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

FORM 8-K

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

Date of Report (Date of earliest event reported): March 7, 2016

TherapeuticsMD, Inc.
(Exact Name of Registrant as Specified in its Charter)

Nevada	**001-00100**	**87-0233535**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

6800 Broken Sound Parkway NW, Third Floor
Boca Raton, FL 33487
(Address of Principal Executive Office) (Zip Code)

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

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

£ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

£ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

£ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

£ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01. Regulation FD Disclosure.

TherapeuticsMD, Inc. is furnishing as Exhibit 99.1 to this Current Report on Form 8-K an investor presentation which will be used, in whole or in part, and subject to modification, on March 7, 2016 and at subsequent meetings with investors or analysts.

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

Item 9.01. Financial Statements and Exhibits.

(d) *Exhibits.*

Exhibit Number	Description
99.1	TherapeuticsMD, Inc. presentation dated March 7, 2016.

SIGNATURES

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

Date: March 7, 2016

THERAPEUTICSMD, INC.

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

EXHIBIT INDEX

Exhibit Number	Description
99.1	TherapeuticsMD, Inc. presentation dated March 7, 2016.

Exhibit 99.1


TherapeuticsMD
REJOICE Trial Data Presentation
March 7, 2016
Rejoice TRIAL
TherapeuticsMD.com

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 therefor; the length, cost and uncertain results of our clinical trials; potential adverse side effects or other safety risks that could preclude the approval of our hormone therapy drug candidates; our reliance on third parties to conduct our clinical trials, research and development and manufacturing; the availability of reimbursement from government authorities and health insurance companies for our products; the impact of product liability lawsuits; the influence of extensive and costly government regulation; the volatility of the trading price of our common stock; and the concentration of power in our stock ownership.

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

YUVVEXY™ (TX-004HR)

Clinical Development Program

YUVVEXY™ is an investigational drug and is not approved for use by the FDA. This is a non-promotional presentation of scientific and development information intended for investor audiences only.

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Agenda

1. Introduction to Vulvar and Vaginal Atrophy (VVA)
2. Rationale for Development
3. Presentation of REJOICE Trial Data
4. Labeling Implications
5. Questions/Answers

Panelists

- **Robert Finizio** – Co-founder and Chief Executive Officer, TherapeuticsMD
- **Brian Bernick, M.D.** – Co-founder and Chief Clinical Officer, TherapeuticsMD
- **Sebastian Mirkin, M.D.** – Chief Medical Officer, TherapeuticsMD
- **Sheryl Kingsberg, Ph.D.*** – Chief, Division of OB/GYN Behavioral Medicine, UH Case Medical Center, Board of Trustees of the North American Menopause Society (NAMS)
- **Lisa Rarick, M.D.*** – Former FDA Medical Officer & Division Director Center for Drug Evaluation and Research (CDER) and FDA Office of Women's Health
- **Ginger Constantine, M.D.*** – President Endoheum Consultants, Former Wyeth Women's Health and Musculoskeletal VP and Therapeutic Area Director, Clinical Research and Development
- **James Simon, M.D.*†** – Professor of Ob/Gyn, George Washington University, Past President of the North American Menopause Society (NAMS), President Elect of the International Society for the Study of Women's Sexual Health (ISSWSH)
- **Steven Goldstein, M.D.*** – Professor of Ob/Gyn, New York University, Past President of the North American Menopause Society (NAMS)

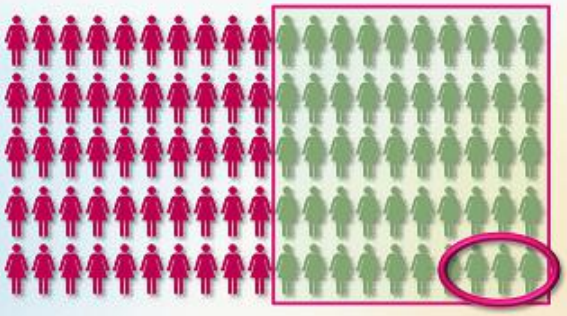
* Consultant to TherapeuticsMD
† Clinical Investigator for TX-004HR REJOICE Trial

Women's Attitudes and Behaviors towards Vulvar and Vaginal Atrophy (VVA)

Sheryl Kingsberg, PhD

University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, OH

The Scope of the Problem



About 50% (~32 million) of all postmenopausal women in the US have VVA/GSM[1]

. . . but only ~7% are treated[2,3]

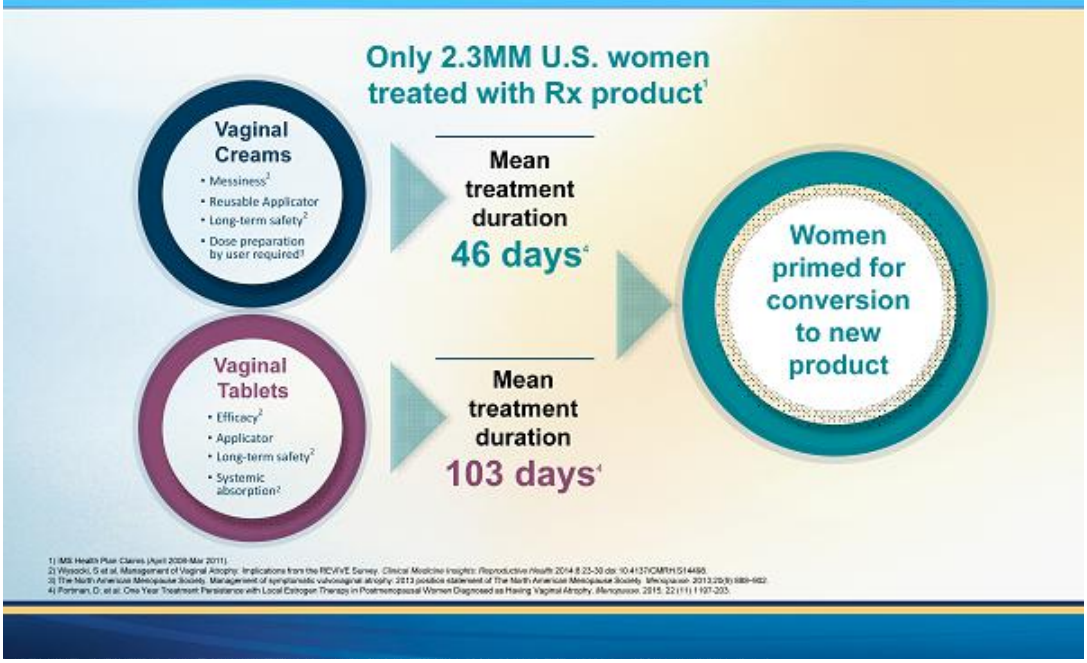
Many women are unaware that symptoms progress without treatment, and that safe and effective treatments are available[4]

1. Simon JA, et al. Menopause. 2013;20:1043-1048.
2. MacBride MB, et al. Mayo Clin Proc. 2010;85:87-94.
3. Prairie BA, et al. J Womens Health. 2014;23:513-518.
4. Nappi RE, et al. Climacteric. 2012;15:36-44.

The Survey Says….

- Several recent surveys on the impact of VVA on Quality of Life, 3 large surveys published within the past 2 years
  - REVIVE: Real Women's Views of Treatment Options for Menopausal Vaginal Changes
    Kingsberg SA, et al. *J Sex Med.* 2013,10:1790-1799
  - VIVA: **V**aginal Health: **I**nsights, **V**iews, and **A**ttitudes
    Nappi RE, Kokot-Kierepa M. *Maturitas* 2010;67(3):233-238
  - CLOSER: **CL**arifying Vaginal Atrophy's Impact **O**n **SE**x and **R**elationships
    Nappi RE et al. J Sex Med 2013,10:2232-2241
- Conclusion:
  - Negative impact of VVA on sexual health and other activities of daily life

VVA Market Dynamics - Ready for New Product



1) IMS Health Plan Claims (April 2009-Mar 2011).
2) 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.S14495.
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.
4) Portman, D. et al. One Year Treatment Persistence with Local Estrogen Therapy in Postmenopausal Women Diagnosed as Having Vaginal Atrophy. *Menopause*. 2015. 22 (11) 1197-203.


VVA Market Opportunity
Brian Bernick, M.D.
– Co-founder & Chief Clinical Officer TherapeuticsMD
TherapeuticsMD
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YUVVEXY™ (TX-004HR): Rationale for Development

- TX-004HR is an investigational **applicator-free** vaginal softgel capsule that contains solubilized **17β-estradiol**
- TX-004HR is designed to provide **improved efficacy, early onset of action** and **lower systemic estrogen** levels vs. currently available products
- TX-004HR is designed to fulfill an unmet need for a more **user-friendly** modern treatment

Established VVA Market

- U.S. sales approximately $1.5 billion in 2015[1]
- U.S. sales more than doubled since 2008[1]
- Global market expected to be $2.1 billion in 2022[4]
- Currently no generic competition
- 32 million U.S. women currently experiencing VVA symptoms[5,6]

Premarin®	Vagifem®	Estrace®	Osphena®	Estring®
				
Reusuable Vaginal Applicator	Vaginal Applicator	Reusuable Vaginal Applicator	Oral Daily SERM	Vaginal Ring
Vaginal Cream	Vaginal Tablet	Vaginal Cream	Oral Tablet	Vaginal Ring
$502MM[1]	$456MM[1]	$420MM[1]	$66MM[1]	$91MM[1]

1) Symphony Health Solutions PHAST 2.0 Prescription Monthly Powered by IDV, 12 months as of December 31, 2015.
2) Femring data is excluded due to VMS indication.
3) Medi-Span Price Rx Basic as of 2/15/16. * for 18 tablets ($156.54 WAC for 6 tablets)
4) GlobalData July 2015 report EDMCSAP/EA
5) 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.
6) Goss 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(1):1

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YUVVEXY™ (TX-004HR)

- **Small digitally inserted rapidly dissolving softgel capsule**
- **No applicator**
- **Proposed dose packaging to optimize compliance and convenience**

YUVVEXY™ is an investigational drug and is not approved for use by the FDA.

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Presentation of
REJOICE Trial Data
Sebastian Mirkin, M.D.
– Chief Medical Officer,
TherapeuticsMD
TherapeuticsMD
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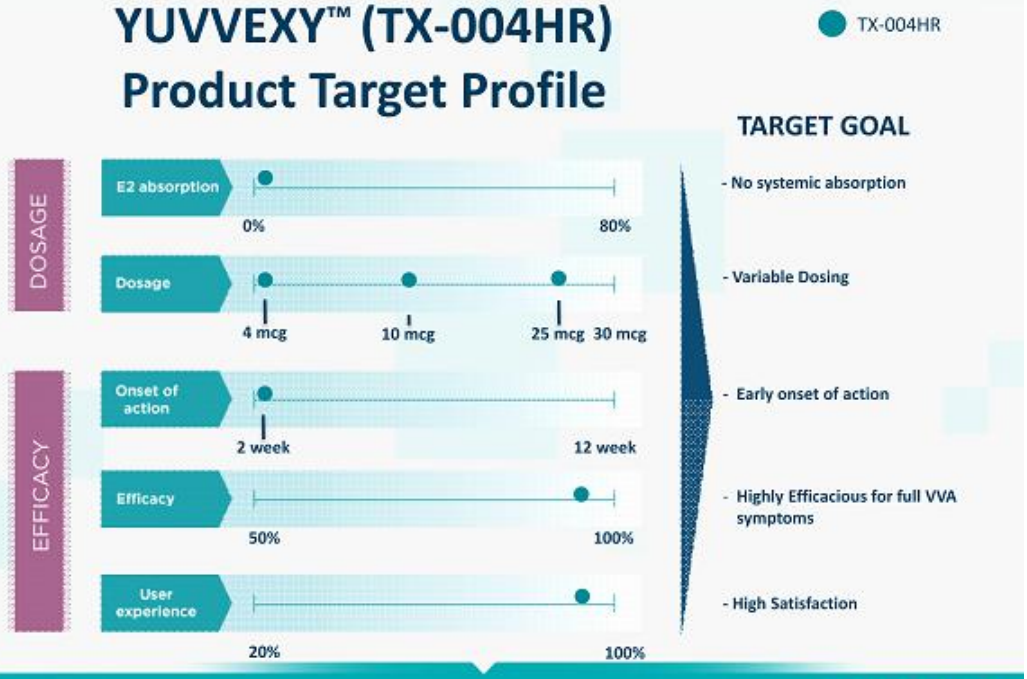
YUVVEXY™ (TX-004HR) Product Target Profile



Clinical Program: YUVVEXY™ (TX-004HR) (Completed)

- ✓ **Phase 1 Studies (499 and 500)**
  - Single dose, randomized, open label, two-way crossover vs. Vagifem®, bioavailability study
- ✓ **Phase 2 Study (TXV-13-01)**
  - A randomized, double blind, placebo controlled trial to evaluate the safety and efficacy of TX-004HR 10mcg on VVA
  - 2 weeks duration
- ✓ **Phase 3 study (TXV-14-01) - REJOICE Trial**
  - A randomized, double blind, placebo controlled trial to evaluated the safety and efficacy of TX-004HR 4, 10 and 25 mcg on VVA

Phase 3 Clinical Study
REJOICE TRIAL

- **12 Week Randomized, Double-blinded, Placebo-controlled**[1]
- **Subjects: 764; 89 Sites across the United States and Canada**
  - **Main inclusion criteria**
    - Postmenopausal
    - Sexually active
    - ≤ 5% superficial cells on vaginal smear
    - Vaginal pH > 5
    - Moderate to severe dyspareunia as most bothersome symptom
  - **4 groups**
    - 4 mcg (N=191)
    - 10 mcg (N=191)
    - 25 mcg (N=190)
    - Placebo (N=192)

1) NCT02253173; https://clinicaltrials.gov/ct2/show/NCT02253173?term=rejoice&rank=1, last accessed November 3, 2015

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REJOICE TRIAL
Co-Primary and Key Secondary Endpoints

- **FDA Required Co-Primary Endpoints – mean change from baseline to week 12 in[1,2]:**
  - ✓ Vaginal superficial cells
  - ✓ Vaginal parabasal cells
  - ✓ Vaginal pH
  - ✓ Moderate to severe dyspareunia (identified as the most bothersome symptom of VVA)
- **Key components of secondary endpoints:**
  - ✓ Efficacy of co-primary endpoints at week 2
  - ✓ Vaginal dryness
- **Additional Endpoints:**
  - ✓ PK measures Days 1, 14, 84
  - ✓ FSFI (Female Sexual Function Index)
  - ✓ Acceptability survey

1) Each arm (4 mcg, 10 mcg, and 25 mcg) tested against each co-primary endpoint.
2) The FDA has previously indicated to us that in order to approve the drug based on a single trial, the trial would need to show statistical significance at the 0.01 level or lower for each endpoint, and that a trial that is merely statistically significant at a higher level may not provide sufficient evidence to support an NDA filing or approval of a drug candidate where the NDA relies on a single clinical trial.

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Baseline Characteristics

	4 mcg N=191	10 mcg N=191	25 mcg N=190	Placebo N=192
Age (years) Mean ± SD	59.8 ± 5.9	58.5 ± 6.3	58.9 ± 6.3	59.3 ± 6.1
Race				
White	87.4%	88.0%	86.8%	84.4%
Black	10.5%	11.0%%	12.6%	12.5%
Other	2.1%	1.0%	0.5%	3.1%
BMI (kg/m^2) Mean ± SD	26.5 ± 4.9	26.8 ± 4.7	26.7 ± 4.8	26.6 ± 4.5
Type of Menopause				
Natural	114 (59.7%)	114 (59.7%)	121 (63.7%)	127 (66.2%)
Surgical	77 (40.3%)	77 (40.3%)	69 (36.3%)	65 (33.9%)

Discontinuation Rates by Reason

	4 mcg (N=191)	10 mcg (N=191)	25 mcg (N=190)	Placebo (N=192)
Number of Subjects Discontinued	**16 (8.4%)**	**17 (8.9%)**	**13 (6.8%)**	**14 (7.3%)**
Adverse Event	2 (1.0%)	3 (1.6%)	4 (2.1%)	5 (2.6%)
Investigator / Sponsor Decision	1 (0.5%)	0 (0%)	1 (0.5%)	0 (0%)
Lack of Efficacy	2 (1.0%)	2 (1.0%)	0 (0%)	0 (0%)
Lost to Follow-up	3 (1.6%)	3 (1.6%)	2 (1.1%)	4 (2.1%)
Protocol Violation	2 (1.0%)	1 (0.5%)	1 (0.5%)	0 (0%)
Withdrew Consent	6 (3.1%)	7 (3.7%)	5 (2.6%)	5 (2.6%)
Other	0 (0%)	1 (0.5%)	0 (0%)	0 (0%)


Rejoice TRIAL
Co-Primary Efficacy Endpoints
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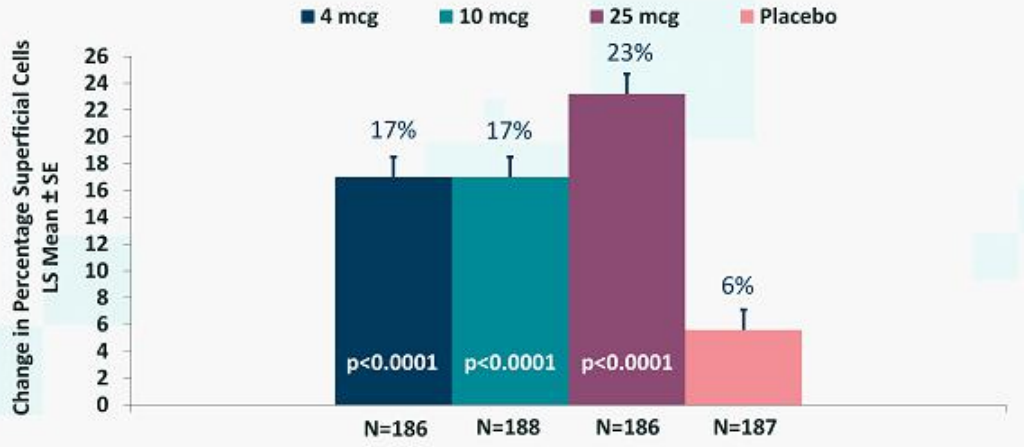
LS Mean Change from Baseline to Week 12: Vaginal Superficial Cells



LS = Least Squares

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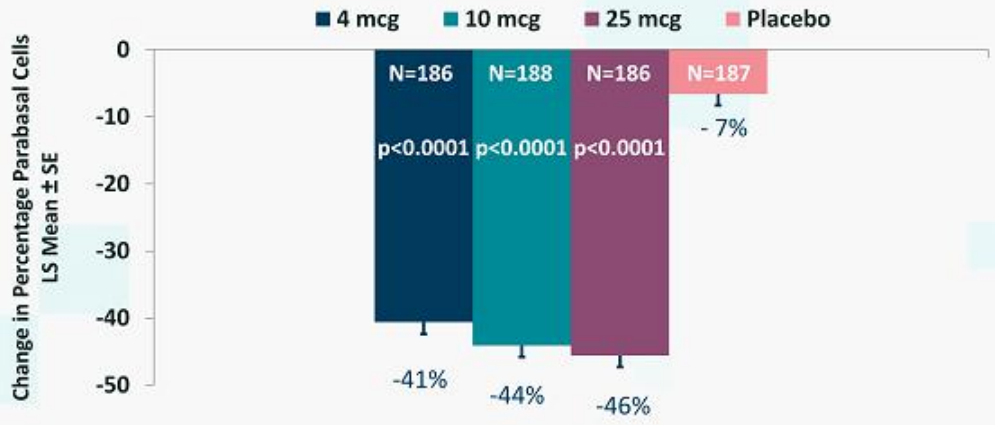
LS Mean Change from Baseline to Week 12: Vaginal Parabasal Cells



LS = Least Squares

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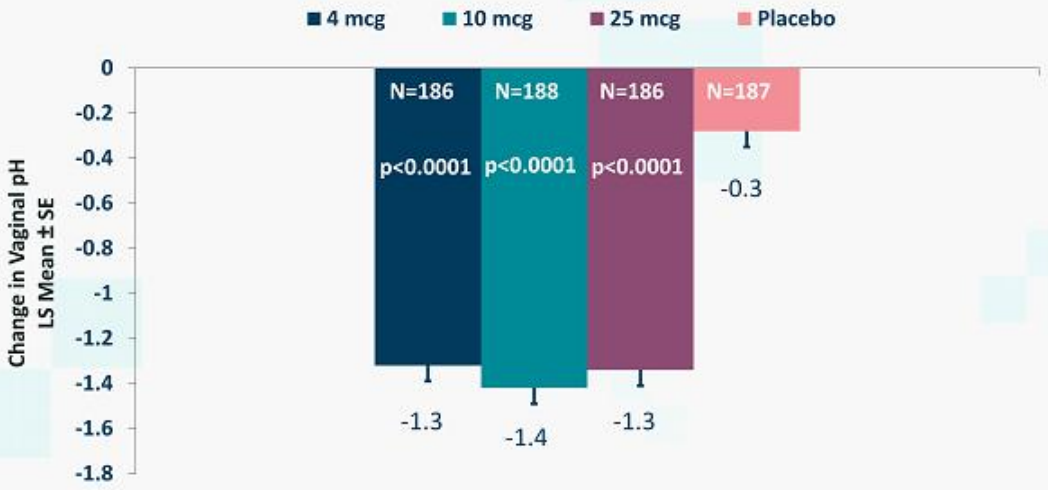
LS Mean Change from Baseline to Week 12: Vaginal pH



LS = Least Squares

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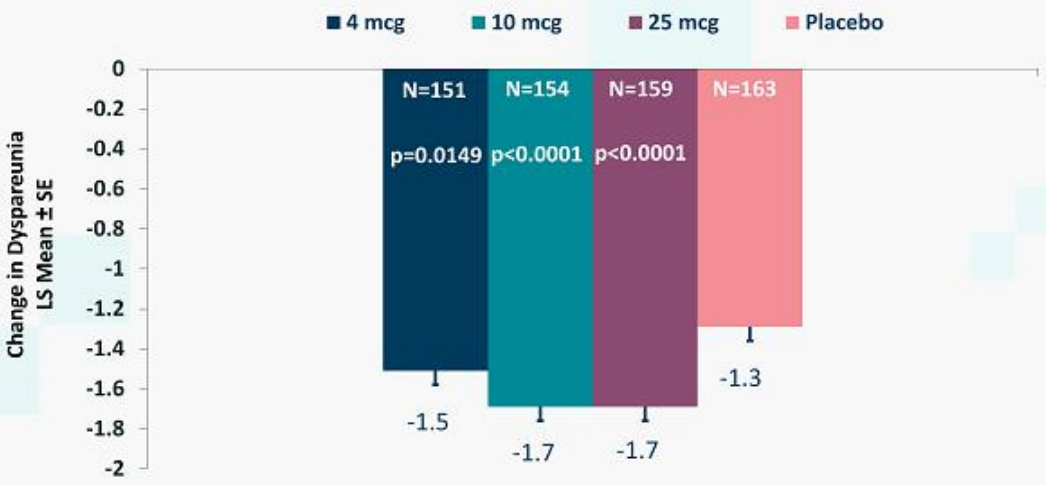
LS Mean Change from Baseline to Week 12: Severity of Dyspareunia



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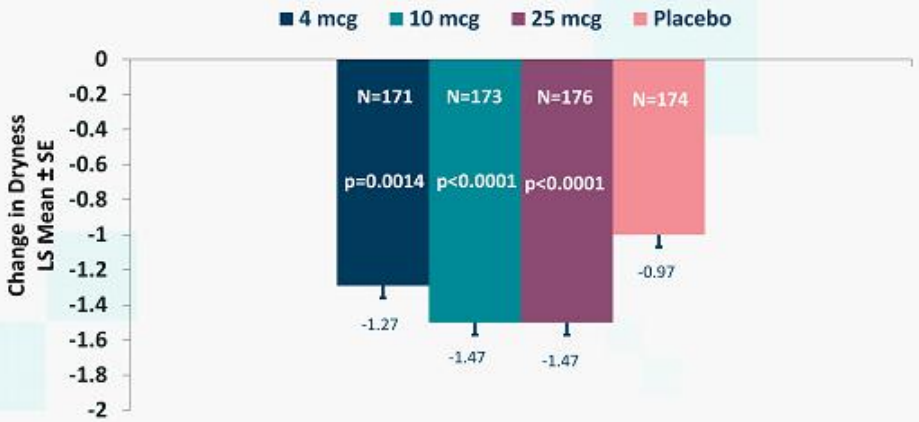
Key Components of Secondary Efficacy Endpoints

Statistical Significance of LS Mean Change from Baseline Severity of Dyspareunia by Study Visit (Week)

	4 mcg	10 mcg	25 mcg
Week 2	0.026	0.0019	0.0105
Week 6	0.0069	0.0009	< 0.0001
Week 8	0.0003	< 0.0001	< 0.0001
Week 12	0.0149	< 0.0001	< 0.0001

MMRM P-value vs placebo

LS Mean Change from Baseline to Week 12: Severity of Vaginal Dryness



LS = Least Squares

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Co-Primary and Key Secondary Endpoints LS Mean Change from Baseline to Week 12 Compared to Placebo

	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

Efficacy and Onset of Action Based on FDA-Approved Labeling and Not Head-to-Head Comparative Studies

	Premarin®	Vagifem®	Estrace®	Osphena®	Estring®
Onset of Action Dyspareunia	Week 4+	Week 8 (composite score)	Approval without dyspareunia and dryness data	Week 12	Approval without dyspareunia and dryness data
Onset of Action Dryness	Not demonstrated			Not demonstrated	

Onset of Action = First efficacy observation

Vagifem [package label] http://www.novo-pi.com/vagifem.pdf
Premarin Vaginal Cream [package label] http://labeling.pfizer.com/showlabeling.aspx?id=133
Estrace Vaginal Cream [package label] http://pi.actavis.com/data_stream.asp?product_group=1880&p=pi&language=E
Osphena [package label] http://www.shionogi.com/pdf/pi/osphena.pdf?400730572
Estring [package label] http://labeling.pfizer.com/showlabeling.aspx?id=667

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Responder Analysis: Severity of Dyspareunia at Week 12

Responder defined as reduction of 2+ points

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Rejoice TRIAL
Results from Pharmacokinetics Substudy
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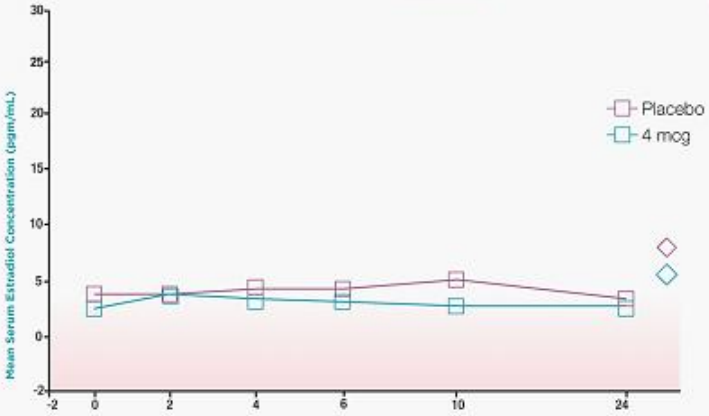
Arithmetic Mean Estradiol Serum Concentrations - Unadjusted
TX-004HR 4 mcg (N=18)



Hours after capsule insertion Day 14

(◇ represents day 84)

	AUC_{0-24} (pg.h/mL)	$C_{avg(0-24)}$ (pg/mL)
4 mcg	87.22 (42.77)	3.634 (1.78)
Placebo	104.16 (66.38)	4.34 (2.76)
P-value vs Placebo	0.3829	0.3829

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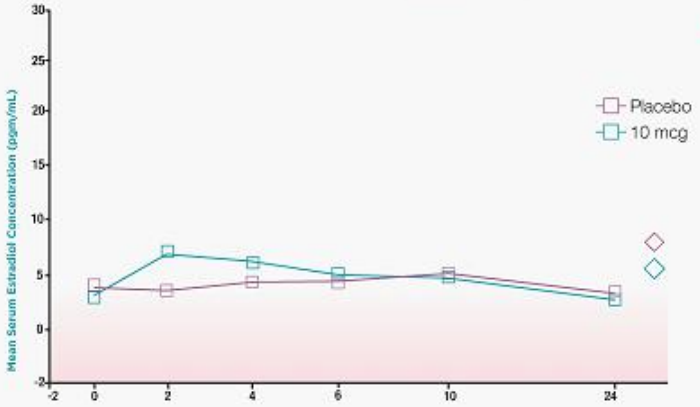
Arithmetic Mean Estradiol Serum Concentrations - Unadjusted
TX-004HR 10 mcg (N=19)



Hours after capsule insertion Day 14
(♀ represents day 84)

	AUC_{0-24} (pg.h/mL)	$C_{avg(0-24)}$ (pg/mL)
10 mcg	110.14 (54.57)	4.58 (2.27)
Placebo	104.16 (66.38)	4.34 (2.76)
P-value vs Placebo	0.7724	0.7724

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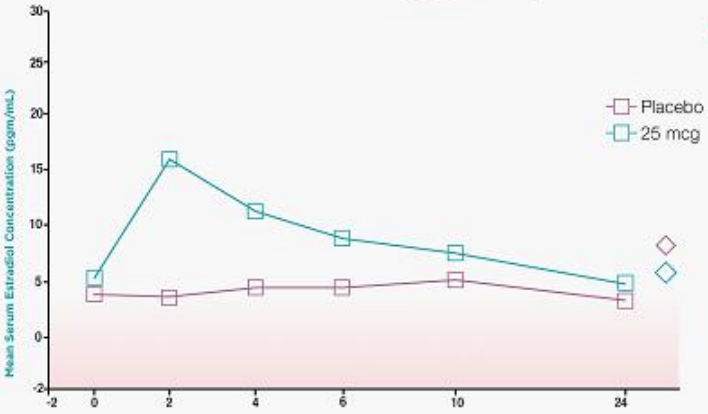
Arithmetic Mean Estradiol Serum Concentrations - Unadjusted
TX-004HR 25 mcg (N=18)



Hours after capsule insertion Day 14
(◇ represents day 84)

	AUC_{0-24} (pg.h/mL)	$C_{avg(0-24)}$ (pg/mL)
25 mcg	171.56 (80.13)	7.14 (3.33)
Placebo	104.16 (66.38)	4.34 (2.76)
P-value vs Placebo	0.0108	0.0108

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Acceptability of Product Administration
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Was the product easy to use?

	4 mcg (N=181)	10 mcg (N=181)	25 mcg (N=184)	Placebo (N=185)
YES	171 (94.5%)	172 (95.0%)	175 (95.1%)	164 (88.9%)

Overall p-value = 0.035

How would you rate the ease of insertion of the capsule?

	4 mcg (N=181)	10 mcg (N=181)	25 mcg (N=184)	Placebo (N=185)
Excellent	79 (44.0%)	83 (46.0%)	83 (45.0%)	65 (35%)
Good	77 (43.0%)	72 (40.0%)	74 (40.0%)	79 (43%)
Fair	20 (11.0%)	23 (13.0%)	18 (10.0%)	25 (14%)
Poor	5 (3.0%)	3 (1.7%)	9 (5.0%)	16 (9.0%)

Overall p-value = 0.037

Level of satisfaction with the product

	4 mcg (N=181)	10 mcg (N=181)	25 mcg (N=184)	Placebo (N=185)
Very Satisfied	74 (40.1%)	84 (46.4%)	83 (45.1%)	41 (22.2%)
Satisfied	57 (31.5%)	55 (30.4%)	62 (33.7%)	68 (36.8%)
Unsure	23 (12.7%)	28 (15.5%)	21 (11.4%)	39 (21.1%)
Dissatisfied	19 (10.5%)	9 (5.0%)	12 (6.5%)	20 (10.8%)
Very Dissatisfied	8 (4.4%)	5 (2.8%)	6 (3.3%)	17 (9.2%)

Overall p-value <0.0001

Safety Endpoints

Overview of Adverse Events (AEs) (Safety Population)

	4 mcg (N=191)	10 mcg (N=191)	25 mcg (N=190)	Placebo (N=192)
Any Subject with Reported AE	113 (59.2%)	105 (55.0%)	107 (56.3%)	124 (64.6%)
Any Subject with Reported TEAE	96 (50.3%)	91 (47.6%)	90 (47.4%)	104 (54.2%)
Any Subject with Drug Related TEAE	38 (19.9%)	28 (14.7%)	34 (17.9%)	47 (24.5%)
Any Reported Serious TEAE	0 (0.0%)	2 (1.0%)	3 (1.6%)	1 (0.5%)
Any AE Leading to Discontinuation	2 (1.0%)	3 (1.6%)	4 (2.1%)	5 (2.6%)

TEAE – Treatment Emergent Adverse Event

TEAEs by Preferred Term Occurring ≥ 3% (Safety Population)

Preferred Term	4 mcg (N=191)	10 mcg (N=191)	25 mcg (N=190)	Placebo (N=192)
Nasopharyngitis	5 (2.6%)	6 (3.1%)	7 (3.7%)	10 (5.2%)
Upper respiratory tract infection	5 (2.6%)	6 (3.1%)	3 (1.6%)	5 (2.6%)
Urinary tract infection	5 (2.6%)	5 (2.6%)	8 (4.2%)	4 (2.1%)
Back pain	9 (4.7%)	1 (0.5%)	4 (2.1%)	7 (3.6%)
Headache	12 (6.3%)	14 (7.3%)	5 (2.6%)	14 (7.3%)
Vaginal discharge	5 (2.6%)	6 (3.1%)	4 (2.1%)	13 (6.8%)
Vulvovaginal pruritus	4 (2.1%)	2 (1.0%)	7 (3.7%)	10 (5.2%)
Oropharyngeal pain	1 (0.5%)	0 (0.0%)	6 (3.2%)	1 (0.5%)

TEAE – Treatment Emergent Adverse Event

Safety Protocol Procedures

- No significant difference in safety labs or vital signs
- No increase in estrogen sensitive tests (i.e., SHBG, Triglycerides)
- No significance difference in EKG findings
- No signal of estrogenic stimulation of the endometrium

Conclusions

TX-004HR at 4, 10 and 25 mcg demonstrated a positive benefit/risk profile for the proposed indication of *"treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy due to menopause"*

- Increased percentage of vaginal superficial cells
- Decreased percentage of vaginal parabasal cells
- Decreased vaginal pH
- Improved dyspareunia as the most bothersome symptom
- Improved vaginal dryness
- Efficacy observed at week 2

- **No difference compared to placebo in incidence of TEAEs or SAEs**
- **Negligible to very low systemic absorption of 17-β estradiol**
  - Significantly lower than Vagifem
- **High patient acceptability and satisfaction rates**
- **Easy to use and insert without the need of an applicator**

Regulatory Strategy

- **Proposed Indication: Treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy due to menopause**
- **Clinical Program Completed**
- **Positive Benefit/Risk profile demonstrated for 4, 10 and 25 mcg**
- **Planned NDA under 505(b)(2) pathway for the 3 doses**
  - Strategy confirmed at Pre-NDA meeting
- **TherapeuticsMD to propose a highly differentiated label**
  - Negligible to very low systemic absorption of 17 β-estradiol
  - Early efficacy/onset of action
  - Applicator-free

Yuvvexy™ (TX-004HR)

Proposed US Regulatory Approach/Labeling

Lisa Rarick, M.D.
Former FDA—Center for Drug Evaluation and Research (CDER)
Medical Officer & Division Director (Division of Bone, Reproductive and Urologic Products)
and FDA Office of the Commissioner, Office of Women's Health (OWH)

FDA Scientific Workshop on Labeling "Lower" Dose Estrogen-Alone Products for Symptoms of VVA - November 10, 2015[1]

- "On the topic of the labeling for lower-dose estrogen products delivered vaginally…"
- "Lower-dose estrogen products [below 0.625 mg conjugated estrogens used in WHI, and below 0.0375 mg of estradiol products] are now approved for treatment of VVA due to menopause, and some in the scientific/medical community have questioned whether the current 'Boxed Warnings' section in the labeling is applicable in whole or in part to these lower-dose estrogen products."
- FDA seeking input on Boxed Warnings section, estrogen exposure data and PK/PD information relative to labeling lower-dose estrogen products…

1. Scientific Workshop on Labeling "Lower" Dose Estrogen-Alone Products for Symptoms of Vulvar and Vaginal Atrophy (VVA) http://www.fda.gov/Drugs/ NewsEvents/ucm459830.htm

TherapeuticsMD proposal for US Labeling—Governed by Regulations and Guidance

- Yuvvexy™ (TX-004HR)—Sections of label to be considered for modification
  - Highlights of Prescribing Information
  - Boxed Warnings
  - Contraindications
  - Warnings and Precautions
  - Adverse Reactions
  - Clinical Pharmacology
  - Clinical Studies
  - Dosage and Administration
  - Patient Counseling/Patient Labeling

Boxed Warning

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, BREAST CANCER and PROBABLE DEMENTIA

See full prescribing information for complete boxed warning.

Estrogen-Alone Therapy

- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens (5.3)
- Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia (5.2, 5.4)
- The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) (5.2)
- The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older (5.4)

Estrogen Plus Progestin Therapy

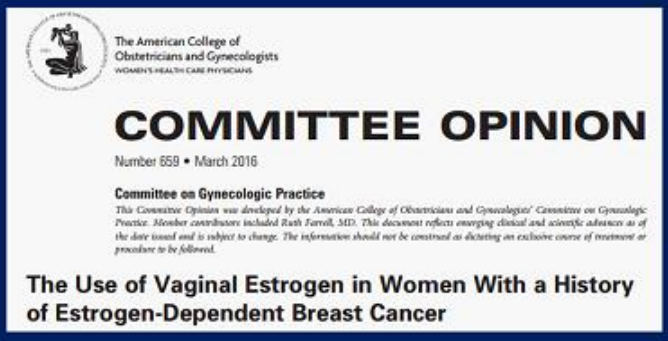
- Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia (5.2, 5.4)
- The WHI estrogen plus progestin substudy reported increased risks of stroke, DVT, pulmonary embolism (PE), and myocardial infarction (MI) (5.2)
- The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer (5.3)
- The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older (5.4)

Proposed Elimination or Modifications to Boxed Warning

- Estrogen-alone boxed warning information
  - Propose removal from Boxed Warning
  - Propose modified language in the "Warnings and Precautions" Section
- Estrogen + Progestin boxed warning information
  - Propose removal from Boxed Warning
  - Propose removal or modification throughout the label
  - Provide data to support that progestin not needed for endometrial protection

Contraindications

- Possible opportunity to remove or modify current Contraindication "Known, suspected, or history of breast cancer"



The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 659 • March 2016

Committee on Gynecologic Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice. Member contributors included Ruth Farrell, MD. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

The Use of Vaginal Estrogen in Women With a History of Estrogen-Dependent Breast Cancer

Warnings and Precautions

- Proposed modification re: "Risks from Systemic Absorption"
- Propose modification of each of the current Warnings with draft language such as "When estrogens are used with resulting systemic absorption higher than demonstrated for Yuvvexy™, an increased risk of XX has been reported"
- May need to add "Although Yuvvexy™ use does not result in the level of systemic exposure associated with this increased risk, long-term safety studies with Yuvvexy™ are not available."
- Proposed removal of "addition of a Progestin" section

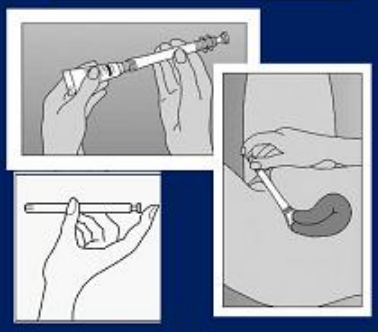
Adverse Reactions
Clinical Pharmacology
Clinical Studies

- Adverse Reactions tables/listings specific to Yuvvexy™ clinical trials
- Clinical Pharmacology to reflect Yuvvexy™ pK data (negligble to very low systemic absorption)
- Clinical Studies
  - Results for co-primary endpoints
  - May be able to include first efficacy timepoint/onset of action (statistical significance at week 2)
  - Propose to include vaginal dryness efficacy

Dosage and Administration Patient Information

Vagifem®, Estrace® and Premarin® Vaginal Cream PI

Instructions for Use of Applicator



YUVVEXY™ PI

2 DOSAGE AND ADMINISTRATION

"A single YUVVEXY capsule should be administered digitally intravaginally"

YUVVEXY™ (TX-004HR)
TherapeuticsMD Label Proposal

- Potential Modification of Boxed Warnings

  Estrogen Warnings
  - —Potential removal from Boxed Warning section
  - —Potential modifications of estrogen warnings

  Estrogen + Progestin Warnings
  - —Potential removal from Boxed Warning section
  - —Potential removal of progestin use for endometrial protection

- DOSAGE AND ADMINISTRATION
  - —Potential language to administer "digitally intravaginally" without instruction for an applicator
  - —Potential removal of progestin use for endometrial protection

- WARNINGS AND PRECAUTIONS
  - —Potential modification of warnings related to higher dose estrogens
  - —Potential removal (or modification) of warnings related to estrogen + progestins
  - —Potential modification of systemic absorption warnings

- CLINICAL STUDIES
  - —Results for co-primary endpoints
  - —Potential labeling to include language regarding demonstration of statistical significance over placebo for the four co-primary endpoints being demonstrated at study visits, including week 2
  - —Potential labeling to include vaginal dryness efficacy

Q&A

- **Robert Finizio** – Co-founder and Chief Executive Officer, TherapeuticsMD
- **Brian Bernick, M.D.** – Co-founder and Chief Clinical Officer, TherapeuticsMD
- **Sebastian Mirkin, M.D.** – Chief Medical Officer, TherapeuticsMD
- **Sheryl Kingsberg, Ph.D.*** – Chief, Division of OB/GYN Behavioral Medicine, UH Case Medical Center, Board of Trustees of the North American Menopause Society (NAMS)
- **Lisa Rarick, M.D.*** – Former Medical Officer & Division Director FDA Office of Women's Health (OWH) and Center for Drug Evaluation and Research (CDER)
- **Ginger Constantine, M.D.*** – President Endoheum Consultants, Former Wyeth Women's Health VP and Therapeutic Area Director, Clinical Research and Development
- **James Simon, M.D.*†** – Professor of Ob/Gyn, George Washington University, Past President of the North American Menopause Society (NAMS), President Elect of the International Society for the Study of Women's Sexual Health (ISSWSH)
- **Steven Goldstein, M.D.*** – Professor of Ob/Gyn, New York University, Past President of the North American Menopause Society (NAMS)

* Consultant to TherapeuticsMD
† Clinical Investigator for TX-004HR REJOICE Trial


THANK YOU
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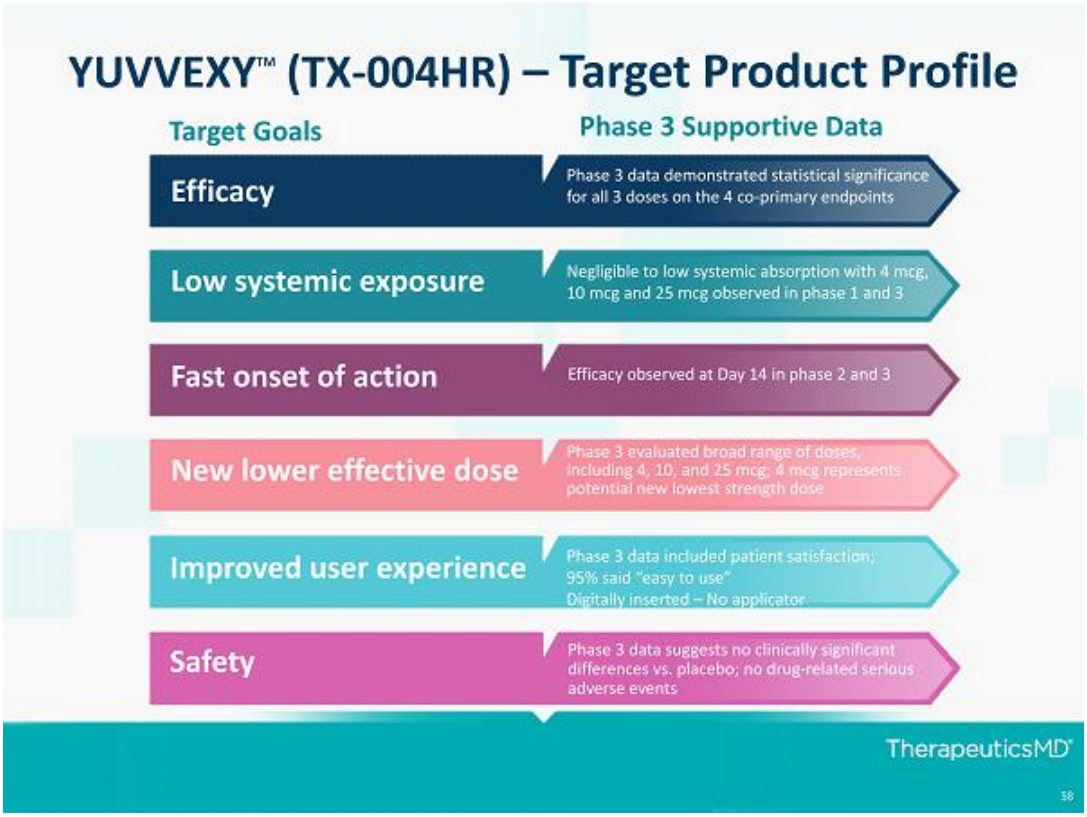
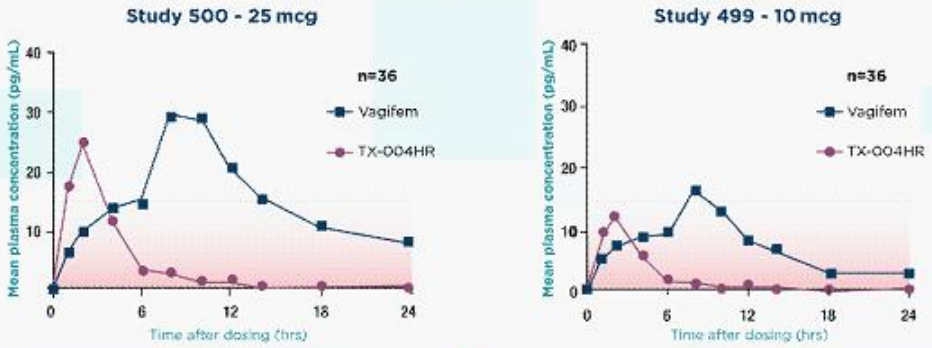
Appendix

YUVVEXY™ (TX-004HR) – Target Product Profile



Phase 1 Single Dose PK Studies
TX-004HR vs. Vagifem®

Systemic absorption AUC (0-24 hours) and C_{avg} (0-24 hours) for estradiol is 2- to 3-fold lower with TX-004HR relative to Vagifem® ($p < 0.0001$)



Vagifem is a registered trademark of Novo Nordisk A/S Corp.
Pickar, et al. *Climacteric* 2016

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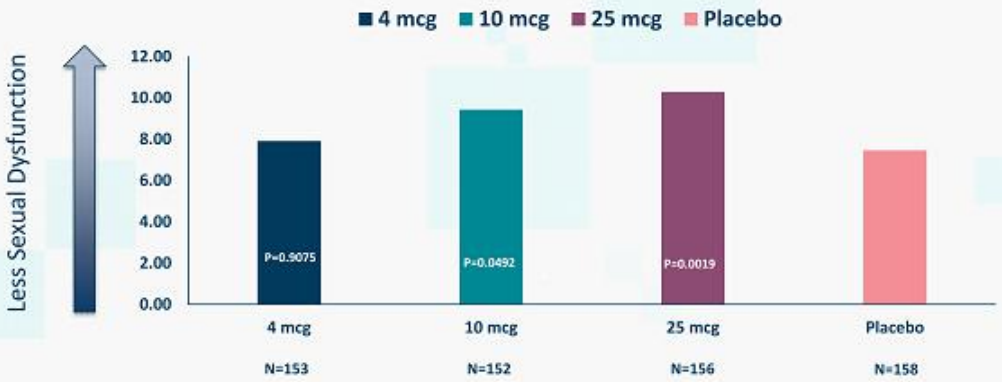
LS Mean Change from Baseline to Week 12 The Female Sexual Function Index (FSFI) Total Score



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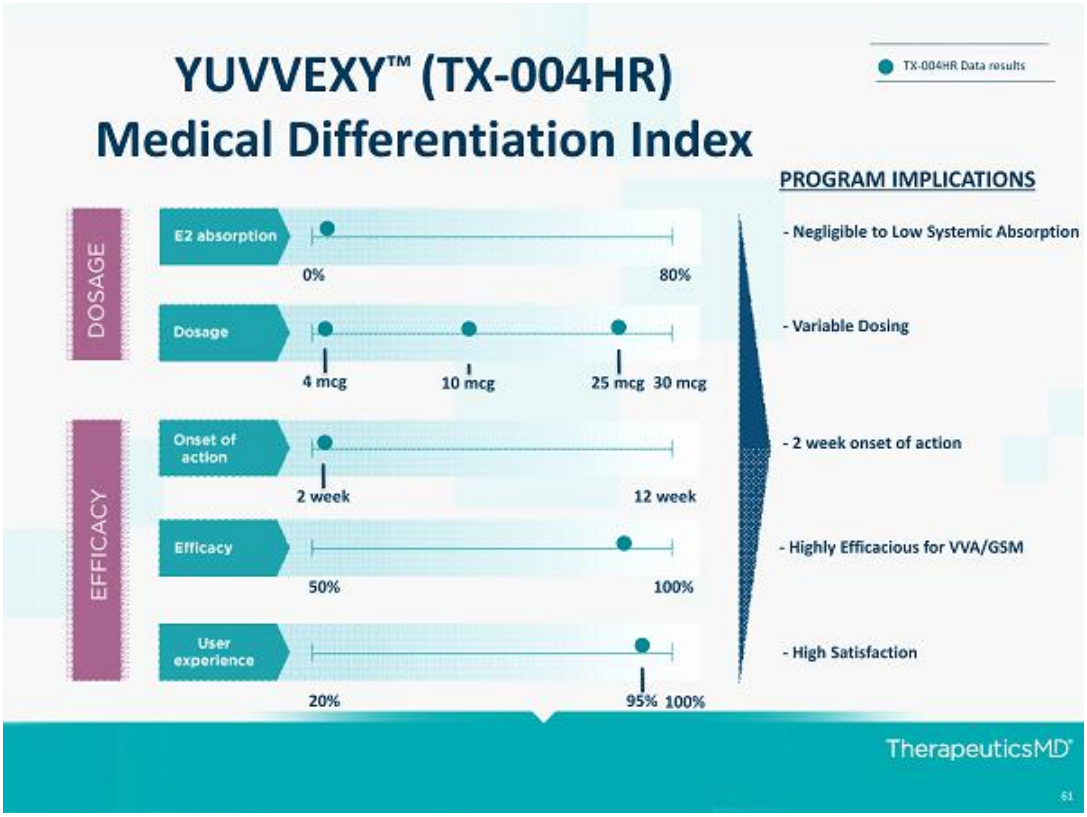
YUVVEXY™ (TX-004HR)
Medical Differentiation Index
TX-004HR Data results
PROGRAM IMPLICATIONS
DOSAGE
E2 absorption
0%
80%
- Negligible to Low Systemic Absorption
Dosage
4 mcg
10 mcg
25 mcg
30 mcg
- Variable Dosing
EFFICACY
Onset of action
2 week
12 week
- 2 week onset of action
Efficacy
50%
100%
- Highly Efficacious for VVA/GSM
User experience
20%
95%
100%
- High Satisfaction
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