did not change their stance towards compounded product, but institutional sales began growing through negotiated contracts
  - Introduced difficult “buy and bill” opportunity with hospitals, clinics, and DOD
- KV Pharmaceutical emerged from bankruptcy in September 2013 and changed the company name to Lumara Health
- **Lumara Health achieved significant growth in 2014 through collaboration with compounding pharmacies**
  - Attained coverage never experienced before
  - Achieved patient and prescriber growth
- **Lumara Health is acquired by AMAG in November 2014 for over \$1B (\$675M upfront and \$350M in sales milestones)**

# Makena<sup>®</sup> Case Study: Collaboration Works

- Collaboration discussions begin with the compounding pharmacy community in 4Q13
- Initial distribution agreements finalized in 1Q14
- Broad distribution implemented in 2Q14 and growth significantly expanded
- 2Q14 volume growth of 38% q/q and 32% y/y
- 2Q14 sales growth of 59% q/q and 77% y/y

## Volume and Sales Growth of Makena<sup>®</sup>



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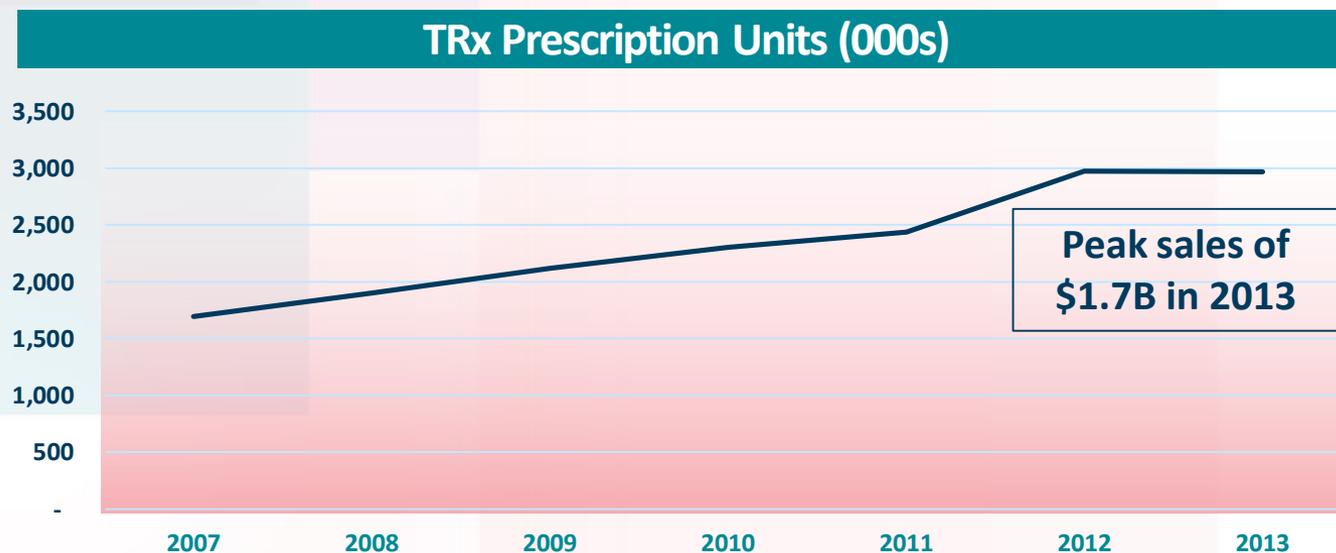
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# Makena<sup>®</sup> Market Launch Dynamics vs Potential TX-001HR Market Launch Dynamics

	Makena <sup>®</sup> 	TX-001HR (if approved) 	
Large Affected Populations	No	Yes	Product Specific
Exorbitant Pricing Model	Yes	No	
Collaborative Approach to Compounders	No	Yes	Corporate Strategy
DQSA Implementation	No	Yes	
Reimbursement for Compounded Products	Yes	No	Regulatory Environment
USP-800 Implementation	No	Yes	

# AndroGel® Case Study: Example of an FDA-Approved Drug Replacing an Unapproved Compounded Product

- Pre-2000, unapproved compounded bio-identical testosterone was heavily compounded whereas synthetic FDA-approved methyltestosterone sales were small
- In 2000, AndroGel® launched as the first FDA-approved bio-identical testosterone and became the leader in the category



# Androgel<sup>®</sup> Market Launch Dynamics vs Potential TX-001HR Market Launch Dynamics

	Androgel <sup>®</sup> 	TX-001HR (if approved) 	
Large Affected Populations	Yes	Yes	Product Specific
Exorbitant Pricing Model	No	No	
Collaborative Approach to Compounders	No	Yes	Launch Strategy
DQSA Implementation	No	Yes	
Reimbursement for Compounded Products	Yes	No	Regulatory Environment
USP-800 Implementation	No	Yes	

# Numerous Other Examples of Prior Success

- **Multiple examples exist where replacing less effective or unapproved compounded options with FDA-approved treatments captured significant market share and became standards of care**

## **Previously Compounded Preparations Evolved to FDA-Approved Products**

- Rectiv – nitroglycerin gel for treatment of anal fissures
- Mitocin – treatment of glaucoma
- Neudexta – treatment of pseudo bulbar affect disorder
- Rogaine – topical treatment for alopecia
- Cleocin Solution/Gel – topical treatment of acne vulgaris
- Endometrin – vaginal suppository formulation of progesterone
- Crinone & Prochieve – progesterone vaginal gel

# Expect Robust Insurance Coverage For TX-001HR, If Approved, In-Line with Product Class

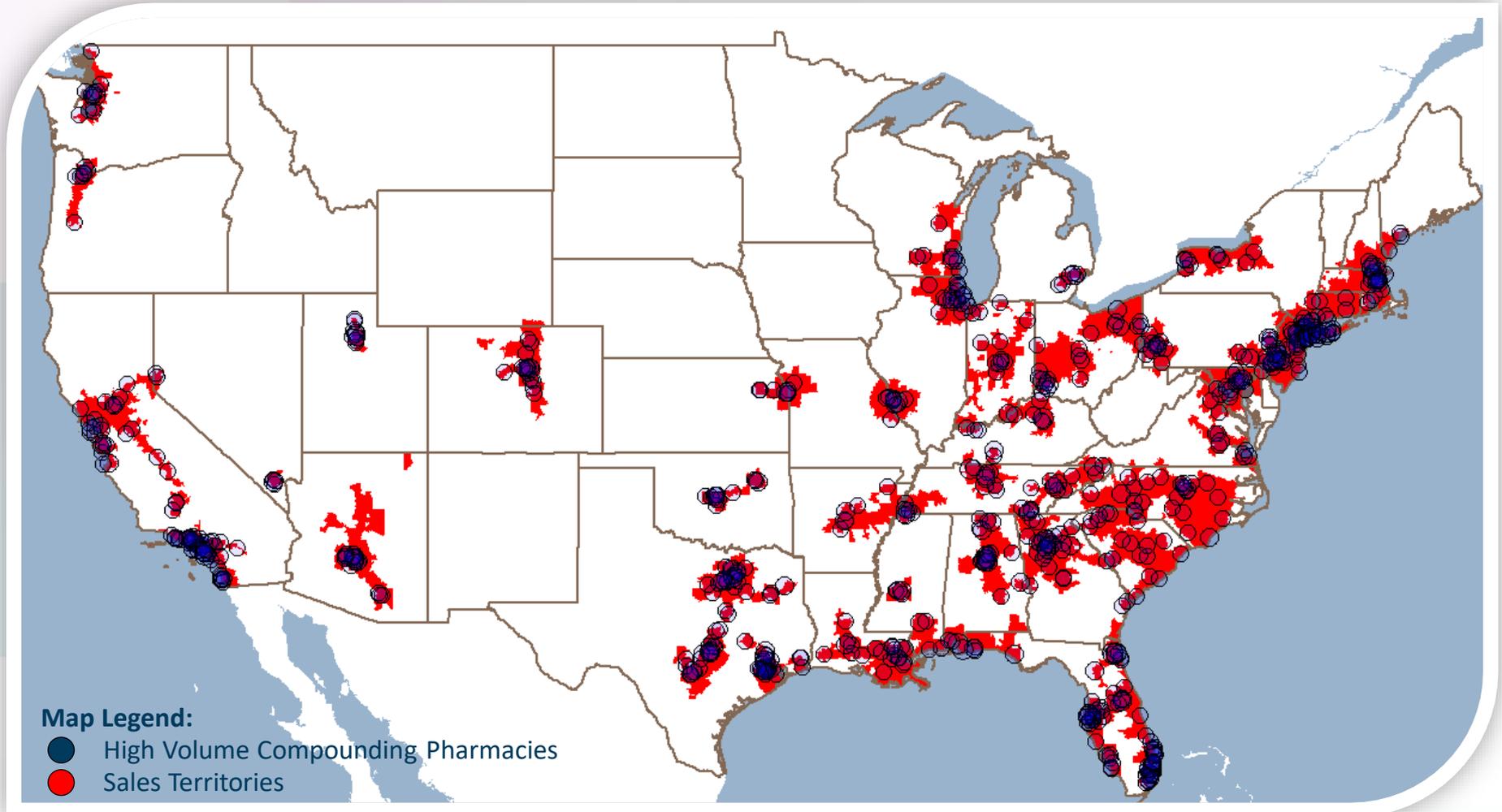
4,315 Commercial Plans	% Unrestricted Access of Commercial Plans	Not Covered
Estrace® (Oral)	96%	1%
Prempro®	94%	5%
CombiPatch®	93%	4%
Climara Pro®	92%	4%
FemHRT®	87%	6%
Duavee®	86%	5%
Vivelle-Dot®	84%	5%
Activella®	83%	8%
Prometrium®	83%	6%

Data Source MMIT August 17, 2016 – 4,300 commercial plans  
All trademarks are the property of their respective owners.

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# TXMD Salesforce Has High Overlap with Targeted Compounding Pharmacies to Drive Successful Conversion



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# Compounding Regulatory Dynamics

David Miller, R.Ph.

- Former Executive VP and CEO for the International Academy of Compounding Pharmacists (2010-2015)
- Director of Pharmacy Affairs at Merck (1996-2010); involved in launch planning, distribution and stocking programs for more than a dozen products
- Advisor and committee member for American Pharmacists Association (APhA), National Community Pharmacists Association (NCPA), National Association of Chain Drug Stores (NACDS), National Alliance of State Pharmacy Associations (NASPA), and many others

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# Regulatory Changes Have Constrained the Compounding Pharmacy Marketplace

**Drug Quality & Security Act of 2013 gave the FDA unprecedented authority and enforcement, which represents an on-going risk burden for compounders**

The FDA is actively enforcing DQSA and coordinating disciplinary action with state regulatory agencies<sup>1</sup>

- 350+ inspections of compounders
- Issued more than 130 warning letters and more than 30 letters referring inspectional findings to state Boards
- Oversaw about 100 recalls involving compounded drugs
- Worked with DOJ on civil and criminal enforcement
- Issued 18 draft guidances, seven final guidances, two proposed rules, a final rule, and a draft memorandum of understanding

Guidance documents and regulations introduce greater risk for compounders

- Prohibits duplication of commercially available products – limiting dose variation, dosage forms – including BHRT
- Prohibits compounding of “demonstrably difficult” products
- Mandates individual patient prescriptions and eliminates sales directly to prescribers – including BHRT
- Limits types of bulk ingredients used by compounders (e.g., positive list, negative list)

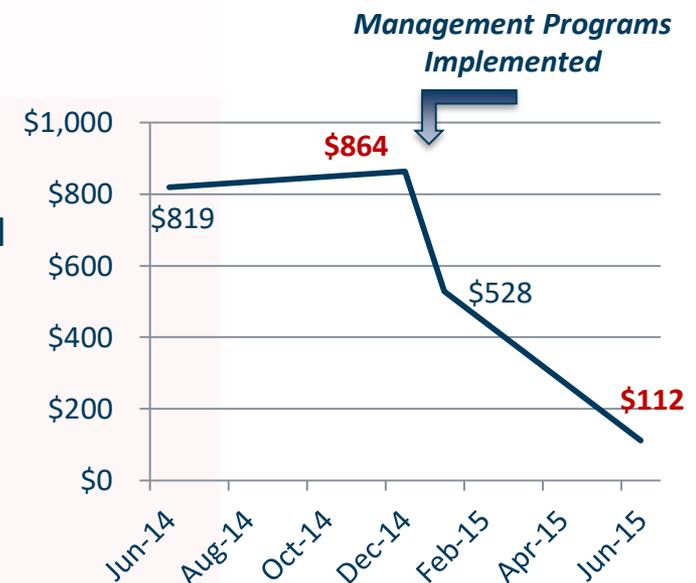
<sup>1</sup>) FDA’s Human Drug Compounding Progress Report: Three Years After Enactment of the Drug Quality and Security Act, January 2017

# Elimination of Coverage and Reimbursement Slashed Compounding Revenue Stream

Questionable billing practices by compounders caused insurers and PBMs to terminate coverage in 2014, reducing revenue by ~90%

Uncontrolled billing by compounders drove the category to the third most PMPM spend for managed care by 2013<sup>1</sup>

- January 2013 – Optum became first PBM to phase in management of compound billing; costs continued to rise<sup>2</sup>
- May 2014 – CVS/Caremark mandated clinical support for all compounds, PAs, and terminated coverage for certain bulk ingredients
- July 2014 – Express Scripts eliminated thousands of bulk ingredients from coverage
- September 2014 – ESI extended prohibition on compounding to include therapeutic categories
- 2014/2015 – DOJ investigations into fraudulent billing to Tricare - \$5 million in 2004 to \$514 million in 2014<sup>3</sup>



Establishing a Well-Balanced Approach to Compound Drug Management. Presented at AMCP Nexus Program, October 2015.

<sup>1</sup> 2014 Annual Drug Spend Trend Report, Express Scripts. <https://lab.express-scripts.com/lab/drug-trend-report/previous-reports>

<sup>2</sup> Restoring trust for compounded medications, Optum, February 2016, <https://www.optum.com/resources/library/restoring-trust-compound-medications.html>

<sup>3</sup> Controls Over Compounds At the Defense Department - Report No. DODIG-2016-105, July 1 2016 <http://www.dodig.mil/pubs/documents/DODIG-2016-105.pdf>

# Mandatory USP-800 Compliance Creates New and Unplanned Expenses by July 2018

**The cost burden of USP-800 will cause many compounders to exit the compounded hormone replacement market space**

*Initial investment of \$100,000 to \$750,000 per pharmacy  
Ongoing costs of ~\$10,000 to \$25,000/month per pharmacy*

**To continue to compound hormones, which are considered hazardous drugs, all pharmacies must comply with new requirements for infrastructure, training, and testing.**

- Investment in externally vented, physically separate, negative pressure environment with ante-room
- Dedicated equipment used only for compounding of hazardous drugs
- Personnel training with annual assessment, and documentation of competency
- Gowning and testing equivalent to sterile drug laboratories
- Every six months sampling of air quality and environmental containment at average cost of \$400 per drug
- Development, review and ongoing compliance with NIOSH lists, internal assessments, and documentation

# What USP-800 Really Means

## Compounding BHRT Today



*Adolphe Pierre-Louis - Albuquerque Journal – 2/13/2017*

## Compounding BHRT after July 2018



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# Compounding Pharmacy Economics

**Richard Moon, PharmD, R.Ph.**

## **Principal, Premier Value Pharmacy Compounding Network**

- Represents one of the largest compounding pharmacy networks
- Owner of Pharmacy Innovations, a group of 7 specialty and compounding pharmacies throughout the United States
- Former IACP President, Treasurer, and Board Member

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# Independent Pharmacy Net Income Per Compounded Script

	Insurance Coverage (before 2H14)	Present Day (2017)	Post USP-800 (July 2018)
<b>Revenue</b>			
Patient Co-Pay	50.00	50.00	50.00
Third-Party Reimbursement	115.00	-	-
<b>Total Net Revenue</b>	<b>\$ 165.00</b>	<b>\$ 50.00</b>	<b>\$ 50.00</b>
Costs of Good Sold	7.50	7.50	7.50
<b>Gross Profit</b>	<b>\$ 157.50</b>	<b>\$ 42.50</b>	<b>\$ 42.50</b>
<i>Gross margin</i>	<i>95.5%</i>	<i>85.0%</i>	<i>85.0%</i>
<b>Operating Expenses</b>			
G&A	15.00	15.00	15.00
S&M	7.50	7.50	7.50
Additional Compounding Costs <sup>1</sup>	15.00	15.00	15.00
<i>Cost of USP-800 Requirements<sup>2</sup></i>	<i>-</i>	<i>-</i>	<i>10.00</i>
<b>Total Operating Expenses</b>	<b>\$ 37.50</b>	<b>\$ 37.50</b>	<b>\$ 47.50</b>
<b>Pre-Tax Profit</b>	<b>\$ 120.00</b>	<b>\$ 5.00</b>	<b>\$ (5.00)</b>
<i>Operating margin</i>	<i>72.7%</i>	<i>10.0%</i>	<i>-10.0%</i>

1) Includes additional labor, pharmacists, technicians, regulatory, and legal expenses

2) July 2018 Implementation; includes >\$150,000 capital expenditure as well as new identification requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administration of hazardous drugs

# Economic Incentives Provide Catalyst to Switch to TX-001HR

Independent Pharmacy Net Income Per Script with TX-001HR			
	Compounded E+P Post USP-800	TX-001HR Launch 2H18	
<b><u>Revenue</u></b>			
Patient Co-Pay	50.00	50.00	
Third-Party Reimbursement	-	200.00	
<b>Total Net Revenue</b>	<b>\$ 50.00</b>	<b>\$ 250.00<sup>1</sup></b>	
Costs of Good Sold	7.50	200.00 <sup>2</sup>	
<b>Gross Profit</b>	<b>\$ 42.50</b>	<b>\$ 50.00</b>	
<i>Gross margin</i>	<i>85.0%</i>	<i>20.0%</i>	
<b><u>Operating Expenses</u></b>			
G&A	15.00	15.00	
S&M	7.50	5.00	
Additional Compounding Costs <sup>3</sup>	15.00	-	
Cost of USP-800 Requirements <sup>4</sup>	10.00	-	
<b>Total Operating Expenses</b>	<b>\$ 47.50</b>	<b>\$ 20.00</b>	
<b>Pre-Tax Profit</b>	<b>\$ (5.00)</b>	<b>\$ 30.00</b>	
<i>Operating margin</i>	<i>-10.0%</i>	<i>12.0%</i>	

1) Assume AWP-18% Third-Party Reimbursement

2) Assume \$250 WAC less 20% distribution discount

3) Includes additional labor, pharmacists, technicians, regulatory, and legal expenses

4) July 2018 Implementation; includes >\$150,000 capital expenditure as well as new identification requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administration of hazardous drugs

# PVPCN Distribution Agreement Rationale

## Innovation

- Potential low-dose local estrogen therapy for VVA
- Potential first and only FDA-approved bio-identical combination of E+P
- Clinical validation of current treatment paradigm for menopausal symptoms

## Regulatory Environment

- Drug Quality and Security Act
- Loss of Third-Party Reimbursement
- USP-800 – Hazardous Drugs

TXMD and PVPCN

## Commercial Opportunity

- 1.5 million annual compounded E+P prescriptions directly substitutable to TX-001HR
- Improved pharmacy economics
- Maintain and grow patient and physician relationships

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# Q&A

## *Panel*

**Joseph Auci**

**David Miller**

**Sebastian Mirkin, M.D.**

**Rich Moon**

**James Pickar, M.D.**

**John Walczyk**

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## Closing Remarks

**Robert Finizio**  
Chief Executive Officer

# TXMD: Financial Snapshot

**Listing  
Exchange**

**TXMD**  
LISTED  
NYSE MKT

**Debt**

**\$0M**

**Shares  
Outstanding**

**197.5M**

(as of Feb. 21, 2017)

**Cash**

**\$131.5M**

(as of Dec. 31, 2016)

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# Worldwide Patent Filings\*

Strong IP Portfolio with 144 Patent Applications, including 74 international filings, and 17 issued U.S. patents



\*Not all patent filings filed in all jurisdictions.

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THANK YOU!

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