

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01 Regulation FD Disclosure**

Cortex Pharmaceuticals, Inc. (the “Company”) has previously furnished via Current Reports on Form 8-K iterations of a slide presentation that it has also posted and updated on its website and shared with various interested parties and presented at conferences and in other contexts. The most recent version of this presentation was filed on a Current Report on Form 8-K/A filed May 18, 2015. Since that filing, the Company’s plans have continued to develop and the Company has accordingly decided to update the slide presentation, specifically to reflect the revised anticipated timing of certain milestones and targets listed therein, in connection with its attendance at the National Angel-VC Summit & Growth Capital Forum being hosted at the Yale Club New York on July 9, 2015. At that forum, and thereafter, the Company may provide the updated slide presentation to interested parties. The updated slide presentation will also be available on the Company’s website.

The updated slide presentation that the Company will be using at the conference is attached as Exhibit 99.1 and is being furnished and not filed pursuant to Item 7.01 of Form 8-K.

**Item 9.01 Financial Statements and Exhibits**

(d) Exhibits.

A list of exhibits that are furnished and filed as part of this report is set forth in the Exhibit Index, which is presented elsewhere in this document, and is incorporated herein by reference.

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**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: July 9, 2015

CORTEX PHARMACEUTICALS, INC.

By: /s/ Arnold S. Lippa  
Arnold S. Lippa  
President and Chief Executive Officer

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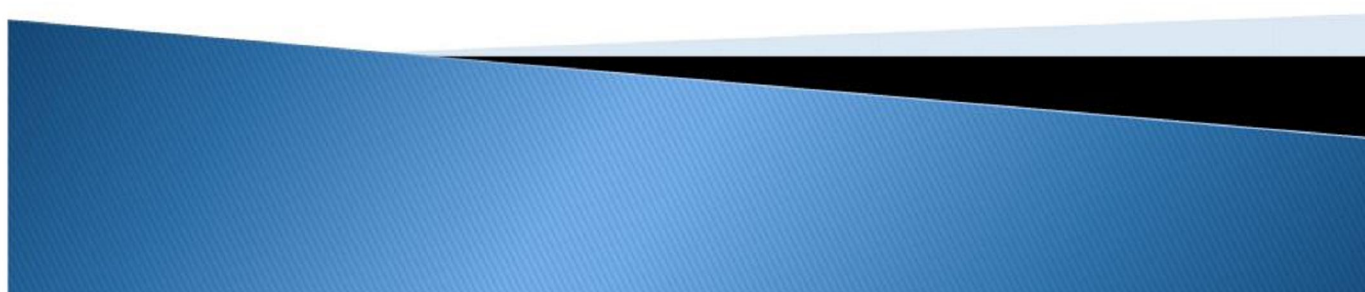
EXHIBIT INDEX

| <u>Exhibit Number</u> | <u>Exhibit Description</u>               |
|-----------------------|--|
| 99.1                  | Slide Presentation (furnished herewith). |



# Cortex Pharmaceuticals, Inc.

July 9, 2015

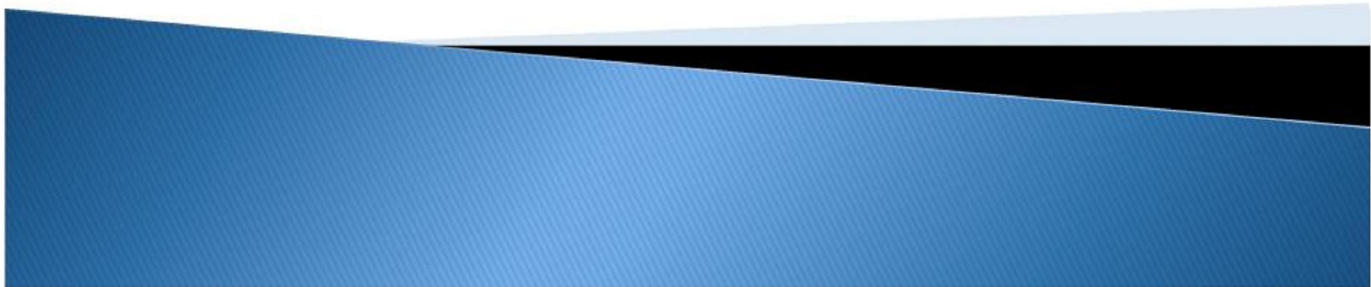


## Forward Looking Statements



*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.*



## Cortex is a leader in the discovery and development of innovative pharmaceuticals for the treatment of breathing disorders

- ▶ **Sleep Apnea**
  - Obstructive sleep apnea (OSA) – dronabinol
  - Central sleep apnea (CSA) - ampakines
- ▶ **Drug-induced respiratory depression (RD) - ampakines**
  - Semi-acute use – post-surgical pain management with opiates
  - Acute use – surgical anesthesia with propofol
  - Chronic use – Outpatient pain management with opiates
- ▶ **Two drug platforms with positive Phase2A efficacy results in RD as well as OSA and CSA**
- ▶ **Strong IP protection for compounds and uses**
- ▶ **Over \$5 million in NIH grants supporting drug development**



# Cortex Drug Platforms

## Cannabinoids

- Dronabinol (D9-THC) is a generic FDA-approved drug
- Positive Phase 2A data for treatment of obstructive sleep apnea
- Phase 2B clinical trial in progress
- Method patent licensed from U. Illinois for the treatment of sleep related breathing disorders

## Ampakines

- Positive allosteric modulators of AMPA glutamate receptors
- Positive effects for treatment of central sleep apnea in Phase 2A clinical trial
- Positive effects for treatment of drug-induced respiratory depression in Phase 2A clinical trial



# Sleep Apnea: A Large Market Opportunity

- ▶ **Sleep Apnea**

- Repetitive episodes of airflow cessation (apnea) or reduction (hypopnea) for more than 10s during sleep
- Three types: Obstructive, Central and Mixed

- ▶ **The Sleep Apnea Market is Large**

- 18 million U.S. adults with moderate or severe sleep apnea
- Market potential for sleep apnea is \$3 - 9 Billion/Year

- ▶ **Current Treatments**

- CPAP device
- Surgery; dental devices

- ▶ **Clear Market Need**

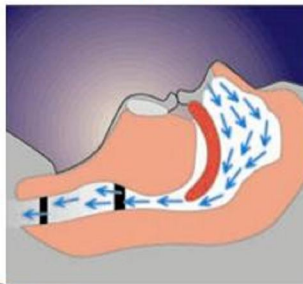
- Poor compliance with CPAP
- No drug treatment available



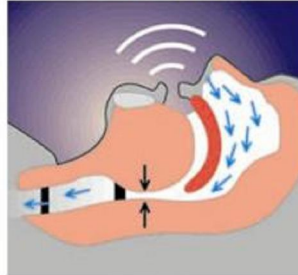
# Obstructive Sleep Apnea (OSA)

- ▶ **Obstructive sleep apnea (OSA) involves a decrease or complete halt in airflow despite an ongoing effort to breathe during sleep**
  - Occurs when the muscles relax during sleep
  - Soft tissue in back of throat collapses and obstructs upper airway
- ▶ **Affects 18 MM adults in the U.S.; no current drug treatment available**
- ▶ **Significant morbidity due to stroke, hypertension, heart failure, diabetes, and other cardiovascular diseases**

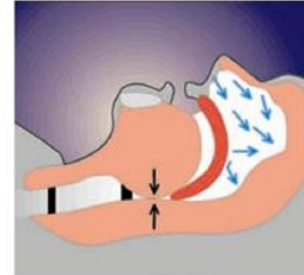
Normal Breathing



Snoring



OSA



# Obstructive Sleep Apnea

## Scope of the Problem in the US

| Disease State                | Estimated US Prevalence | Annual Estimated Cost to Society | Annual Indicated Drug Therapy Expenditures |
|------------------------------|-------------------------|----------------------------------|--|
| OSA <sup>1-5</sup>           | 18.0 MM                 | \$75.0 Billion                   | \$ 0                                       |
| Asthma <sup>6,7</sup>        | 16.4 MM                 | \$18.3 Billion                   | \$13.5 Billion                             |
| Hypertension <sup>8-10</sup> | 43.2 MM                 | \$73.4 Billion                   | \$48.5 Billion                             |
| Diabetes <sup>11,12</sup>    | 23.5 MM                 | \$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

## CPAP Efficacy is Greatly Limited by Patient Compliance

Works as an air splint to keep upper airway open during sleep

- ▶ 30% of patients prescribed CPAP never initiate treatment when prescribed a machine
- ▶ Over 50% of patients stop using CPAP in the first year of use; may only wear 3-4h/night





# Dronabinol: a Breakthrough Treatment for OSA

## ▶ Mechanism of Action

- Dronabinol is (D-9)THC, a cannabinoid agonist

## ▶ Stage of Development

- Schedule III drug available by prescription, 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 demonstrates clear signal of activity in OSA
- Phase 2B study in OSA in progress

## ▶ Intellectual Property

- Issued method-of-use patent in the US for the use of dronabinol for treating OSA (expires 2025) and pending patents on modified release formulations

## ▶ Funding

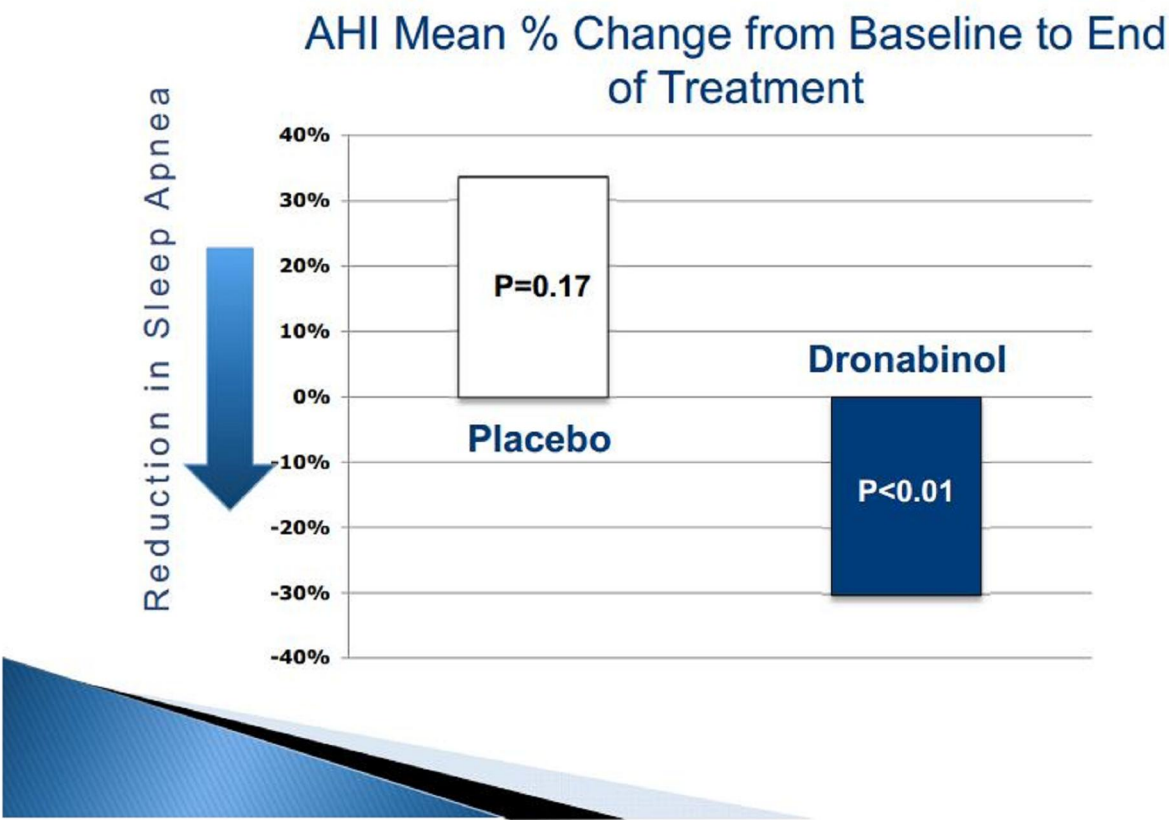
- NIH funded \$5MM grant for Phase 2B study in OSA

## Dronabinol Phase 2A Clinical Study in OSA

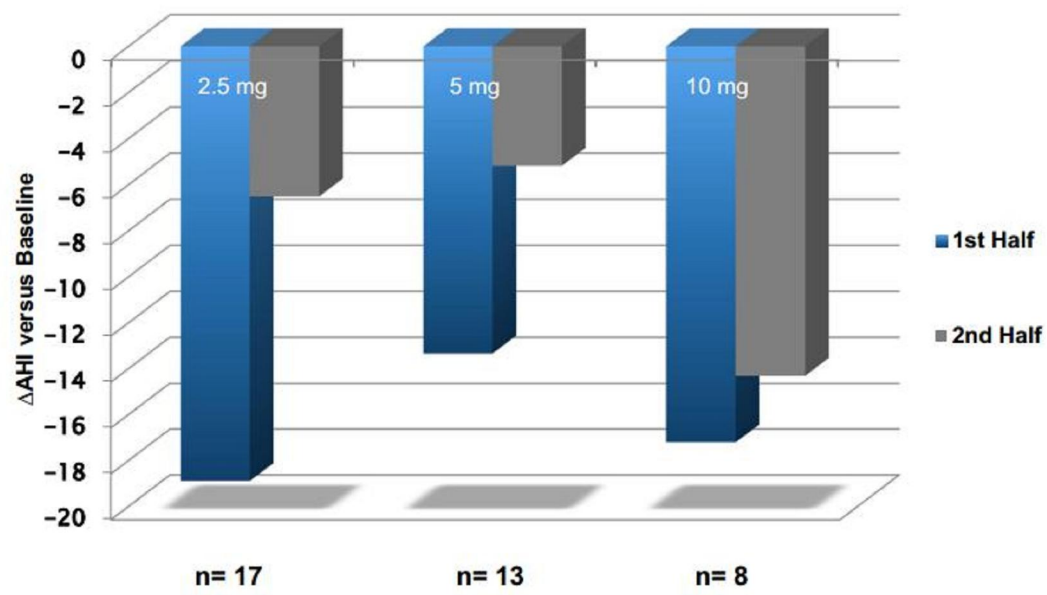
- ▶ **Randomized, double-blind, placebo-controlled dose escalation study in 22 patients with OSA**
- ▶ **Randomized to Placebo (N=5) or Dronabinol (N=17) for 21 days**
  - 2.5, 5 and 10 mg/night studied with weekly dose escalation
- ▶ **Overnight polysomnogram (PSG) at baseline, and after 7, 14 and 21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



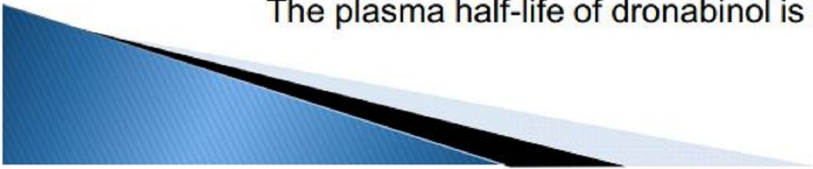
# Dronabinol Reduced the AHI in OSA Subjects



# Apnea Suppression as a Function of Dose and Time



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





## Dronabinol Phase 2B Trial in OSA

- Ongoing clinical study at 4 major medical centers
- Potentially pivotal for NDA approval
- 120 subjects (40/group, 6 wks dosing)
- Doses: Placebo, 2.5 mg, 10 mg qd
- \$5 MM NIH Grant
- Completion by May 2016



# Protecting Dronabinol in the Marketplace

- ▶ **Issued Method-of-Use patent for dronabinol and 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 third party payers**



# Dronabinol – A Game Changer

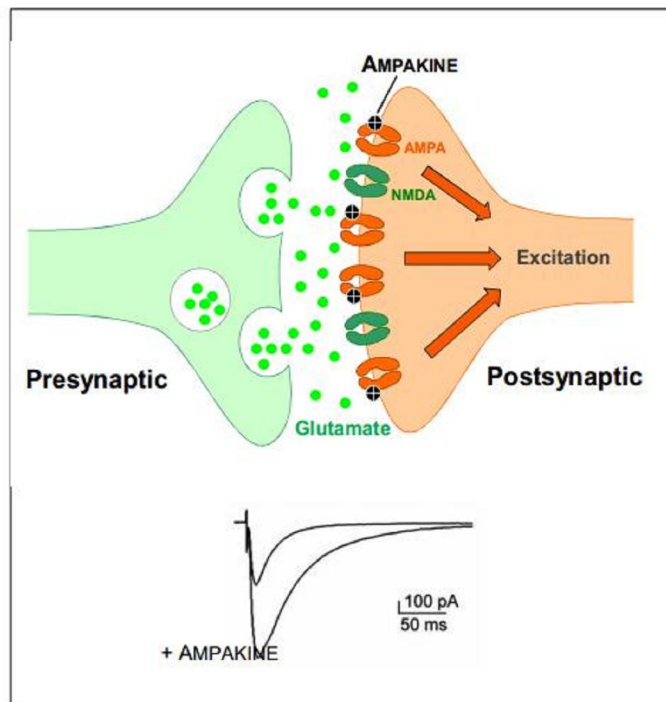
| Impact on Patient                            | Commercial Opportunity  |
|--|---|
| First drug available for OSA                 | Changes the nature of OSA treatment   |
| Ease of Use/Better Patient Compliance        | Broadly expands prescriber base from sleep specialists to include primary care physicians and cardiologists |
| Low cost                                     | Recurring lifetime sales rather than one time sale 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                     |



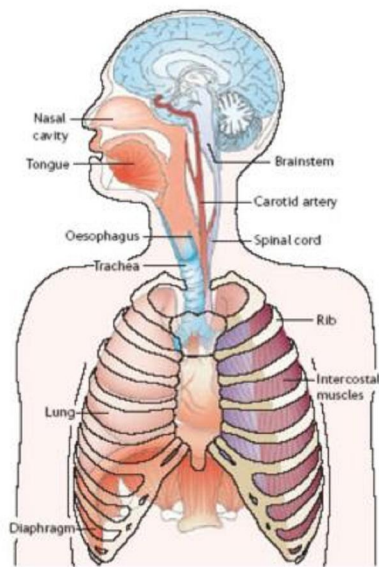
# AMPAKINES – A NOVEL CLASS OF DRUGS

## AMPA Receptors Mediate Synaptic Transmission in the Brain

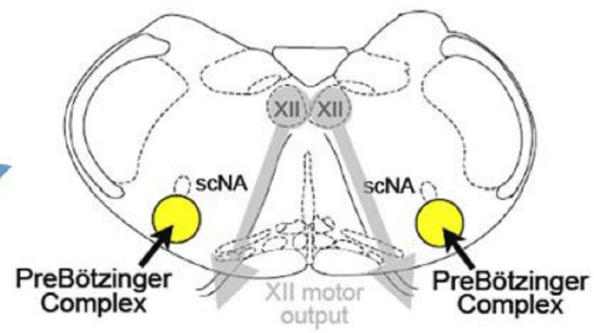
- ▶ Glutamate is the major excitatory neurotransmitter in the CNS
- ▶ Fast excitatory transmission is mediated by AMPA-type glutamate receptors
- ▶ Ampakines are positive, allosteric modulators of the AMPA-type glutamate receptor
- ▶ Prolong and strengthen synaptic transmission



## AMPAKINES – Novel Treatment for Respiratory Depression



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
- Opiates and other depressants mediate their inhibitory effects on breathing at this site
- Ampakines normalize breathing by enhancing firing of PreBotC respiratory rhythm neurons



# CX1739: An Oral Phase 2 Ampakine

## ▶ **Stage of Development**

- Completed Phase 1 in healthy volunteers and Phase 2a in central sleep apnea
- Ready for Phase 2 studies in opiate and propofol induced respiratory depression

## ▶ **Targeted Indications**

- Oral therapy for opiate and propofol induced respiratory depression
- Oral therapy for central sleep apnea
- Combination formulation with opiate for treatment of chronic pain

## ▶ **Intellectual Property**

- Protected by an issued Composition-of-Matter Patent (expires 2028), filed worldwide; a method-of-use patent (expires 2030)

## ▶ **Strong Preclinical Pharmacology**

- Broad-spectrum reversal and prevention of drug-induced respiratory depression



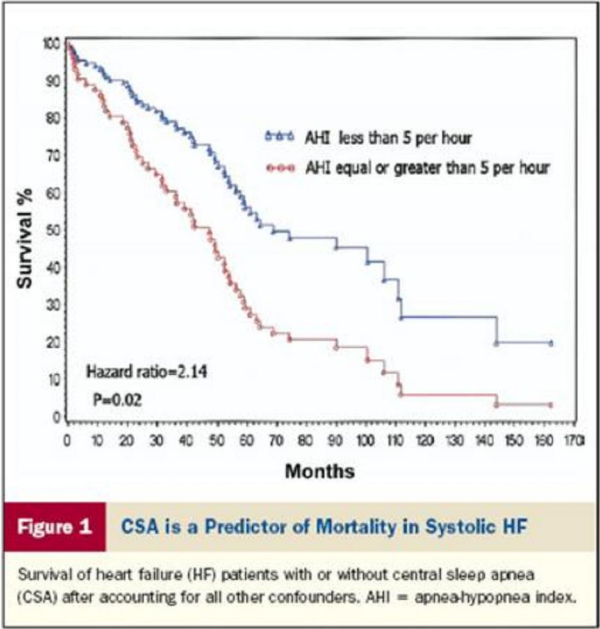
# Central Sleep Apnea

- ▶ **Characterized by a lack of drive from the brain to breathe during sleep – similar response as in treatment of RD**
- ▶ **Manifestations of CSA**
  - Narcotic-induced central apnea (70% chronic users)
  - Heart failure patients (up to 40%)
  - Idiopathic CSA (5% sleep apnea patients)
- ▶ **Standard CPAP therapy is not effective for central sleep apnea**



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

Reducing Central Sleep Apnea May Reduce Mortality in Heart Failure Patients

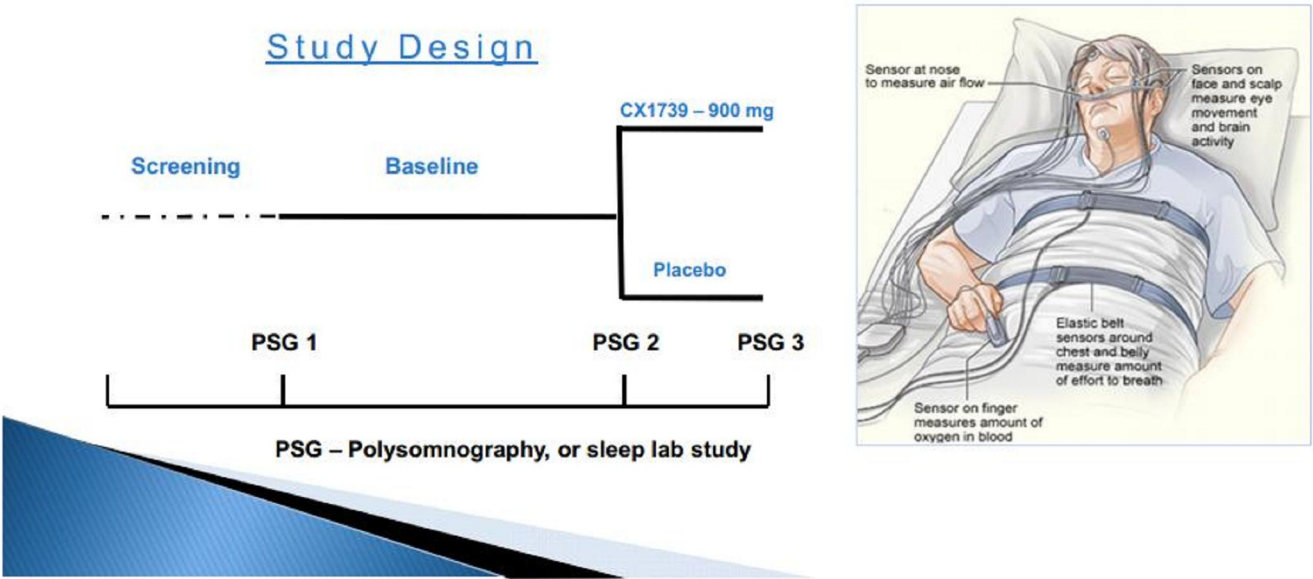


Javaheri et al, J. Amer. Coll. Cardiology 49:20, 2007



# CX1739 Sleep Apnea Clinical Study Design

|                  |  |
|------------------|--|
| Design           | Randomized, double-blind, placebo-controlled study   |
| Population       | 20 adults with moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)   |
| Dosing           | Each subject receives 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<br>(Apnea: no airflow for >10s; Hypopnea: reduced airflow for >10s) |



# Apnea-Hypopnea Response to CX1739

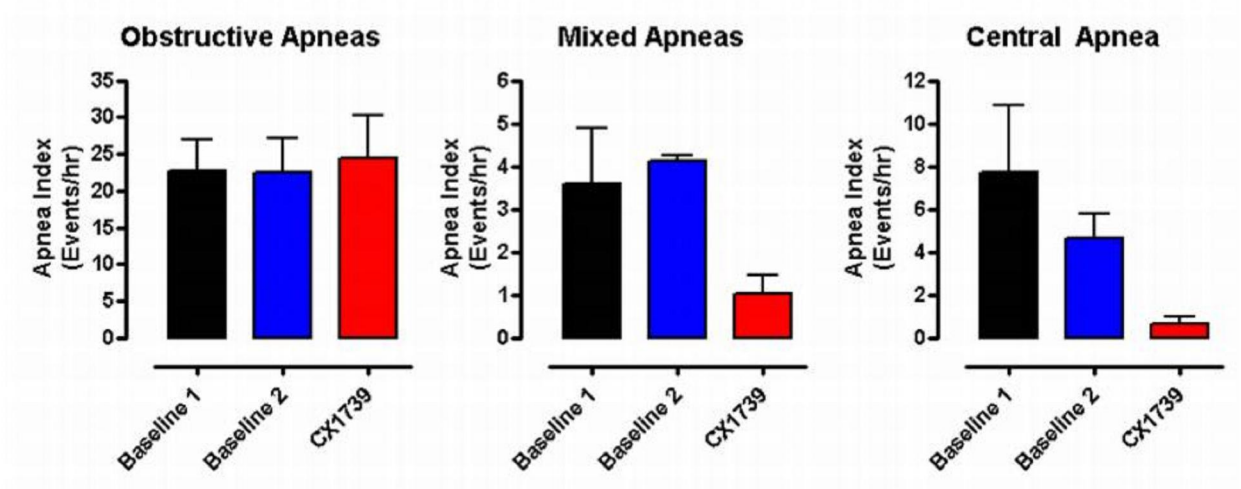
| Measure                    | Group   | No. Responders* |
|----------------------------|---------|-----------------|
| Apnea-Hypopnea Index (AHI) | CX1739  | 3 / 15          |
|                            | Placebo | 0 / 4           |
| Apnea-Hypopnea Time (AHT)  | CX1739  | 5 / 15          |
|                            | Placebo | 0 / 4           |

Why do some patients respond, and others not ?

\* A responder has at least a 40% decrease in the respective parameter



# CX1739 Was More Effective on Mixed and Central Sleep Apneas



# Acute Drug-induced Respiratory Depression

- **Most frequent lethal side effect of opiate use is respiratory depression (RD)**
- **In-patient, post-surgical opiate use (~12M patients/year) increases risk for RD**
- **RD also occurs during surgery and procedures (e.g., colonoscopy) that use propofol as an anesthetic (20 MM procedures/year)**
- **Large market potential in excess of \$1 Billion/year in the US**
- **Unmet Need: Therapeutic drug treatment that can counter and reduce respiratory depression without interfering with analgesia or anesthesia**
- **Short-term studies that can be conducted rapidly and inexpensively**



# Respiratory Failure: A Very Serious Hospital Safety Problem

HealthGrades Patient Safety in American Hospitals Study 2010 - 28  
Appendix E: Patient Safety Events and Attributable Mortality and Excess Charge

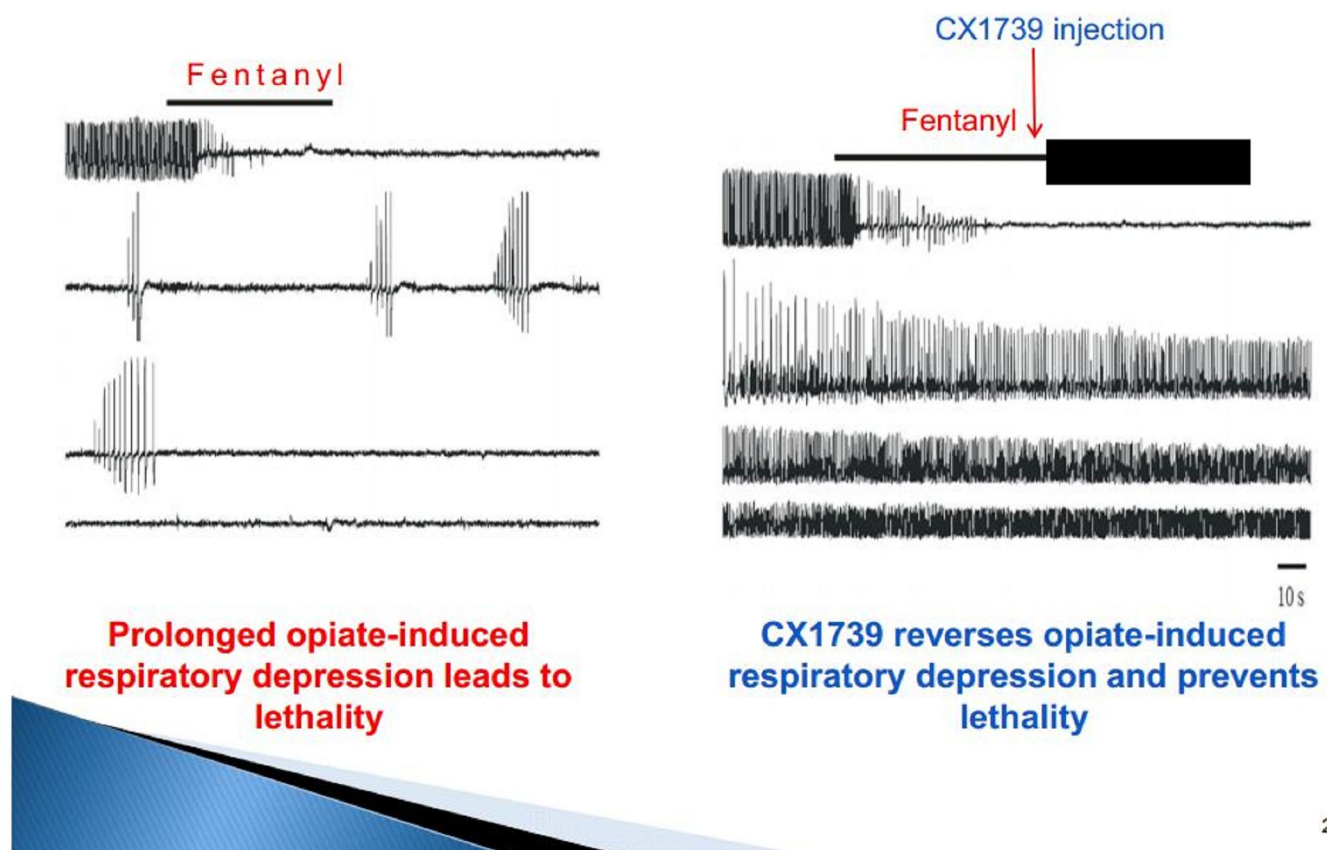
## Appendix E: Patient Safety Events and Their Attributable Mortality and Excess Charge Among Medicare Beneficiaries by Patient Safety Indicator (2006 – 2008)

| Patient Safety Indicator                                  | Actual Number of National Events | Percentage of Total Number of Events | Attributable Mortality Rates** | Number of Deaths Attributable to PSI (Attributable Mortality**) | Attributable Charge** | Excess Charge Attributable to PSI** (Millions) | Excess Cost Attributable to PSI ^^ (Millions) |
|---|----------------------------------|--------------------------------------|--------------------------------|---|-----------------------|--|---|
| Decubitus ulcer   | 487,718                          | 50.90%                               | 7.23%                          | 35,262  | \$10,845              | \$5,289.30                                     | \$2,644.65                                    |
| Post-operative pulmonary embolism or deep vein thrombosis | 143,699                          | 15.00%                               | 6.56%                          | 9,427   | \$21,709              | \$3,119.56                                     | \$1,559.78                                    |
| Accidental puncture or laceration                         | 96,082                           | 10.03%                               | 2.16%                          | 2,075   | \$8,271               | \$794.69                                       | \$397.35                                      |
| Post-operative respiratory failure                        | 69,078                           | 7.21%                                | 21.84%                         | 15,087  | \$53,502              | \$3,695.81                                     | \$1,847.91                                    |
| Selected infections due to medical care                   | 50,165                           | 5.24%                                | 4.31%                          | 2,162   | \$38,656              | \$1,939.18                                     | \$969.59                                      |

**Highest mortality rate**  
**2<sup>nd</sup> highest attributable number of deaths**  
**2<sup>nd</sup> largest overall excess cost to Medicare system**



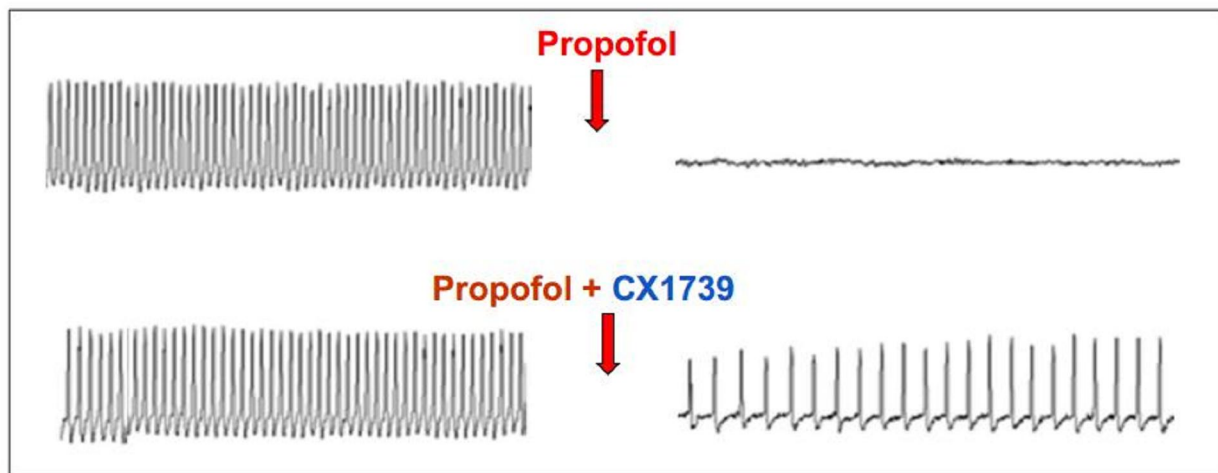
# Reversal of Opioid-induced Respiratory Depression with an Ampakine in Rats



## Reversal of Propofol-induced RD With an Ampakine in the Rat

### Experimental Design:

- Administer a lethal dose of propofol to rats
- Inject CX1739 within 1 minute



## Ampakines Prevent Opioid-induced Respiratory Depression in Humans

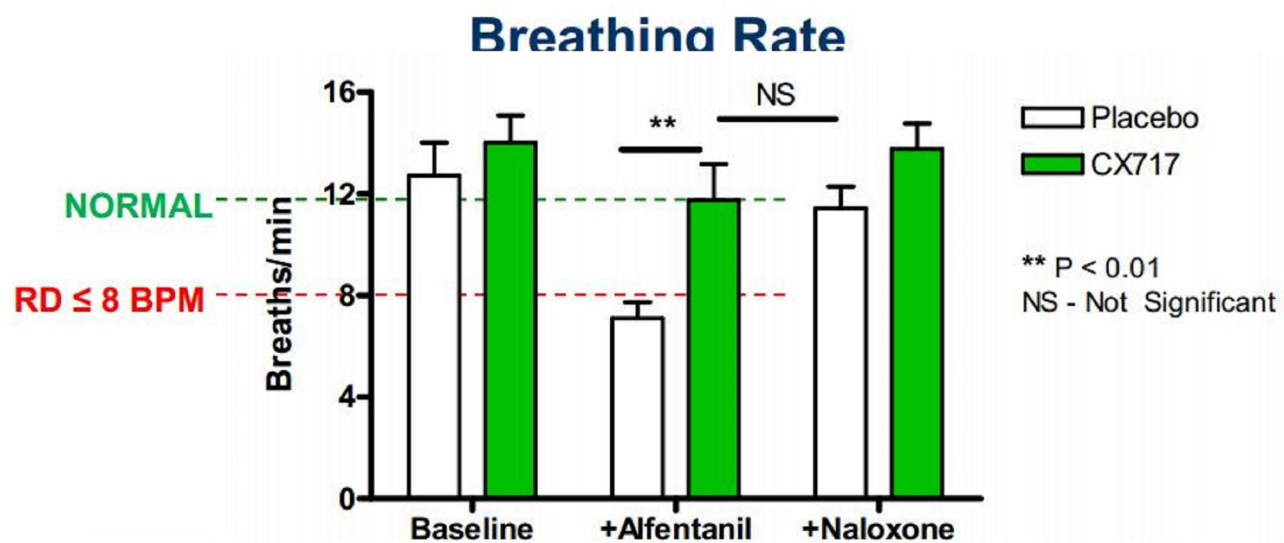
- ▶ Two clinical studies were run in normal, healthy volunteers with CX717 an earlier Ampakine
- ▶ Moderate respiratory depression was induced experimentally by infusion of the opioid, Alfentanil
- ▶ Respiratory and analgesia end-points were measured

Oral CX717 prevented and reversed the respiratory depression without impacting the pain-relieving properties of the opioid





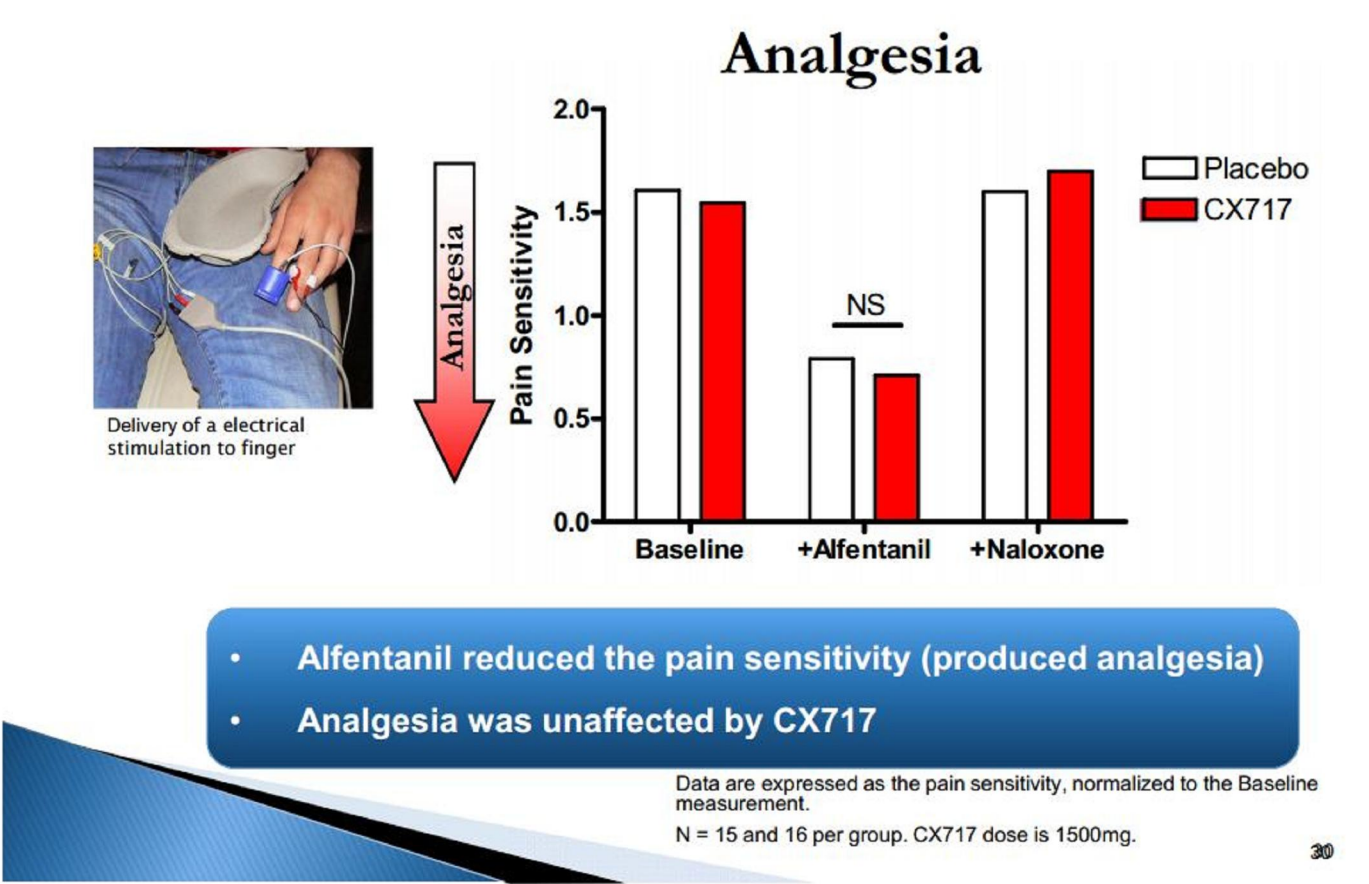
## CX717 Prevents Opiate-induced Respiratory Depression in Humans



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

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

# CX717 Maintains the Analgesic Properties of Opioids



# CX1942: A Soluble Ampakine

- ▶ **Mechanism of Action**

- Positive Allosteric Modulator of AMPA receptors
- Water-soluble - allowing for injectable dosage forms

- ▶ **Stage of Development**

- Injectable routes have been studied in animal models of respiratory depression
- Exploratory studies supported by SBIR contract

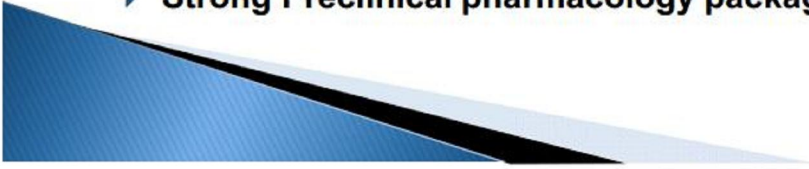
- ▶ **Targeted Indication**

- Injectable therapy for opiate and propofol-induced respiratory depression

- ▶ **Intellectual Property**

- Protected by an issued Composition-of-Matter Patent (expires 2028), filed worldwide; a method-of-use patent (expires 2030)

- ▶ **Strong Preclinical pharmacology package**



# Status of Product Pipeline - Respiratory Disorders

| Indication                                       | Compound          | Stage of Development |              |         |         |
|--|-------------------|----------------------|--------------|---------|---------|
|  |                   | Drug Discovery       | Pre-clinical | Phase 1 | Phase 2 |
| Obstructive Sleep Apnea                          | <i>Dronabinol</i> | →                    |              |         |         |
| Central Sleep Apnea in CHF                       | <i>CX1739</i>     | →                    |              |         |         |
| Drug-induced Respiratory Depression (oral)       | <i>CX1739</i>     | →                    |              |         |         |
| Drug-induced Respiratory Depression (injectable) | <i>CX1942</i>     | →                    |              |         |         |



Key Objectives for the Next 12 Months  
(Pending Availability of Finance)

| Compound     | Indication                               | Status               | Estimated Start Date | Estimated Completion |
|--------------|--|----------------------|----------------------|----------------------|
| Dronabinol   | Obstructive Sleep Apnea                  | Phase IIB            | started              | 3Q2015               |
| CX1739       | Opiate-induced RD                        | Phase IIA            | 3Q2015               | 1Q2016               |
|              | Propofol-induced RD                      | Phase IIA            | 4Q2015               | 2Q2016               |
| CX1739/CX717 | Pompe Disease, Spinal Cord Injury, other | Phase IIA            | 1Q2016               | 3Q2016               |
| CX1942       | Injectable for RD                        | Pre-clinical studies | 4Q2015               | 3Q2016               |





# Summary

- Two drug platforms
- Three Phase 2 or Phase 2 ready programs
- Blockbuster markets
- IP protection with the ability to add additional IP
- Low valuation entry point
- Experienced management team
- Strategic collaborative opportunities
- Availability of non-dilutive finance
- Public company with stock as potential currency



# Background

## 2013

- Insolvent and near bankruptcy
- No ongoing operations
- Lost dronabinol license
- Deficient in SEC reporting
- Approx. \$3M market cap

## Today

- Non-bankruptcy reorganization
- New capital raised
- Re-gained dronabinol license
- Current in SEC reporting
- Approx. \$15M market cap
- Newly organized research program
- Phase 2B dronabinol clinical trial in progress with completion in mid-2016
- Phase 2A ampakine clinical trial to begin 3Q, pending financing
- Committed management team and board of directors

# Management and Directors

|                          |   |
|--------------------------|---|
| <b>Arnold Lippa</b>      | <b>Chairman, CEO</b>  |
| <b>Jeff Margolis</b>     | <b>VP, Sec/Treas, Director</b>  |
| <b>Robert Weingarten</b> | <b>CFO, Director</b>  |
| <b>Richard Purcell</b>   | <b>Senior VP R&amp;D</b>  |
| <b>John Greer</b>        | <b>Chairman, Scientific Advisory Board</b><br>Prof & Dir. Neuroscience Ctr., U. Alberta |
| <b>Katie MacFarlane</b>  | <b>Director, CCO Agile Therapeutics</b>   |
| <b>James Sapirstein</b>  | <b>Director, CEO ContraVir Pharm</b>  |

