Orexigen Second Quarter 2017 Earnings Conference Call

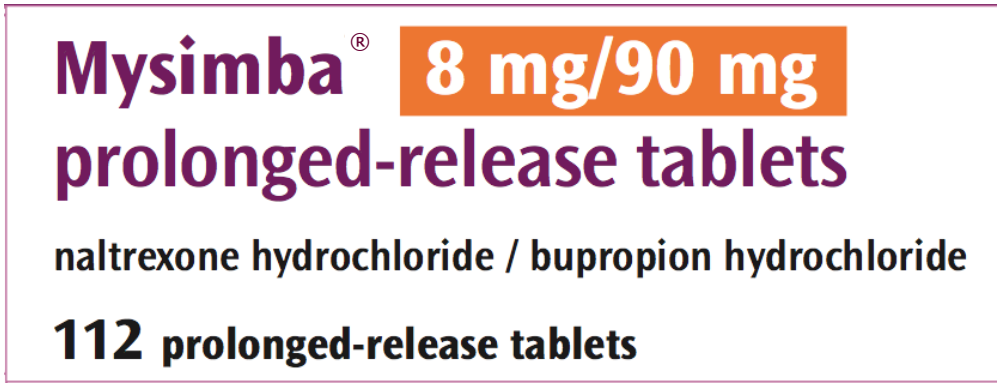
August 8th 2017

Forward Looking Statements

This presentation contains forward-looking statements about Orexigen Therapeutics, Inc. and its Contrave® product. Words such as “believes,” “anticipates,” “plans,” “expects,” “indicates,” “will,” “should,” “intends,” “potential,” “suggests,” “assuming,” “designed” and similar expressions are intended to identify forward-looking statements. These statements are based on the Company‘s current beliefs and expectations. These forward-looking statements include statements regarding: the potential success of marketing and commercialization efforts for Contrave in the United States; the potential for Contrave and Mysimba™ to achieve commercial success globally, including through potential partnership arrangements outside the United States, and the potential timing of related regulatory filings; the Company’s future financial and sales projections, including future expectations regarding net sales, cash operating expense and market share, its expectation for profitable operations by 2019 and its sales growth projections through 2019; and the status of various strategic plans and initiatives.

The inclusion of financial modeling, forward-looking statements and potential financing and transaction plans and terms should not be regarded as a representation by Orexigen that any of its plans will be achieved. Actual results may differ materially from those expressed or implied in this presentation due to the risk and uncertainties inherent in the Orexigen business, including, without limitation: the potential that the marketing and commercialization of Contrave/Mysimba will not be successful; the Company’s ability to obtain and maintain partnerships and the ability of it or its partners to maintain marketing authorization globally; the Company’s ability to adequately inform consumers about Contrave; the Company‘s ability to successfully commercialize Contrave with a specialty sales force in the United States; the capabilities and performance of various third parties on which it relies for a number of activities related to the manufacture, development and commercialization of Contrave/Mysimba; the estimates of the capacity of manufacturing and the Company’s ability to secure additional manufacturing capabilities; the Company’s ability to successfully complete the post-marketing requirement studies for Contrave; the therapeutic and commercial value of Contrave/Mysimba; competition in the global obesity market, particularly from existing therapies; the Company’s failure to successfully acquire, develop and market additional product candidates or approved products; the Company’s ability to obtain and maintain global intellectual property protection for Contrave and Mysimba; the potential for a Delaware court to determine that one or more of the Company’s patents is not valid or that Actavis' proposed generic product is not infringing each of the patents at issue; other legal or regulatory proceedings against Orexigen, as well as potential reputational harm, as a result of misleading public claims about Orexigen; the Company’s ability to maintain sufficient capital to fund its operations for the foreseeable future; the Company’s ability to satisfy covenants in the indentures for its outstanding indebtedness, including one requirement that the Company generate consolidated net product sales of least $100 million for fiscal 2017; the Company’s ability to satisfy the applicable listing standards of the NASDAQ Global Market; and other risks described in Orexigen’s filings with the Securities and Exchange Commission.

You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and Orexigen undertakes no obligation to revise or update this news release to reflect events or circumstances after the date hereof. Further information regarding these and other risks is included under the heading "Risk Factors" in Orexigen's Quarterly Report on Form 10-Q, which is planned to be filed with the Securities and Exchange Commission on or about August 9, 2017 and its other reports, which are available from the SEC's website (www.sec.gov) and on Orexigen's website (www.orexigen.com) under the heading "Investors." All forward-looking statements are qualified in their entirety by this cautionary statement. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.



Indicated for use as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of 30 kg/m^2 or greater (obese), or 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition. Approved with the brand name Contrave® in the United States and Mysimba® in the European Union.

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Suicidality and Antidepressant Drugs

CONTRAVE® is not approved for use in the treatment of major depressive disorder or other psychiatric disorders. CONTRAVE contains bupropion, the same active ingredient as some other antidepressant medications (including, but not limited to, WELLBUTRIN, WELLBUTRIN SR, WELLBUTRIN XL, and APLENZIN). Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term trials. These trials did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in subjects over age 24; there was a reduction in risk with antidepressant use in subjects aged 65 and older. In patients of all ages, monitor closely for worsening, and for the emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber. Not approved for use in pediatric patients.

Full Prescribing Information, including Medication Guide, for Contrave is available at http://www.contrave.com/. The Mysimba summary of product characteristics is available at ema.europe.eu.

OREXIGEN®

Mike Narachi
President and Chief Executive Officer

Q2 2017 Introduction

Second Quarter Results: Key Takeaways

- Strong 2Q17 net sales and TRx growth
- Projecting strong future net sales growth
- Projecting lower future operating expense
- Remain on track for profitable operations by 2019

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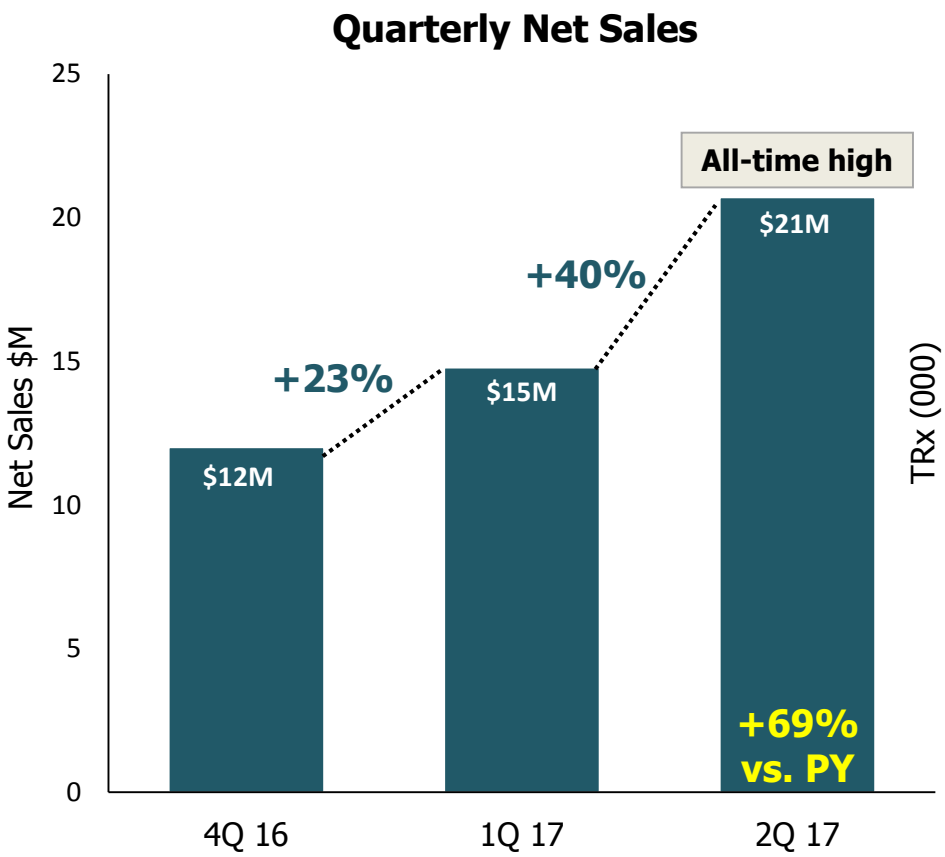
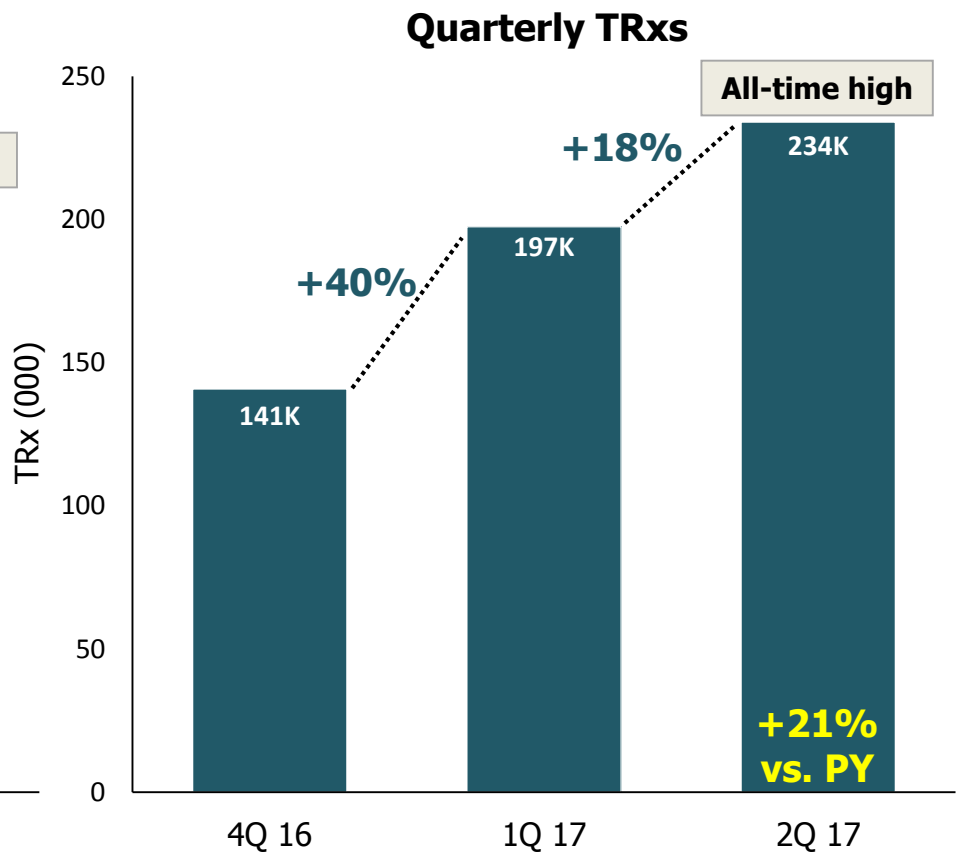
Dr. Thomas Cannell
Chief Operating Officer, President of Global Commercial Products

Q2 2017 Commercial Update

Strong US Sales Growth Driven by Increasing TRx Volume and Revenue/Unit

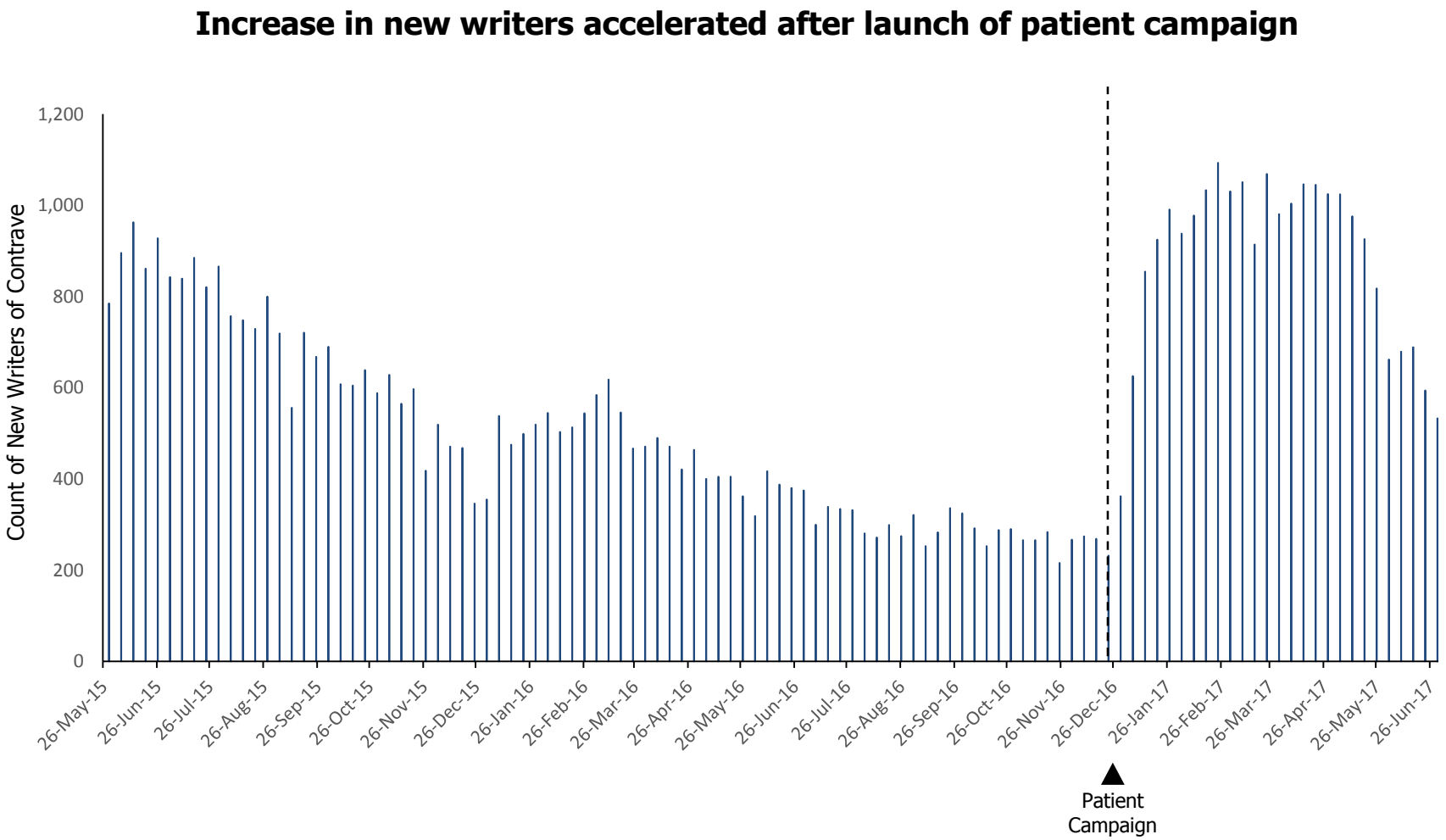




Note: Orexigen assumed commercial responsibility August 1, 2016

Source: Orexigen reported sales, IMS NPA

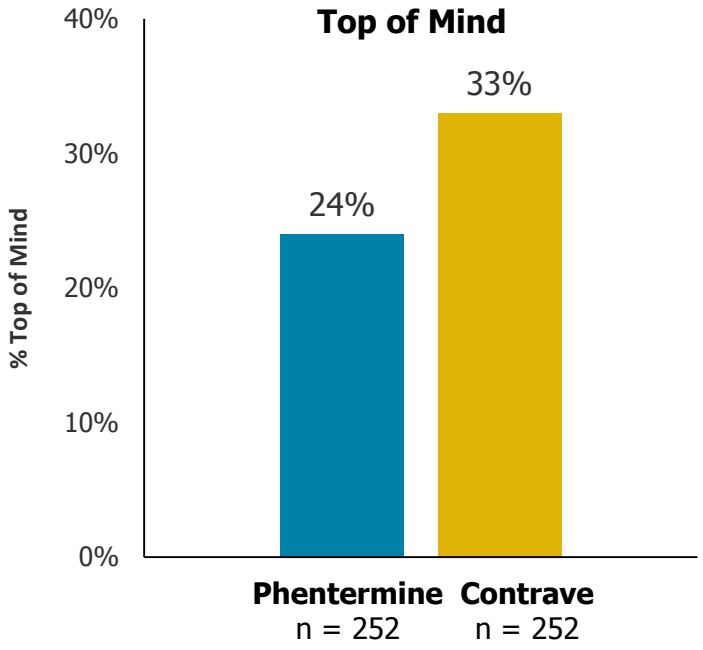
Contrave Has Nearly 100,000 Unique Prescribers in the US Since Launch



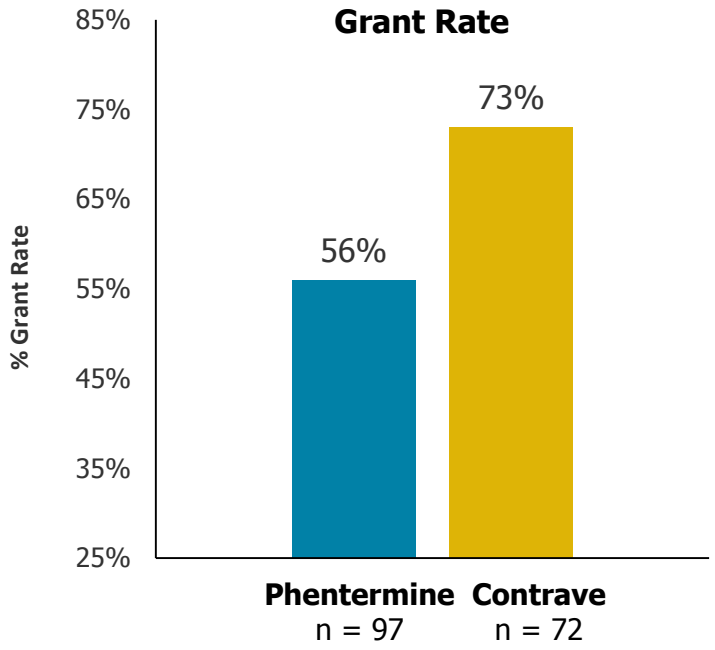
Source: QuintilesIMS Xponent Week Ending 6/30/2017

Significant Differentiation of Contrave vs. Phentermine Among HCPs

Q (HCP): When thinking about prescription medications to treat obesity, what one brand first comes to mind?



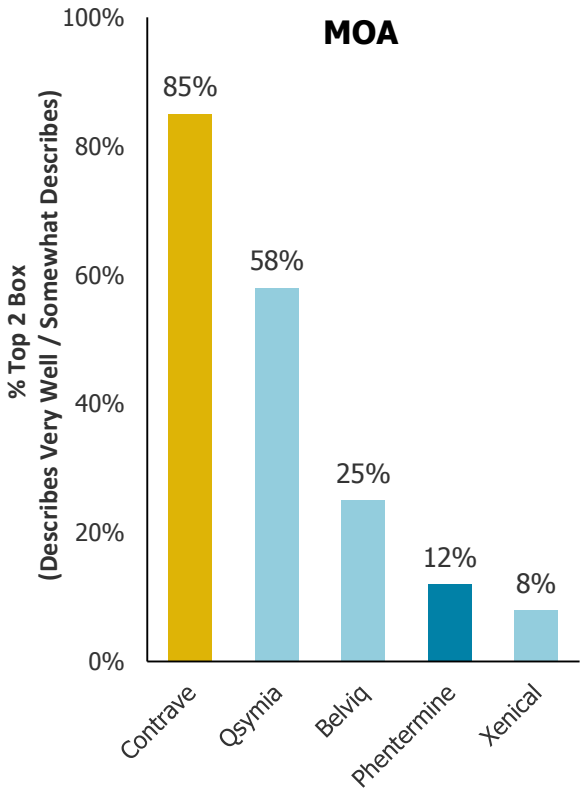
Q (HCP): When a patient asks for a prescription for [brand], what percent of the time do you grant the patients request for that specific prescription?



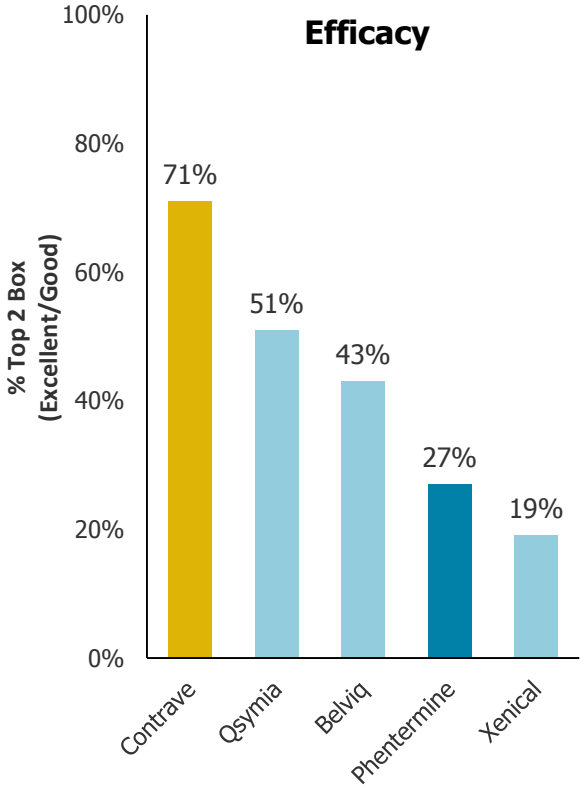
Source: HCP ATU Survey; n=253 sampled from 20,000 rep target physicians; Feb/Mar 2017

Contrave is Favorably Differentiated vs. Branded and Generic Competition

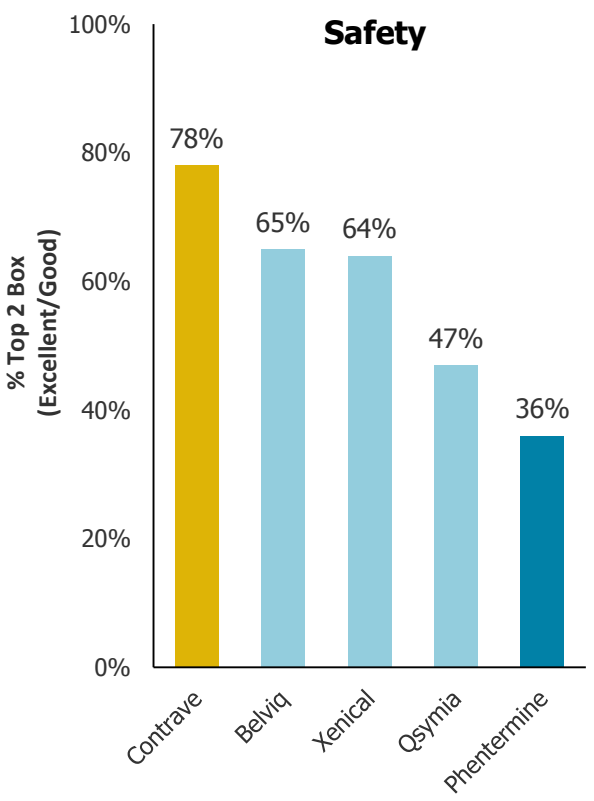
Q (HCP): Evaluate how well the following statement describes [brand]: "Works on two areas of the brain"



Q (HCP): Please rate [brand] on the following attributes: "Effective for long term weight loss"



Q (HCP): Please rate [brand] on the following attributes: "Overall safety"



Source: HCP ATU Survey; n=253 sampled from 20,000 rep target physicians; Mar/Apr 2017

Digital/Social Strategy Rollout

Website Launch

Facebook Page Launch

Instagram Page Launch

Pinterest Pilot Launch

YouTube Pilot Launch

Dec. | **Jan.** | **Feb.** | **Mar.** | **Apr.** | **May** | **2H 2017**

Get Contrave Now Pilot (CA/TX)

Paid Video & Banner

Paid Facebook

Paid Get Contrave Now Facebook

Paid Instagram

Telemedicine & Free Home Delivery National Pilot Launch

Facebook/ Instagram Testimonial Posts

Twitter Pilot Launch

Patient Activation Campaign is Driving a Significant Increase in Patient Interest and Action

Digital/Social Campaign Metrics			
Key Strategic Metrics	**Status**		**Status**
Total DTC Impressions	1.8B	Digital Impressions	288M
Contrave.com Sessions	3.1M	Contrave.com Engagements* (%)	36%
KPIs	**Status**		**Status**
Unique Site Visitors	2.2M	Find a Doctor Pageviews	403K
% of Contrave.com Sessions from Search	58%	Doctor Discussion Guide Prints	13K
% of Contrave.com Sessions from Video	20%	Get Contrave Now Pageviews	208K
Savings Card Pageviews	276K	Emails Sent	190K
Savings Card Enrollments on Web	132K	Video Views on Social Media	2.4M
Savings Card Conversion to Rx Rate	63%	Facebook Reach	22.8M

*Engagement rate = [(FAD + GCN + Enrollment pageviews) + (Savings Card Enrollments + DDG Prints)] / Contrave.com sessions

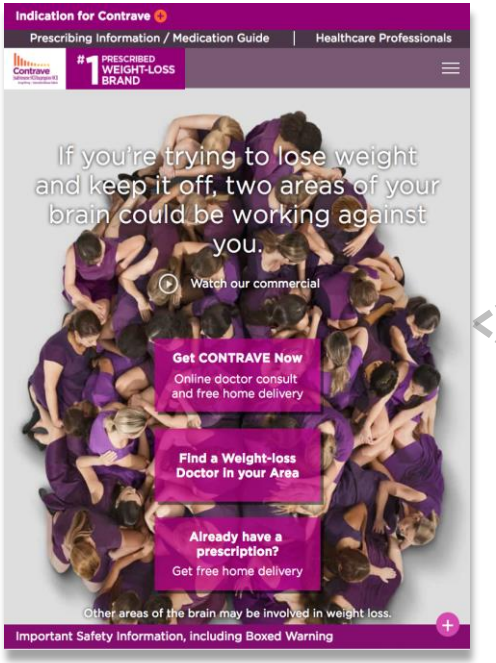
Orexigen is driving a fundamental change in the patient journey

End-to-end Telemedicine Process for Contrave

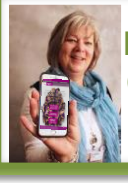
Broadcast TV

Digital Activation

Branded Site: Contrave



Return to Contrave Rx



Telemedicine*

Virtual Consultation

Patient chooses preferred HCP interaction

Patient Visits HCP Office

Traditional

eRx

eRx

Rx

Free Home Delivery*

On-line Pharmacy
Ships to Patient

Patient chooses preferred pharmacy

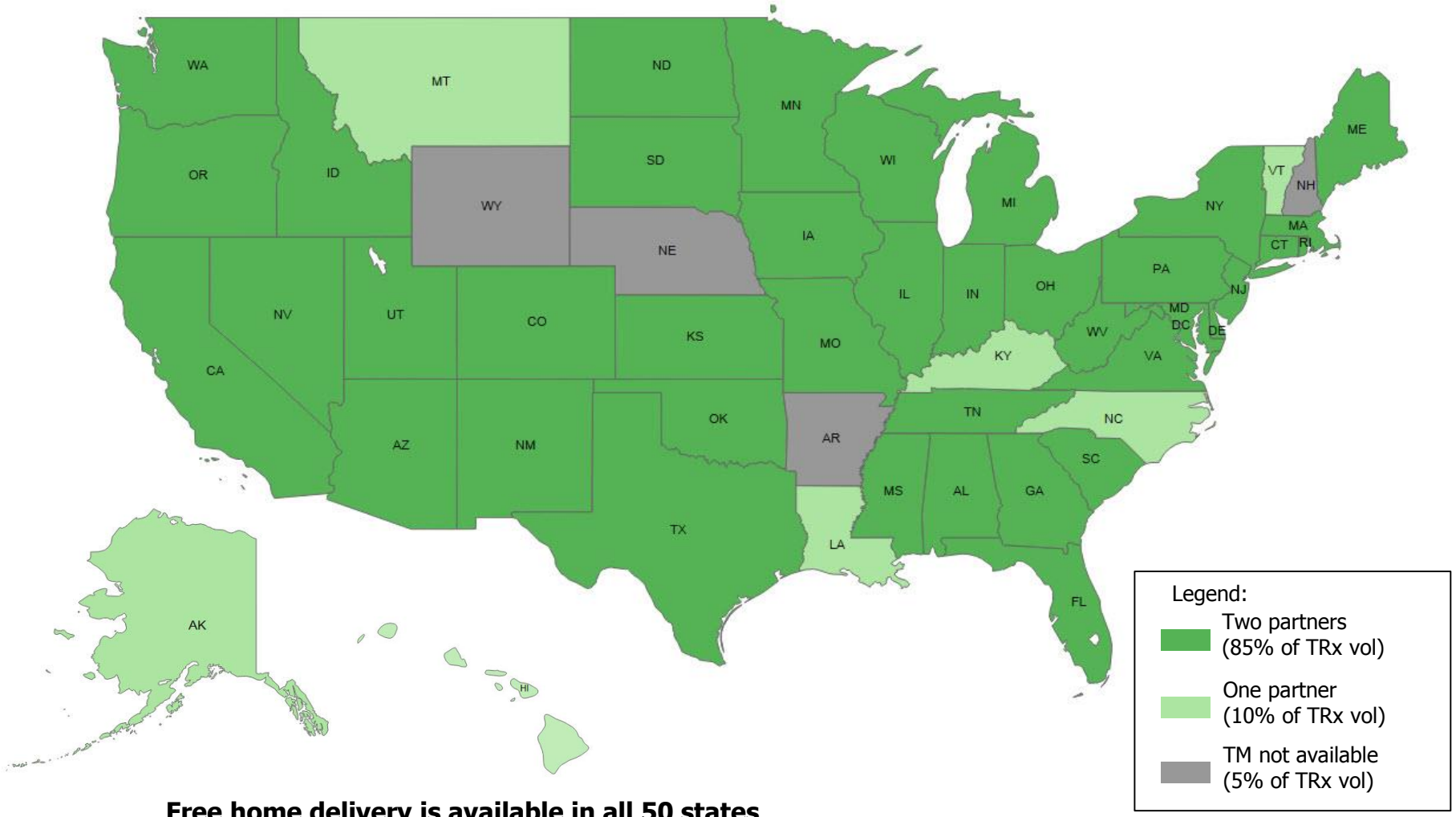
Patient Picks Up at Retail Pharmacy

Traditional

Patient engagement data is gathered at every step of the treatment process to improve end-to-end patient experience

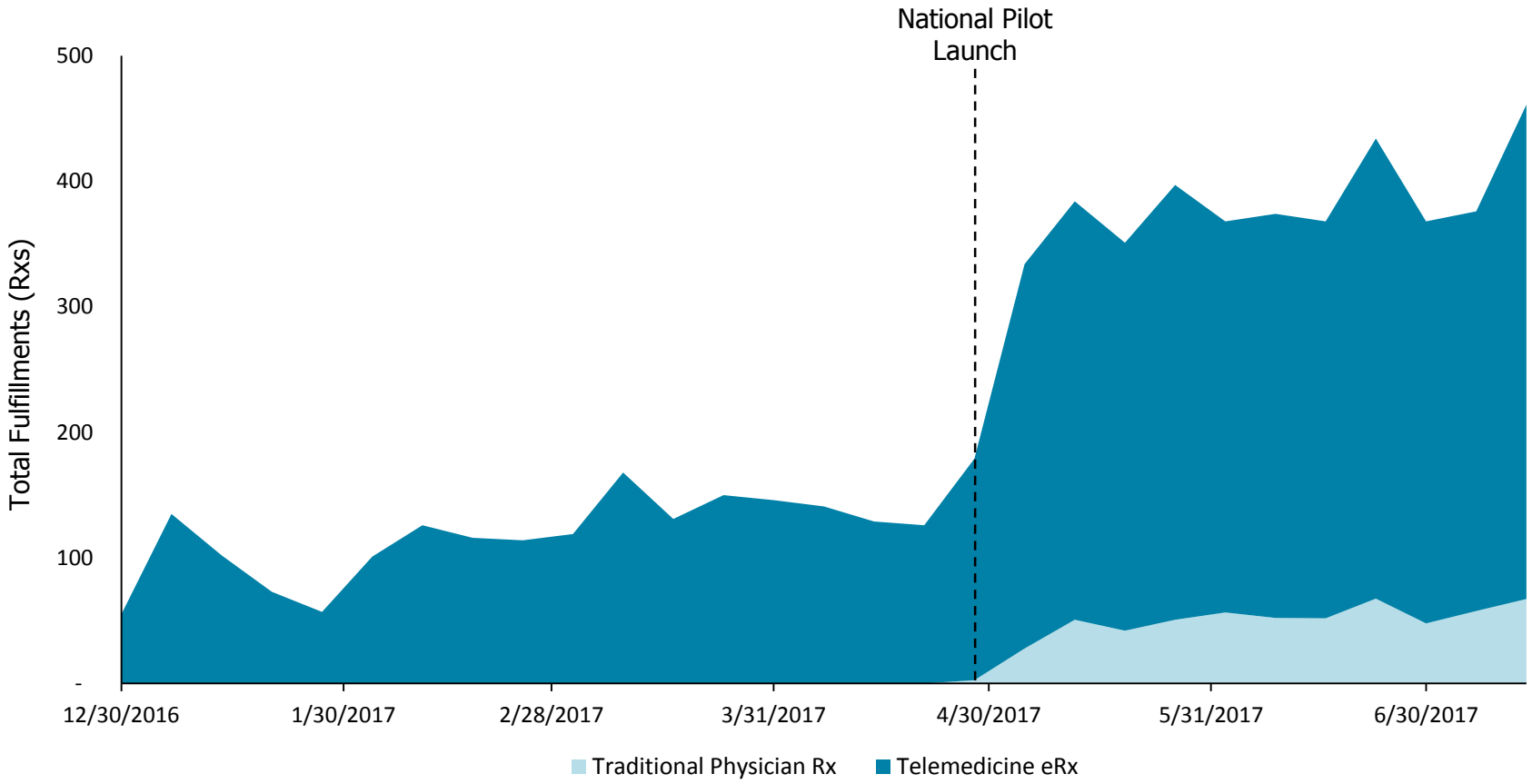
* The online doctor consult and free home delivery services are offered by our partners

Telemedicine is now available in 46 states with patient choice in provider available in 39 states



Free home delivery is available in all 50 states

Strong Growth in Our Free Home Delivery Channel, Driven by Telemedicine



Source: Partner provided fulfillment reports

Commercial Coverage of Contrave Driven by National Health Plan/PBM Coverage and Employer Opt-in

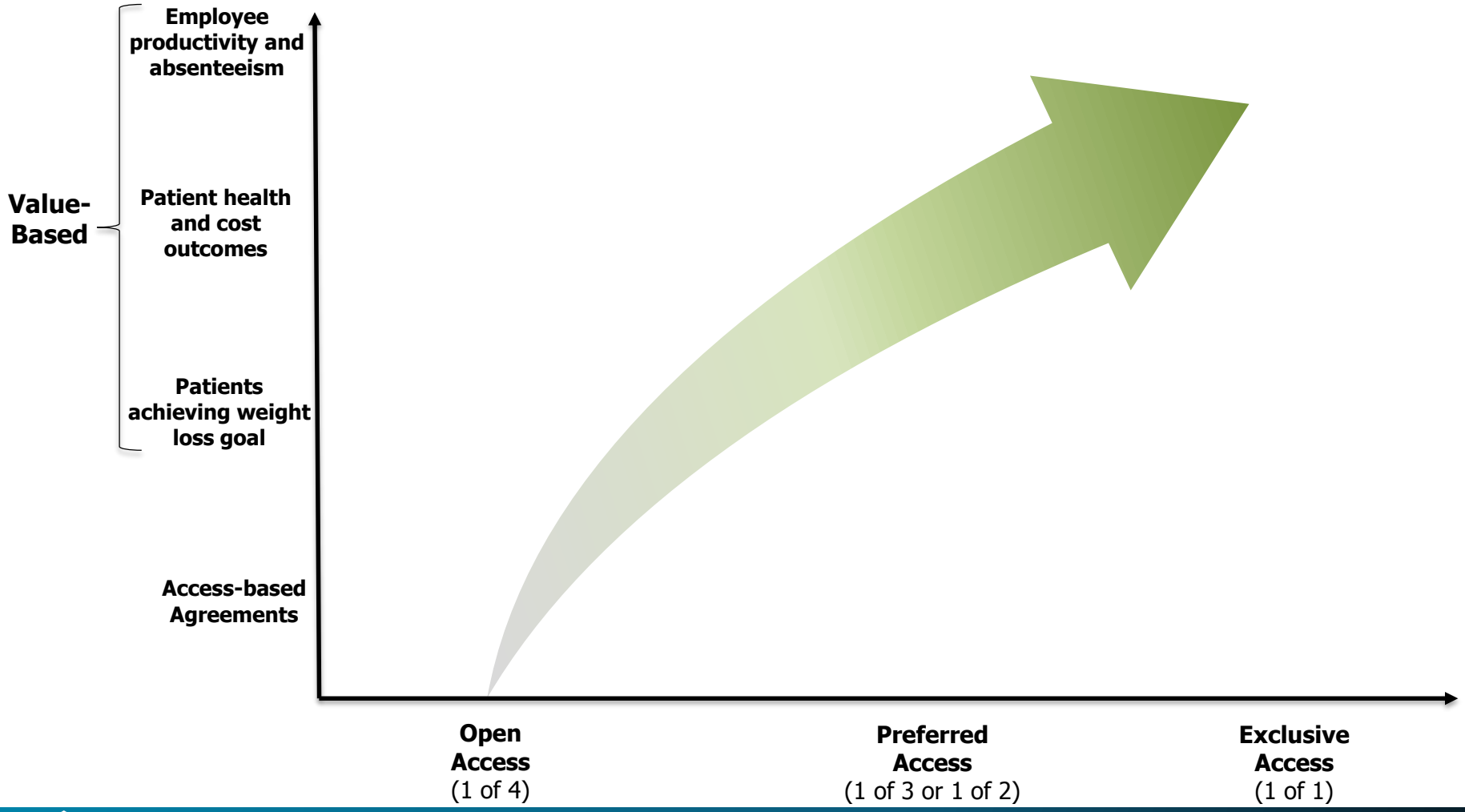
73% National Coverage (~100M Lives)

>200 Large Employers (opted in to obesity Rx coverage)

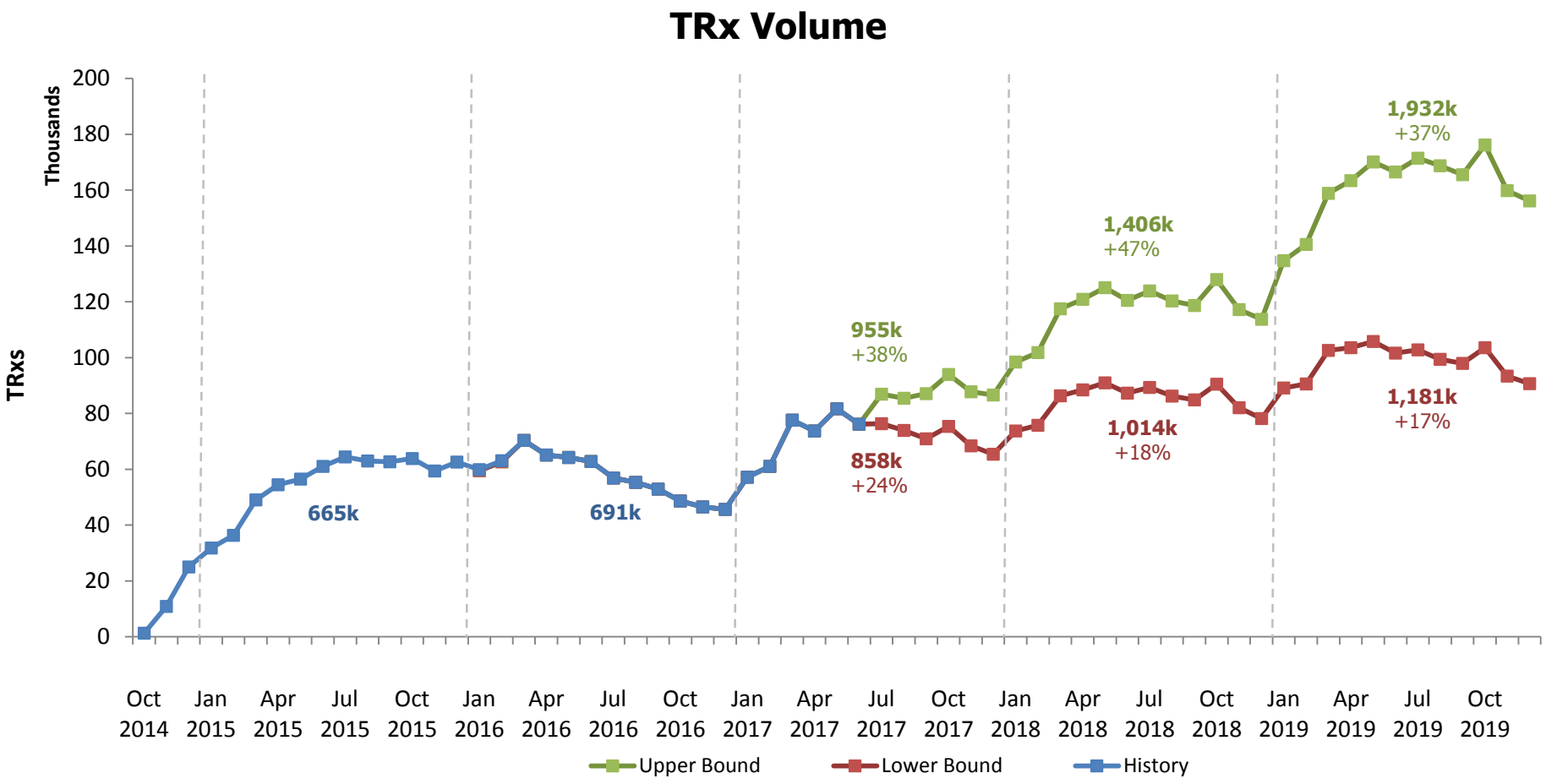
Source: Fingertip Formulary, June 2017
Note: Coverage includes tier 1-5; may be understated due to data limitation (N/A); N/A for Contrave ~6%

Orexigen Contracting Strategy: Value-Based Agreements

Orexigen Strategy is to vary the price of Contrave based on patient outcome achieved



We Project Strong Double Digit Growth of Contrave



Source: IMS NPA; Orexigen estimates.

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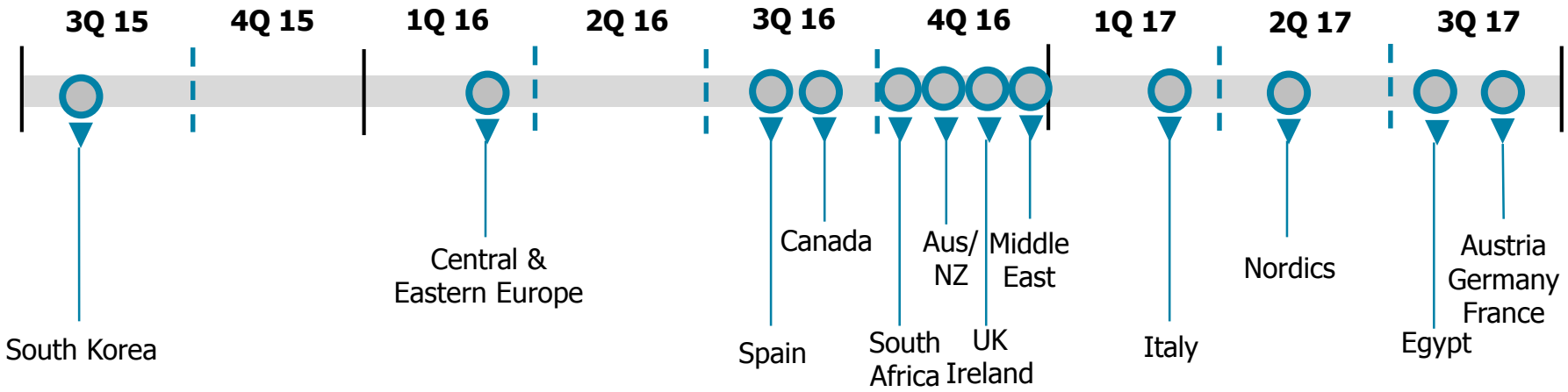
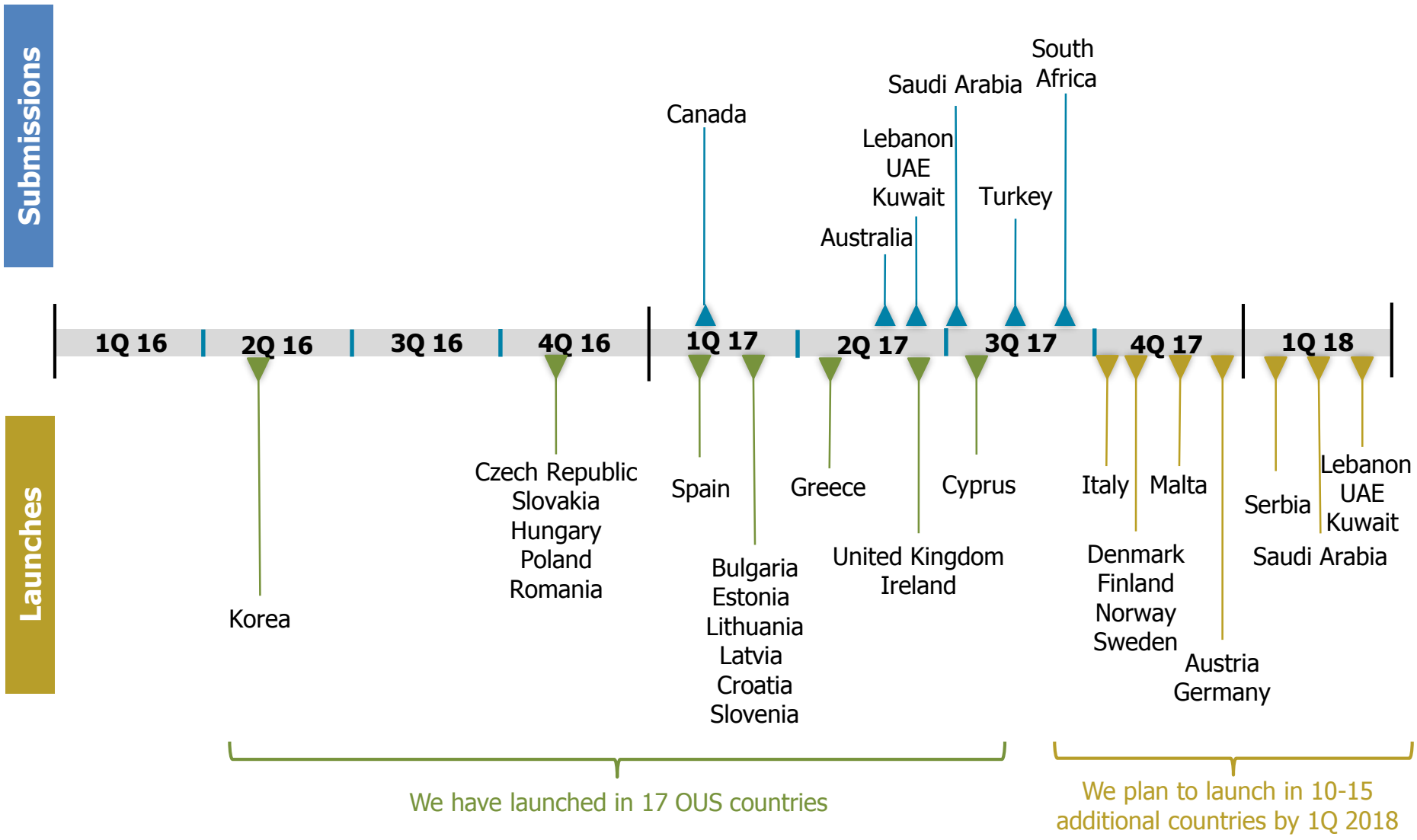
Now Partnered in 48 Countries Outside the U.S.



2017 Goal: Add 10-15 additional countries, with a focus on Latin America and Europe

Now Launched in 17 Countries Outside the U.S.



Commercial Summary

- **Execution Excellence:** speed and quality exceeding expectations
- **Strong Sustainable Growth:** projecting strong and sustainable growth over planning horizon
- **Innovative Commercial Model:** increasing efficiency and profitability as model evolves

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Pete Flynn
Global Head of Development, Regulatory & Safety

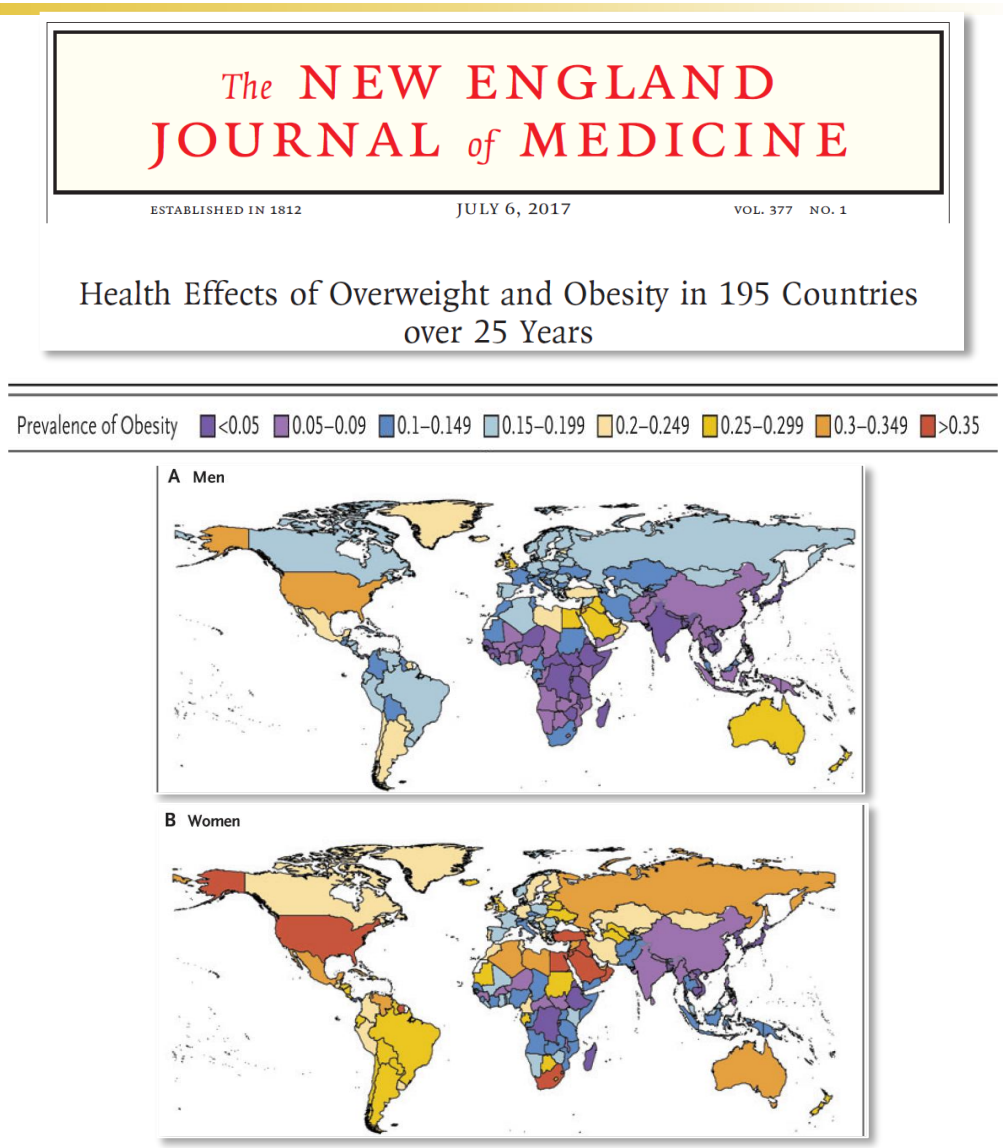
Q2 2017 Update

Q2 Regulatory Update: Submissions

- Completed regulatory submissions for marketing authorization in Canada, Australia, Lebanon, UAE, Kuwait and Saudi Arabia
  - Working with local distribution partners and regulatory authorities
  - Potential regulatory approvals throughout 2018
- Several additional submissions in Q3-Q4 2017

Obesity: A Global Epidemic

- Global Burden of Disease study data analyzed from 68.5 million persons between 1980 and 2015 across 195 counties
- Assessed the trends in the prevalence of overweight and obesity among children and adults
- Since 1980 the prevalence of obesity has doubled in more than 70 countries
- Global levels now at >600M adults and >100M children
- Prevalence of Obesity ~20-35% across most of the developed and developing world



Medical Affairs Support for Global Partners

2017 EUROPEAN CONGRESS ON OBESITY
INDUSTRY-SUPPORTED SATELLITE SYMPOSIUM

Integrating Pharmacotherapy Into Obesity Management

Thursday, 18 May 2017
13:15–14:45
Alfândega Porto Congress Centre
Infante Hall
Porto, Portugal

Overview

Integrating pharmacotherapy into obesity management has, until recently, been limited. Increased understanding of the neural pathways associated with regulating hunger, cravings, and eating behaviour has led to a different approach for managing obesity as a chronic disease: by targeting the brain. By aligning treatment to these mechanisms of disease, clinicians can more effectively assist patients in achieving not only clinically meaningful weight loss, but also broader benefits such as reductions in cardio-metabolic risk and an improved quality of life.

Join your colleagues and a distinguished panel of obesity experts as they discuss the important role of pharmacotherapy in the management of obesity, and learn more about the clinical trial evidence and practical experience with naltrexone HCl/bupropion HCl as a component of an effective weight loss and maintenance treatment plan in patients who struggle with obesity.

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This symposium is sponsored by Orexigen Therapeutics, Inc.
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MYS-0082-001 April 2017

Programme Agenda and Faculty

Obesity Pharmacotherapy: Evolving Clinical Practice to Align With Mechanism of Disease
Prof. Mike Lean, MA, MB, BChir, FRCP, FRCPS
Professor, Human Nutrition
University of Glasgow School of Medicine, Dentistry and Nursing
Glasgow, United Kingdom

Naltrexone HCl/Bupropion HCl Clinical Evidence: Reducing Hunger, Controlling Cravings, Sustaining Weight Loss
Prof. Felipe F. Casanueva, MD, PhD
Head, Department of Endocrinology and Nutrition
Complejo Hospitalario Universitario de Santiago
Santiago, Spain

Insights Into the Use of Naltrexone HCl/ Bupropion HCl: Clinical Experience in the United States
Deborah Bade Horn, DO, MPH, MFOMA
President, Obesity Medicine Association
Medical Director, Center for Obesity Medicine and Metabolic Performance
University of Texas Health Science Center
Houston, Texas, United Sates

- NB is Well Tolerated and Had No Effect on Serious Adverse Events in Participants Receiving Antidepressant Medication, Including SSRIs, in a Large Randomized Double-Blind Study

- Effect on Body Weight of Naltrexone/Bupropion (NB) in Overweight and Obese Participants with Cardiovascular Risk Factors in a Large Randomized Double-Blind Study

- **Halseth A[1], Gilder K[1], Shan K[1], Acevedo L[1], Smith S[2], Buse J[3]**

Ongoing Data Publications Supporting the Medical Impact of Contrave

Early improvement in food cravings are associated with long-term weight loss success in a large clinical sample

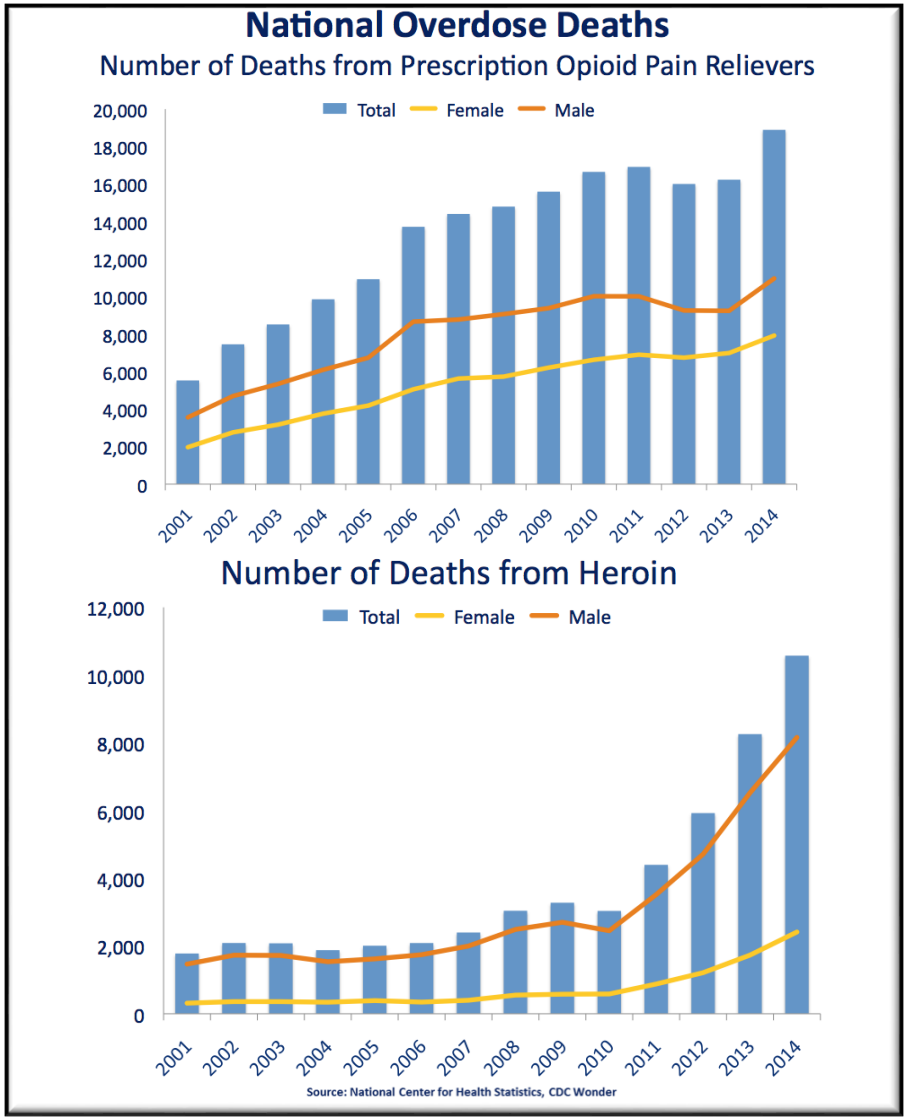
M Dalton, G Finlayson, B Walsh, A Er Halseth, C Duarte, J E Blundell

- April 4th 2017: Study published examining whether early changes in control of food craving was predictive of long-term weight loss
- Data collected across all four naltrexone/bupropion phase 3 studies
- Conclusion: patients with the greatest craving control at 8 wks had the greatest weight-loss at week 56

Opioid Epidemic: Burden of Disease

- 259M opioid prescriptions in 2012 written for the 48M people treated
- It is estimated that only 10% of patients treated with prescription opioids develop dependence
- In 2014, the most recent year for which data is available, >10M individuals reported using prescription opioids non-medically and 1M reported heroin use
- Admissions to substance-abuse treatment programs more than quadrupled (2002-2012)
- In 2014 there were 18,893 deaths from prescription-opioid overdose (a 4x increase over 2001) and 10,574 deaths from heroin (a 5x increase over 2001)

With ~30,000 overdose deaths in 2014, opioid addiction is being recognized as an urgent public health epidemic in the U.S.



Sources: NEJM 2016;374:154-63; CDC Wonder

Opioid Addiction: A Need for New Treatments

- Recent NEJM special report on the opioid crisis
  - Francis Collins, Director NIH
  - Nora Volkow, Director NIDA

- Highlighted:
  - Need for new strategies and medication for the treatment of opioid addiction
  - Need for novel treatments for chronic pain that do not have the abuse profile of standard
  - Need for new strategies for overdose prevention and reversal
  - Public/private partnerships

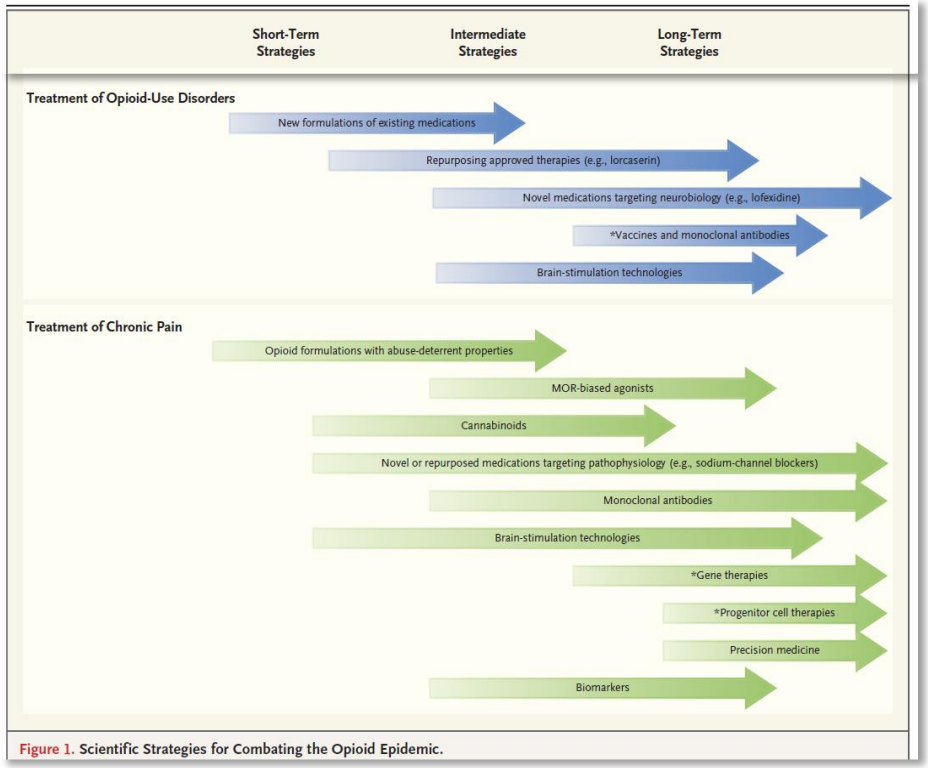


Figure 1. Scientific Strategies for Combating the Opioid Epidemic.

OREX-1038 Preclinical Asset: Profile and Key Data

Therapeutic Area	Chronic, out-patient analgesic medication for the treatment of nociceptive, inflammatory and neuropathic pain.
Value Proposition	Potent analgesic for chronic administration. Reduced abuse liability and adverse events associated with standard of care opioids, leading to greater regulatory, medical and patient acceptance.

- Member of 25 molecule naltrexone analogue series exclusively licensed by Orexigen
- Novel partial agonist activity at Mu opioid and Nociceptin receptors
- Significant, long-lasting analgesia in primates at doses >100x lower than Morphine
- Significant analgesia in models of postoperative and inflammatory pain
- Limited tolerance effect
- Significantly improved profile in primate self-administration addiction models and dependency studies compared to SOC opioid analgesics
- No constipation in preclinical models
- No pruritus in preclinical models
- No observed respiratory depression in preclinical models
- Promising ADME/safety profile
- Lead molecule + back-ups, national-stage IP

OREX-1019 Preclinical Asset: Profile and Key Data

Therapeutic Area	Opioid addiction treatment and relapse prevention
Value Proposition	Market currently fulfilled by few compounds: Methadone, Buprenorphine-containing products and Naltrexone. Potential niche for a product that has less inherent opioid-associated adverse effects than buprenorphine but without the withdrawal induction of naltrexone.

- Member of 15-molecule novel orvinol series exclusively licensed by Orexigen
- Novel opioid receptor activity profile places OREX-1019 between buprenorphine and naltrexone as a opioid antagonist
- Significant inhibition of opioid (prescription and heroin) self-administration in primates
- Significantly lower abuse liability profile than standard of care buprenorphine in primates
- Promising ADME/safety profile
- Issued IP: Composition, method of making, method of treating addiction and relapse prevention

OREXIGEN®

Jason Keyes
Chief Financial Officer

Q2 2017 Financial Results

Second Quarter 2017 Financial Results

- Revenue of $23.4M
  - $20.7M in US net sales of Contrave, a 69% increase compared to Q2 2016[a]
  - $2.7M in OUS net sales of Contrave to partners
- US average net revenue per unit sold of approximately $96, a 37% increase compared to Q2 2016
- Cost of Product Sales of $6.8M, reflecting US gross margins of 75%
- Operating expenses totaled $58.5M
  - Non-GAAP Cash Operating Expense of $53.2M[b]
- Operating Loss of $42.0M
  - Non-GAAP Operating Loss of $36.3M[b]
- Net Loss of $30.5M or $2.00 per share
  - 15.2M shares used for computing Q2 2017 net loss per share
- $86.6M in cash and marketable securities at the end of Q2 2017

a) In Q2 2016, Contrave net sales were booked by our former partner, and Orexigen earned royalties on those net sales
b) Reconciliation from GAAP to non-GAAP figures are provided at the end of this presentation

2017 Net Sales Expectations

	2017 Guidance
Orexigen Net Sales	$85M - $100M
US Net Sales	$75M - $85M
OUS Net Sales	$10M - $15M
Partner-Reported OUS Net Sales of Contrave / Mysimba	$10M - $15M

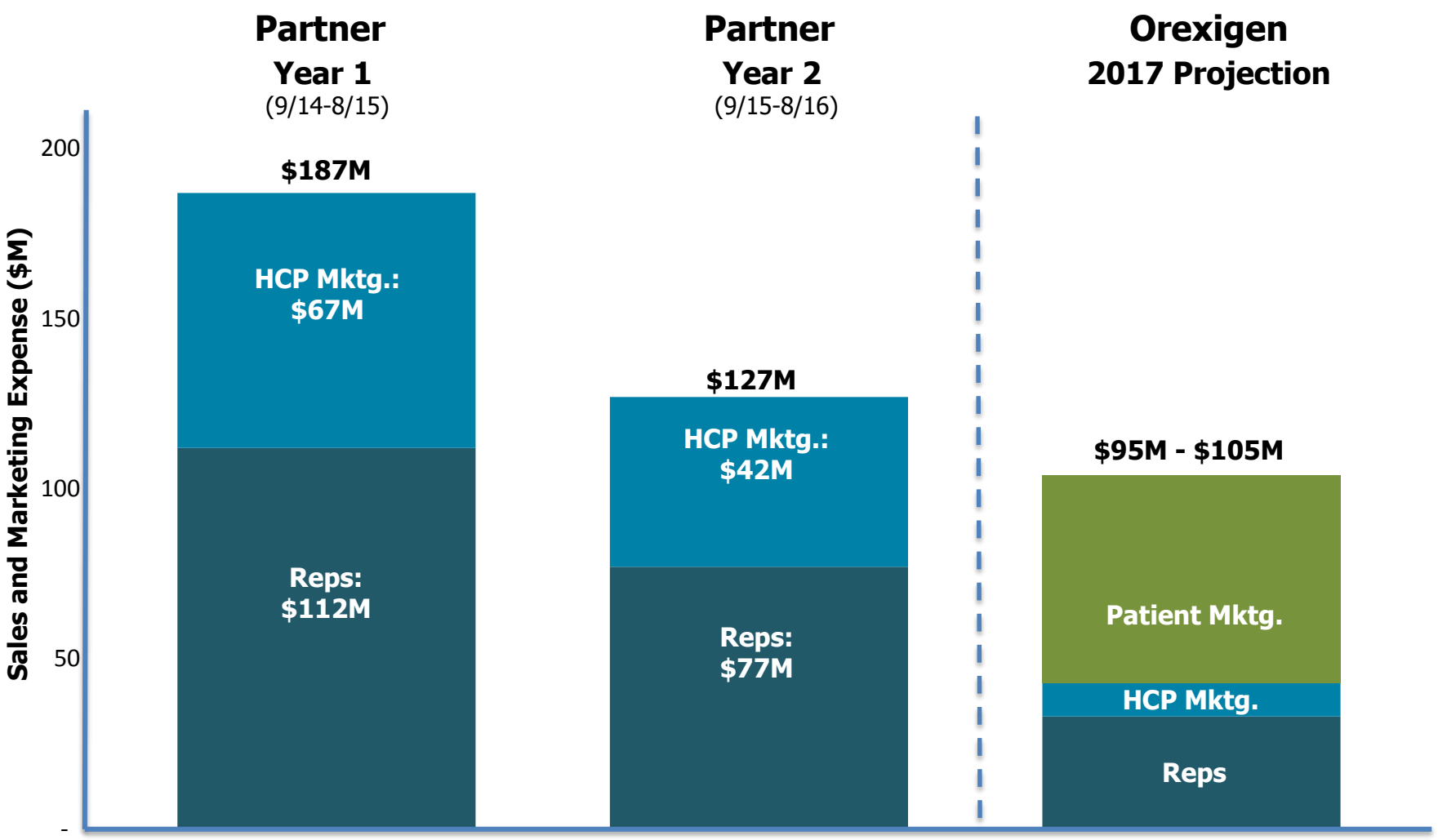
2017 Expense Guidance

	1H 2017 Actual	Full-Year 2017 Estimate
Total Cash Operating Expenses[1]	$113.7M	$180M - $200M
R&D[2]	$14.8M	$30M - $35M
Commercial	$82.5M	$125M - $135M
G&A	$16.4M	$25M - $30M
Ending Cash Balance[3]	$86.6M	$40M - $50M

Notes:
1. Defined as GAAP operating expense less stock compensation, depreciation, and other non-cash expenses outside the normal course of business operations
2. Includes the following areas: Research, Development, Regulatory Affairs, Safety, Technical Operations and Quality
3. Cash, cash equivalents, restricted cash, and marketable securities

Appendix

Re-Launch of Contrave: Aim to Significantly Grow Sales with a Lower Overall Sales and Marketing Spend by Changing the Approach



Note: Year 1 and 2 base sales expense assume $125 per PDE with 800K and 600K PDEs, respectively with sales training and logistic expenses added incrementally ($12M and $2M); 2. Year 1 and 2 HCP Promotion and DTC spend is an estimated split based on guidance provided in publicly available 8K documents; 3. Year 2 marketing spend estimated to be flat to contractual obligations of $50M

Non-GAAP Financial Measures

- This presentation includes information relating to non-GAAP operating expense and non-GAAP operating results, which the Securities and Exchange Commission has defined as "non-GAAP financial measures." Non-GAAP operating expense and non-GAAP operating results have been included in this presentation because they have been adjusted for non-cash items such as depreciation, amortization and stock-based compensation, as well as certain one-time non-recurring accounting charges. These metrics aid Orexigen management and its board of directors in understanding and comparing the financial performance for the quarter to core operating performance and trends, and to develop short- and long-term operational plans. The presentation of this financial information, which is not prepared under any comprehensive set of accounting rules or principles, is not intended to be considered in isolation or as a substitute for the financial information prepared and presented in accordance with generally accepted accounting principles in the United States ("GAAP").

- Non-GAAP operating expense and non-GAAP operating results have limitations as analytical tools, and you should not consider them in isolation or as substitutes for analysis of Orexigen's financial results as reported under GAAP. Because of these limitations, you should consider non-GAAP operating expense and non-GAAP operating results alongside other financial performance measures, including GAAP operating expense and GAAP operating results. For a reconciliation of non-GAAP financial measures to the nearest comparable GAAP measures, see the non-GAAP reconciliations included at the end of this presentation.

Reconciliation of GAAP to Non-GAAP Financial Measures

Reconciliation from GAAP Operating Expenses to Non-GAAP Cash Operating Expenses ($000)
Quarter Ended June 30, 2017

	R&D	Sales & Marketing	G&A	Amortization Expense of Intangible Assets	Change in Fair Value of Contingent Consideration	Total
GAAP Operating Expense	$7,509	$38,128	$10,183	$1,984	$700	$58,504
Stock Compensation	($301)	($810)	($1,443)	---	---	($2,554)
Depreciation	---	---	($81)	---	---	($81)
Amortization Expense of Intangible Assets	---	---	---	($1,984)	---	($1,984)
Change in Fair Value of Contingent Consideration	---	---	---	---	($700)	($700)
Non-GAAP Cash Operating Expense	$7,208	$37,318	$8,659	$0	$0	$53,185

Reconciliation of GAAP to Non-GAAP Operating Loss

Reconciliation of GAAP to non-GAAP Operating Loss	Three Months Ended June 30, 2017 ($000)	Three Months Ended June 30, 2016 ($000)
GAAP Operating Loss	($41,990)	($33,233)
Amortization Expense of Intangible Assets	$1,984	---
Change in Fair Value of Contingent Consideration	$700	---
Stock Compensation Expense	$2,846	$2,311
Depreciation	$115	$117
Non-GAAP Operating Loss	($36,345)	($30,805)