RespireRx Pharmaceuticals Inc

OTC QB: RSPI

CANTOR FITZGERALD 2ND ANNUAL HEALTHCARE CONF.
JULY 13, 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.

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. In addition, any investment in the Company is subject to numerous risks. Investors must be able to afford the loss of their entire investment. Any such representations and warranties and further discussion of risk factors would be made solely in formal agreements executed by the Company with its investors.

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

Innovative Medicines for Respiratory Diseases

RespireRx Pharmaceuticals Inc

- Two proprietary, small molecule platforms
- Three Phase 2 or Phase 2-ready development programs
- Three pre-clinical programs
- Focus on blockbuster markets with unmet clinical needs
- More than 120 + patents and patent applications
- Multiple opportunities for strategic collaborations
- Non-dilutive financing from NHLBI and NIDA
- Experienced and accomplished management team

Company Focus

RespireRx Pharmaceuticals Inc

- **Sleep Apneas**
  - Dronabinol for Obstructive Sleep Apnea (**OSA**)
  - Ampakines for Central Sleep Apnea (**CSA**)
- **Drug-induced Respiratory Depression (RD) - Ampakines**
  - Acute use – surgical anesthesia/sedation
  - Semi-acute use – post-surgical pain management with opioids
  - 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**
- **More than $5 million in NIH grants supporting two programs**

Respiratory Diseases Product Pipeline

RespireRx Pharmaceuticals Inc

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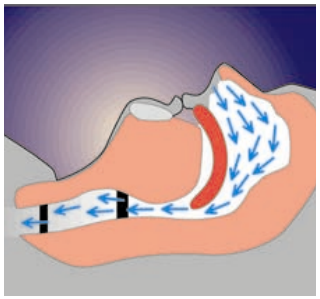
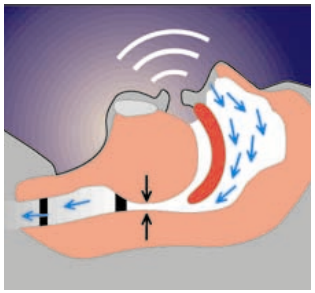
- **Obstructive Sleep Apnea (OSA):** a decrease or complete halt in airflow during sleep
  - Induced by relaxation of muscles during sleep
  - Soft tissue in back of throat collapses and obstructs upper airway
- **Significant morbidity due to stroke, hypertension, heart failure, diabetes, and other cardiovascular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

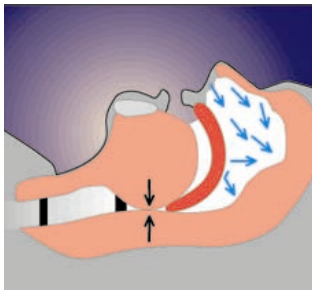
Normal Breathing



Snoring



OSA



CPAP Efficacy is Severely Limited by Patient Compliance

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- Standard of Care
- 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: Breakthrough Treatment for OSA

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- **Mechanism of Action**
  - Dronabinol is (delta 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 with 120 patients 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**
  - $5MM NIH-funded 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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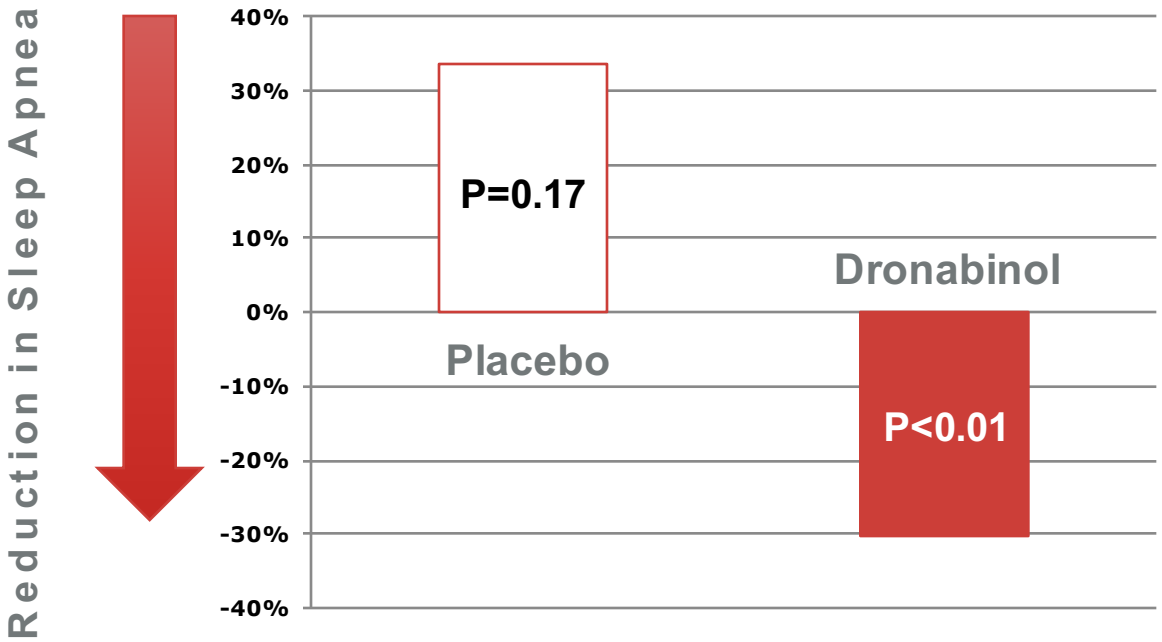

Apnea Suppression as a Function of Dose and Time

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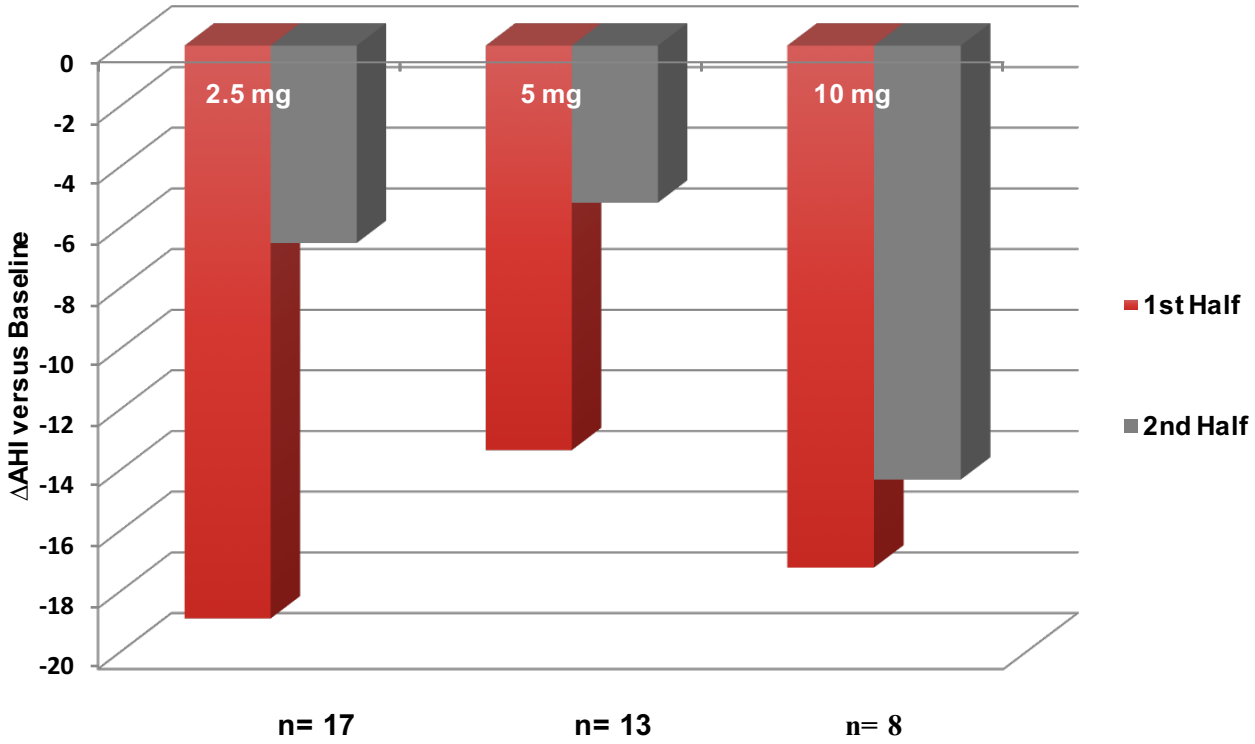

The plasma half-life of dronabinol is 2 – 4 hours.

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 NDA submission
- Doses: Placebo, 2.5 mg, 10 mg qd
- All 120 subjects dosed (40/group, 6 weeks dosing)
- Data analysis underway; readout in Q3/2016
- Meet with FDA after trial completion to determine registration path forward

Protecting Dronabinol in the Market

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- Licensed 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 and manufacturing protection

The Dronabinol Opportunity

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Impact on Patient	Commercial Opportunity
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

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 medicine or device is approved for the CSA indication**

Severity of CSA is Correlated with Increased Mortality in Heart Failure Patients

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Reducing Central Sleep Apnea May Reduce Mortality in Heart Failure Patients

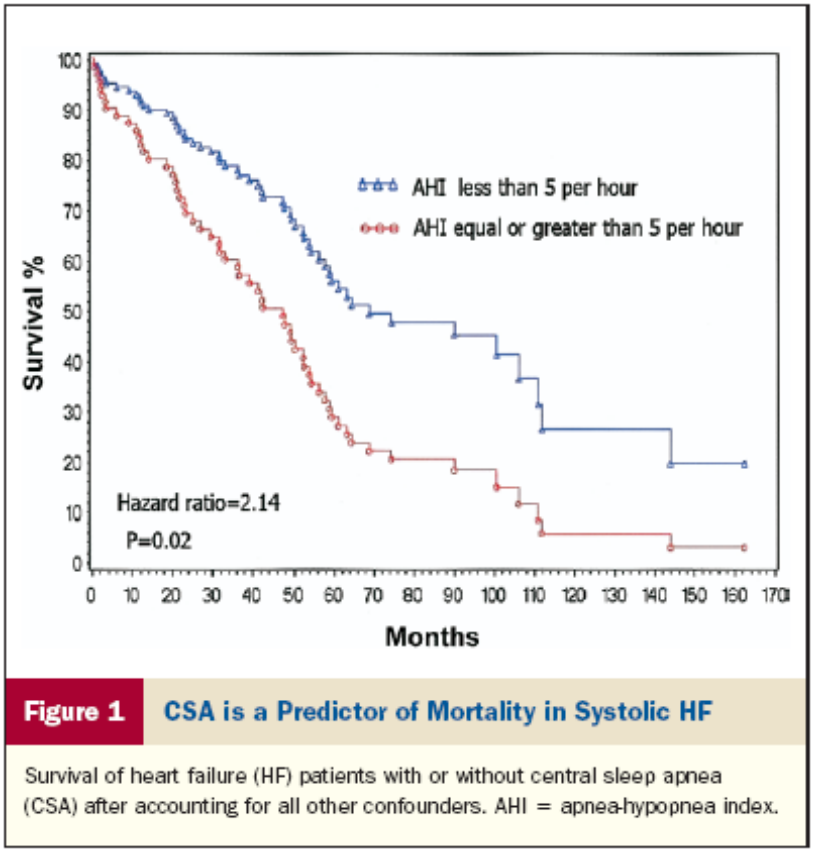

Figure 1 **CSA is a Predictor of Mortality in Systolic HF**

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 Medicines

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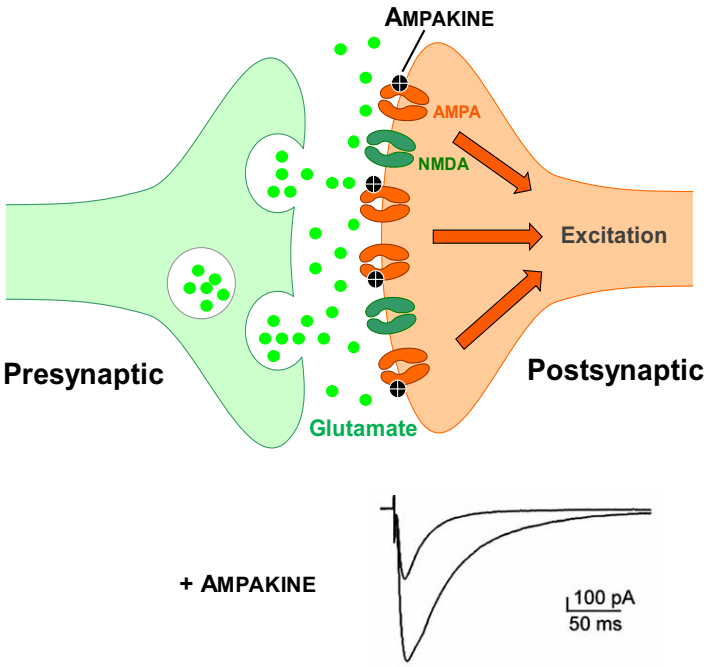
AMPA Receptors Mediate Synaptic Transmission in the Brain

- 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 Treatments for Respiratory Depression

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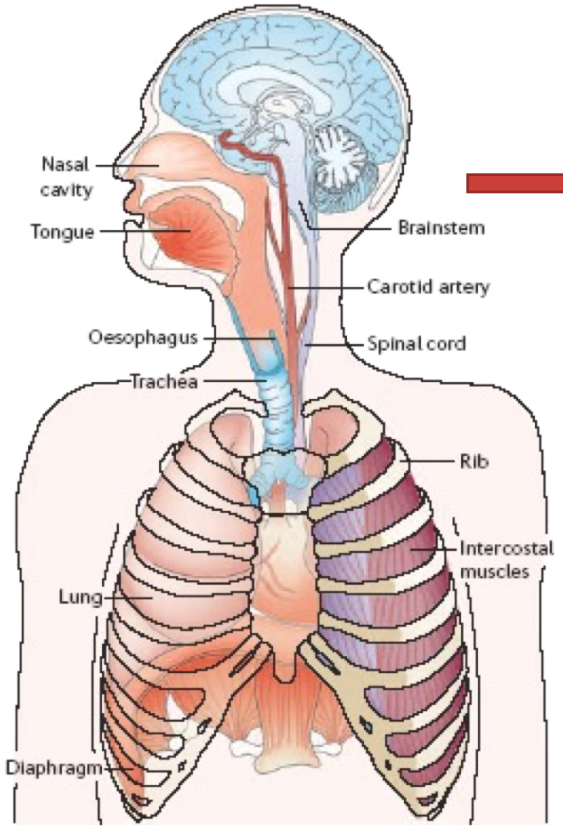
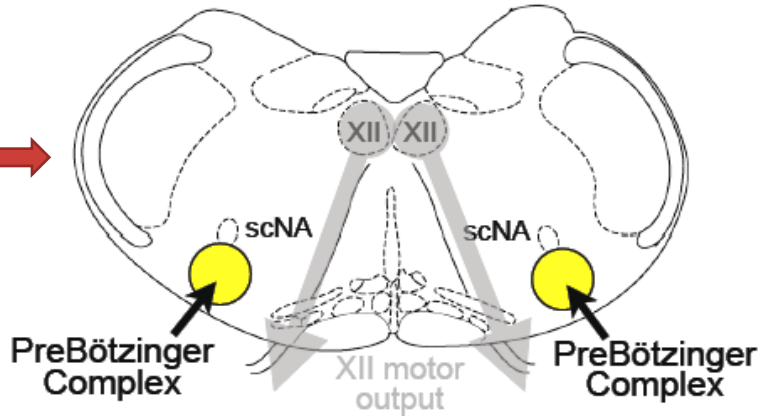


Initial research conducted by Dr. J. Greer, U. Alberta
Ren et al, Anesthesiology. 110:1364-1370, 2009



- 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
  - Combination formulation with an opioid for treatment of chronic pain

- **Stage of Development**
  - Successfully completed four Phase 1 studies
  - Efficacy signals observed in CSA
  - Phase 2 trial in opioid-induced RD initiated at Duke University

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

CX1739: Completed Phase 2A in Sleep Apnea

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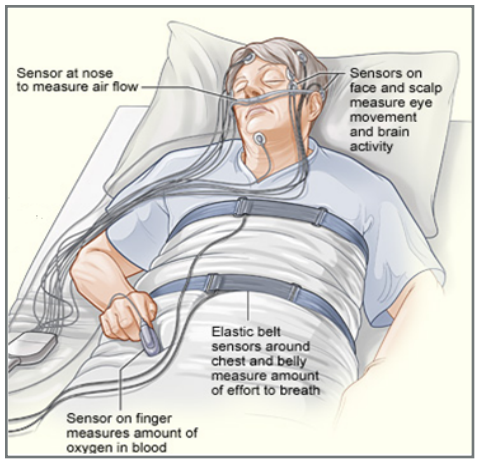
Design	Randomized, double-blind, placebo-controlled study
Population	20 adults with all types of moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)
Dosing	Each subject received either placebo or a single dose of 900mg CX1739 one hour before lights out
Primary Measures	Apnea-Hypopnea measures;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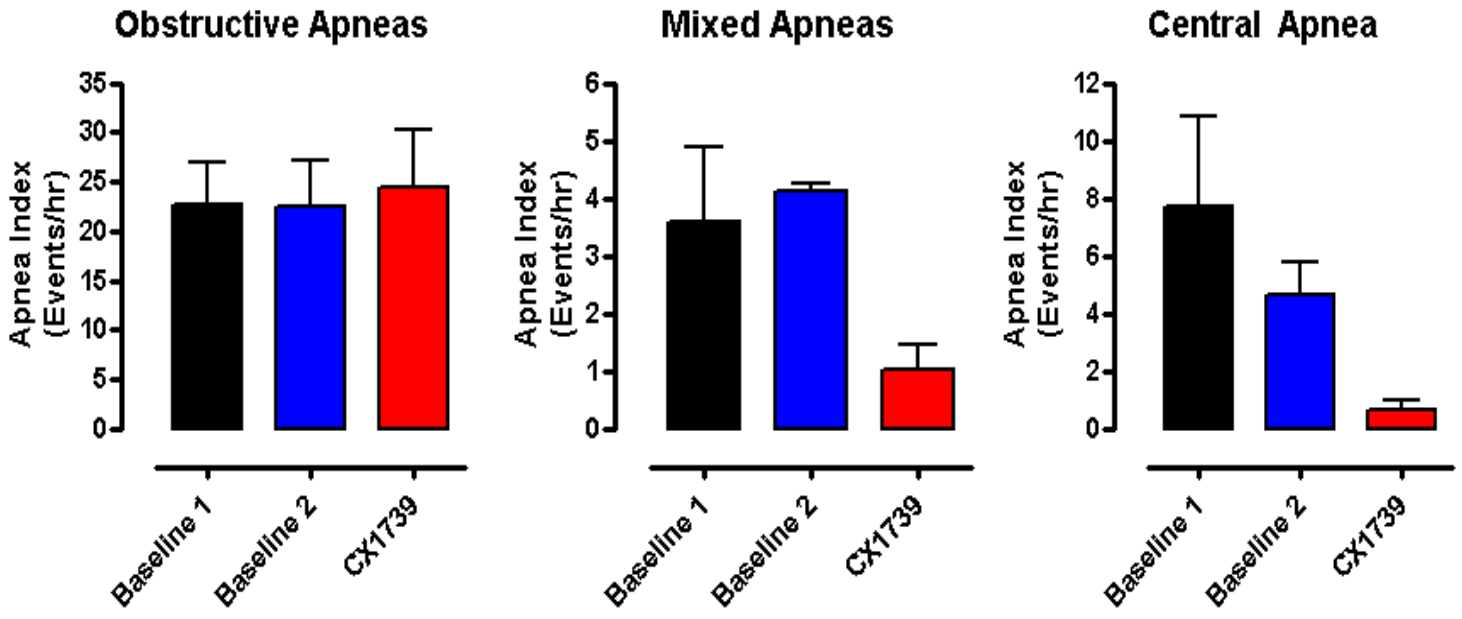

Drug-induced Respiratory Depression

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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 Respiratory Depression (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
- **Multi-billion dollar per year market potential**

Ampakines Prevent Opioid-induced Respiratory Depression

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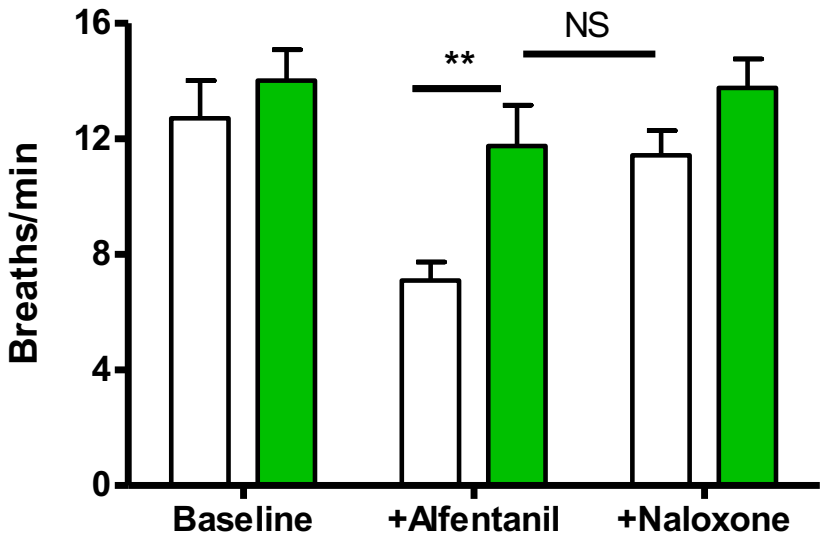
- Two clinical studies in normal, healthy volunteers with CX717, a second-generation Ampakine
- Moderate Respiratory Depression was induced experimentally by infusion of the opioid, Alfentanil
- Respiratory and analgesia end-points were measured

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

RespireRx Pharmaceuticals Inc



** 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 Does Not Interfere With the Analgesic Properties of Opioids

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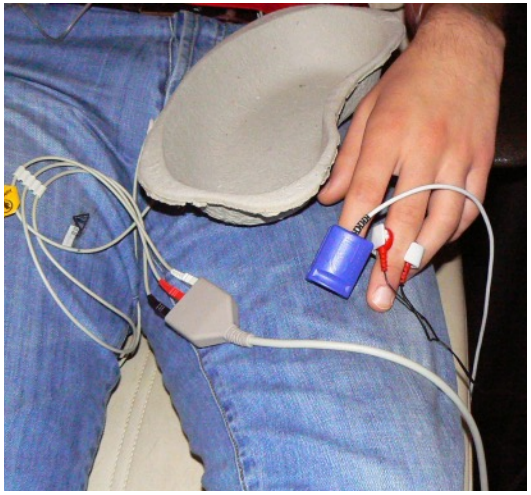
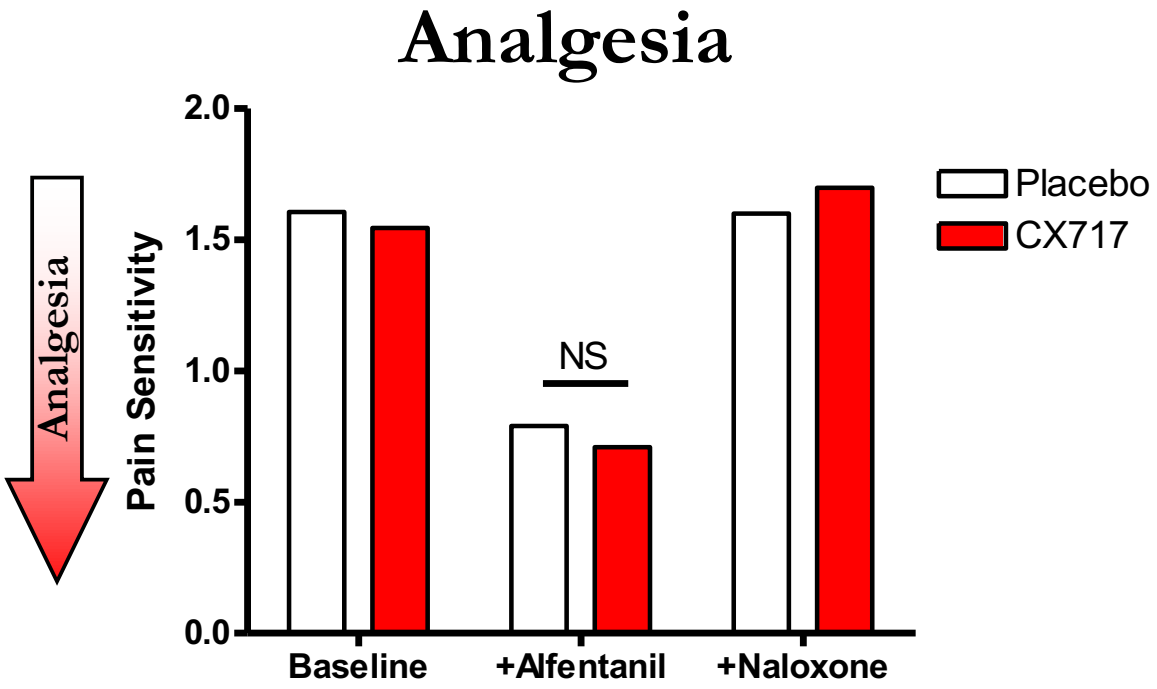


Delivery of a electrical stimulation to finger

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.

CX1739: Phase 2A in Opioid-Induced Respiratory Depression

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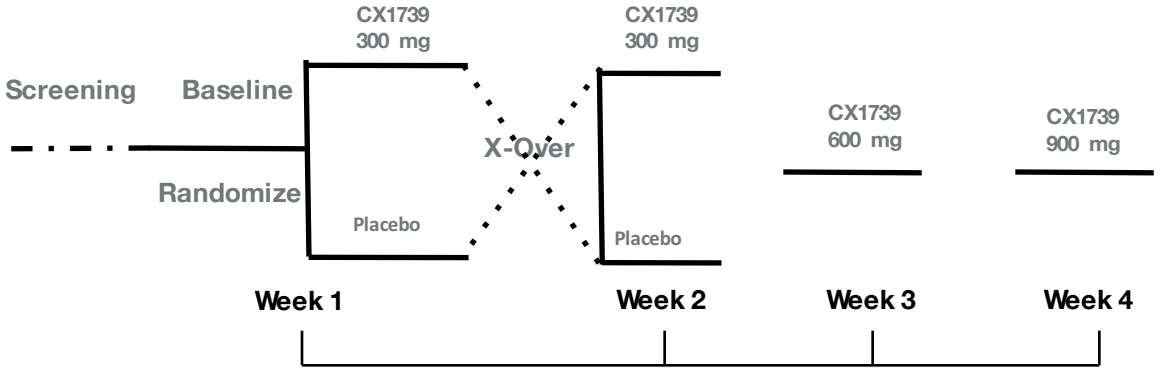
Protocol	Antagonism of Opioid-Induced Respiratory Depression by CX1739 with Preservation of Opioid Analgesia
Design	Randomized, Blinded, Placebo-controlled, Cross-Over with Dose Escalation
Dosing	Each subject will receive acute doses of placebo, 300 mg, 600 mg, and 900mg CX1739 once per week for four consecutive weeks; Each week, subjects will receive doses of remifentanil 3 hours (Tmax) after CX1739 or placebo.
Study Objectives	Primary: What is the efficacy of ascending doses of CX1739 to antagonize remifentanil-induced RD in healthy subjects, as measured by plethysmography? Is CX1739 safe when used in conjunction with remifentanil? Secondary: Does CX1739 reduce the analgesic effects of remifentanil? Does CX1739 alter the bispectral index (BIS) measure of sedation?



Respiratory Diseases Product Pipeline

RespireRx Pharmaceuticals Inc

Compound	Indication	Preclinical	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 Repertory Depression			
CX1942	Drug-induced Respiratory Depression (injectable)			

NIH-Supported Programs in Drug Abuse

RespireRx Pharmaceuticals Inc

- **Non-Core Programs in Drug Abuse and Addiction**
  - Cocaine and Amphetamines
  - Research and development program with NIDA
  - NIDA contracts with specialist labs and pays for animal studies
  - Company provides compounds and retains all rights

Capital Structure (thousands of shares) & Market Metrics

RespireRx Pharmaceuticals Inc

	Total as of May 31, 2016
Common Stock	648,768
Common Stock Equivalents of Convertible Notes	9,153
Common Stock Equivalents of all Options and Warrants Granted	556,251
Total	1,214,172

	May 31, 2016
Closing price per share of Common Stock	$0.021
Fully diluted market capitalization ($ rounded)	$25,498,000

* Preliminary Proxy Statement has been filed with the SEC for Special Stockholders' meeting to be held on August 16, 2016 to approve 325:1 reverse stock split and adjust the number of authorized shares

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

Innovative Medicines for Respiratory Diseases

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- Multiple opportunities for strategic collaborations
- Non-dilutive financing from NHLBI and NIDA
- Experienced and accomplished management team

Strategic Considerations, Post-Phase II Results

RespireRx Pharmaceuticals Inc

- Prepare RSPI for an up-listing to NASDAQ
- Engage advisor to assist with capital raising
- Directly manage all trials of medicines in development
- Partner/License/Sell one or more medicines in development
- Partner/License select applications of ampakine platform

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