OREXIGEN®

2017 BIO Investor Forum

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Chief Executive Officer

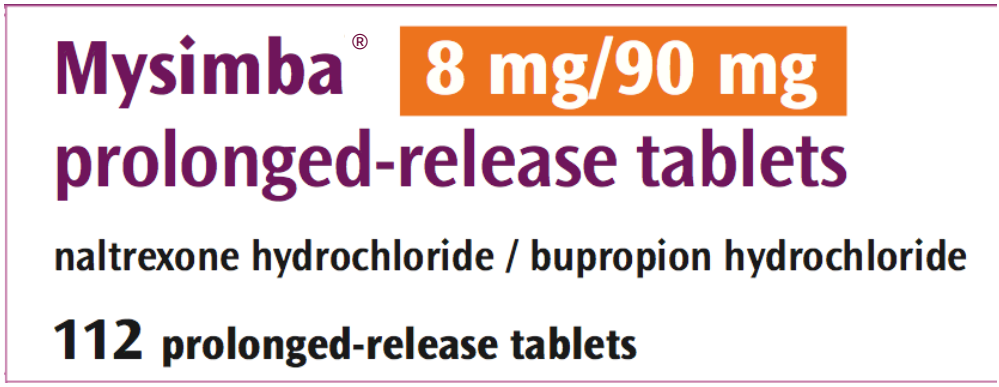
October 17, 2017

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 presentation 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 was filed with the Securities and Exchange Commission on 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.

Recent Patent Judgment provides exclusivity to 2030

- U.S. District Court for the District of Delaware issued ruling in favor of Orexigen in the litigation against Actavis on October 13 upholding the validity of all of three patents involved in the case
- As Orexigen progresses on its path to profitability by 2019, the exclusivity through 2030 supports many valuable years of growing profitability for Contrave, especially given the high barriers to entry faced by potential new competitors
- Orexigen filed the suit in response to an Abbreviated New Drug Application (ANDA) filed by Actavis, which sought to market and sell a generic version of Contrave tablets, prior to the expiration of U.S. patents listed in the FDA's Orange Book

Patent	Claim Description	Expiration	Ruling
7,375,111	Fixed dose of bupropion SR and naltrexone SR for treatment of obesity	**3/26/25**	**Favorable**
7,462,626	Methods of treating obesity with a combination of bupropion and naltrexone	**7/20/24**	**Favorable**
8,916,195	Treating obesity using 360 mg of bupropion and 32 mg of naltrexone where the naltrexone meets a specified sustained-release dissolution profile	**2/2/30**	**Favorable**

Overall Business Performance: Key Takeaways

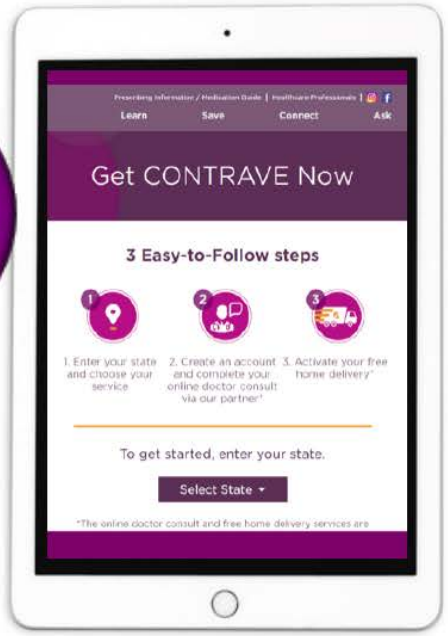
- First year results after re-purchasing US rights from our former partner are very positive, with about half of the prior spend
- Aided by Orexigen's consumer-focused campaign, Contrave achieved new all time highs in volume, share, and net revenue per Rx
- Learning from our first year of commercialization, we have begun our second year with innovative strategies that we believe will drive even greater efficiencies
- Projecting strong 2018 net sales growth, building from a new, larger base of consumer awareness and overall demand
- Projecting lower operating expenses for 2018 and Long Range Plan
- Remain on track for profitability by 2019, with patent coverage through 2030

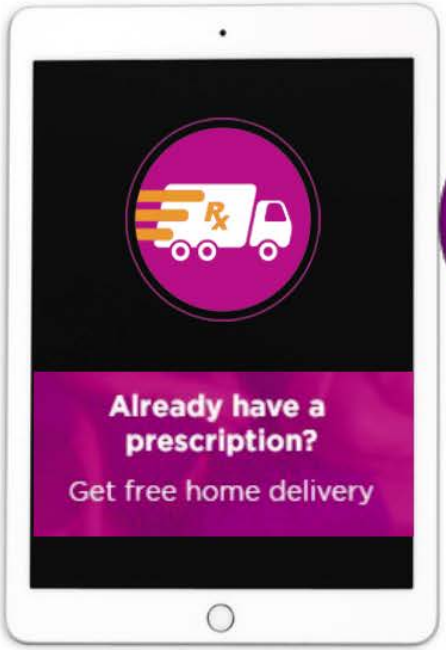
September 2017 Commercial Campaign

- Plan to activate patients during the Fall season where “back to school, back to routine, back to you” themes can activate weight loss patients
- Focus patients on Telemedicine and Free Home Delivery via “Get Contrave Now”
- Main activity runs from mid August to mid October
- Key Elements of Plan:
  - Fall Season TV Advertising Campaign
  - New Call to Action for Television Ad
  - New Digital/Social Executions
  - New Targeting Strategy
  - Customer Relationship Database e-blasts
  - Sales Force Messaging Aligned with Campaign
  - Active promotion of Free Home Delivery for all customers
- Learnings to be applied to launch of 2018 season – start 2018 from a higher base of awareness and demand

Get Contrave Now: Telemedicine and Free Home Delivery are Creating a Retail Experience for Patients

Specific types of patients **online**



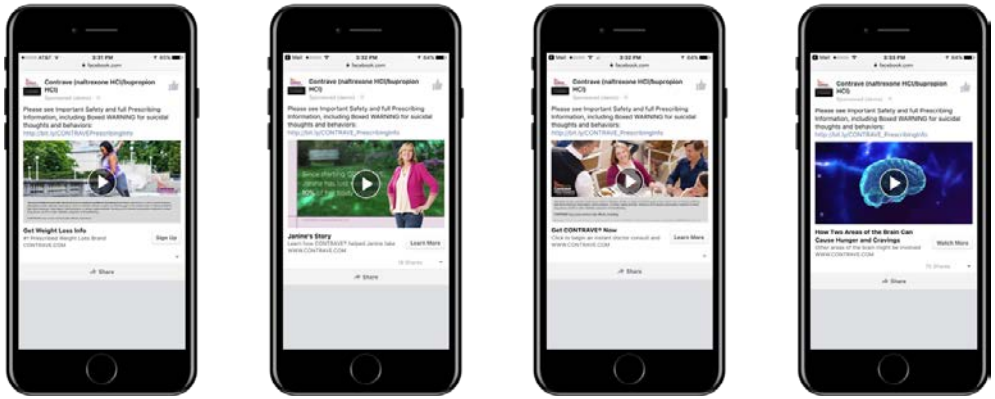


Any cash patient **online and in office**

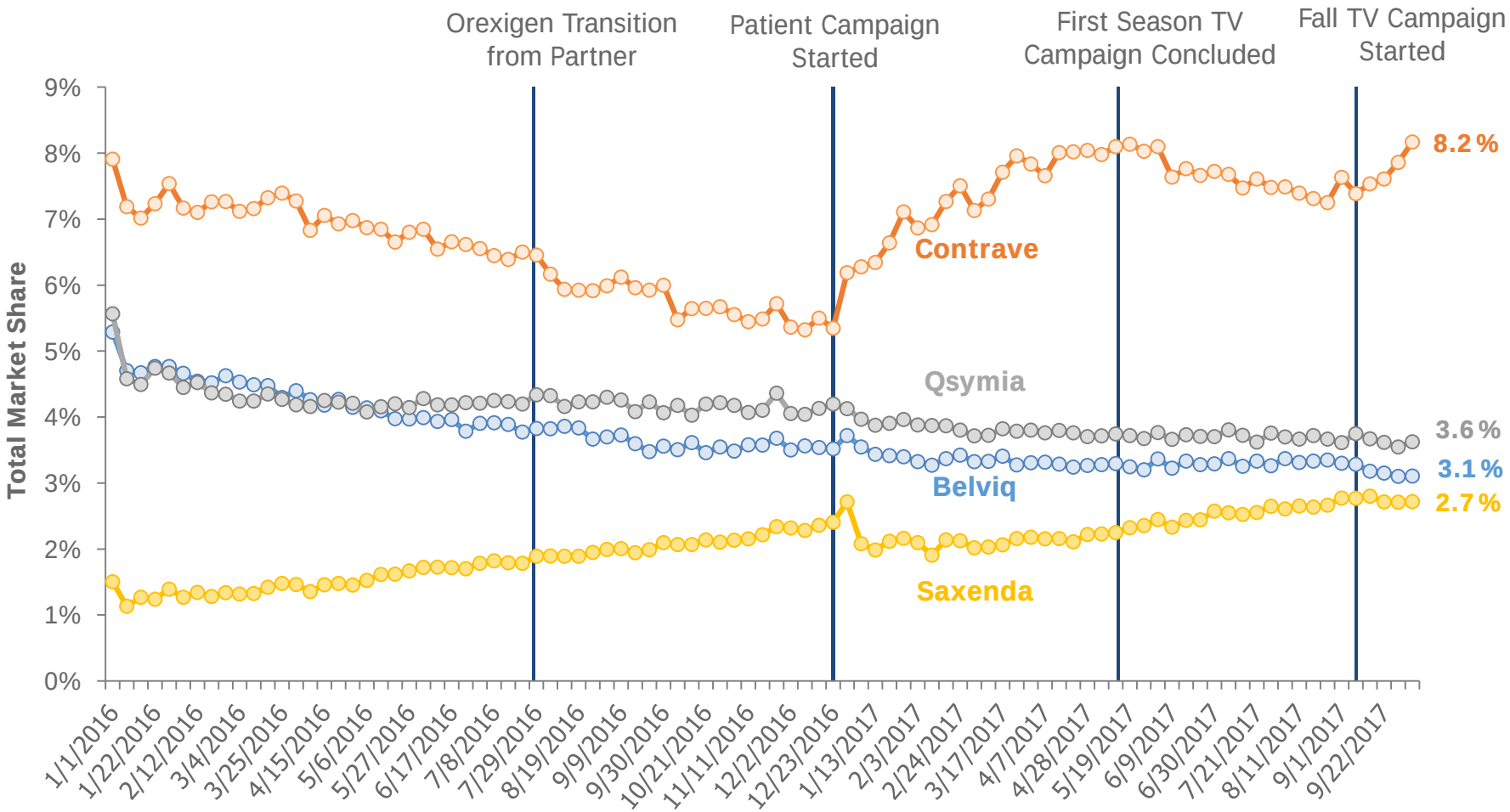
Normalizing Prescription Therapy as Part of Weight Loss Regimens

Fall Campaign and a New Call to Action for “Get Contrave Now” with getcontravenow.com URL in all TV/Digital DTC ads

“Now you can talk to a doctor online and get free shipping at getcontravenow.com”
(URL directs to homepage)



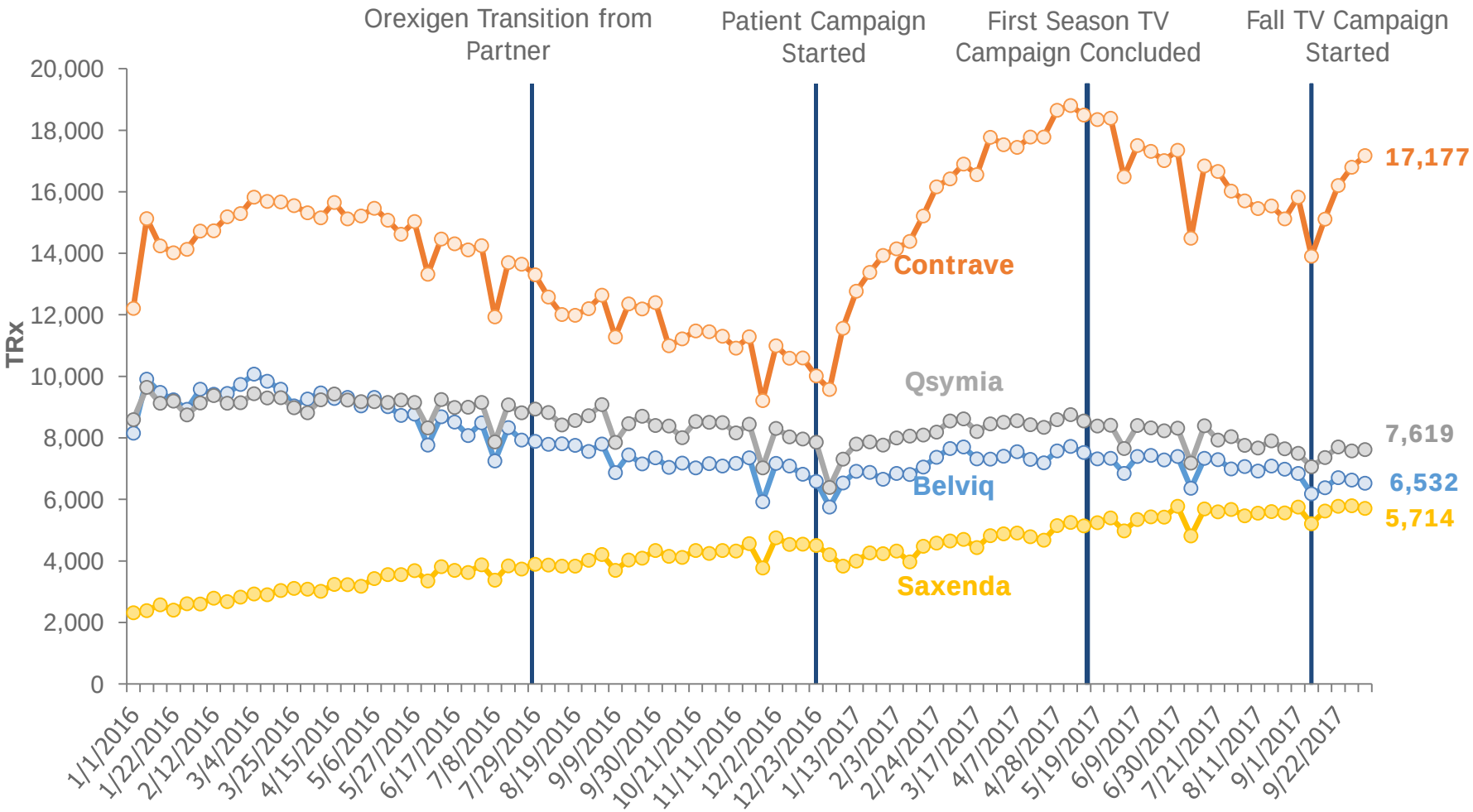
Contrave Weekly Market Share – All Time Market Share High



Source: QuintilesIMS NPA Weekly, Week Ending 10/06/17

Note:
Digital and Print Ads are still active after 2nd week of May
Fall Campaign started 9/10

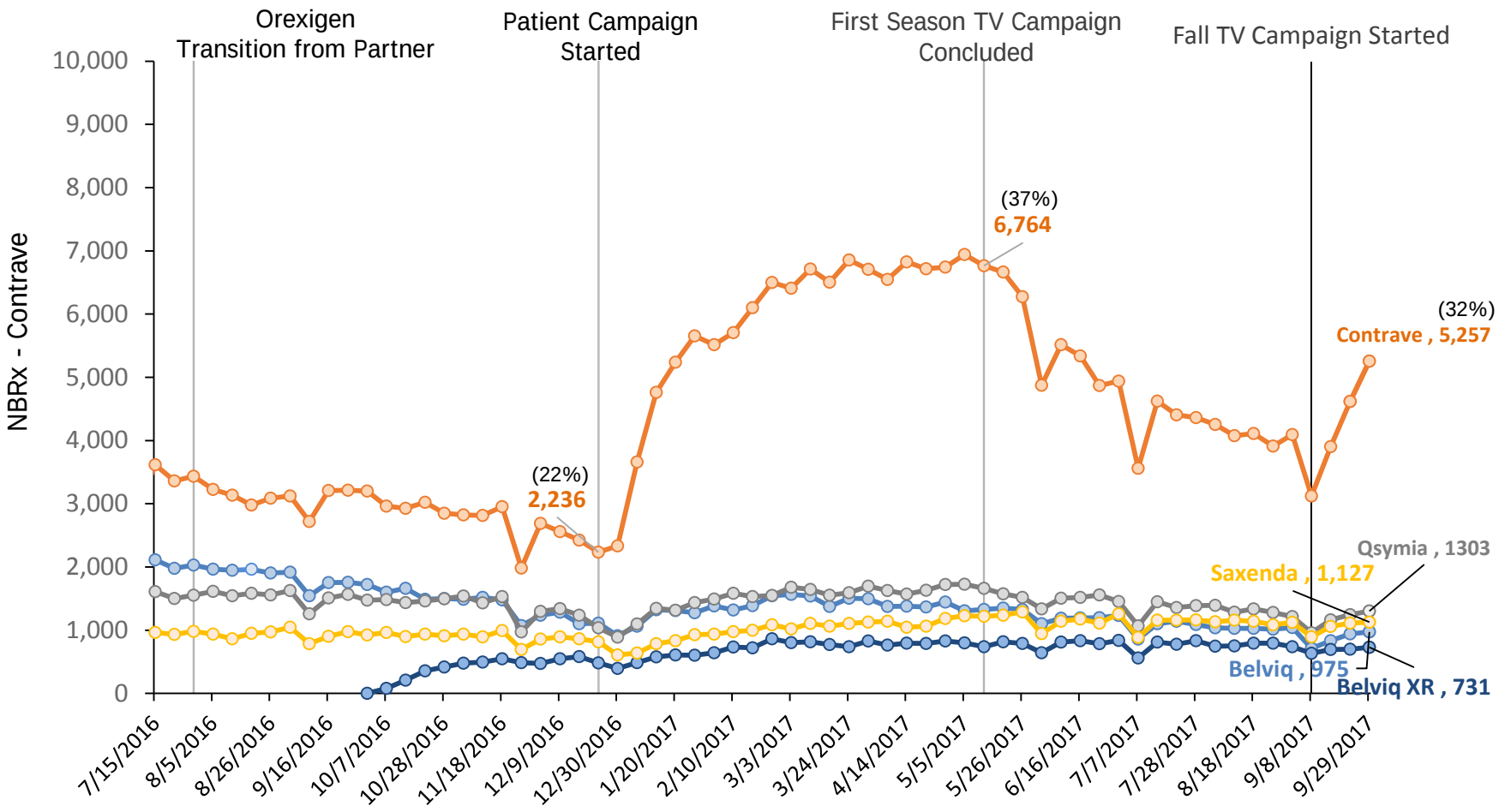
Contrave TRx Volume Approaching Prior Highs, Responding Well to the Promotional Campaign Kicked Off in September



Source: QuintilesIMS NPA Weekly, Week Ending 10/06/17

Contrave NBRx Volume has Jumped Nearly 70% in Response to Recent Promotional Tactics

(%) = NBRx as % of TRx



Source: QuintilesIMS Market Dynamics, Week Ending 9/29/17

Note:
Digital and Print Ads are still active after 2nd week of May
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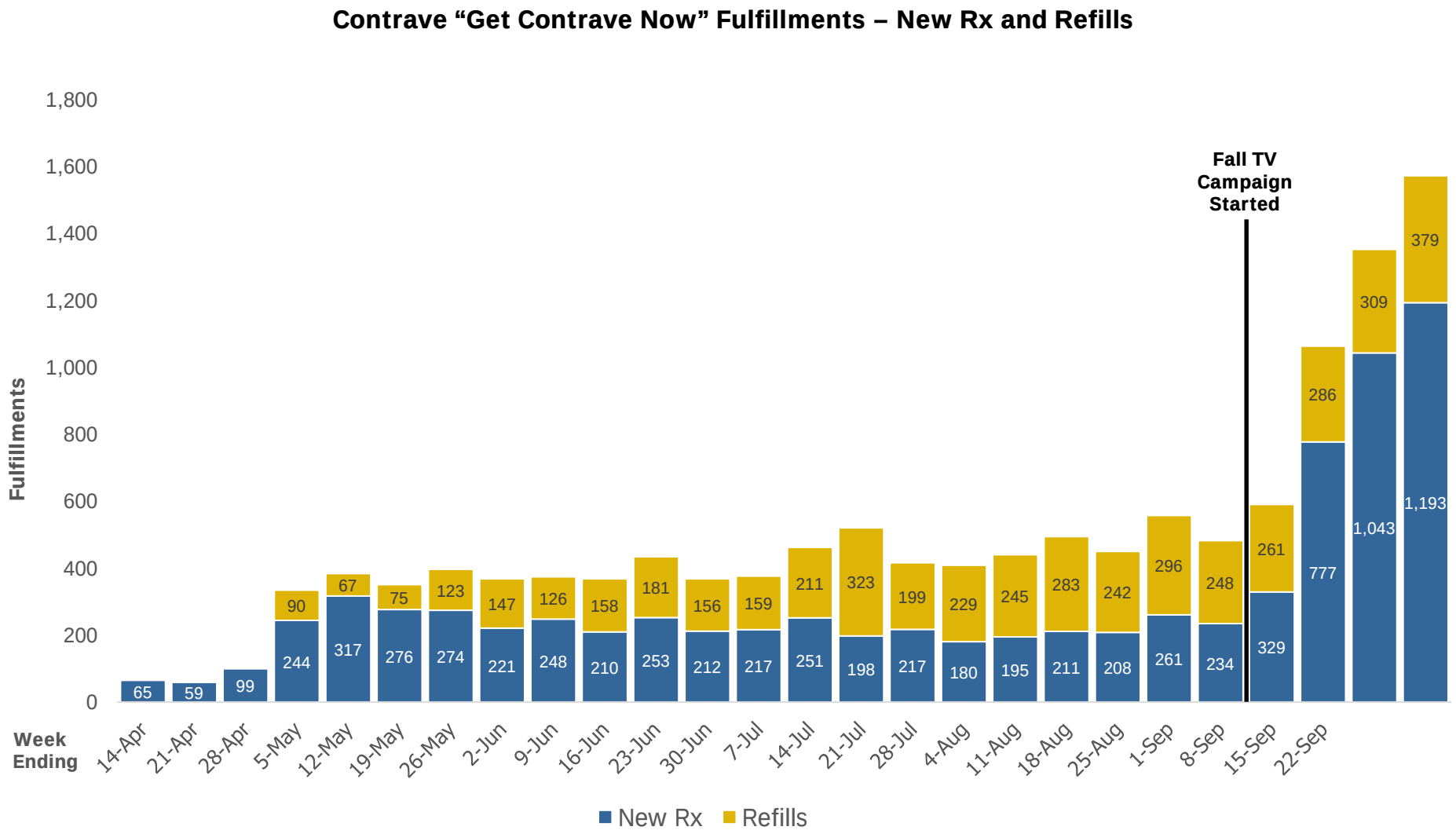
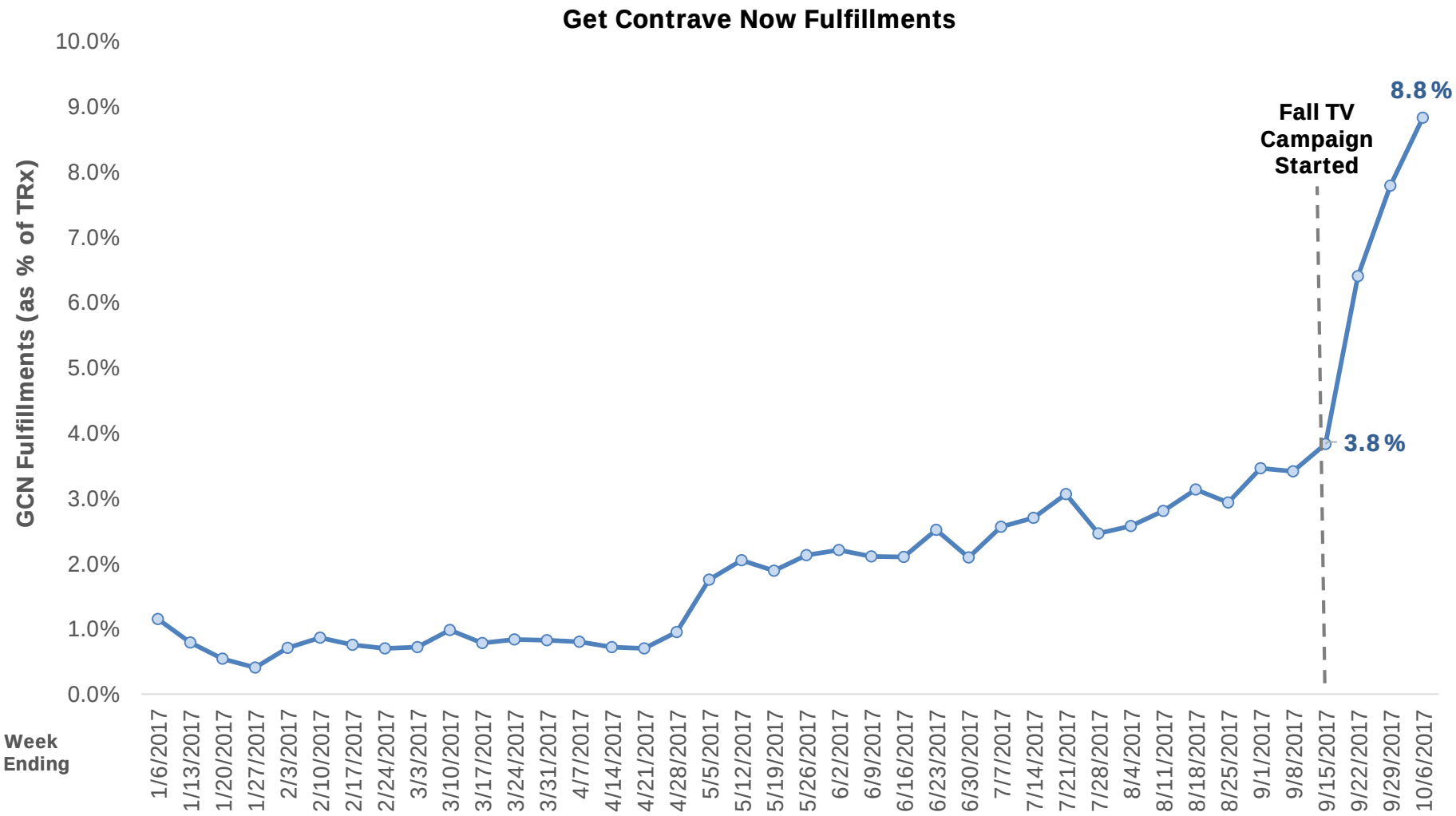
Telemedicine and Home Delivery New Prescription and Refill Rates Supported by Customer Service Model



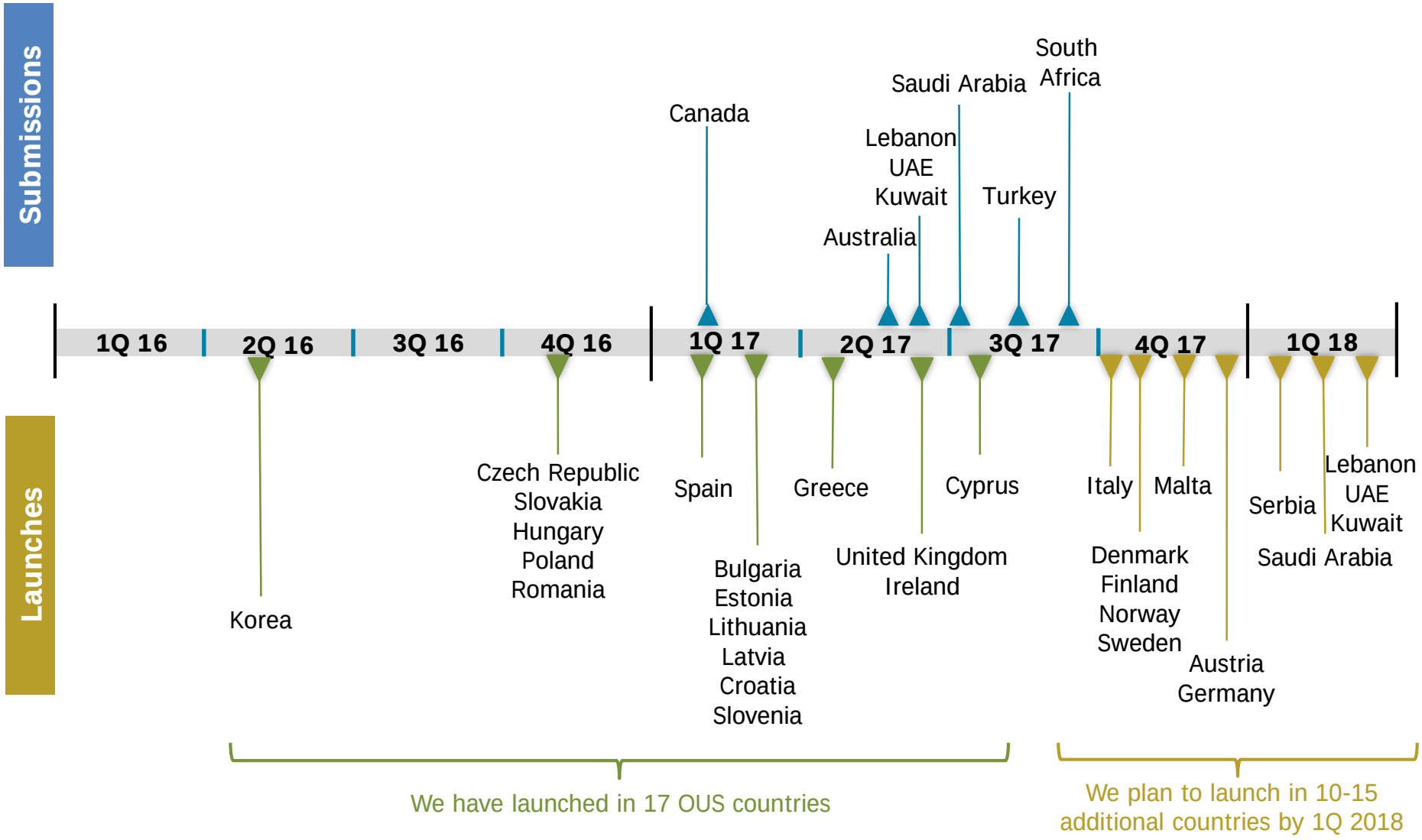
Source: Orexigen Therapeutics

Get Contrave Now fulfillments as % of TRx



Source: Orexigen Therapeutics, QuintilesIMS

Contrave/Mysimba Launched in 17 Countries Outside the U.S., with 10-15 New Launches on Track and Expected by the End of Q1 2018



OREXIGEN®

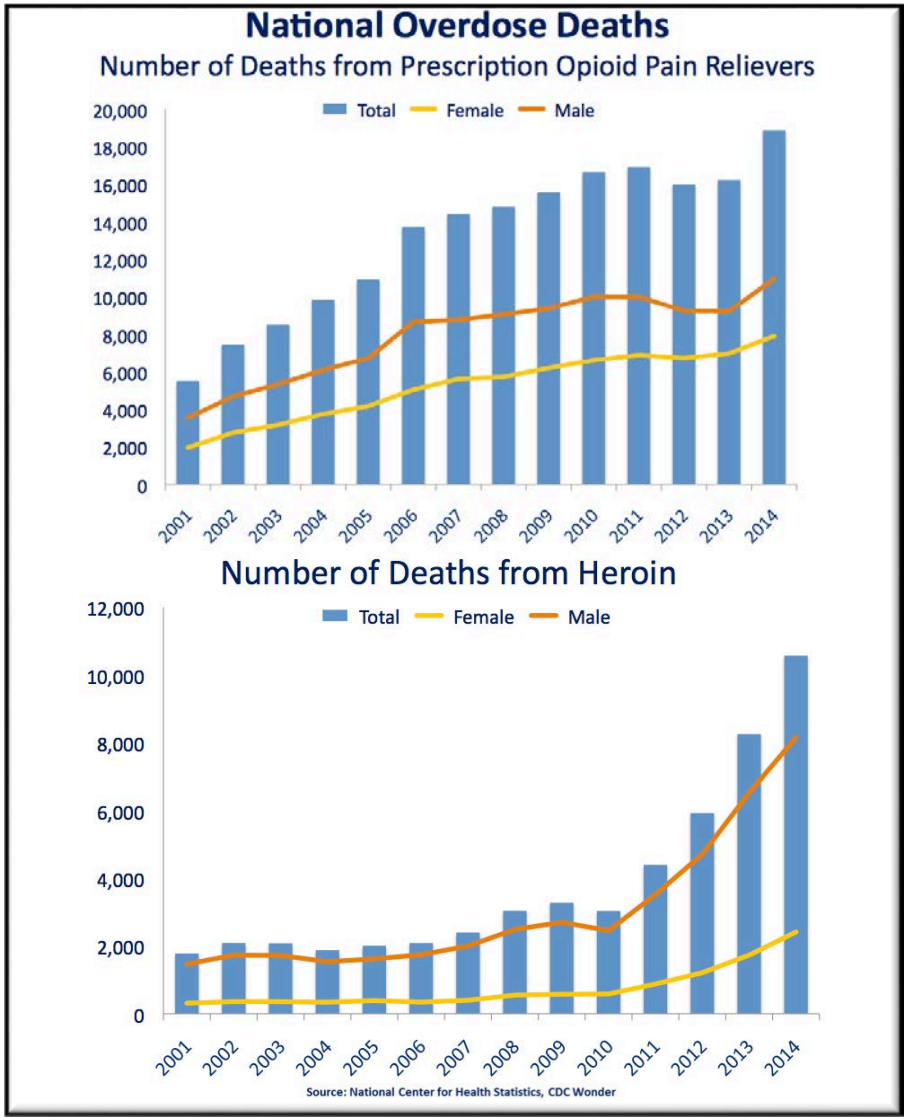
Preclinical Development Assets

Orex-1038: Chronic Pain Analgesic
Orex-1019: Opioid Addiction Management

The Opioid Addiction Public Health Epidemic

- 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, >10,000,000 individuals reported using prescription opioids non-medically and 1,000,000 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 US.



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

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 SoC 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 on chronic dosing (unlike Morphine)
- 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
- 9 months to IND, 2 years to Human POC

OREX-1019 Preclinical Asset: Profile and Key Data

Therapeutic Area	Opioid addiction treatment and relapse prevention (Stress-induced and drug induced relapse prevention)
Value Proposition	Large market potential currently fulfilled by a few compounds Buprenorphine is only chronic management methadone step-down molecule but remains schedule III, addictive and can cause respiratory depression

- 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
- 12 months to IND, 2 years to Human POC

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