

OTC QB: RSPI

James S. Manuso, Ph.D., President & CEO

BIOTECH SHOWCASE

San Francisco, January 9, 2018

Medicines for Respiratory Diseases

Forward Looking Statements



The matters discussed in this presentation that are not historical facts are "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and we intend that such forward-looking statements be subject to the safe harbor created thereby. Forward-looking statements include, but are not limited to, statements containing the words "believes," "anticipates," "intends," "estimates," "plans," "expects," "projects" and words of similar import. Readers are cautioned not to place undue reliance on these forward-looking statements, which are based on the information available to management at this time and which speak only as of the date of this presentation. The Company undertakes no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise. These forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements of the Company or its industry to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. All forward-looking statements should be evaluated with the understanding of their inherent uncertainty and in the context of the Company's filings with the Securities and Exchange Commission, including the risk factors contained therein. While the Company believes the information contained herein is reliable, the Company makes no representations or warranties regarding the accuracy or completeness of this information.

Breath



"Breath is the universal factor of life. We are born the first time we inspire, and we die the last time we expire. Breath is life itself. In Sanskrit the same word means both breath and life."

.....Abbot George Burke

Innovative Medicines for Respiratory Diseases



Corporate Overview

Focused on the development of novel medicines to treat very large respiration-related diseases with no pharmaceutical treatments: sleep apnea/hypopnea, respiratory depression and respiratory distress

Value Drivers

- Cannabinoid: Dronabinol (D9-THC)
 - Treatment of Obstructive Sleep Apnea (OSA)
 - Phase 3 ready
- Ampakines: CX1739, CX717 & CX1942
 - Opioid induced respiratory depression (RD) and central sleep apnea
 - 3 successful phase 2A trials for CX1739 and CX717
 - Pre-IND studies for CX1942

Compound	Indication	Preclinical	Phase 1	Phase 2
Dronabinol	Obstructive Sleep Apnea			
CX1739	Opioid Induced Sleep Apnea			
	Spinal Cord Injury			
CX717	Spinal Cord Injury			
CX1942	Drug-induced RD (Soluble Formulations)			

Apneas: Types, Their Measurement, Epidemiology and Economics



Sleep Apnea: A National Health Epidemic



3 Types of Sleep Apnea

- **Obstructive** (OSA) - a peripheral phenomenon that occurs when throat muscles intermittently relax and block airway during sleep
 - May be accompanied by snoring
- **Central** (CSA) – a brain-mediated phenomenon that occurs when breathing control centers in the brain reduce activity
 - Frequently caused by opioid consumption
- **Mixed** - a combination of OSA and CSA



Over 35 million Americans stop breathing
every night from 5-50 times per hour

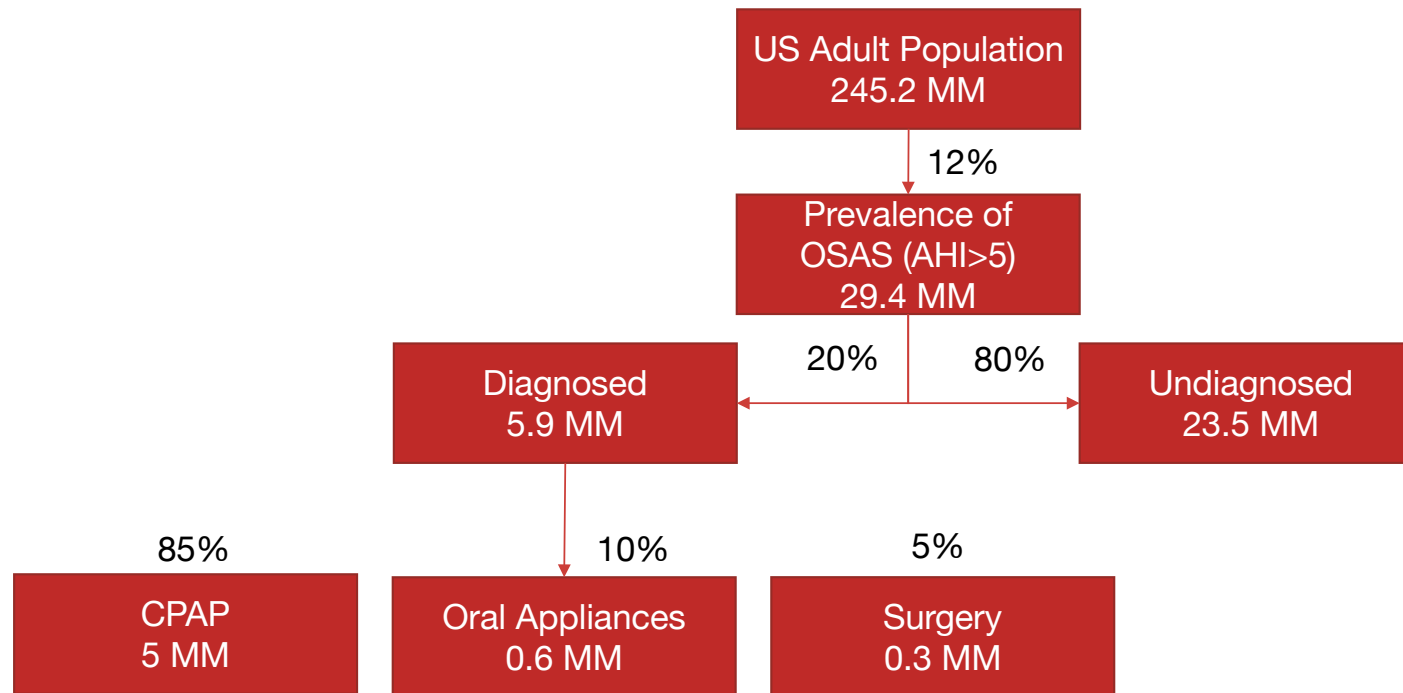
THIS IS NOT MERELY SNORING!

Sleep Apnea and its Measurement



- **Apnea:** Cessation of breathing for ≥ 10 seconds
- **Hypopnea:** Abnormal, severe slowing of breathing for ≥ 10 seconds
- **Apnea - Hypopnea Index (AHI):** Average number of apnea-hypopnea events per hour during sleep (indicator of the severity of sleep apnea)
- **Severity of Sleep Apnea:**
 - Normal: AHI < 5 incidents per hour
 - Mild: $5 \leq \text{AHI} < 15$ incidents per hour
 - Moderate: $15 \leq \text{AHI} < 30$ incidents per hour
 - Severe: AHI ≥ 30 incidents per hour

OSA Afflicts Nearly 30 Million People in the US and There Are No Approved Medicines for OSA

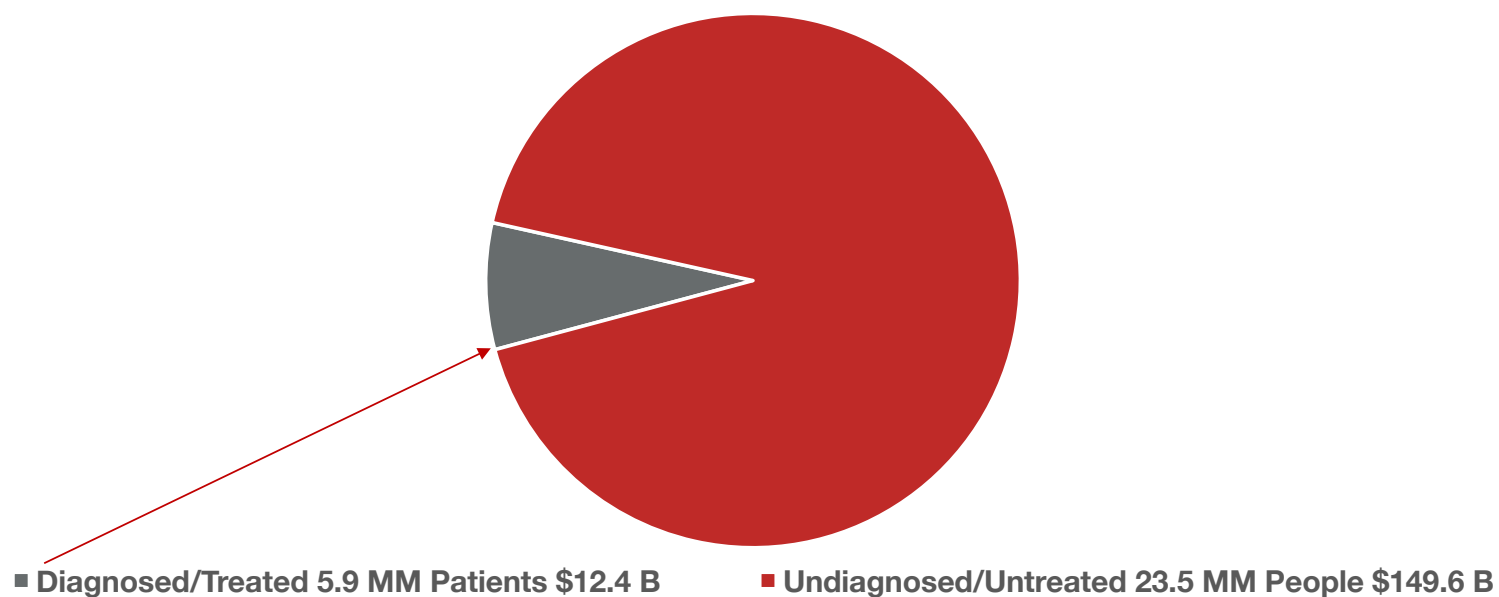


Source: U.S. Census (2014) [Am J Epidemiol](#). 2013 May 1;177(9):1006-14. doi: 10.1093/aje/kws342. Epub 2013 Apr 14.
Frost & Sullivan Report for the American Academy of Sleep Medicine

The Economic Impact of OSAS in the US is \$162 Billion



Only 20% of Sleep Apnea Patients are Diagnosed



Source: [Am J Epidemiol](#). 2013 May 1;177(9):1006-14. doi: 10.1093/aje/kws342. Epub 2013 Apr 14.
Frost & Sullivan Report for the American Academy of Sleep Medicine

OSA – Costs of the Problem in the US



<u>Disease State</u>	<u>Estimated US Prevalence</u>	<u>Annual Cost to US Economy</u>	<u>Annual Indicated Drug Therapy Expenditures</u>
OSA ¹⁻⁵	29.4 Million	\$162.0 Billion	\$ 0
Asthma ^{6,7}	16.4 Million	\$18.3 Billion	\$13.5 Billion
Hypertension ⁸⁻¹⁰	43.2 Million	\$73.4 Billion	\$48.5 Billion
Diabetes ^{11,12}	23.5 Million	\$174 Billion	\$20.6 Billion

¹ Obstructive sleep apnea and sleep. National Sleep Foundation Web site.

² Manufacturer Recommendations

³ Qualitative Market Research, Physician / Patient interviews, 2010

⁴ CPAP Supply USA,

⁵ American Sleep Apnea Association, 2010

⁶ Asthma & Allergy Foundation of America

⁷ Espicom Business Intelligence's New Drug Futures, 2006

⁸ Burt, V., et al., Hypertension, 2005

⁹ Lloyd-Jones, D., et al., Circulation 119(3):e21-181, 2009

¹⁰ Acmite Market Intelligence, 2008

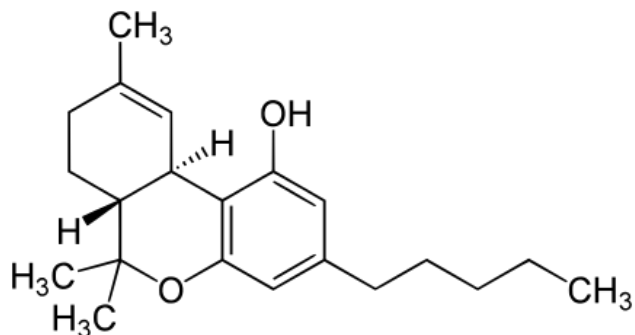
¹¹ Arrowhead, Global Diabetes Market, 2006

¹² American Diabetes Assoc., 2007

Dronabinol: Breakthrough Treatment for Obstructive Sleep Apnea



Dronabinol: A Breakthrough Treatment for OSA



- Dronabinol is Δ^9 -THC
- Oral, small molecule
- Cannabinoid receptor agonist
- Reduces apnea by acting on spinal ganglia controlling muscle tone in throat
- Positive Phase 2A and 2B clinical trials in OSA

- **Dronabinol Background**

- FDA approved for the treatment of anorexia in AIDS patients and nausea and vomiting in cancer patients undergoing chemotherapy (Marinol®)
- Schedule III drug available by prescription, with a low risk of addiction

- **Intellectual Property**

- Exclusive worldwide license from the University of Illinois
- Patents issued for the use of dronabinol in the treatment of OSA
- Pending patents on dosage and modified release formulations

- **NIH Support**

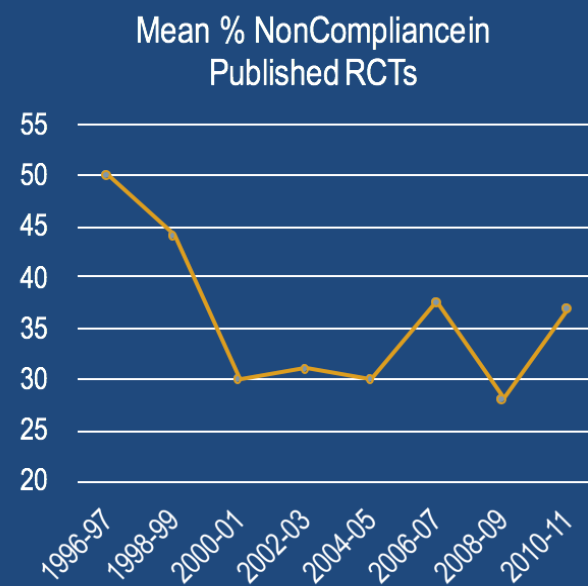
- >\$5MM NIH-funded grant PACE Phase 2B trial in OSA

CPAP Efficacy and Patient Non-Compliance



There are No Approved Medicines for the Treatment of OSA

- 30% of patients prescribed CPAP never initiate treatment when prescribed a machine
- Over 50% of patients stop using CPAP in the first year
- Dronabinol Indication for Patients who Cannot or Will Not Tolerate CPAP



J Otolaryngol Head Neck Surg. 2016; 45: 43

The Phase 2B “PACE” Clinical Trial: Pharmacotherapy of Apnea by Cannabimimetic Enhancement



PACE INVESTIGATORS

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Boris Vern, MD, PhD

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The **PACE Clinical Trial** was funded by the National Heart, Lung & Blood Institute of NIH with Grants: UM1HL112856 UL1TR001422 UL1TR002003

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Clinical Trial

Design of The Phase 2B PACE Trial in OSA



- **Study Design**

- Six week, double-blind, placebo controlled clinical study in 73 patients with OSA

- **Dosage / Administration**

- Placebo, 2.5 mg, or 10 mg dronabinol at night

Fully funded by
NIH ~\$5 Million

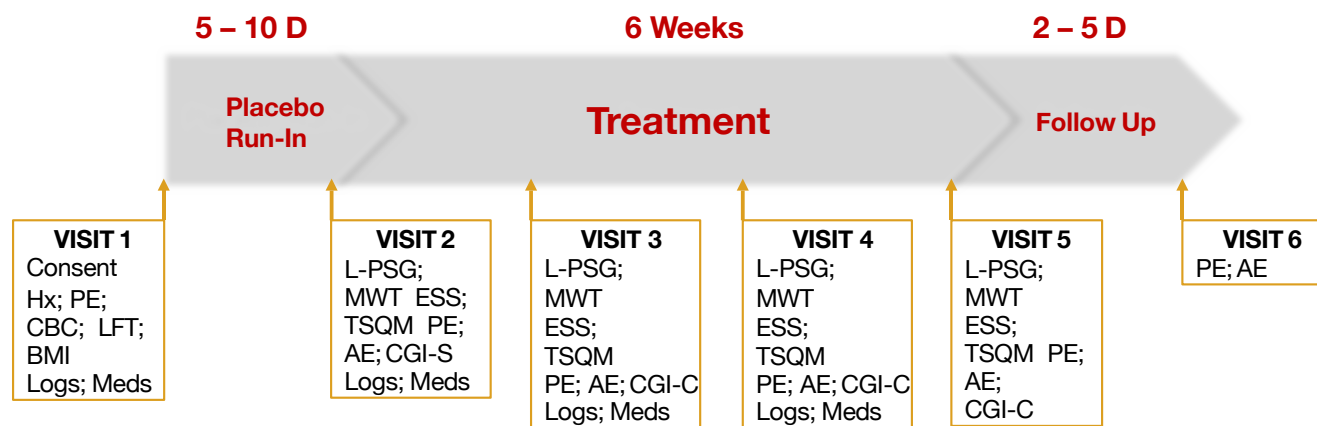
- **Patient Randomization**

- Of 73 randomized patients 56 completed study and were evaluable
- Placebo, n = 17
 - Placebo, n = 17
 - 2.5 mg dronabinol, n = 19
 - 10 mg dronabinol, n = 20

THE PACE Clinical Trial: Pharmacotherapy of Apnea by Cannabimimetic Enhancement – A Phase 2B Study



- Randomized, Placebo-controlled, Parallel Groups, Multi-site Trial in Patients with Moderate to Severe OSA
- Study Drug: Dronabinol (Overencapsulated Marinol®): 2.5 mg or 10 mg QD
- Dose Administration: 60 minutes before bedtime
- Inclusion: Age 21 – 64; AHI 15 – 50; Epworth Sleepiness Scale (ESS) ≥ 7 ; Body Mass Index (BMI) ≤ 45
- Exclusion: Shift Work or OSA Tx within 1 mo; Medical Co-morbidity; Psych Dx; CNS Active Meds



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Clinical Trial

The Phase 2B PACE Trial in OSA: Final Overall Results



- Statistically significant improvement in Primary Outcome Measures
 - Apnea-Hypopnea Index (AHI) (2.5 and 10 mg)¹
 - ESS Sleepiness Scale (10 mg)²
 - Overall Patient Satisfaction (10 mg)³

¹ p<.02 and p<.001, respectively, compared to placebo

² p<.001, compared to placebo

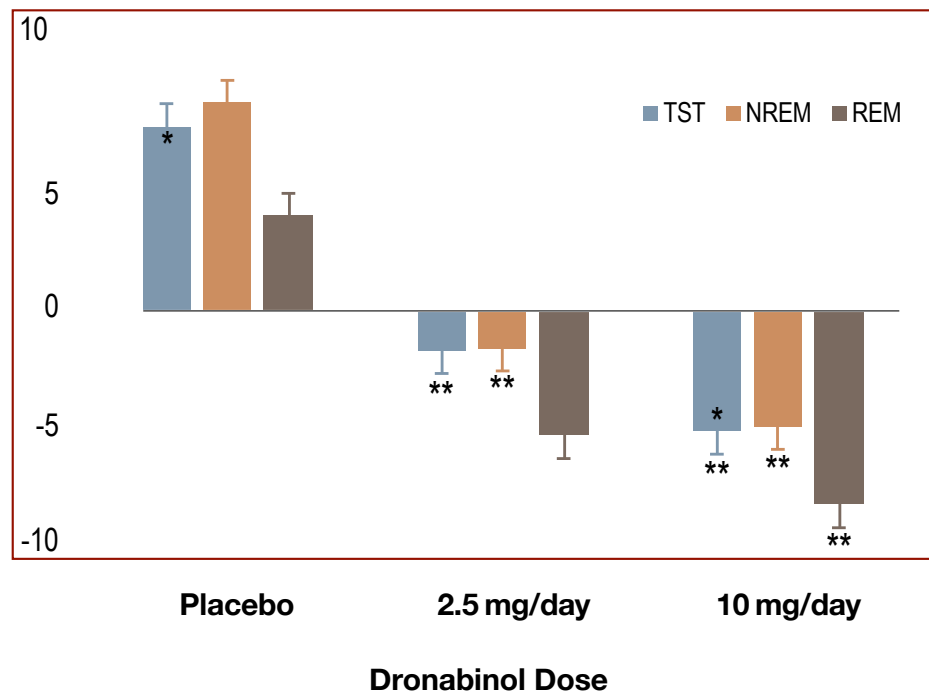
³ p<.02, compared to placebo

Results of 6-Week Treatment: Dronabinol Reduces AHI⁺



Positive Effects of Dronabinol vs. Placebo in TOTAL, REM & NREM Sleep Demonstrate Efficacy

Change in Apnea/Hypopnea Index



*P=0.02

**P=0.001

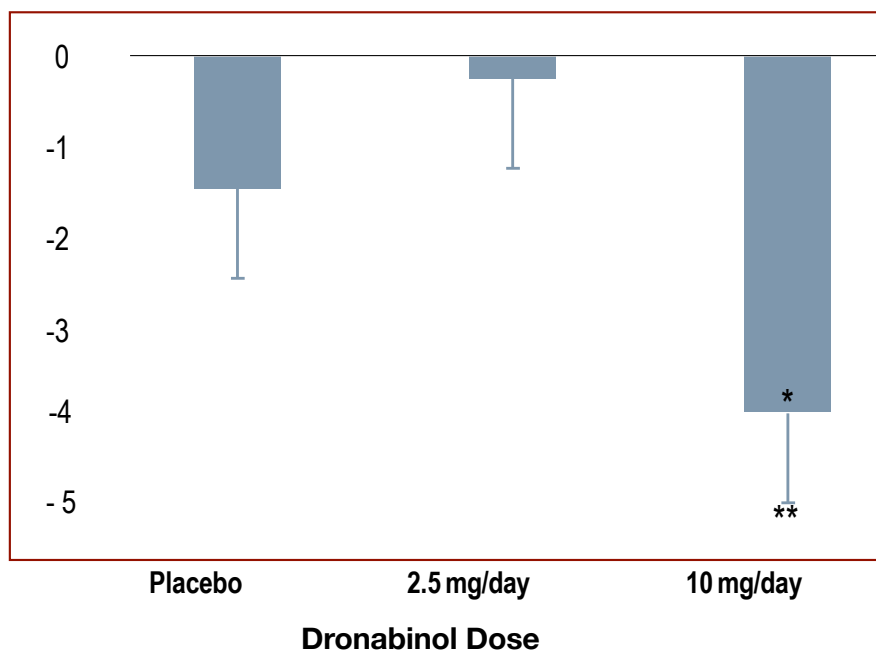
+ Primary Endpoint

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Dronabinol Reduces Daytime Sleepiness⁺



Change in Epworth Sleepiness Scale

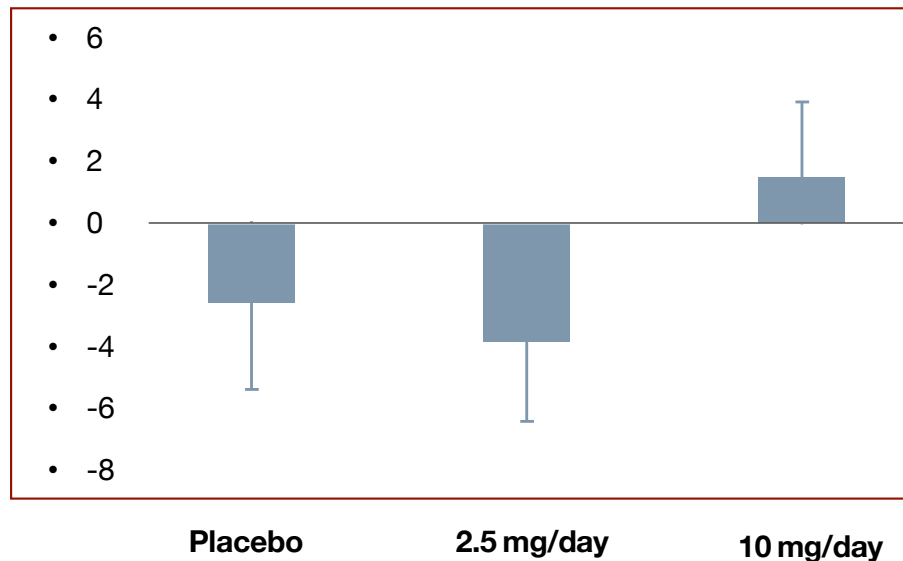


+ Primary Endpoint

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Clinical Trial

Dronabinol Improves MWT

Change in Mean Wakefulness Testing (MWT)



Dronabinol Dose

PACE enhancement
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Clinical Trial

Dronabinol Has an Excellent Safety Profile and Patients are Highly Satisfied With Treatment



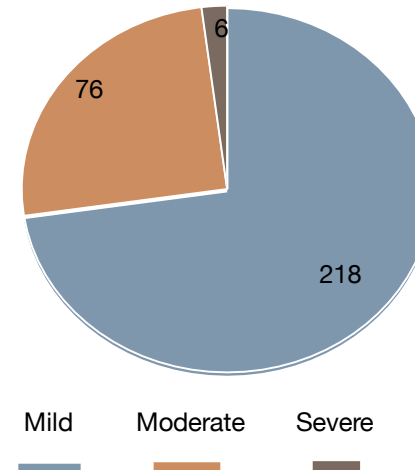
TSQM Response: End of Treatment

Tx Response	Placebo	2.5 mg/day	10 mg/day
Extremely Dissatisfied	3	2	1
Very Dissatisfied	1	2	0
Dissatisfied	0	3	0
Somewhat Satisfied	5	6	4
Satisfied	1	4	4
Very Satisfied	5	1	5
Extremely Satisfied	1	1	6
Total	16*	19	20

p=0.04 for Tx Effect

*TSQM data missing for one placebo subject

- Average Number of AEs = 4.1 ± 4.0
 - Did not differ by Tx group
- Most Frequent Verbatim AEs Reported
 - Sleepiness/Drowsiness (N=25)
 - Headache (N=24)
 - Nausea/Vomiting (N=23)



A Clinical View of the Pace Trial Results



Comments by David Rapoport, MD Professor of Medicine Mount Sinai School of Medicine*

“OSA may affect....long term cardiovascular and cerebrovascular health,.....memory loss and progression of Alzheimer Disease biomarkers.”

“...dronabinol is effective in lowering AHI in patients with moderate obstructive sleep apnea.”

“The results of the PACE trial are among the first to show sustained effect of a drug therapy targeting the behavior of the upper airway. Dronabinol is easy to take, appears to have a low side effect profile and now has been shown to be effective. “

dronabinol “may help address the significant medical need for alternative treatments for OSA.”

*RespireRx press release, November 30, 2017

Dronabinol – Phase 3 Regulatory Strategy*



- Meet with FDA during Q1/2018
- Finalize the Phase 3 trial plan required for approval
- Position dronabinol as a breakthrough medicine
- Seek fast track designation
- Facilitate and hasten the development path

* Pending Finance

FDA Expedited Approval Opportunities for Dronabinol



Breakthrough Therapy Designation	Preliminary clinical data	Substantial improvement on clinically significant endpoint(s) over available therapies <i>No Drug Therapy for OSAS</i>	More frequent meetings with FDA More frequent FDA communication Rolling review Intensive guidance on an NDA FDA help to expedite development
Accelerated Approval Pathway	Not specified; Sponsor should make justification of alternate endpoint based scientific support	Generally provides a meaningful advantage over available therapies AND demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or a clinical endpoint that can be measured earlier than irreversible morbidity or mortality <i>Cannot or Will Not Use CPAP</i>	Approval based on a surrogate or intermediate endpoint (often allows for shorter development time) Note: FDA requires clinical trials to be conducted post-approval to confirm clinical benefit <i>AHI & ESS Endpoints</i>
Priority Review Designation	Data contained in the final NDA submission	Significant improvement in safety or effectiveness of the treatment, prevention, or diagnosis of a serious condition <i>OSAS Health & Economic Impact</i>	Review of application in 6 months

Dronabinol in the Marketplace: Strategies to Capture the Sleep Market



- **Issued Method-of-Use Patents**
 - Expires in 2025
 - Pending patent applications to 2030 & beyond
- **FDA Designations for Market Exclusivity**
 - Fast-Track
 - Breakthrough
 - Hatch-Waxman
- **Develop a “Branded Generic” Formulation of Dronabinol (R-Nabinol) for Phase 3 Pivotal Trial**
- **Develop Proprietary Dosage Formulations for Product Line Extensions**
- **Execute Commercial & Market Strategies**

The Dronabinol Opportunity



Impact on Patient	Commercial Potential
First medicine available for OSA	Changes the nature of OSA treatment
Ease of Use/Better Patient Compliance	Broadly expands prescriber base from sleep specialists to include primary care physicians and cardiologists
Low cost	Recurring lifetime sales versus one time sale or ongoing rental of a device
Safe and effective	Market will expand into the currently undiagnosed/untreated population
Potential for better cardiovascular outcomes	Potential for reducing systemic healthcare costs by reduced cardiac re-hospitalizations

Potential Dronabinol Economics



If FDA approves dronabinol for the treatment of OSA:

- Initial target market: Mild to moderate OSA patients who are diagnosed but do not use CPAP
- 1,770,000 adults (i.e., 30% of 5.9 million diagnosed adults).
- Daily price per pill is \$5.00
- Patient compliance – assume patients take the pill only 50% of the time (i.e., 183 days per year)
- Gross Sales = \$1.6 billion

Ampakines for Opioid Induced Apneas

The Opioid Epidemic - Prologue

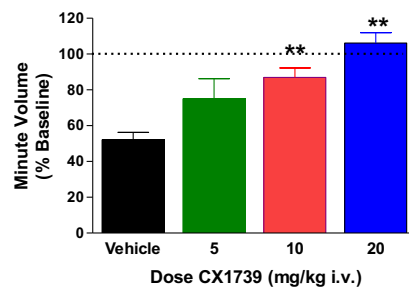
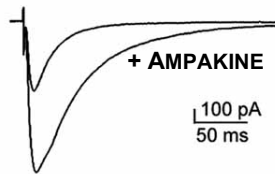
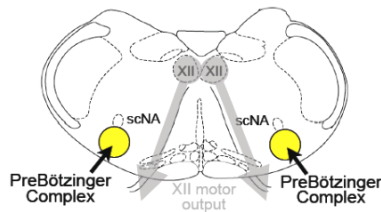


- 11 million Americans take chronic opioids for pain management and 50% of them have central sleep apnea¹.
- The majority of opioid deaths occur in non-substance abusing patients
- Sleep apnea is a primary risk factor for opioid overdose².
- Opioid-induced death is caused by respiratory depression.
- Tolerance to opioids develops rapidly, causing dose escalation, whereas tolerance develops less so to the respiratory depressant effects.

¹ Rose AR, Catcheside PG, McEvoy RD, Paul D, Kapur D, Peak E, Vakulin A, Antic NA. J Clin Sleep Med 2014;10(8):847-852

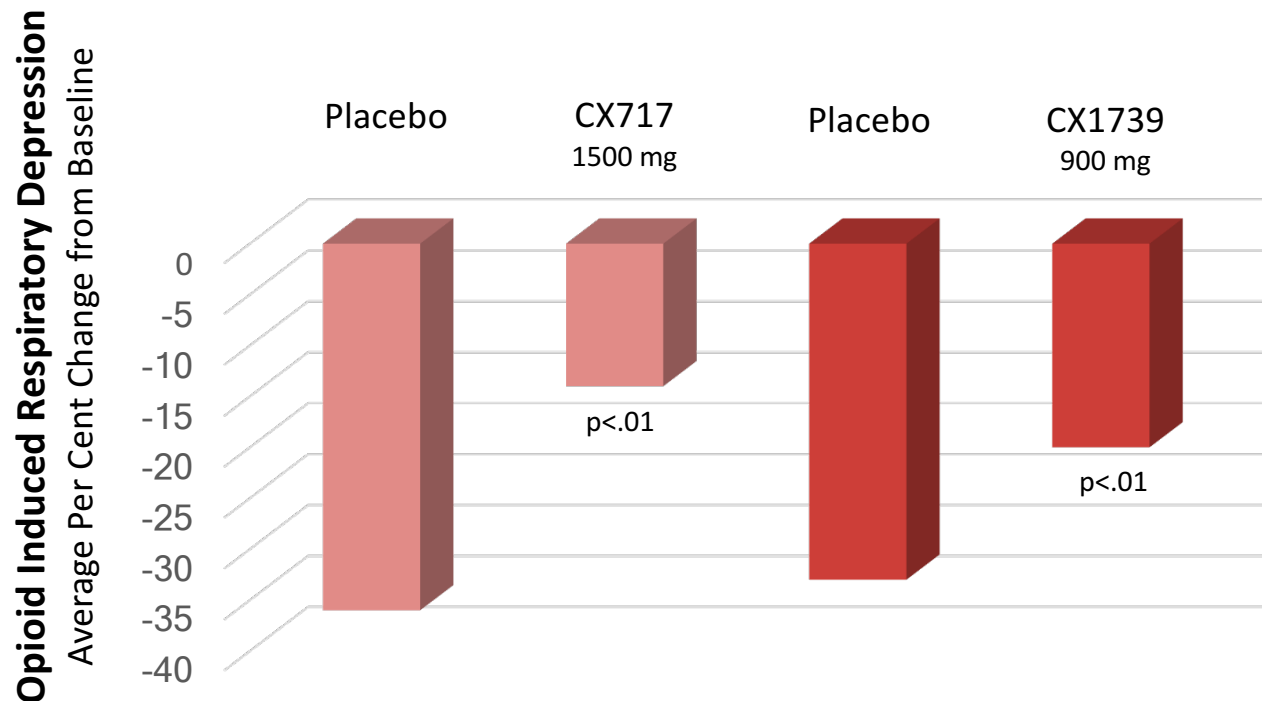
² Nora D. Volkow, M.D., and A. Thomas McLellan, Ph.D, National Institute of Drug Abuse, N Engl J Med 2016;374:1253-63.

Translational Approach to Respiratory Disorders



- Brain stem nuclei that regulate breathing contain opiate and AMPA glutamate receptors that inhibit and excite cell activity, respectively
- Ampakines act as positive, allosteric modulators of the AMPA-type glutamate receptor to enhance excitation and prolong and strengthen synaptic transmission
- In animal models, ampakines antagonize opioid-induced respiratory depression

Ampakines Reduce Opioid Induced Respiratory Depression in Phase 2A Clinical Trials

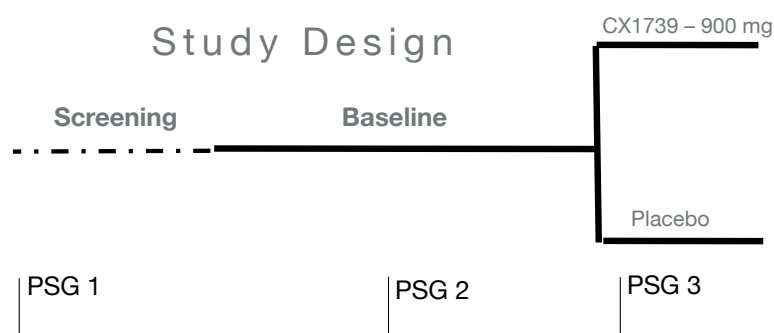


Ampakines reduce opioid induced respiratory depression without altering analgesia

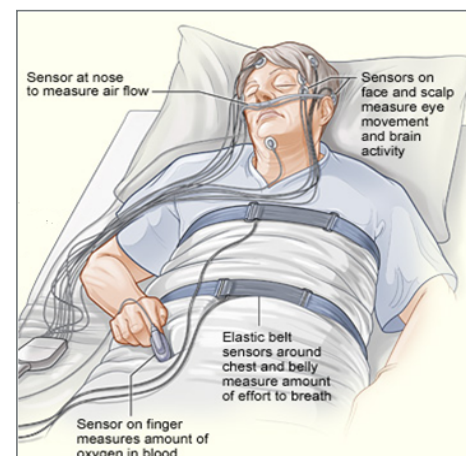
CX1739: Completed Phase 2A in Sleep Apnea – Single Dose



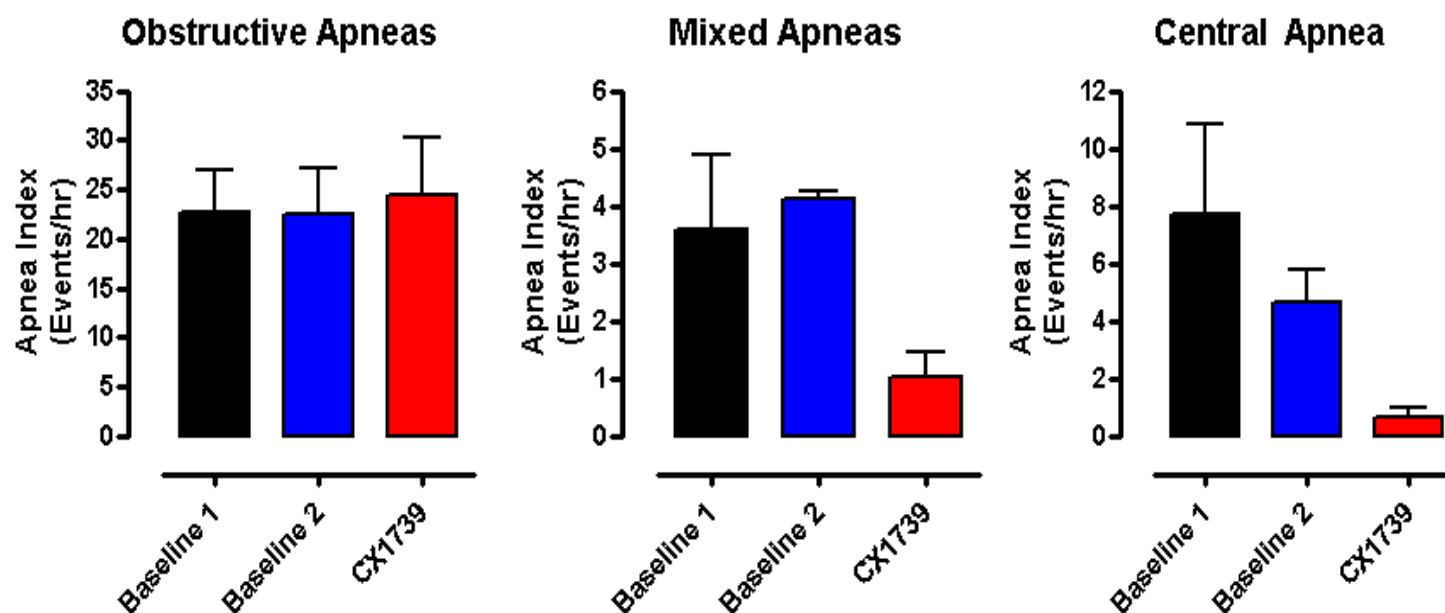
Design	Randomized, double-blind, placebo-controlled study
Population	20 adults with all types of moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)
Dosing	Each subject received either placebo or a <u>single</u> dose of 900mg CX1739 one hour before lights out
Primary Measures	Apnea-Hypopnea measures; Oxygen saturation; Sleep quality, measured by PSG (Apnea: no airflow for >10s; Hypopnea: reduced airflow for >10s)



PSG – Polysomnography, or sleep lab study



Patient Selection: CX1739 Was More Effective in Treating Mixed and Central Sleep Apneas



The RespireRx Ampakine™ Pipeline



Compound	Indication	Status	Start Date*	Completion*
CX1739	Opioid-induced Apnea	Phase 2A	2Q2016	✓ 4Q2016
	Opioid Induced Sleep Apnea*	Phase 2B	2Q2018	1Q2019
CX717/CX1739	Spinal Cord Injury*	Phase 2A	2Q2018	4Q2018
CX717/CX1739	Orphan Diseases: Autism, Pompe*	Pre-Clinical to Clinical	Ongoing	Ongoing
* Pending finance				

Ampakine Indications and IP



- **Targeted Indications**
 - CSA in Chronic opioid patients
 - Spinal cord injury
 - Combination formulation with an opioid for treatment of chronic pain
- **Intellectual Property Protection (owned and licensed)**
 - Issued Composition-of-Matter Patents (expire 2028)
 - Method-of-use patents (expire 2030)

Capital Structure and Market Metrics



	September 30, 2017 ProForma to December 19, 2017
Common Stock (as of November 13, 2017)	2,633,000
Common Stock Equivalents of Convertible Notes	32,000
Common Stock Equivalents of Options and Warrants Granted (excludes 3,102,000 shares reserved for equity plans, after 2015 Plan size increase. Includes grants on December 9, 2017)	4,700,000
Total	7,365,000

	Market Metrics at December 19, 2017
Closing price as of December 19, 2017	\$1.51
Fully diluted market capitalization (rounded)	\$11,121,000

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CX1739	Opioid Induced Sleep Apnea			
	Spinal Cord Injury			
CX717	Spinal Cord Injury			
CX1942	Drug-induced RD (Soluble Formulations)			

Management Team and Directors



James Manuso, PhD, President, CEO & Vice Chairman

- *Biotechnology/pharmaceuticals industry CEO*
- *Formerly served as Chairman and CEO of Astex Pharmaceuticals*
- *Author of over 30 chapters, articles and books on topics including healthcare cost containment and biotechnology company management*

Arnold Lippa, CSO & Executive Chairman

- *Founder of DOV Pharmaceuticals and Praxis Pharmaceuticals*
- *Serial life science company entrepreneur*
- *Indirect managing member of Aurora Capital LLC*

Jeff Margolis, CFO, SVP, Treasurer, Secretary, Director

- *Founder, President and indirect managing member of Aurora Capital LLC (FINRA, SIPC), life science focused investment bank, 22 years*

Richard Purcell, Senior VP, R&D

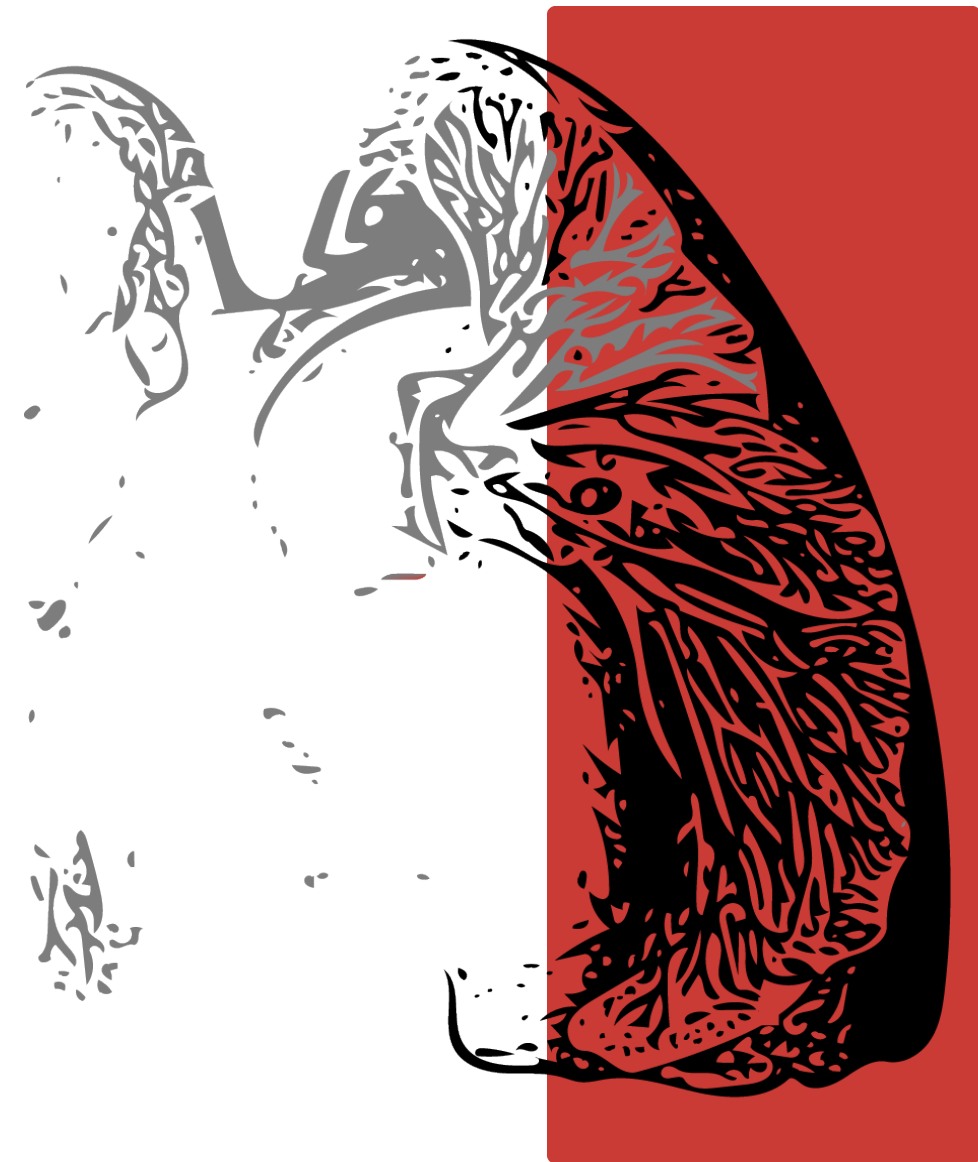
- *Biopharmaceutical development specialist with consulting experience for financial, venture capital and start-up companies*
- *Formerly, President of CRO*

Katie MacFarlane, Director

- *Senior VP, Napo Pharmaceuticals*
- *Owner and Managing Director of SmartPharma, a pharmaceuticals consulting firm*
- *More than 25 years of experience and expertise in marketing, new product planning and commercialization*

James Sapirstein, Director

- *CEO of ContraVir Pharmaceuticals*
- *Founder and former CEO of Tobira Therapeutics*



OTC QB: RSPI

James S. Manuso, Ph.D., President & CEO

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