RespireRx Pharmaceuticals Inc

OTC QB: RSPI

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

BIO Investor Forum, 2016
San Francisco, October 18-19, 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" 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

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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

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**
  - Acute use – surgical anesthesia/sedation
  - Semi-acute use – post-surgical pain management with opioids
  - Chronic use – outpatient pain management with opioids
- **Spinal Cord Injury – Ampakines**

Innovative Medicines for Respiratory Diseases

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- Two proprietary, small molecule platforms
- Three Phase 2 development programs
- Additional 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

Respiratory Diseases Product Pipeline

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

Dronabinol for Obstructive Sleep Apnea

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Obstructive 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

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: 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 completed and awaiting data
- **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

Dronabinol Proven to Reduce Apnea in OSA Subjects

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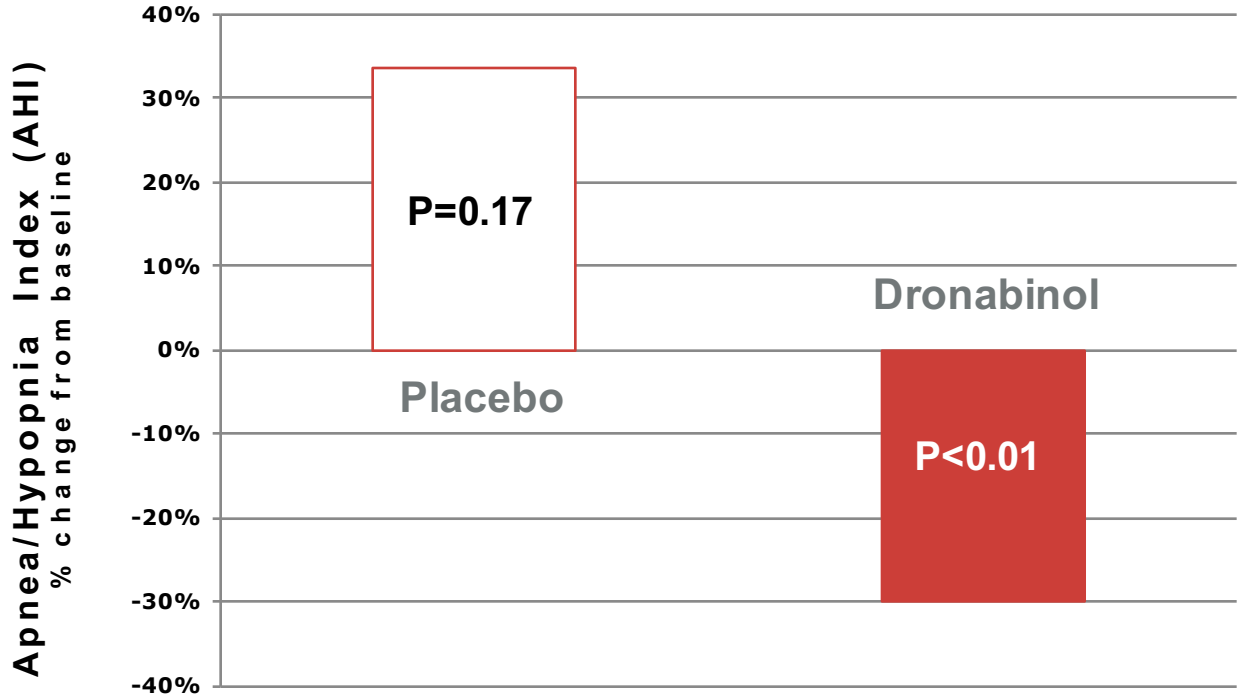

Apnea Suppression as a Function of Dose and Time

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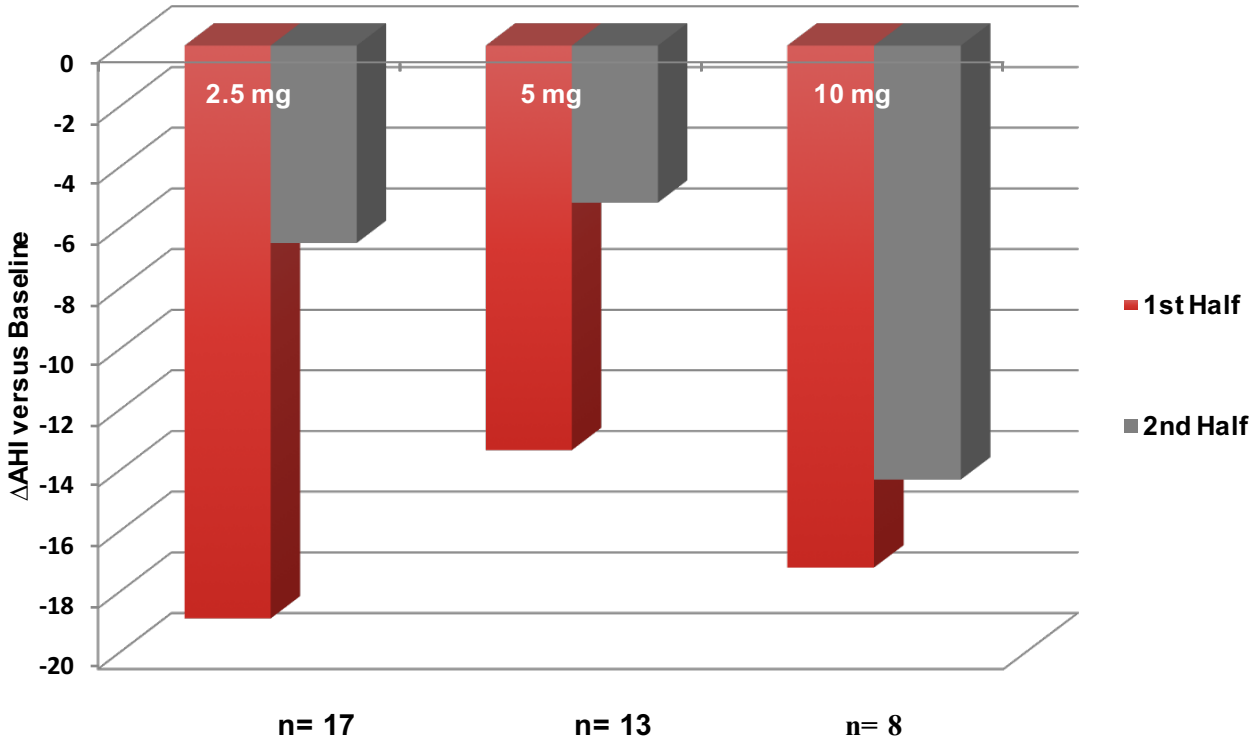

The plasma half-life of dronabinol is 2 – 4 hours.

Completed 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
- Doses: Placebo, 2.5 mg, 10 mg qd
- 6 weeks dosing
- Trial completed
- Data expected Q4/2016
- Meet with FDA after trial completion to determine registration path forward

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

Protecting Dronabinol in the Market

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- 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

Ampakines for Opioid-Induced Respiratory Depression

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Translational Approaches to Respiratory Disorders – A Short Course

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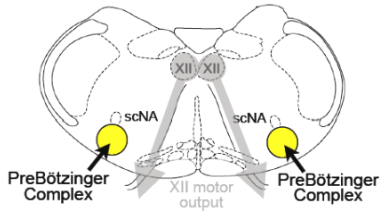
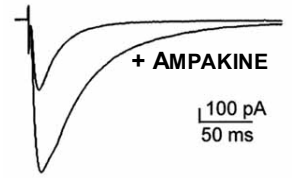
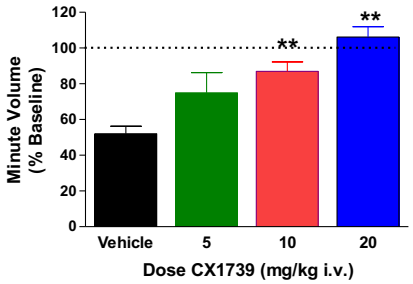


- Brain stem nuclei that regulate breathing contain opioid and AMPA glutamate receptors that inhibit and excite, respectively



- 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 opiate-induced respiratory depression

CX717 Prevents Opioid-induced Respiratory Depression in Humans – Target Engagement

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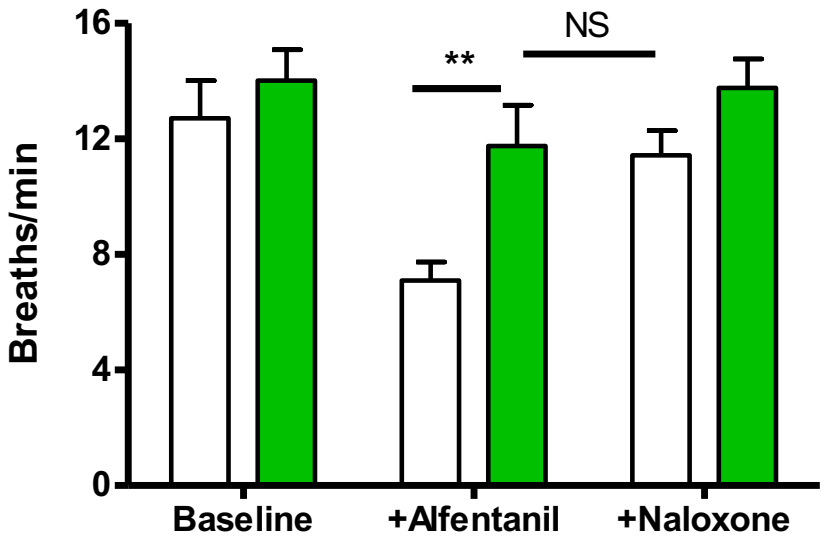

** P < 0.01
NS - Not Significant

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

Oertel et al., (2010) Clin Pharmacol Ther. 87(2):204-11

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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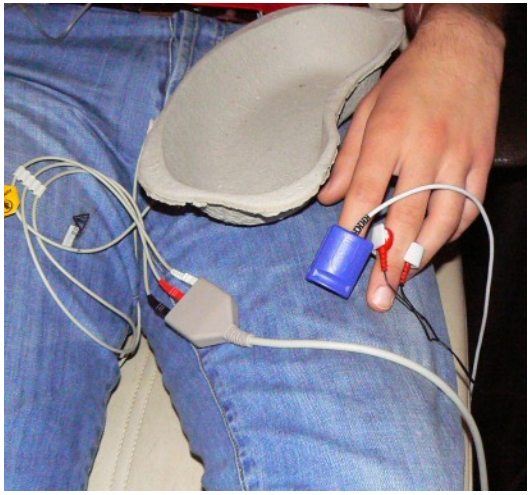
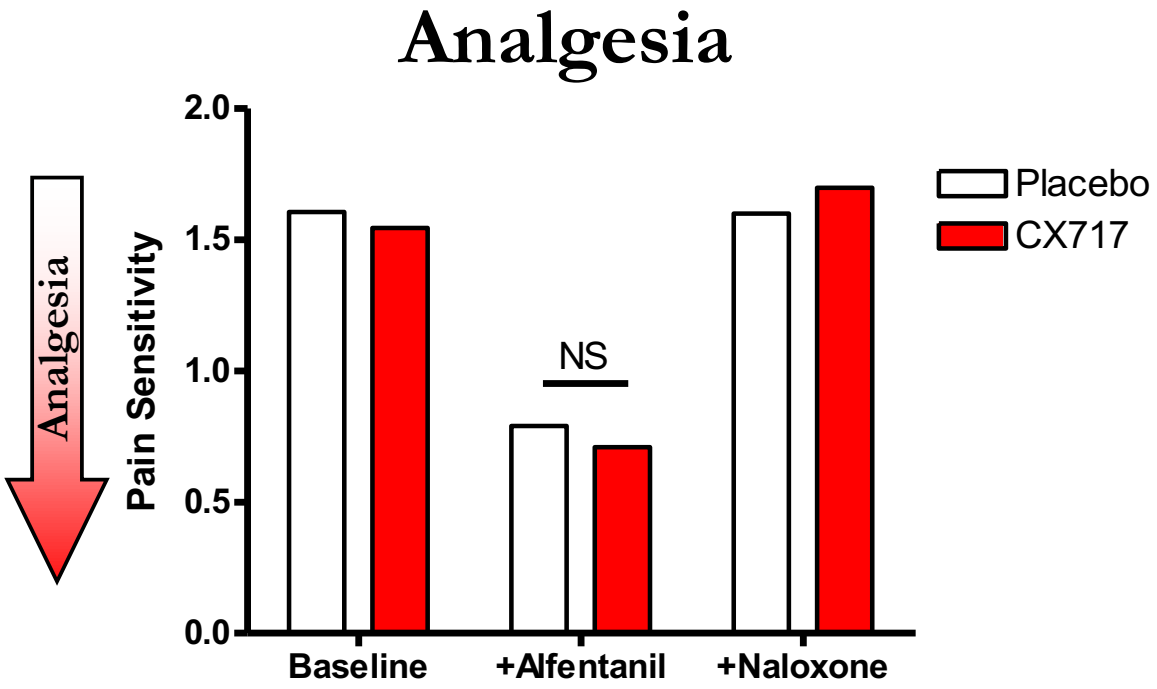


Delivery of a electrical stimulation to finger

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: 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 and 2 Phase 2A studies
  - Phase 2A trial in opioid-induced RD completed at Duke University
  - Safe and well tolerating
  - Re-analyzing efficacy data resulting from un-blinding error

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

CX1739: Phase 2A in Opioid-Induced Respiratory Depression

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Protocol	Antagonism of Remifentanil-Induced Respiratory Depression by CX1739 in Two Clinical Models of Respiratory Depression
Design	Randomized, Blinded, Placebo-controlled, Cross-Over with Dose Escalation
Dosing	17 subject received and completed acute doses of placebo, 300 mg, 600 mg, and 900mg CX1739 (during separate weekly visits) followed by two protocols for remifentanil administration (REMI 1 and REMI 2)
Study Objectives	Primary: Time to respiratory recovery following remifentanil-induced RD during REMI 1 protocol Reduction in respiratory rate during REMI 2 protocol Safety when used in conjunction with remifentanil Secondary: Impact on analgesic effects of remifentanil Impact on volunteer bispectral index (BIS) measure of sedation

CX1739: Phase 2A – Overall Study Design

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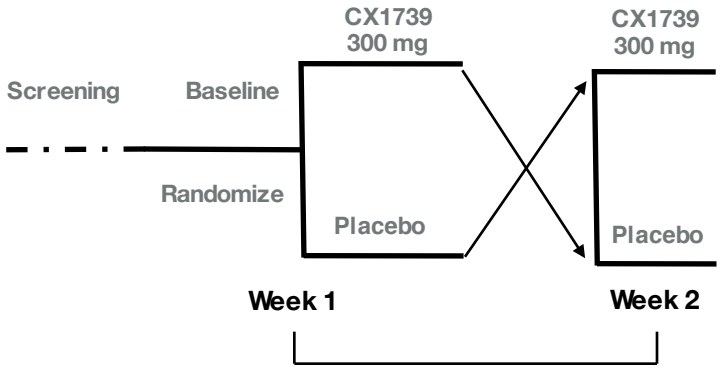
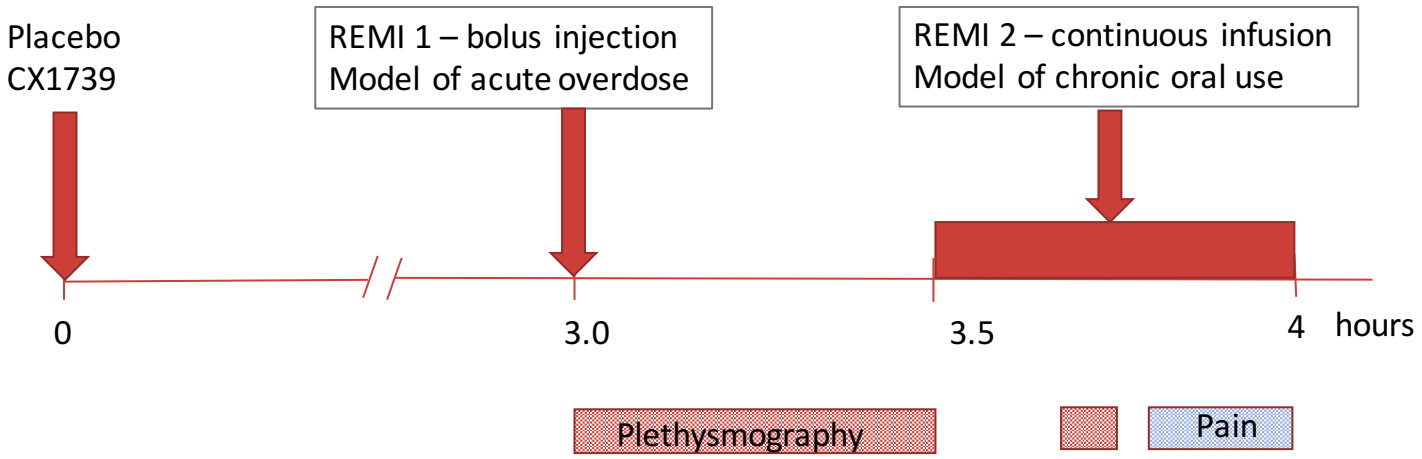
STAGE 1
Double-blind, Placebo-Controlled Crossover

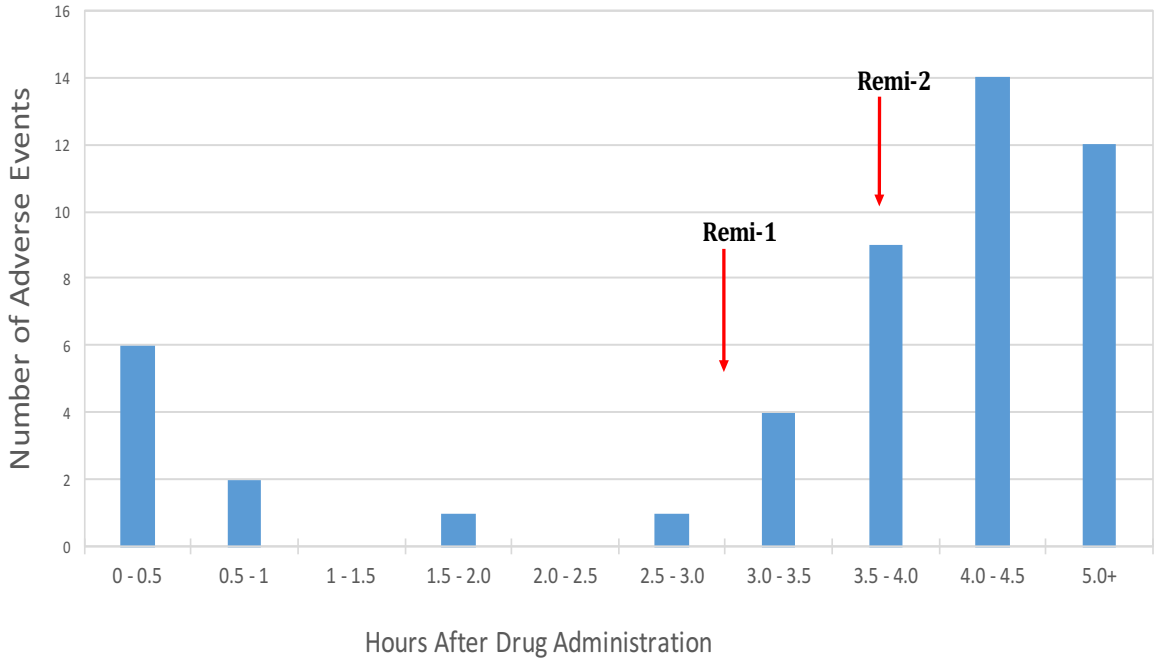


STAGE 2
Open-label, Dose Ascending

CX1739: Phase 2A – Daily Protocol



CX1739: Phase 2A – Safety



SAFETY DATA

- CX1739 was safe and well tolerated with no SAEs
- Most frequent AEs were nausea, vomiting, headache and dizziness, all of which are common side effects of opioids
- 39 of 49 AEs occurred after remifentanil
- 8 AEs occurred less than one hour after ampakine or placebo

Ampakines for Central Sleep Apnea

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Central Sleep Apnea (CSA)

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- **Lack of drive from the brain to breathe during sleep**
- **CSA Patients**
  - 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 CSA**

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

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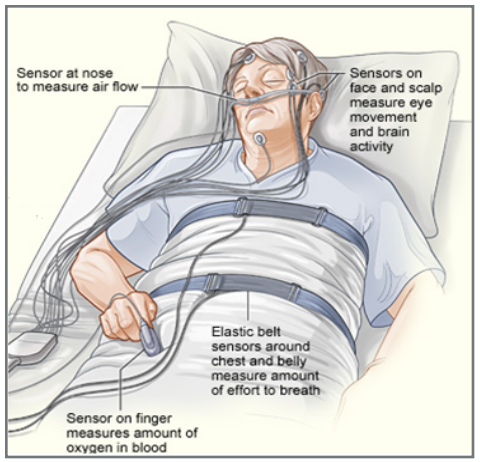
Design	Randomized, double-blind, placebo-controlled study
Population	20 adults with all types of moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)
Dosing	Each subject received either placebo or a single dose of 900mg CX1739 one hour before lights out
Primary Measures	Apnea-Hypopnea measures;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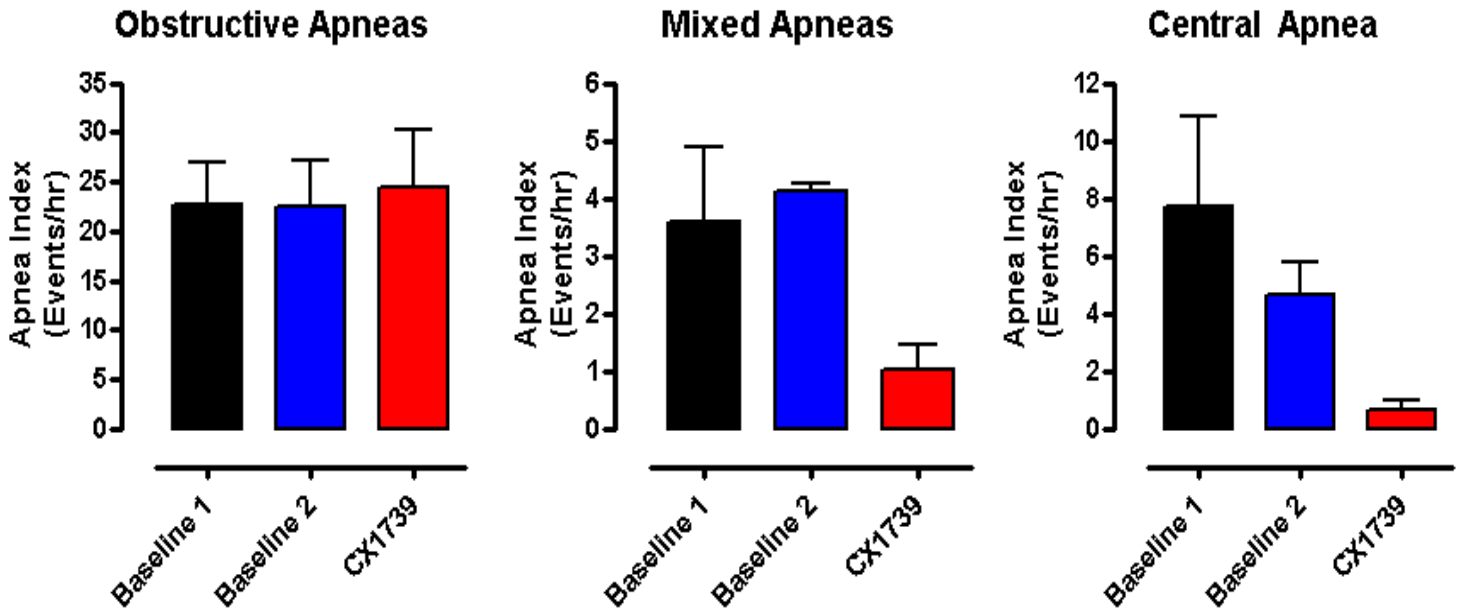

Oertel et al., (2010) Clin Pharmacol Ther. 87(2):204-11

CX1739: Proposed Phase 2 in Sleep Apnea – Multiple Dose

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Protocol	Evaluation of CX1739 for the Treatment of Central Sleep Apnea in Patients on Chronic Opioid Therapy
Design	• Randomized, Blinded, Placebo-controlled, Multiple Dose Study at Multiple Sites • Subjects with a documented history of chronic opioid use for pain management and a diagnosis of Central Sleep Apnea (CSA) as confirmed by plethysmography and EEG
Dosing	28 days of BID doses
Study Objectives	Primary: To evaluate the ability of daily, BID doses of CX1739 to reduce AHI, AHT and daytime sleepiness Secondary: To evaluate whether CX1739 reduces the analgesic effects of opioids for pain management To evaluate whether CX1739 improves Sleep Architecture To evaluate the safety of CX1739 when used in conjunction with oral opioids

Ampakines for Breathing Disorders due To Spinal Cord Injury

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CX717: Second Generation Oral Ampakine in Phase 2

RespireRx Pharmaceuticals Inc

- **Targeted Indications**
  - Spinal Cord Injury
  - Combination formulation with an opioid for treatment of chronic pain
- **Stage of Development**
  - Completed 6 Phase 1 and 4 Phase 2 studies
  - Two positive Phase 2A trials in opioid-induced RD
  - Positive clinical effects in ADHD and cognition
- **Intellectual Property Protection**
  - Method-of-use patent (expires 2030)
  - Hatch/Waxman Amendment
  - Potential breakthrough status for SCI

CX717: Spinal Cord Injury

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Incidence

- Estimated 276,000 people with SCI in the US, with 12,000 new cases per year
- ~92,000 with respiratory distress
- Eligible for Orphan Status

Breathing problems are substantial after SCI

- Approximately half of all SCIs occur in the cervical region, leading to increased morbidity and mortality
- More than two-thirds of acute cervical SCI patients require respiratory support (usually mechanical ventilation) and 40% require continued ventilatory support after acute care discharge

Current Treatments

- Mechanical ventilation
- Resistive breathing exercises
- Diaphragm pacing using electrical nerve stimulation

Clear Market Need

- Respiratory disorders are the leading cause of death for SCI patients
- There exists a significant and unmet need for translatable strategies to improve respiratory motor function after incomplete cervical SCI

CX717 – Animal Models of Spinal Cord Injury

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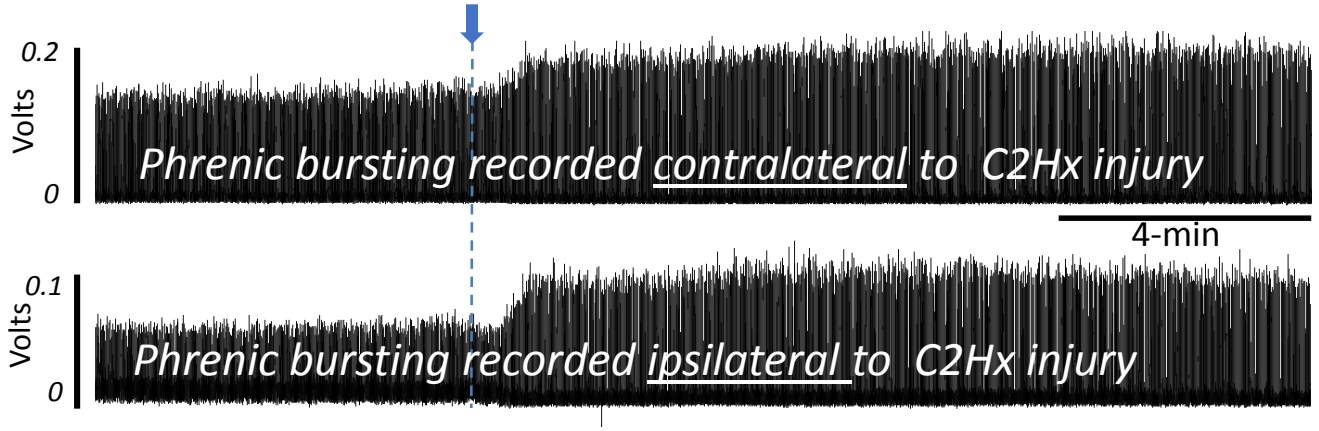
Unilateral hemi-transections at the level of the 2nd cervical vertebra are performed on rats and electrical activity is recorded from phrenic nerves, which innervate the diaphragm and contribute to the regulation of breathing.



8 weeks following surgery, CX717 (15 mg/kg) increases amplitude in electrical recordings taken from rat phrenic nerves

CX717: Proposed Phase 2 in Spinal Injury – Multiple Dose

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Protocol	Evaluation of CX717 for the Treatment of Breathing Disorder in Patients with SCI
Design	Ascending Dose Study
Dosing	BID doses of 250 mg, 500mg and 750 mg CX717 daily for 28 days
Study Objectives	Primary: To evaluate the ability of daily, BID doses of CX717 to improve breathing Secondary: To evaluate whether CX717 improves Sleep Architecture

Summary

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Respiratory Diseases Product Pipeline

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

Development Milestones

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	4Q2016	1Q2017	2Q2017	3Q2017	4Q2017	1Q2018
CX1739						
RD Clinical Trial at Duke						
CSA Clinical Trial pending results of RD Trial						
Formulation, PK and ADME						
CX717						
FDA Regulatory						
Spinal Cord Injury Clinical Trial						
Ampakine/Opiate Combination Formulation						
Formulation Design						
Phase I Clinical Trials for Efficacy & PK						
Dronabinol						
FDA Regulatory						
Formulation						

Capital Structure (rounded) & Market Metrics

RespireRx Pharmaceuticals Inc

	Total as of October 13, 2016
Common Stock	2,019,000
Common Stock Equivalents of Convertible Notes (estimated)	29,000
Common Stock Equivalents of all Options and Warrants Granted (excludes 371,000 reserved for equity plans)	1,745,000
Total	3,793,000

Closing Price range (high → low), October 1 – October 13, 2016	$4.25 → $2.60
Fully diluted market capitalization range October 1 – October 13, 2016 (rounded)	$16,120,000 → $9,862,000

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 Senior VP, Napo Pharmaceuticals
James Sapirstein	Director CEO, ContraVir Pharmaceuticals
John Greer	Chairman, Scientific Advisory Board Prof & Dir. Neuroscience Ctr., U. Alberta

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