RespireRx Pharmaceuticals Inc

OTC QB: RSPI

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

January 11, 2016

BIOTECH
SHOWCASE 2016

Medicines for Respiratory Diseases

Forward Looking Statements

RespireRx Pharmaceuticals Inc

The matters discussed in this presentation that are not historical facts are "forward-looking statements." Forward-looking statements include, but are not limited to, statements containing the words "believes," "anticipates," "intends," "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.

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Breath

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"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

The RespireRx Story: Innovative Medicines for Respiratory Diseases

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- Two drug platforms
- Three Phase 2 or Phase 2-ready programs
- One pre-clinical program
- Blockbuster markets
- IP protection with the ability to add additional IP
- Multiple opportunities for strategic collaborations
- Availability of non-dilutive financing
- Experienced management team

Company Focus

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- **Sleep Apneas**
  - Dronabinol for Obstructive Sleep Apnea (**OSA**)
  - Ampakines for Central Sleep Apnea (**CSA**)
- **Drug-induced Respiratory Depression (RD) - Ampakines**
  - Semi-acute use – post-surgical pain management with opioids
  - Acute use – surgical anesthesia/sedation
  - Chronic use – outpatient pain management with opioids
- **Positive Phase 2A efficacy results in RD, OSA and CSA**
- **Commercial and IP protection for compounds and uses**
- **$5 million in NIH grants supporting OSA drug development**

Respiratory Diseases Product Pipeline

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Compound	Indication	Pre-clinical	Phase 1	Phase 2
Dronabinol	Obstructive Sleep Apnea			
CX1739	Central Sleep Apnea Opioid-induced RD Spinal Damage/Pompe			
CX717	Combination Formulation with Opioids for Reduced RD			
CX1942	Drug-induced Respiratory Depression (injectable)			

Sleep Apnea

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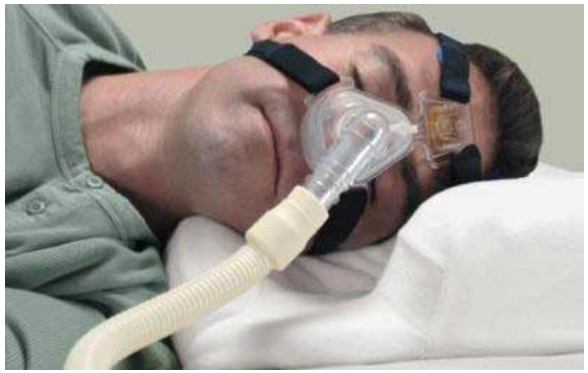
- **Sleep Apnea**
  - Repetitive episodes of airflow cessation (apnea) or reduction (hypopnea) for more than 10 seconds during sleep
  - Three types: Obstructive, Central & Mixed

- **The Sleep Apnea Market is Large**
  - 18 million U.S. adults suffer from moderate or severe sleep apneas
  - Market potential for sleep apneas is $3 - 9 Billion/Year

- **Current Treatments**
  - CPAP device
  - Surgery; dental devices

- **Clear Market Need**
  - Poor compliance with CPAP
  - No drug treatment available



Obstructive Sleep Apnea (OSA)

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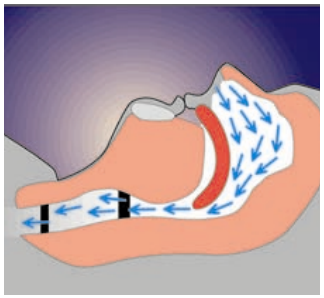
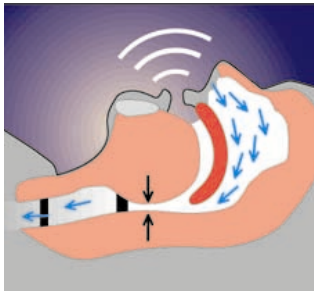
- **Obstructive Sleep Apnea (OSA):** a decrease or complete halt in airflow during sleep
  - Induced by relaxation of muscles during sleep
  - Soft tissue in back of throat collapses and obstructs upper airway
- **Significant morbidity due to stroke, hypertension, heart failure, diabetes, and other cardiovascular diseases**

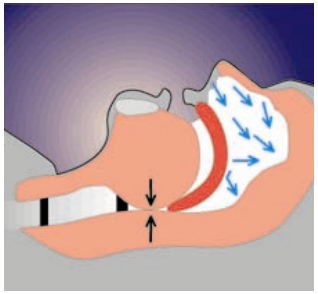
Normal Breathing



Snoring



OSA



CPAP Efficacy is Severly Limited by Patient Compliance

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- Works as an air splint to keep upper airway open during sleep
- 30% of diagnosed patients never initiate CPAP treatment when prescribed a machine
- Over 50% of patients stop using CPAP in the first year
- Many CPAP users wear the device for less than 4 hours per night, limiting efficacy

Dronabinol: a BreakthroughTreatment for OSA

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- **Mechanism of Action**
  - Dronabinol is (D-9)THC, a cannabinoid agonist
- **Background**
  - Schedule III drug available by prescription, with a low risk of addiction
  - Approved for the treatment of anorexia in AIDS patients and nausea and vomiting in cancer patients undergoing chemotherapy
  - Phase 2A data demonstrated clear signal of activity in OSA
  - Phase 2B study in OSA in progress
- **Intellectual Property**
  - License to issued method-of-use patent in the US for the use of dronabinol for treating OSA (expires 2025)
  - Pending patents on modified release formulations
- **Funding**
  - NIH funded $5MM grant for Phase 2B study in OSA

Completed Phase 2A Trial of Dronabinol in OSA

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- **Randomized, double-blind, placebo-controlled dose escalation study in 22 patients with OSA**
- **Placebo (N=5) or dronabinol (N=17) for 21 days**
  - 2.5, 5 and 10 mg/night studied with weekly dose escalation
- **Overnight polysomnogram (PSG) at baseline, and after 7, 14 and 21 days of treatment**
- **FDA-accepted Efficacy tests:**
  - Apnea-Hypopnea Time (AHT)
  - Apnea-Hypopnea Index (AHI)
  - Stanford Sleepiness Scale (SSS)

Dronabinol Proven to Reduce Apnea in OSA Subjects

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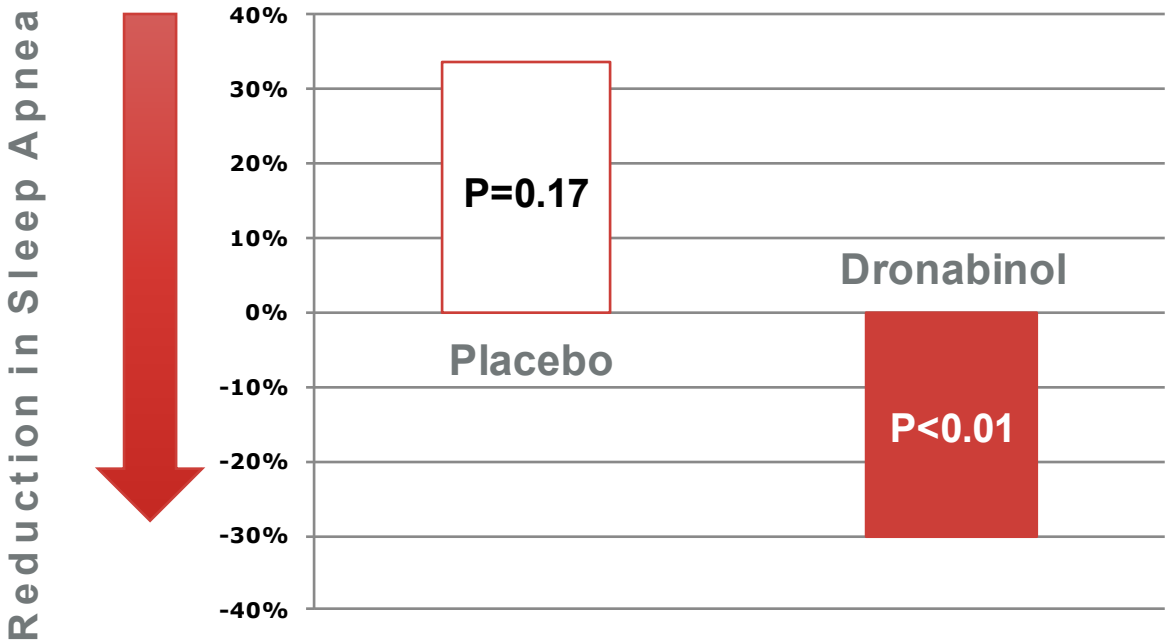

Apnea Suppression as a Function of Dose and Time

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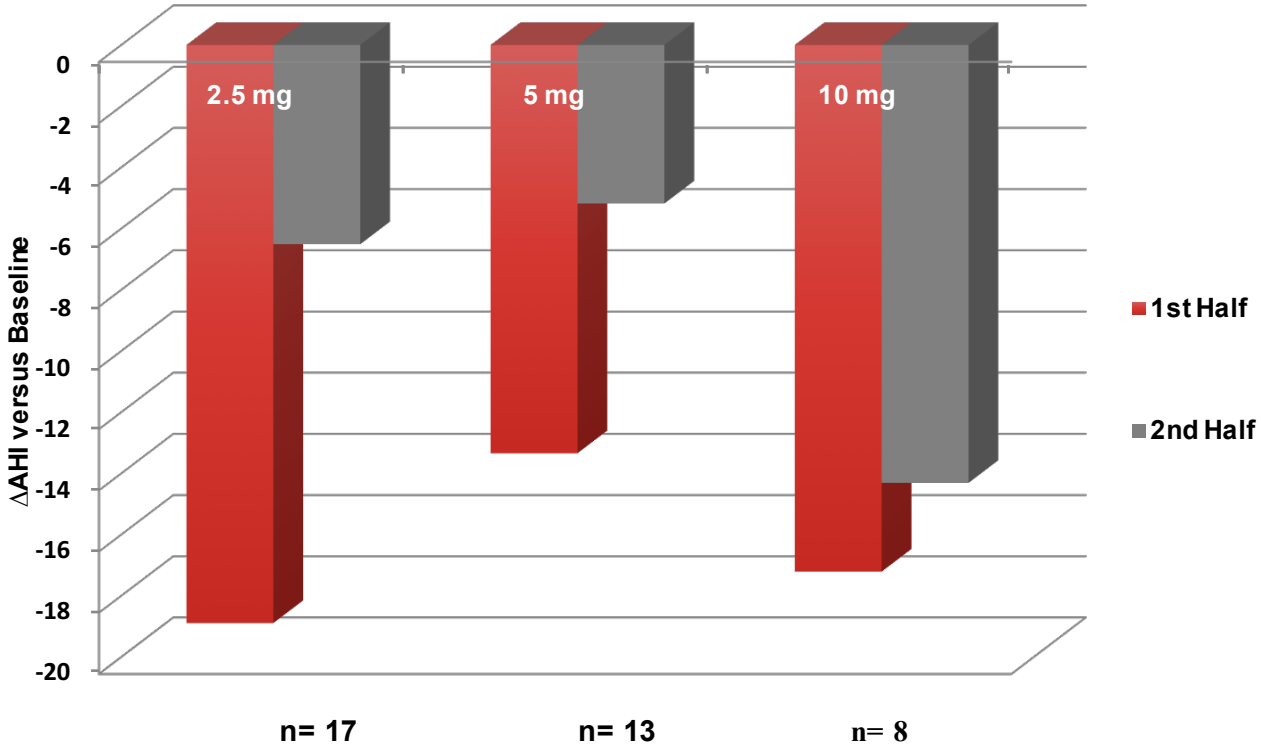

The plasma half-life of dronabinol is 2 – 4 hours.

Ongoing Dronabinol Phase 2B Clinical Trial in OSA

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- Sponsored and led by U of Illinois
- 4 major centers, fully funded by NIH
- Potentially pivotal for an accelerated NDA
- 120 subjects (40/group, 6 wks dosing)
- Doses: Placebo, 2.5 mg, 10 mg qd
- Data expected Q3/2016
- Plan to meet with FDA after study completion to determine registration path forward

Protecting Dronabinol in the Market

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- License to issued Method-of-Use patent for dronabinol in OSA
  - Expires in 2025
- Schedule III drug: off-label use monitored by US government, discouraging generic manufacturers from selling off-label
- Off-label use of generics and medical marijuana are not covered by insurers
- Market pricing protection

The Dronabinol Opportunity

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Impact on Patient	Commercial Opportunity
First pharmacotherapeutic 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

Central Sleep Apnea

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- **Caused by a lack of drive from the brain to breathe during sleep**
- **Manifestations of CSA**
  - 70% of chronic narcotic users
  - Up to 40% of heart failure patients
  - 5% of sleep apnea patients are idiopathic
- **No therapeutic or device is approved for the indication**

The Severity of CSA is Correlated with Increased Mortality in HF Patients

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Reducing Central Sleep Apnea May Reduce Mortality in Heart Failure Patients

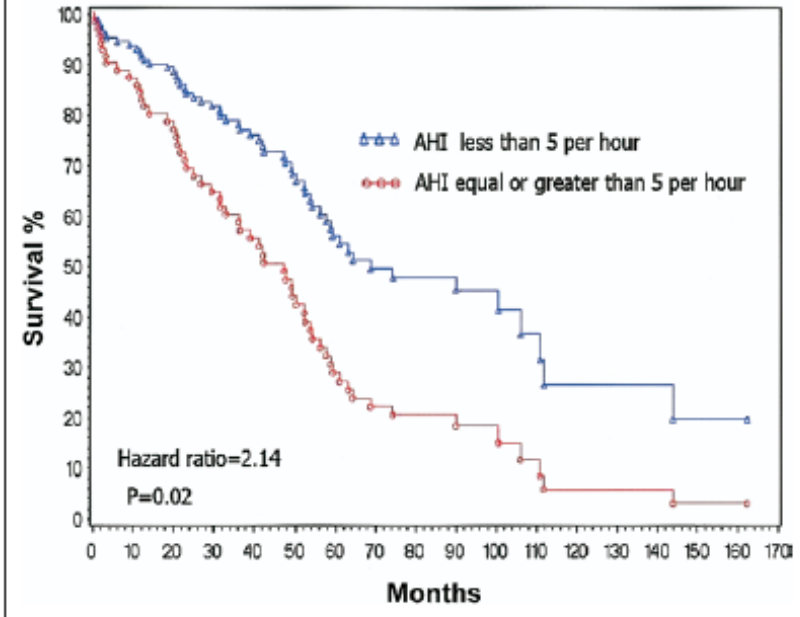

Figure 1 **CSA is a Predictor of Mortality in Systolic HF**

Survival of heart failure (HF) patients with or without central sleep apnea (CSA) after accounting for all other confounders. AHI = apnea-hypopnea index.

Javaheri et al, J. Amer. Coll. Cardiology 49:20, 2007

AMPAKINES – A NOVEL CLASS OF DRUGS

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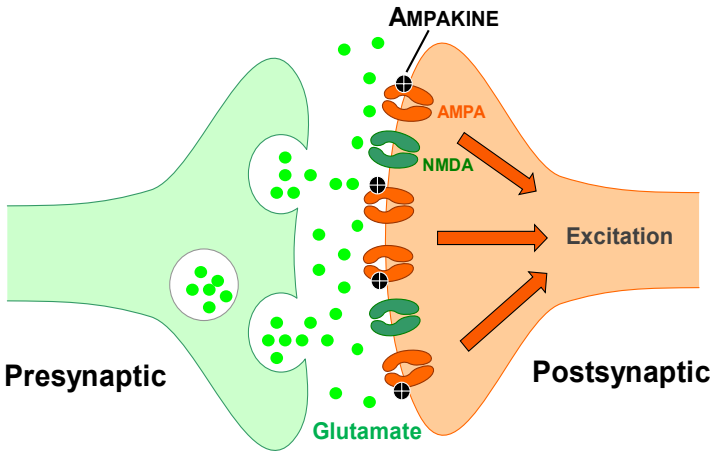
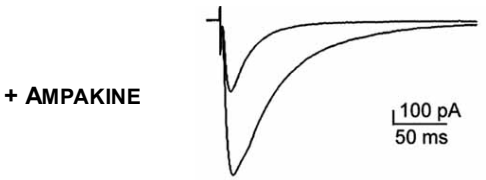
AMPA Receptors Mediate Synaptic Transmission in the Brain

- Glutamate is the major excitatory neurotransmitter in the CNS
- Fast excitatory transmission is mediated by AMPA-type glutamate receptors
- Ampakines are positive, allosteric modulators of the AMPA-type glutamate receptor
- Prolong and strengthen synaptic transmission





AMPAKINES – Novel Treatment for Respiratory Depression

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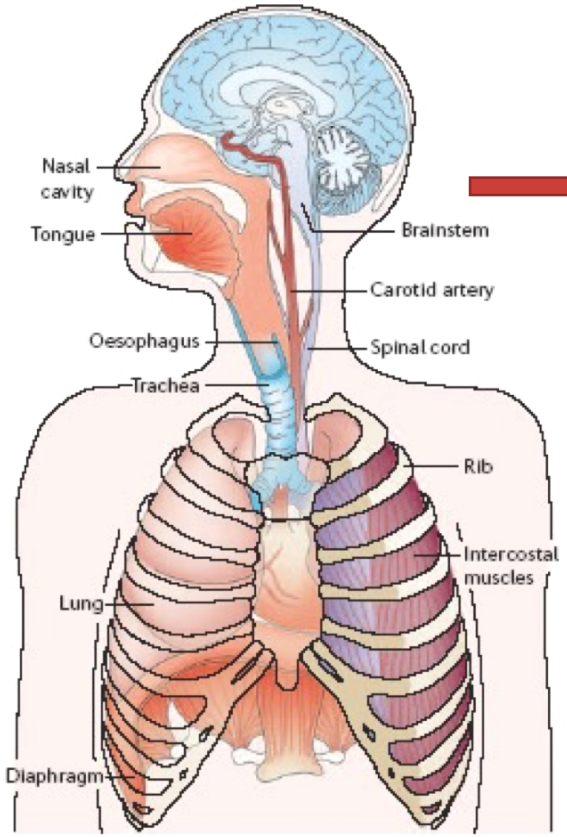
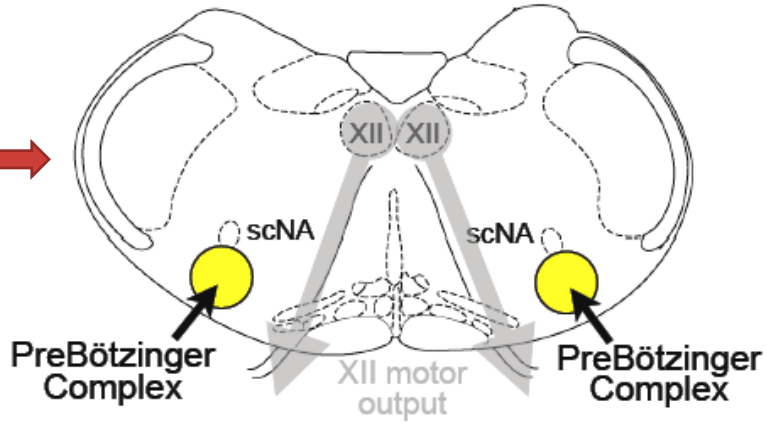


Initial research conducted by Dr. J. Greer, U. Alberta
Ren et al, Anesthesiology. 110:1364-1370, 2009



- Neurons in this brainstem region control inspiratory breathing rhythm
- PreBotC neurons use AMPA receptors for signaling
- Opioids and other depressants mediate their inhibitory effects on breathing at this site
- Ampakines normalize breathing by enhancing firing of PreBotC respiratory rhythm neurons

CX1739: A Third Generation, Oral Ampakine in Phase 2

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- **Targeted Indications**
  - Central Sleep Apnea (CSA)
  - Reversal and prevention of opioid-induced Respiratory Depression (RD)
  - Combination formulation with an opioid for treatment of chronic pain

- **Stage of Development**
  - Successfully completed four Phase 1 studies
  - Indications of efficacy in CSA
  - Phase 2 trial in opioid-induced RD planned

- **Intellectual Property Protection (owned and licensed)**
  - Issued Composition-of-Matter Patent (expires 2028), filed worldwide
  - Method-of-use patent (expires 2030)

CX1739: IND Status

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- **IND**
  - Opioid induced respiratory depression study
  - Submitted to FDA on September 18, 2015

- **FDA noted two deficiencies**
  - Myocardial Histology
    - ✓ FDA requested tissue analysis for all rats at all doses
    - ✓ Analysis completed
    - ✓ No drug-related histopathology observed by two independent board certified pathologists

  - FDA requested an additional study of neuro-histopathology measured at 1, 3 and 14 days after single doses of 250, 750 and 1500 mg/kg
    - ✓ Prior studies showed no histopathology when CX1739 was dosed for 14 and 28 days
    - ✓ Top line results from the additional study show no histopathology
    - ✓ Independent pathologist report in preparation

- **Anticipate filing complete response to FDA within 30 days**

CX1739: Completed Phase 2A in Sleep Apnea

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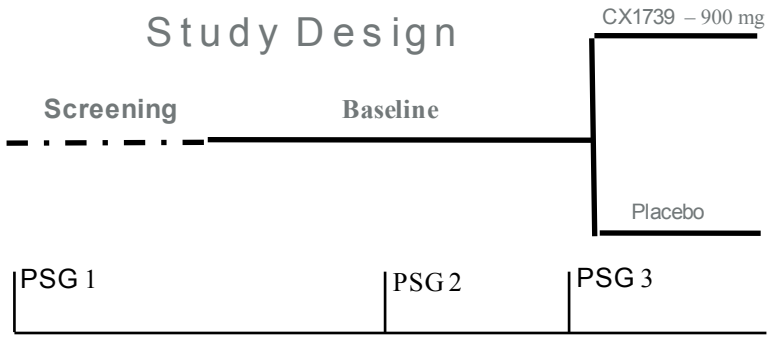
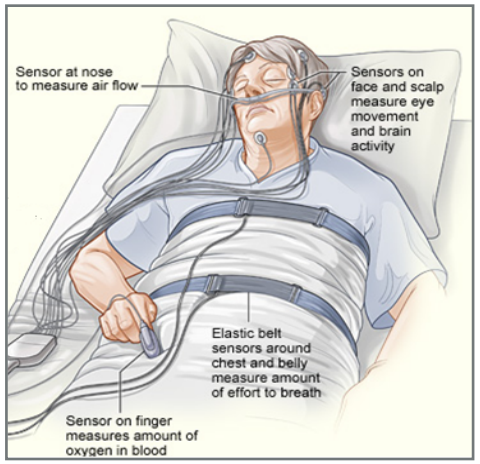
Design	Randomized, double-blind, placebo-controlled study
Population	20 adults with all types of moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)
Dosing	Each subject received either placebo or a single dose of 900mg CX1739 one hour before lights out
Primary Measures	Apnea-Hypopnea measures; 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

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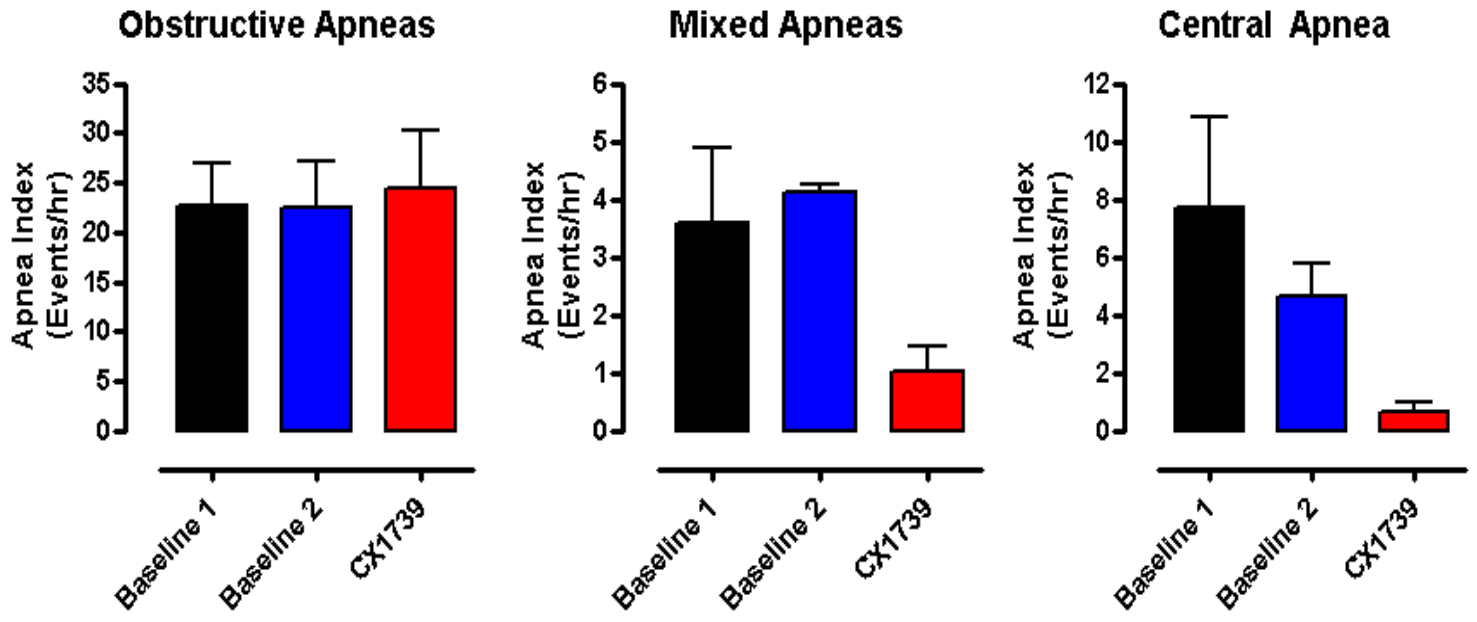

Drug-induced Respiratory Depression

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RD is the most frequent lethal side effect of opioid use

- **Acute and Semi-Acute Use of opioids**
  - ~25M patients/year at risk for RD (hospitalized, peri- and post-surgical opioid patients)
- **Chronic Opioid Use**
  - Use of Ampakines in combination with other drugs to prevent RD
- **Unmet Need: Medicine to counter or reduce RD without interfering with analgesia or anesthesia**
- **Large multi-$ billion/year market potential**

Ampakines Prevent Opioid-induced Respiratory Depression in Humans

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- Two clinical studies in normal, healthy volunteers with CX717, a second-generation Ampakine
- Moderate Respiratory Depression was induced experimentally by infusion of the opioid, Alfentanil
- Respiratory and analgesia end-points were measured

Oral CX717 prevented and reversed the Respiratory Depression without impacting the pain-relieving properties of the opioid

CX717 Prevents Opioid-induced Respiratory Depression in Humans

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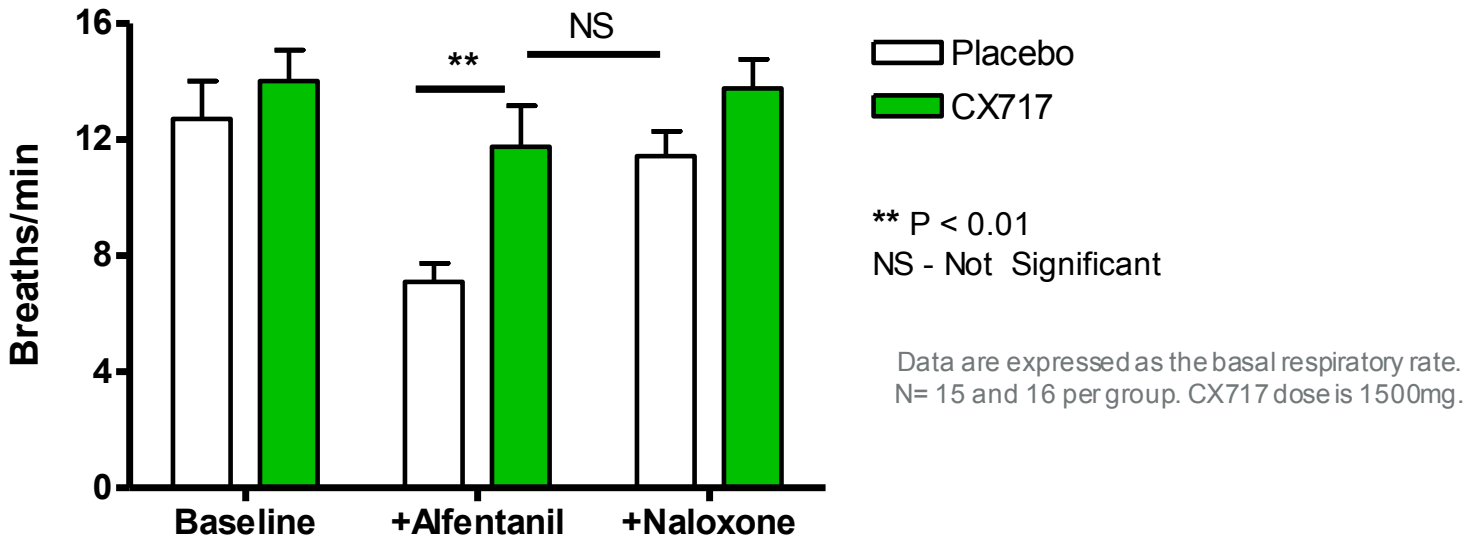

** P < 0.01
NS - Not Significant

Data are expressed as the basal respiratory rate.
N= 15 and 16 per group. CX717 dose is 1500mg.

- Alfentanil reduced breathing rate & produced Respiratory Depression
- CX717 maintains respiratory rate in the presence of Alfentanil

CX717 Maintains the Analgesic Properties of Opioids Without Affecting Rescue Therapy

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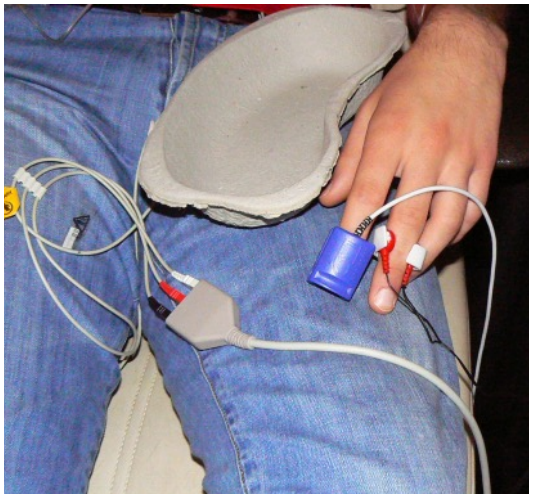
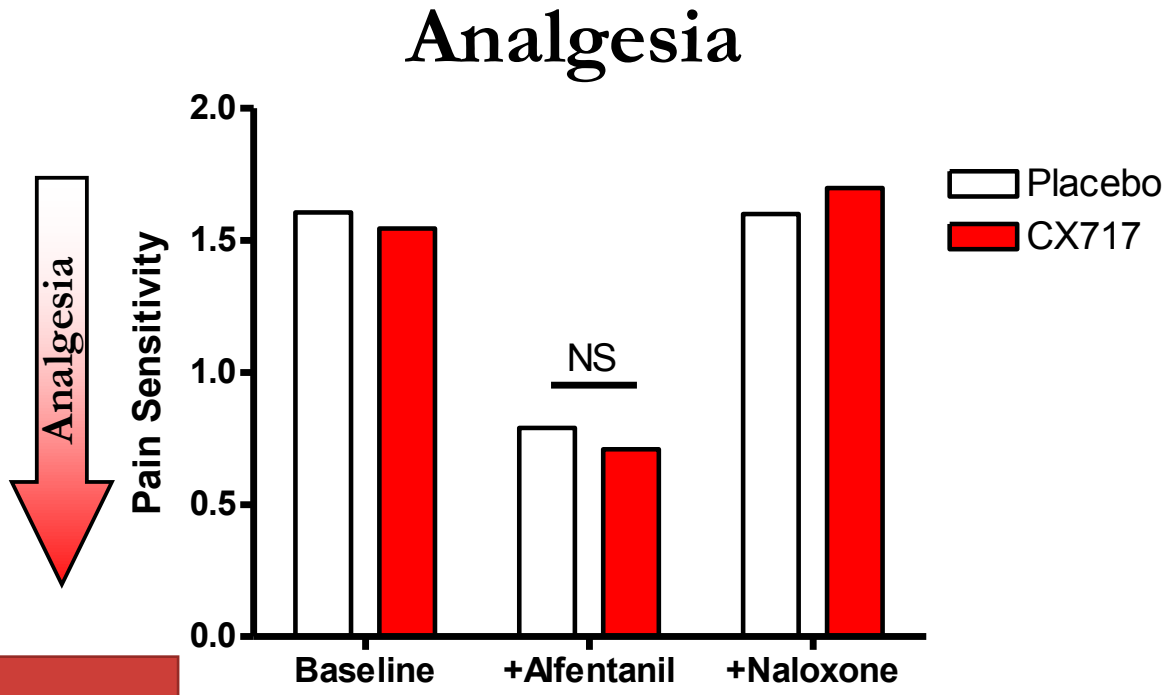


Delivery of a electrical stimulation to finger



- Alfentanil reduced the pain sensitivity (produced analgesia)
- Analgesia was unaffected by CX717

Data are expressed as the pain sensitivity, normalized to the Baseline measurement. N = 15 and 16 per group. CX717 dose is 1500mg.

Respiratory Diseases Product Pipeline

RespireRx Pharmaceuticals Inc

Compound	Indication	Pre-clinical	Phase 1	Phase 2
Dronabinol	Obstructive Sleep Apnea			
CX1739	Central Sleep Apnea Opioid-induced RD Spinal Damage/Pompe			
CX717	Combination Formulation with Opioids for Reduced RD			
CX1942	Drug-induced Respiratory Depression (injectable)			

Key Objectives for 2016 (Pending Financing)

RespireRx Pharmaceuticals Inc

Compound	Indication	Status	Estimated Start Date	Estimated Completion
Dronabinol	Obstructive Sleep Apnea	Phase 2B	Underway	3Q2016
CX1739	Opioid-induced RD	Phase 2A	1Q2016	2Q2016
	Central Sleep Apnea	Phase 2A	3Q2016	2Q2017
CX1739 / CX717	Spinal Cord Injury, Pompe Disease, other	Phase 2A	3Q2016	1Q2017
CX717	Combination formulation with opioid	Pre-clinical studies	1Q2016	4Q2016
CX1942	Injectable for RD	Pre-clinical studies	3Q2016	4Q2017

Capital Structure (in thousands of shares) & Market Metrics

RespireRx Pharmaceuticals Inc

	Total As of September 30, 2015
Common Stock	477,221
Common Stock Equivalents of all Convertibles (Preferred Stock and Convertible Notes)	95,934
Common Stock Equivalents of all Options and Warrants	380,247
Total	953,402

	January 6, 2015
Closing price per share of Common Stock	$0.0216
Fully diluted market capitalization ($ rounded)	$20,593,000

Management and Directors

RespireRx Pharmaceuticals Inc

James Manuso	President, CEO & Vice Chairman
Arnold Lippa	CSO & Chairman
Jeff Margolis	VP, Secretary/Treasurer, Director
Robert Weingarten	CFO, Director
Richard Purcell	Senior VP, R& D
Katie MacFarlane	Director CCO Agile Therapeutics
James Sapirstein	Director CEO ContraVir Pharmaceuticals
John Greer	Chairman, Scientific Advisory Board Prof & Dir. Neuroscience Ctr., U. Alberta

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