

## **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 are 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 Current Reports on Form 8-K, and include the following: our ability to resolve the deficiencies identified by the FDA in our new drug application for our TX-004HR product candidate and the time frame associated with such resolution; whether the FDA will approve the amended NDA for our TX-004HR product candidate and whether such approval will occur by the PDUFA target action date; whether the FDA will approve the NDA for our TX-001HR product candidate and whether such approval will occur by the PDUFA target action date; 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 therefor; the length, cost and uncertain results of our clinical trials; the potential of 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 and other 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-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.



## Therapeutics MD (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

Therapeutics MD°

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

#### **TX-001HR TX-004HR** Moderate to severe dyspareunia, a Moderate to severe hot flashes **Proposed Indication** symptom of VVA, due to menopause due to menopause **Condition Description VVA due to Menopause** Menopause **Bio-Identical 17 β-Estradiol + Active Ingredients** Bio-Identical 17 β-Estradiol **Bio-Identical Progesterone Form** Vaginal softgel capsule Oral softgel capsule Potential first and only bio-identical Easy to use, negligible systemic exposure, **Key Value Proposition** designed to support long-term use **FDA-approved combination product Affected US Population** 36 million women<sup>3</sup> 32 million women<sup>1,2</sup> **US TAM Opportunity** >\$25B<sup>4,5</sup> >\$20B<sup>5</sup> NDA resubmitted Nov. 29, 2017 NDA submitted Dec. 28, 2017 **Status** PDUFA Target Action Date: Oct. 28, 2018/ **PDUFA Target Action Date: May 29, 2018**

Therapeutics MD°

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.

<sup>2)</sup> 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.

<sup>3)</sup> Derived from U.S. Census data

<sup>4)</sup> Based on pre-WHI annual scripts of FDA-approved HT products

<sup>5)</sup> Based on market pricing of current FDA-approved HT products

## **Significant Catalysts Within Next 12 Months**







#### **December 2017**

Acceptance of the NDA for TX-004HR

May 29, 2018

PDUFA target action date for TX-004HR

3Q 2018

Potential launch of TX-004HR\*



#### December 2017

Submission of the NDA for TX-001HR

#### **March 2018**

Acceptance of the NDA for TX-001HR

#### October 28, 2018

PDUFA target action date for TX-001HR

#### 1Q 2019

Potential launch of TX-001HR\*\*



TX-001HR





<sup>\*</sup>Assumes approval on or before PDUFA target action date of May 29, 2018

<sup>\*\*</sup>Assumes approval on or before PDUFA target action date of October 28, 2018

## **Complete Financing Strategy In Place**

Phase 1
Equity
Financing

# Phase 2 Term Loan Debt Financing

Phase 3
Partnership

**Opportunities** 

- \$68.6M equity offering, closed on September 28<sup>th</sup>
- Secures near term financing needs for TX-004HR launch, if approved
- Strengthens Phase 2 debt financing negotiating position

- Targeting commitments of \$150M-\$200M in debt financing
- Anticipate first draw of debt financing following approval of TX-004HR or TX-001HR
- Secures medium term financing needs for TX-004HR and TX-001HR launches, if approved

 Potential for upfront payments and royalty revenue streams to further support additional product opportunities

Phase 1 and Phase 2 provide potential access to ~\$300M of capital to support commercialization of TX-004HR and TX-001HR\*

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



- 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



- 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



- 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



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



- 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



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



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



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



- 30+ years of regulatory, quality, and drug development experience
- Sr. Vice President, Drug Development at Sirion Therapeutics
- VP of Regulatory Affairs and Quality Assurance at Santarus



- 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



- 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®



- 16+ years of experience in the pharmaceuticals and biotech
- Created a national sales channel, led the Specialty Diagnostics business at ViaCell. Inc.
- Product launch and sales management roles at Eli Lilly & Company and KV Pharmaceutical

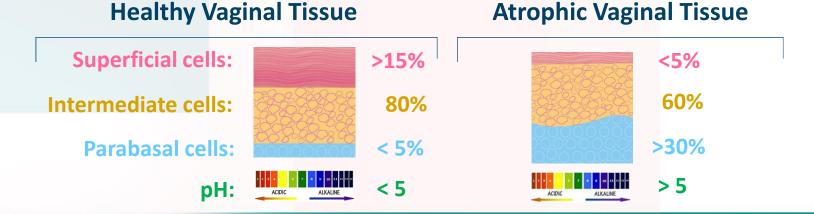
Insiders own approximately ~23% of total outstanding shares

**Therapeutics MD®** 



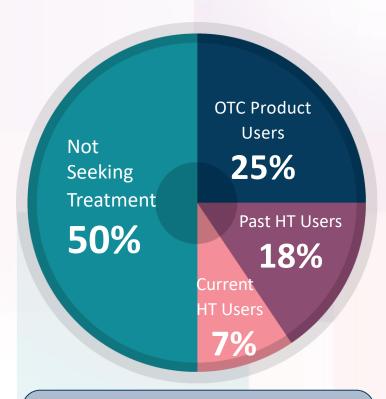
## **Vulvar and Vaginal Atrophy (VVA)**

- 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



Therapeutics MD°

#### **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

4) TherapeuticsMD "EMPOWER" Survey, 2016

Therapeutics MD°

<sup>1)</sup> 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.

<sup>3)</sup> IMS Health Plan Claims (April 2008-Mar 2011)

<sup>5)</sup> Based on current FDA-approved market pricing

<sup>5)</sup> Based on current FDA-approved market pricing

<sup>6)</sup> 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

### **Current FDA-Approved VVA Products**

	Estrace Cream®	Premarin Cream®	Vagifem®	Estring®	Osphena®	Intrarosa®
Products	COMMANDE OF THE PARTY OF THE PA	Service (S	The second secon	Estring Veget trep	Osphicus Use friend and fing the same	INTRAROSA (prasterone)
	::: Allergan	Pfizer	novo nordisk	Pfizer	DUCHESNAY USA	ENDOCEUTICS amag
FDA Approval	1984	1978	1999	1996	2013	2016
TRx Dollars 2017 <sup>1</sup>	\$583,612,698	\$533,386,029	\$525,321,410ª	\$120,499,734	\$75,683,654	\$4,187,571
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	Week 4+	Mark 9	Approval Without	Week 12	Week 6
Onset of Action* Dryness	Dyspareunia and Dryness Data	Not Demonstrated	Week 8	Dyspareunia and Dryness Data	Approval Without Dryness Data	Week 12

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

1. Symphony Health Solutions PHAST Data powered by IDV; Annual 2017
a. 2017 Vagifem, Yuvafem (authorized generic of Vagifem), and Teva generic
Vagifem [package label] http://www.novo-pi.com/vagifem.pdf

Therapeutics MD®

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

Osphena [package label] 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

All trademarks are the property of their respective owners

For Her. For Life.

\*Onset of Action = First efficacy observation

### **Compliance and Fills Per Year Drives Top-Line Revenue**

#### **Current VVA Market**

**Vaginal Creams:** 

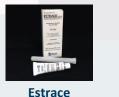
**Reasons Women Stop** 

**Vaginal Tablets:** 

**Reasons Women Stop** 

Average:

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



**Premarin** 

Messiness<sup>1</sup>

Reusable Applicator<sup>1</sup>

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

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

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



Vagifem

Efficacy1

Applicator<sup>1</sup>

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

Systemic Absorption<sup>1</sup>

Product	TRx Dollars <sup>4</sup>	Patient Count⁵	Patient Share⁵
Estrace	\$583,612,698	900,618	41%
Premarin	\$533,386,029	696,125	32%
Vagifem/Generics	\$525,321,410°	448,745	20%

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

5) IMS SDI's Total Patient Tracker; Annual 2017

Therapeutics MD°

<sup>1)</sup> 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

<sup>3)</sup> 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.

<sup>4)</sup> Symphony Health Solutions PHAST Data powered by IDV; Annual 2017

a. 2017 Vagifem, Yuvafem (authorized generic of Vagifem), and Teva generic

### **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

Therapeutics MD°

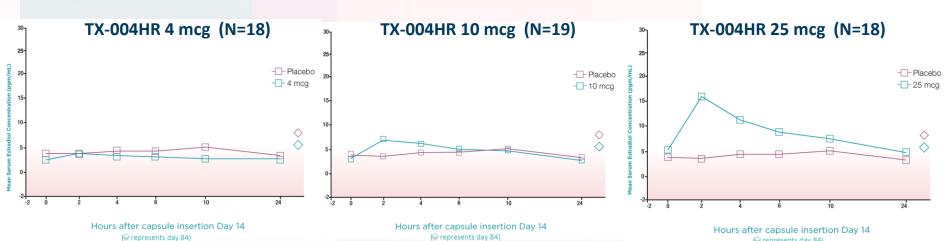
### Co-Primary and Key Secondary Efficacy Endpoints



	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

#### <u>Arithmetic Mean Estradiol Serum Concentrations – Unadjusted</u>



	AUC <sub>0-24</sub> (pg.h/mL)	C <sub>avg(0-24)</sub> (pg/mL)	
4 mcg	87.22 (42.77)	3.634 (1.78)	10 m
Placebo (pl)	104.16 (66.38)	4.34 (2.76)	Place

0.3829

0.3829

P-value vs Pl

	AUC <sub>0-24</sub> (pg.h/mL)	C <sub>avg(0-24)</sub> (pg/mL)
10 mcg	110.14 (54.57)	4.58 (2.27)
Placebo (Pl)	104.16 (66.38)	4.34 (2.76)
P-value vs Pl	0.7724	0.7724

( represents day 84)	
AUC <sub>0-24</sub> (pg.h/mL)	C <sub>a</sub>

	(pg.h/mL)	(pg/mL)
25 mcg	171.56 (80.13)	7.14 (3.33)
Placebo (Pl)	104.16 (66.38)	4.34 (2.76)
P-value vs. Pl	0.0108	0.0108

## **TX-004HR Approval and Launch Timelines**

January - March (Pre-Approval) April - June (FDA-Approval)

3Q 2018 (Launch)

- Sales force build and preparedness
- Payer pipeline discussions
- Launch planning
- National Sales Meeting

- Territory readiness with expanded sales force
- PDUFA date May 29<sup>th</sup>
- Payer outreach
- Experience First program
- Launch Meeting

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

Therapeutics MD°

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

#### **Drive Market Share**

#### **Targeted Market Expansion**

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



Elevate importance of VVA by demonstrating true impact of disease







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

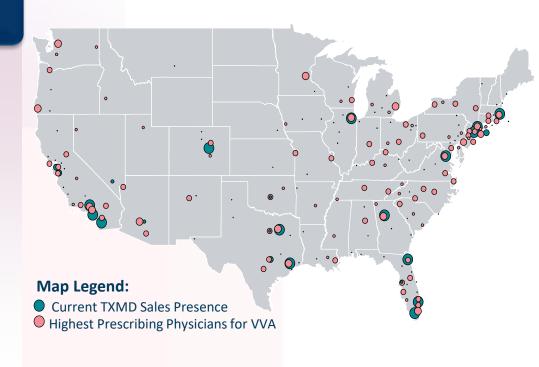
#### **Commercial Execution**



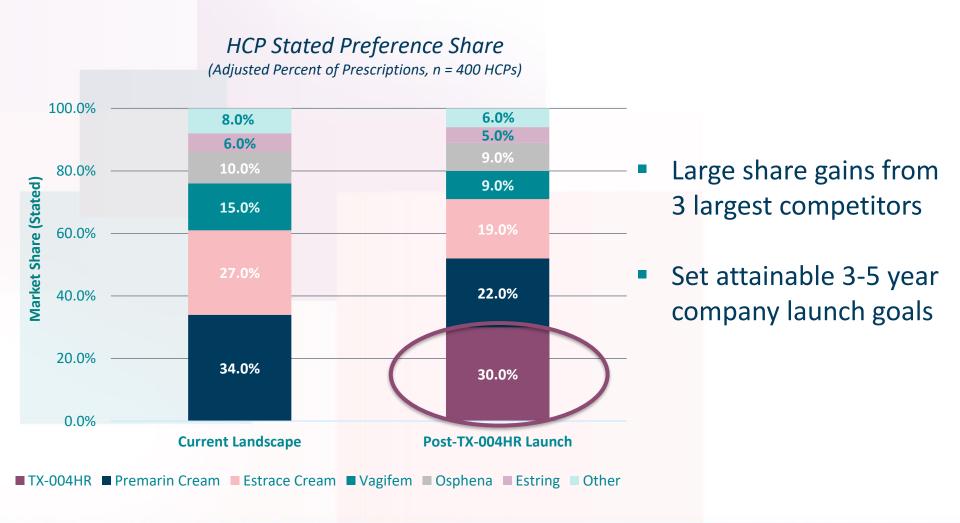
## **Foundation Already Built for a Strong Launch**

## TXMD Sales Force Currently in OB/GYN Offices

- 40% overlap with current prenatal vitamins business
- Currently calling on VVA targets with disease awareness campaign
- Sales force of 150 hired and in place for TX-004HR launch
- Partnership with inVentiv, leading contract sales organization
- Operational and analytic systems



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





## Efficacy, Safety, and Positive User Experience Redefines Relief

#### **Perceived Shortcomings**

#### **TX-004HR Solution**

#### **Efficacy**

- 1 in 4 women achieve limited relief<sup>1</sup>
- Delayed onset of efficacy<sup>1</sup>

#### Early efficacy observed at week 2

Efficacy for vaginal dryness

## Safety/ Side Effects

- Hormone exposure concerns<sup>1</sup>
- Messiness<sup>1</sup>

- Negligible systemic exposure
- No messiness

#### Convenience

- Products difficult to use<sup>1</sup>
- Inadequate instructions on use<sup>1</sup>

- No applicator; any time of day use
- Simple dose pack; easy instructions

Patients Choose TX-004HR

Rejoice Trial	4 mcg	10 mcg	25 mcg
Survey Results	(N=119)	(N=113)	(N=128)
TX-004HR preferred over	73.9%	67.3%	74.2%

Therapeutics MD°

# Increasing Compliance Through National Care Model Represents TXMD Core Competency

#### **Prenatal Vitamins Market**

- Market Dynamics:
  - No Drug Claims
  - 9 month condition
- Industry Average Patient Compliance:
  - 2.5 fills per pregnancy
- TXMD Compliance with National Care Model:
  - 8 fills per pregnancy

#### **VVA Market**

- Market Dynamics:
  - Clinical and physical product differentiation
  - Chronic, progressive condition
- Industry Average Patient Compliance:
  - Vaginal Creams: 1.5 fills per year
  - Vaginal Tablets: 3.5 fills per year
- Potential Compliance with National Care Model:
  - Greater than 4 fills per year



Therapeutics MD°

## Market Share Gains and Fills Per Year Drive TX-004HR Net Revenue at Year 5 of Launch

Year 5 Assumptions	
Total VVA Patients on HT <sup>1</sup>	2,207,517
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%

## TX-004HR Net Revenue at Year 5 >\$400 Million

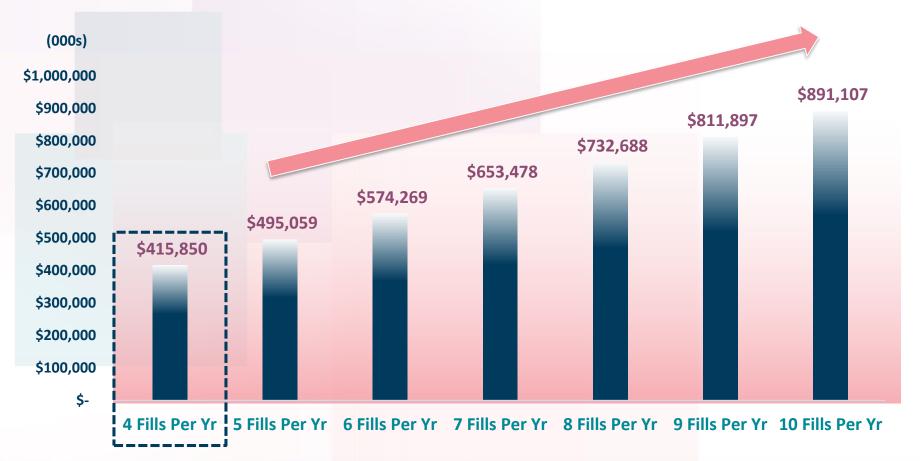
4 Fills Per Year

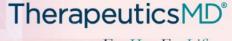
- Pricing at parity to Vagifem
- Zero price increases
- Zero market growth



# Incremental Fills Per Year Drives Significant Upside to TX-004HR Net Revenues

Each incremental fill per year adds >\$75M to TX-004HR net revenues





## Payers are Continuing to Provide Choice

#### 85% of Top 25 Payers Prefer 2+ Products

Vulvar and Vaginal Atrophy		Estrace Cream	Estring	Intrarosa	Osphena	Premarin Cream	Vagifem	Yuvafem
Controlling Payer/PBM	Lives	Univ. Status	Univ. Status	Univ. Status	Univ. Status	Univ. Status	Univ. Status	Univ. Status
Express Scripts PBM	28,537,095	Preferred	Covered	Covered	Covered	Preferred	Covered	Preferred
CVS Caremark RX	27,321,765	Preferred	Covered	Not Covered	Preferred	Preferred	Preferred	Covered
Anthem, Inc.	14,420,468	Preferred	Covered	Covered (PA/ST)	Covered (PA/ST)	Preferred	Covered	Preferred
JnitedHealth Group, Inc.	13,604,482	Covered	Preferred	Not Covered	Covered	Covered	Covered	Preferred
OptumRx	11,780,939	Preferred	Covered	Covered	Covered	Preferred	Covered	Preferred
Aetna, Inc.	7,921,969	Covered	Covered	Covered	Covered	Preferred	Covered	Preferred
Caiser Foundation Health Plans, Inc.	7,433,618	Preferred	Preferred	Not Covered	Not Covered	Preferred	Not Covered	Not Covered
CIGNA Health Plans, Inc.	7,426,248	Covered	Preferred	Covered	Covered	Preferred	Covered	Preferred
Department of Defense - TRICARE	7,022,233	Preferred	Preferred	Preferred (PA/ST)	Preferred	Preferred	Preferred (PA/ST)	Preferred
Blue Cross Blue Shield Association Corporation	5,418,801	Preferred	Covered	Covered	Covered	Preferred	Covered	Covered
Health Care Service Corporation	5,303,089	Covered (PA/ST)	Covered	Covered	Covered	Covered	Covered	Preferred
Department of Veterans Affairs (VHA)	4,782,573	Covered (PA/ST)	Covered (PA/ST)	Covered (PA/ST)	Covered (PA/ST)	Preferred	Covered (PA/ST)	Covered (PA/ST)
nvision Pharmaceutical Services	3,129,698	Covered	Covered	Covered	Covered	Preferred	Covered	Preferred
ndian Health Service (IHS)	2,192,083	Covered (PA/ST)	Covered (PA/ST)	Covered (PA/ST)	Covered (PA/ST)	Preferred	Covered (PA/ST)	Covered (PA/ST)
Blue Shield of California	1,844,906	Preferred	Preferred	Covered (PA/ST)	Covered (PA/ST)	Preferred	Covered	Preferred
CareFirst, Inc.	1,521,549	Covered	Covered	Covered	Preferred	Preferred	Covered	Preferred
EmblemHealth, Inc.	1,480,759	Preferred	Preferred	Covered	Covered	Preferred	Covered	Preferred
Blue Cross Blue Shield of Michigan	1,402,930	Covered	Preferred	Covered	Covered	Preferred	Covered	Covered
Humana, Inc.	1,215,671	Covered	Covered	Not Covered	Not Covered	Not Covered	Not Covered	Not Covered
Blue Cross and Blue Shield of Florida, Inc.	1,210,282	Covered	Covered	Covered	Covered	Preferred	Preferred	Preferred
Blue Cross Blue Shield of Minnesota	1,175,995	Preferred	Covered	Covered	Covered	Covered	Covered	Preferred
State of New York	1,095,141	Preferred	Covered	Not Covered	Preferred	Preferred	Covered	Covered
Blue Cross Blue Shield of North Carolina	1,063,705	Covered	Covered	Covered	Covered	Preferred	Covered	Preferred
Centene Corporation	1,014,607	Preferred	Covered	Not Covered	Covered	Preferred	Covered (PA/ST)	Covered
Blue Cross Blue Shield of Alabama	993,558	Preferred	Covered	Covered	Covered	Covered	Preferred	Not Covered
Blue Cross Blue Shield of Massachusetts	913,779	Preferred	Covered	Covered	Not Covered	Preferred	Covered	Preferred

Therapeutics MD°

## Why are Payers Providing Open Access?

- Overall low cost category compared to other therapeutic areas
- Importance of providing choice for women
- Prior authorizations and step edits are not economically favorable for payers and do not currently exist
- Cost of a prior authorization runs between \$80-\$140 per patient per year depending on payer



## Favorable Payer Dynamics: No Substitution Across Branded Products

**Case Study: Yuvafem Authorized Generic Launch (Year 1)** 

Yuvafem launch in October 2016

	VVA TRx Market Share (%) Oct 2015-Sept 2016	VVA TRx Market Share (%) Oct 2016-Sept 2017	Gains (Losses)
Vagifem	29.2%	9.3%	(19.9%)
Yuvafem	-	19.7%	19.7%
Total	29.2%	29.0%	(0.2%)

- Yuvafem continues to take market share from only Vagifem
- Total Vagifem and Yuvafem TRx have lost 20 bps of VVA TRx market share to other branded products
- No substitution or cannibalization of other branded products





## **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>



## **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 2015¹
    - Today, patients have the choice between three treatment options:
      - FDA-approved, synthetic combination hormones
      - FDA-approved, separate bio-identical hormone products
      - Unapproved, <u>compounded</u> 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



<sup>1)</sup> Symphony Health Solutions PHAST Data powered by IDV; Annual 2015

<sup>2)</sup> 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)

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 Estrogen/Ineffective Progesterone leads to increased risk of endometrial hyperplasia / cancer

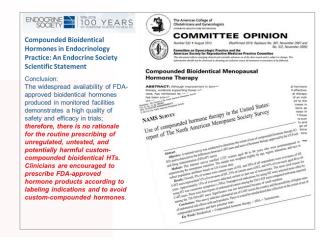






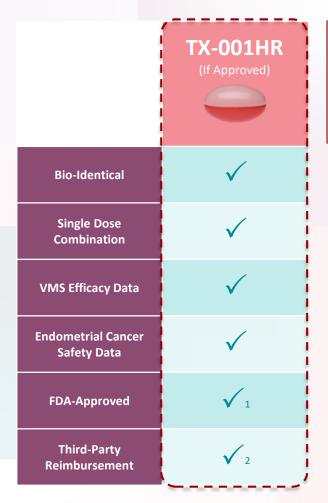








### TX-001HR - Potential Best in Class Therapy



#### 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

Therapeutics MD°

## **Replenish Trial Co-Primary Endpoints**

Primary Efficacy Endpoints: M		uency and Sever 12, VMS-mITT Po	-	es Per Week Versu	s Placebo at
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: In	cidence of Consens	us Endometrial H	lyperplasia or M	lalignancy up to 1	2 months,
		rial Safety Popula	· · <u>-</u>	, ,	·
Endometrial Hyperplasia	0% (0/280)	0% (0/303)	0% (0/306)	0% (0/274)	0% (0/92)

MITT = Modified intent to treat

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</li>

Therapeutics MD°

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

## **TX-001HR New Drug Application Acceptance**

No Filing Review Issues Identified

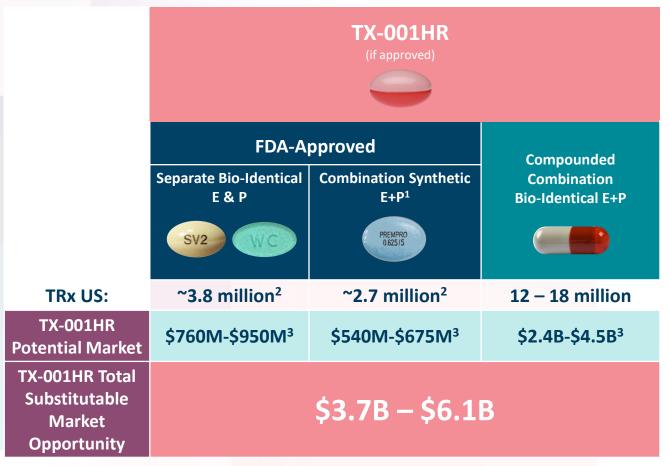
 Application sufficiently complete to permit a substantive review

The FDA has not identified any potential review issues\*

PDUFA target action date of October 28, 2018



### **Multi-Billion Dollar Total Substitutable Market Opportunity**



#### 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

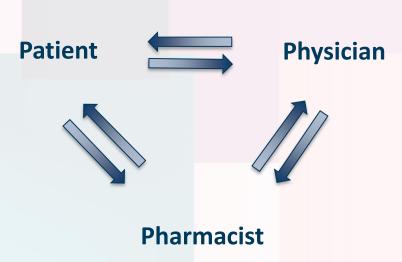
Therapeutics MD°

<sup>1)</sup> Oral and transdermal combinations, including: 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, 2017

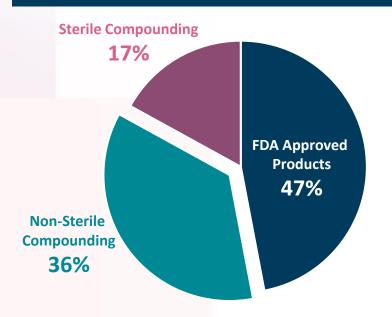
<sup>3)</sup> Assume WAC pricing between \$200-250

### **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>

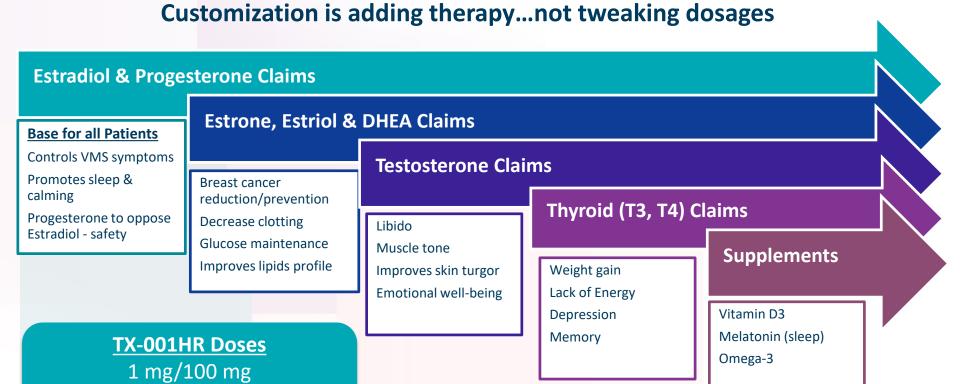


<sup>(1) 2013</sup> National Community Pharmacists Association Digest: Financial Benchmarks (Sponsored by Cardinal Health)

<sup>(2)</sup> NCPA Community Pharmacy Compounding Survey (November 2012)

<sup>(3)</sup> NPI Database: using taxonomy codes

### **Compounding Pharmacy Menopausal Treatment Paradigm**



**Continued Testing**Blood, Saliva, Urine

0.5 mg/100 mg

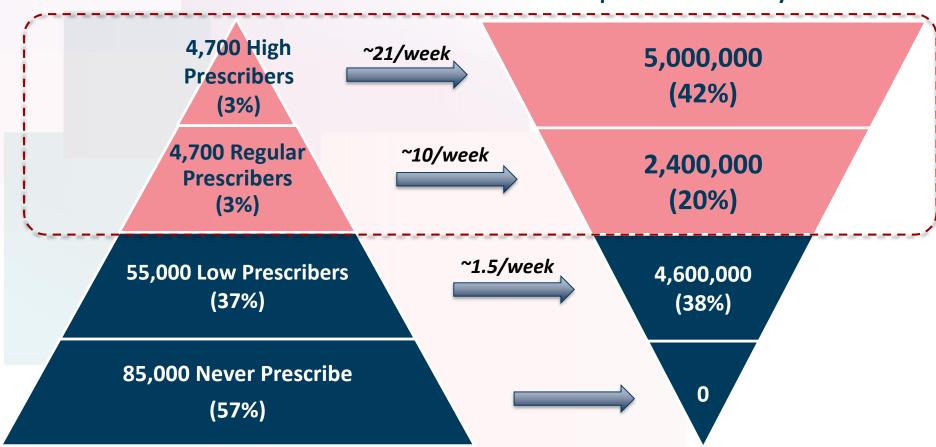
Covers >80% of Compounded E+P



## **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





### **BIO-IGNITETM**

## **Compounding Pharmacy Partnership Strategy**

BIO-IGNITE<sup>TM</sup> 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



## **BIO-IGNITETM** Progress and Results

Partnerships with Large Pharmacy Network and Individual Pharmacies

**Pharmacy Network and Combination** # of Pharmacies **Individual Pharmacy Partners Bio-Identical E+P Scripts** Premier ~1,500,000 >300 Pharmacies Value **In Network** prescriptions annually >400 Pharmacies >500,000 **TXMD Outreach to** with Prescription **Individual Pharmacies** prescriptions annually **Data** 

Therapeutics MD°

# Adverse Reimbursement and Regulatory Environments Continue to Erode Independent Pharmacy Margins



**November 2013:** Congress enacts Drug Quality and Security Act (DQSA), which prohibits compounding of essential copies of an FDA-approved drug except in limited circumstances such as drug shortage<sup>1</sup>



**June 3, 2014:** ESI launches a "Compound Management Solution," creating a list of excluded ingredients that eliminated almost 95% of all compound claims<sup>2</sup>



**July 2014:** Optum initiates a comprehensive compound management program, including prior authorizations and step therapy for all compounded prescriptions<sup>3</sup>



**December 1, 2019:** USP-800 implementation will set new identification requirements for receipt, storage, mixing, preparing, compounding, dispensing, and administration of hazardous drugs<sup>4,5</sup>

- Considered "prohibitively expensive" requiring major pharmacy upgrades and renovations to be compliant
- Large fixed capital expenditure requirements, with some totaling
   >\$150,000 per pharmacy to implement

Therapeutics MD°

<sup>1)</sup>http://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/ucm376829.htm

<sup>2)</sup> http://www.iacprx.org/general/custom.asp?page=CCIns161314

<sup>3)</sup> http://www.optum.com.br/content/optum/en/optumrx/pharmacy-insights/restoring-trust-compound-medications.html

<sup>4)</sup> http://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

<sup>5)</sup> https://www.ascp.com/sites/default/files/Joint%20USP%20letter%202015%20FINAL.pdf

## **Independent Pharmacy Net Income Per Compounded Script**

	Insurance Coverage (before 2H14)		Present Day (2017)		Post USP-800 (Dec. 2019)	
Revenue						
Patient Co-Pay	50.00		50.00		50.00	
Third-Party Reimbursement		115.00	-			-
Total Net Revenue	\$	165.00	\$	50.00	\$	50.00
Costs of Good Sold		7.50		7.50		7.50
<b>Gross Profit</b>	\$	157.50	\$	42.50	\$	42.50
Gross margin	95.5%		85.0%		85.0%	
Operating Expenses						
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
Cost of USP-800 Requirements <sup>2</sup>		-		-		10.00
<b>Total Operating Expenses</b>	\$	37.50	\$	37.50	\$	47.50
Pre-Tax Profit	\$	120.00	\$	5.00	\$	(5.00)
Operating margin		72.7%		10.0%		-10.0%



<sup>1)</sup> Includes additional labor, pharmacists, technicians, regulatory, and legal expenses

<sup>2)</sup> December 2019 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 1Q19			
<u>Revenue</u>						
Patient Co-Pay		50.00		50.00		
Third-Party Reimbursement		-		200.00		
Total Net Revenue	\$	50.00	\$	250.00 <sup>1</sup>		
Costs of Good Sold		7.50		$200.00^2$		
Gross Profit	\$	42.50	\$	50.00		
Gross margin	85.0%		20.0%			
Operating Expenses						
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		-		
Total Operating Expenses	\$	47.50	\$	20.00		
Pre-Tax Profit	\$	(5.00)	\$	30.00		
Operating margin	-10.0%		12.0%			

Therapeutics MD°

<sup>1)</sup> Assume AWP-18% Third-Party Reimbursement

<sup>2)</sup> Assume \$250 WAC less 20% distribution discount

<sup>3)</sup> Includes additional labor, pharmacists, technicians, regulatory, and legal expenses

<sup>4)</sup> December 2019 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 FDAapproved 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



# 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 <sup>®</sup>	94%	5%
 CombiPatch®	93%	4%
 Climara Pro®	92%	4%
 FemHRT®	87%	6%
 Duavee <sup>®</sup>	86%	5%
 Vivelle-Dot®	84%	5%
Activella®	83%	8%
 Prometrium®	83%	6%



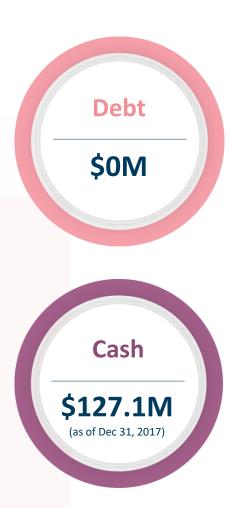
## **TXMD:** Financial Snapshot



Shares
Outstanding

216.4M
(as of Feb 20, 2018)

Insider Ownership
~23%
(as of Feb 20, 2018)





# **Worldwide Patent Filings\***

Strong IP Portfolio with 158 Patent Applications, including 82 international filings, and 18 issued U.S. patents





## Women's Health Initiative Observational Study

- First ever study to evaluate the long-term safety of women using **only** U.S. FDA-approved vaginal estrogen products
  - 2,953 users of vaginal estrogen without progestin with an intact uterus
  - Median duration of use of 2-3 years and median duration of follow-up of 7.2 years, representing over 21,000 patient years of data
  - Risks of breast cancer, endometrial cancer, colorectal cancer, stroke, and pulmonary embolism/deep vein thrombosis were not statistically significant between vaginal estrogen users and nonusers
    - 11 total cases of endometrial cancer

Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study

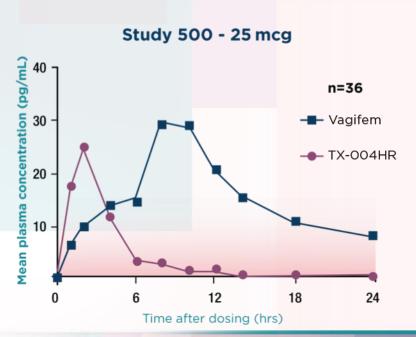
Carolyn J. Crandall, MD, MS,<sup>1</sup> Kathleen M. Hovey, MS,<sup>2</sup> Christopher A. Andrews, PhD,<sup>3</sup> Rowan T. Chlebowski, MD, PhD,<sup>4</sup> Marcia L. Stefanick, PhD,<sup>5</sup> Dorothy S. Lane, MD, MPH,<sup>6</sup> Jan Shifren, MD,<sup>7</sup> Chu Chen, PhD,<sup>8</sup> Andrew M. Kaunitz, MD,<sup>9</sup> Jane A. Cauley, DrPH,<sup>10</sup> and JoAnn E. Manson, MD, DrPH<sup>11</sup>

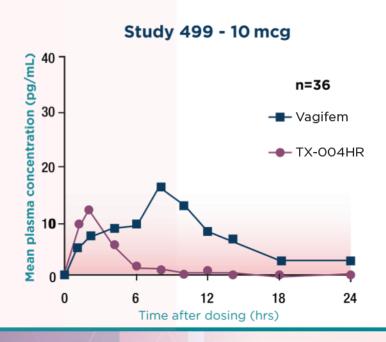


# TX-004HR vs. Vagifem<sup>®</sup> Phase 1 Single Dose PK Studies

#### **Key Findings**

- Tmax ~2 hours with TX-004HR and ~8 hours with Vagifem
- Systemic absorption of estradiol AUC (0-24 hours) is 2- to 3-fold lower with TX-004HR relative to Vagifem





# 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> *	903,680	1,596,847	902,733	399,665	3,802,925 <sup>1</sup>
<u>Estradiol</u>	2,297,141	5,033,146	2,722,199	1,476,272	11,578,758 <sup>1</sup>

<sup>\*</sup>Menopausal use of progesterone directly substitutable to TX-001HR

~3.8M Potential Prescriptions for TX-001HR (if approved)

Market Opportunity = \$760M-950M<sup>2</sup>

- This regimen carries <u>significant risk</u> of endometrial hyperplasia/cancer if the patient is noncompliant 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

Therapeutics MD°

<sup>1)</sup> Symphony Health Solutions PHAST Data powered by IDV; 12 months as of December 31 2017

<sup>2)</sup> Assume WAC pricing between \$200-250

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

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







AGES	AGES	AGES	AGES	AGES	Unknown	TRx
31-40	41-50	51-60	61-70	71+	Ages	Totals
45,564	341,778	1,487,018	646,172	134,137	71,718	2,726,387 <sup>1</sup>

~2.7M Potential Prescriptions for TX-001HR (if approved)

Market Opportunity = \$540M-675M<sup>2</sup>

1) Symphony Health Solutions PHAST Data powered by IDV; 12 months as of December 31 2017

Therapeutics MD®

Oral and transdermal combinations, including: Activella®, FemHRT®, Angeliq®, Generic 17β + Progestins, Prempro®, Premphase®, Duavee®, Brisdelle® 2) Assume WAC pricing between \$200-\$250