Cortex Pharmaceuticals, Inc.

May 4, 2015

Forward Looking Statements

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Background

2013

- Insolvent & 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. $25M market cap
- Newly organized research program
- Phase 2B dronabinol clinical trial to be completed mid-year
- Phase 2A ampakine clinical trial to begin 3Q, pending financing
- Committed management team and board of directors

Management and Directors

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

Cortex Drug Platforms

Ampakines

- Positive allosteric modulators of AMPA glutamate receptors
- Positive effects for treatment of drug-induced respiratory depression in Phase 2A studies
- Positive effects for treatment of central sleep apnea in Phase 2A study
- Positive effects for treatment of ADHD in Phase 2A study
- Positive preclinical results in Pompe disease, neonatal apnea and spinal disorders

Cannabinoids

- Dronabinol (Δ9-THC) is a generic FDA-approved drug
- Positive Phase 2A data for treatment of obstructive sleep apnea
- Phase 2B clinical trial in progress
- Use patent for the treatment of sleep related breathing disorders

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

Key Company Highlights

- Drug-induced respiratory depression (RD) - ampakines
  - Acute use – surgical anesthesia with propofol
  - Semi-acute use – post-surgical pain management with opiates
  - Chronic use – in conjunction with opiates
- Sleep Apnea
  - Obstructive sleep apnea (OSA) – dronabinol
  - Central sleep apnea (CSA) - ampakines
- Orphan Diseases – Pompe & Perinatal Apnea
- Strong IP protection for compounds and uses
- Over $5 million in NIH grants supporting drug development

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

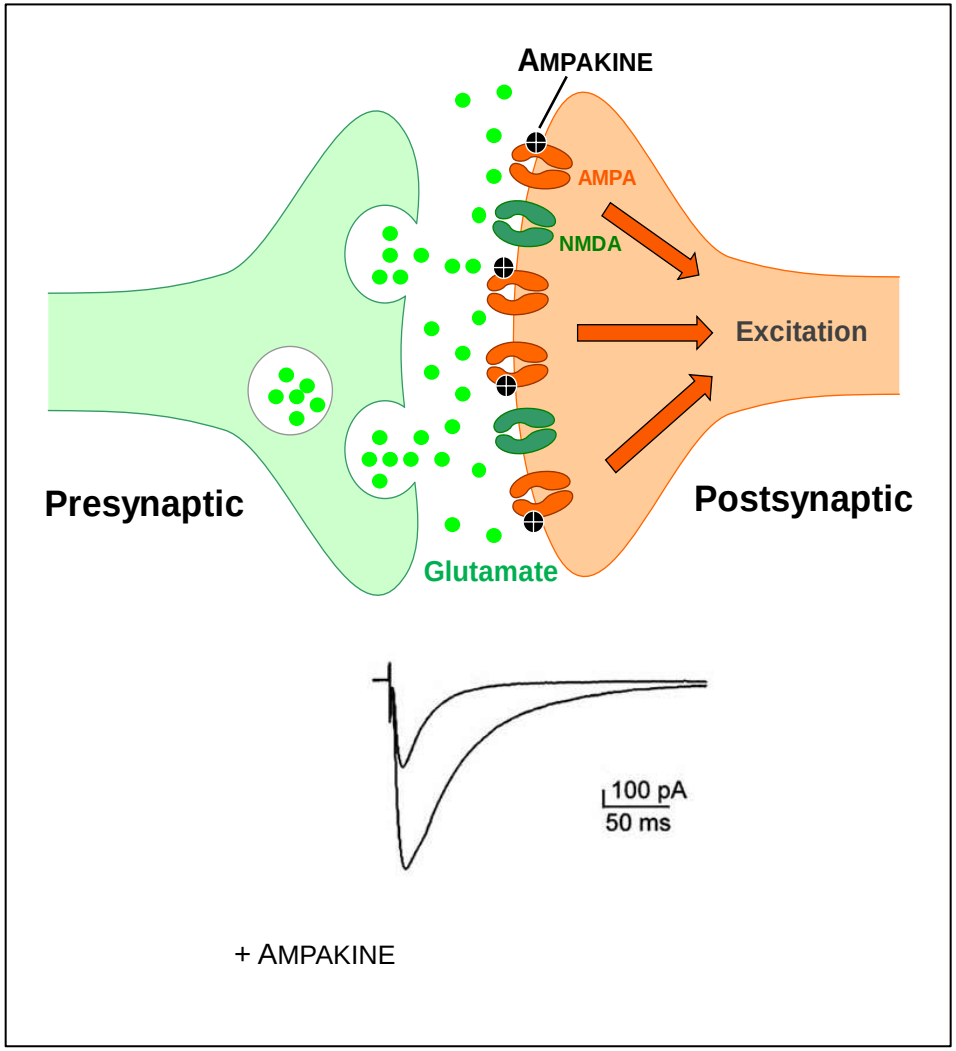
Large Market with Unmet Need

- **Drug-Induced Respiratory Depression (RD)**
  - Patients treated with anesthetic, analgesic and/or sedatives in association with surgery (12 million/yr) or medical procedures (17 million/yr) are at risk for RD, which can be lethal (cardio-respiratory arrest) or require intubation & longer hospital stay
- **Obstructive Sleep Apnea**
  - 18 million patients in the US
  - CPAP is very problematic due to high non-compliance
  - Associated morbidity (hypertension, heart disease) and mortality issues
- **Central Sleep Apnea**
  - Affects > 5 million heart failure patients in the US with high morbidity and mortality
  - Approx 40% of heart failure patients have CSA, which promotes heart disease progression and increases the risk of mortality. No current therapy for treatment of CSA in CHF

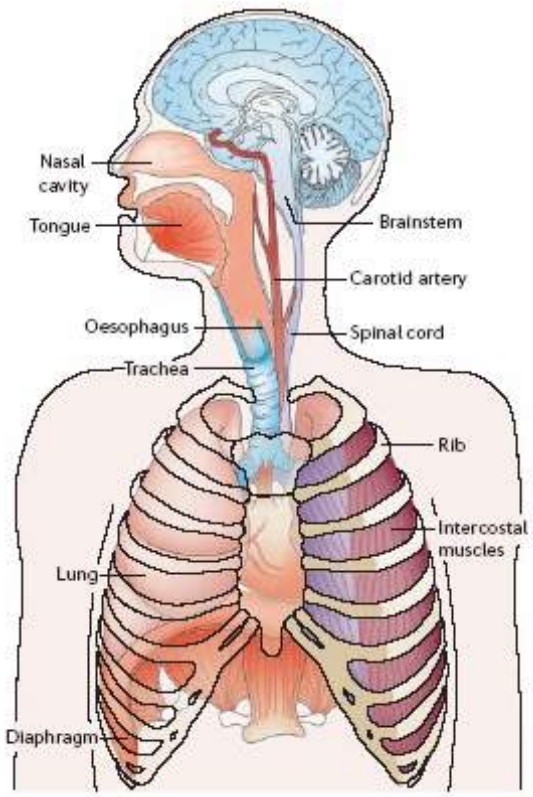
AMPAKINES – Positive Allosteric Modulators at AMPA Glutamate Receptors

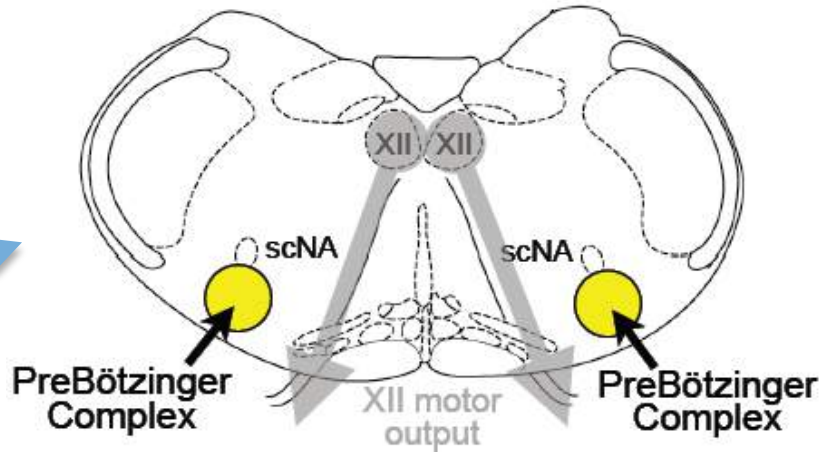
AMPA Receptors Mediate Synaptic Transmission in the Brain

- **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





- 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
- AMPA-PAMs normalize breathing by enhancing firing of PreBotC respiratory rhythm neurons

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

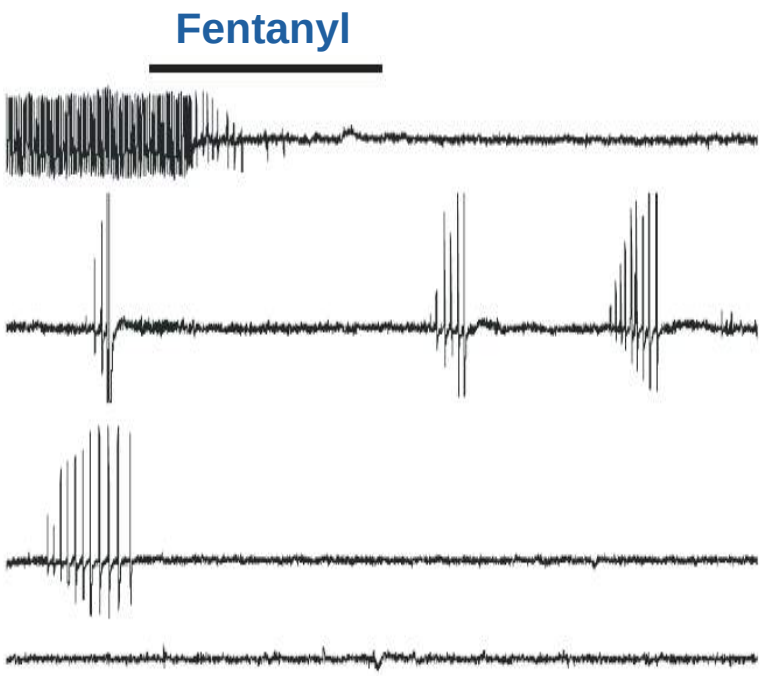
Acute Drug-induced Respiratory Depression

- **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 anesthetic procedures (e.g. colonoscopy) with propofol (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**

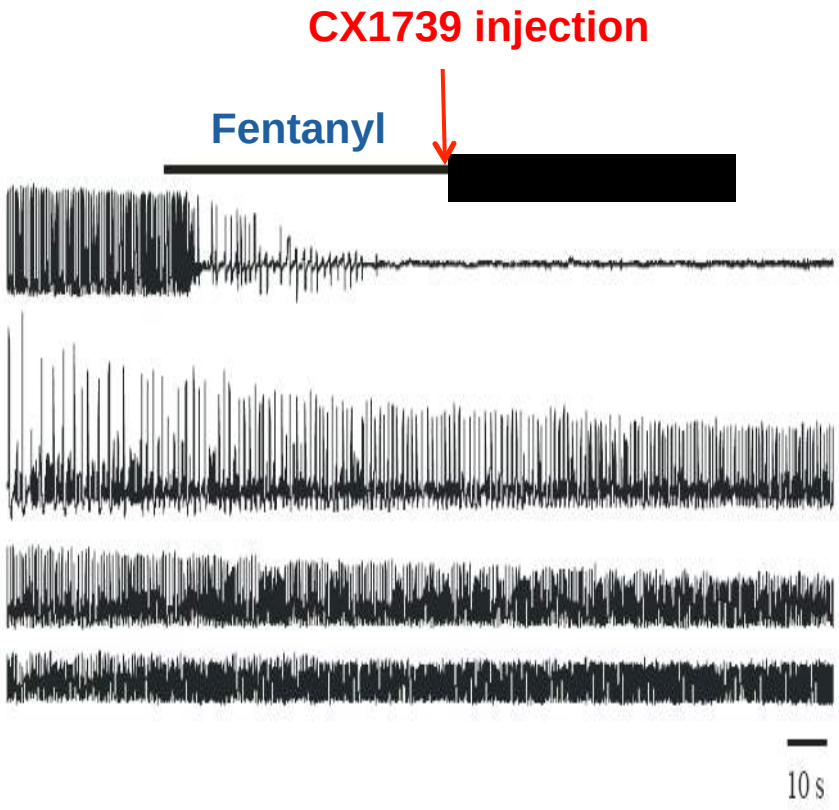
CX1739: An Oral Phase 2 Ampakine

- **Stage of Development**
  - Completed Phase 1 in healthy volunteers and Phase 2a in central sleep apnea
  - Ready for Phase 2A studies in opiate- and propofol-induced respiratory depression and central sleep apnea
- **Targeted Indication**
  - Prevention of propofol-induced respiratory depression during surgery
  - Post-surgical prevention of opiate-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**
  - Broad-spectrum reversal & prevention of drug-induced respiratory depression

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



Prolonged opiate-induced respiratory depression leads to lethality

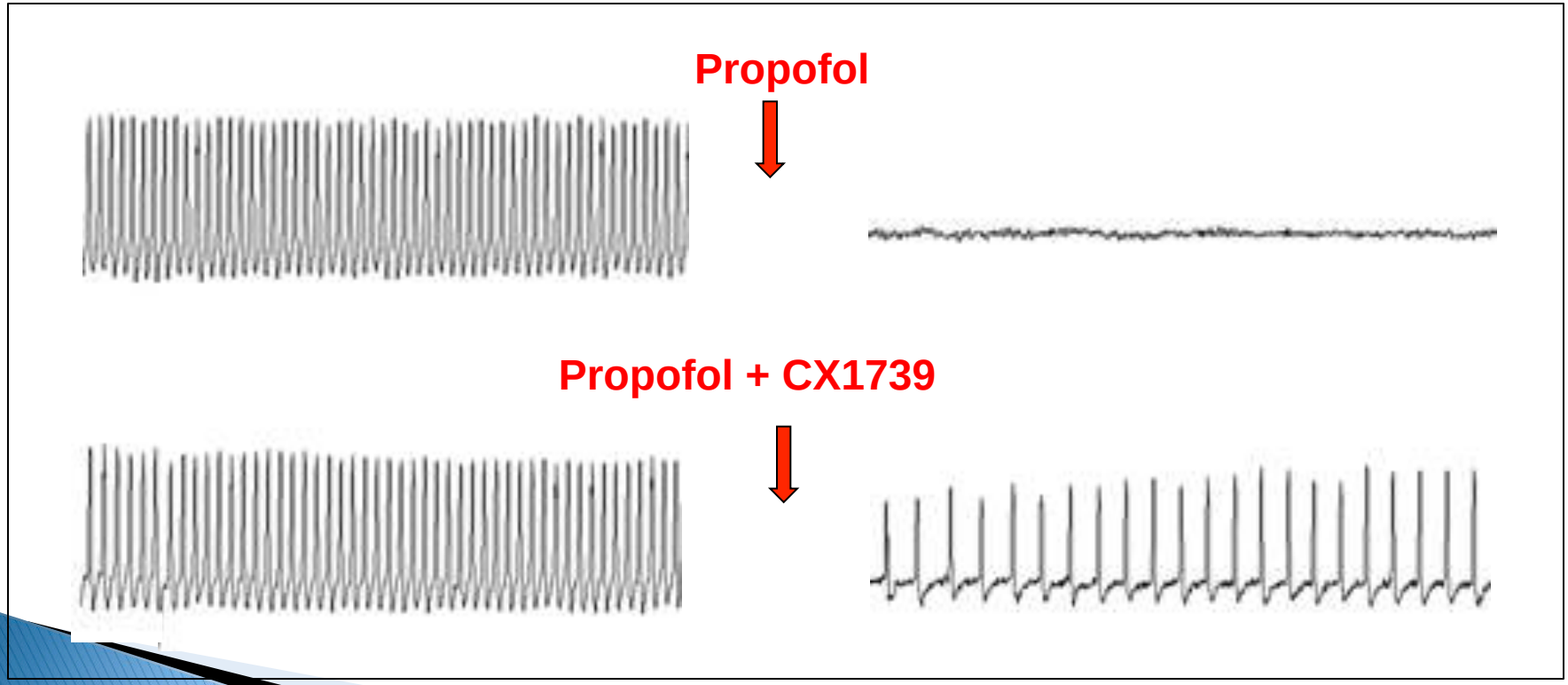


CX1739 reverses opiate-induced respiratory depression and prevents lethality

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

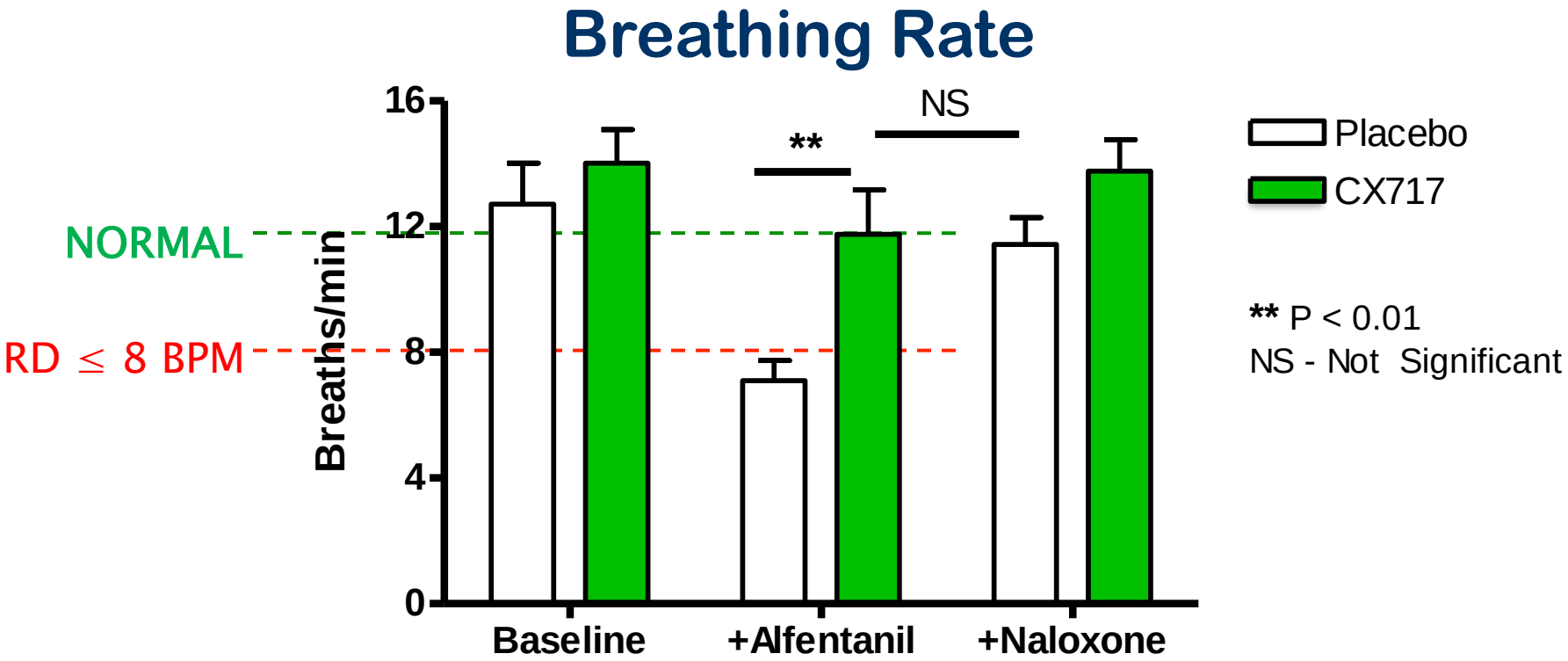


Ampakines Prevent Opioid-induced Respiratory Depression in Humans

- **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 the onset of respiratory depression without impacting the pain-relieving properties of the opioid

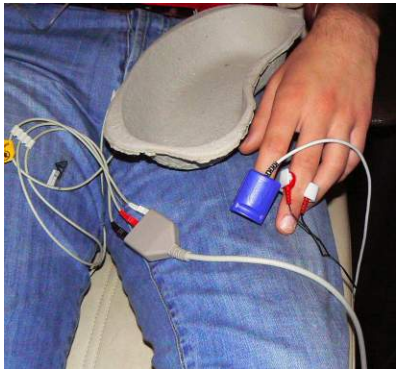
CX717 Prevents Opiate-induced Respiratory Depression in Humans



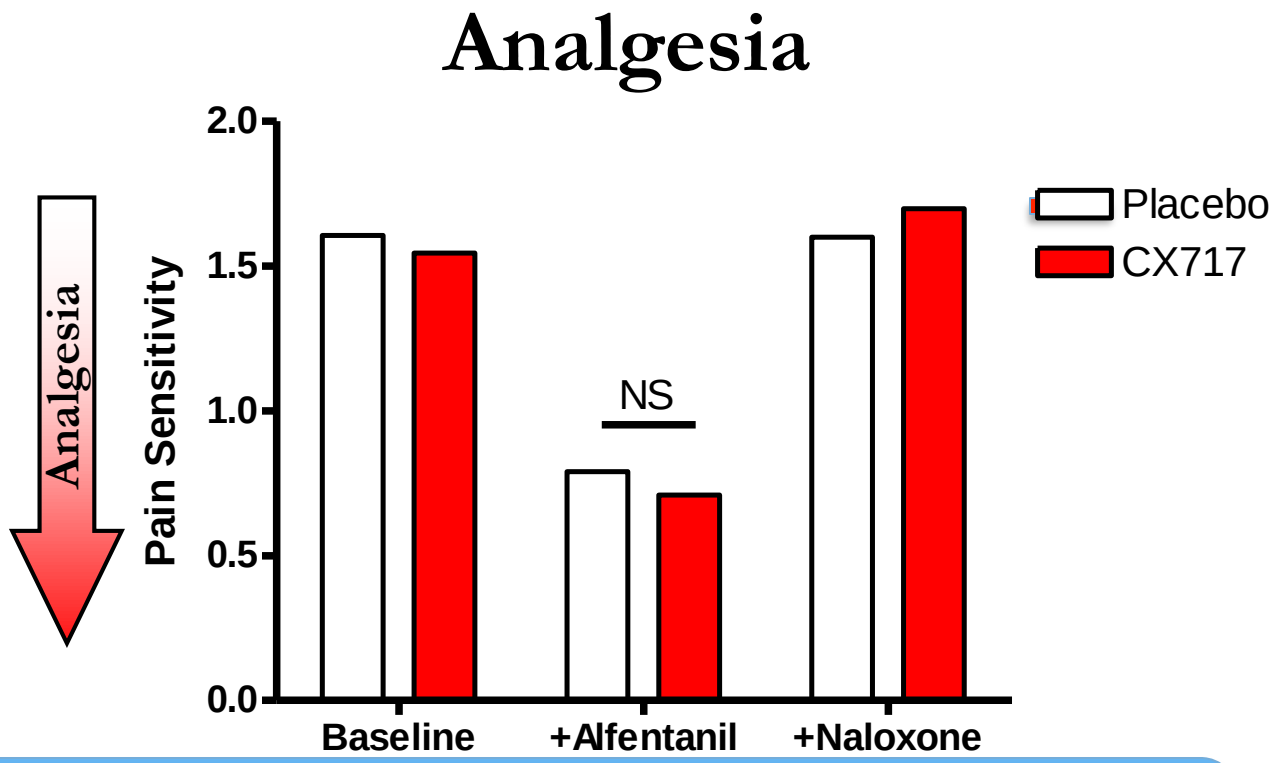
- Alfentanil reduced breathing rate & produced respiratory depression
- CX717 maintains respiratory rate in the presence of Alfentanil

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



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.

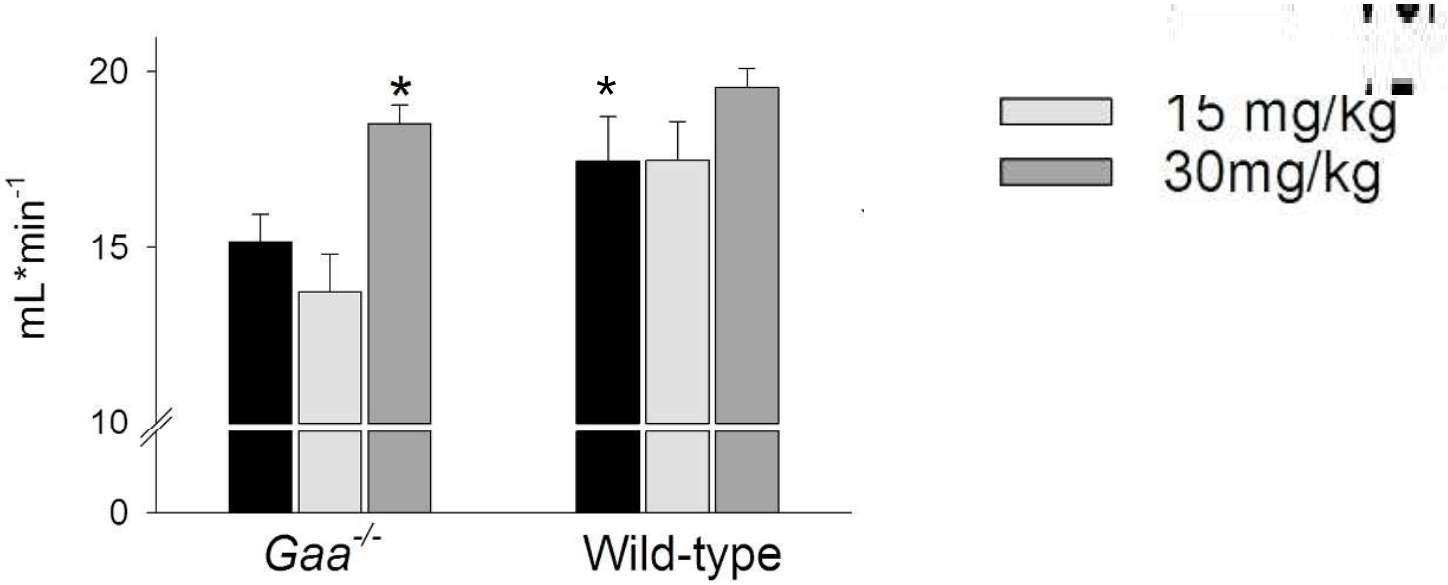
N = 15 and 16 per group. CX717 dose is 1500mg.

POMPE DISEASE

- Autosomal recessive metabolic disorder caused by an accumulation of lysosomal glycogen due to a deficiency of alpha glucosidase
- Damages muscle and nerve cells throughout the body
- Respiratory failure is the most common cause of death
- Replacement enzyme therapy

MOUSE MODEL OF POMPE DISEASE

Effects of Ampakine on Minute Volume



* p<.05, compared to vehicle
** p<.05, compared to mutant

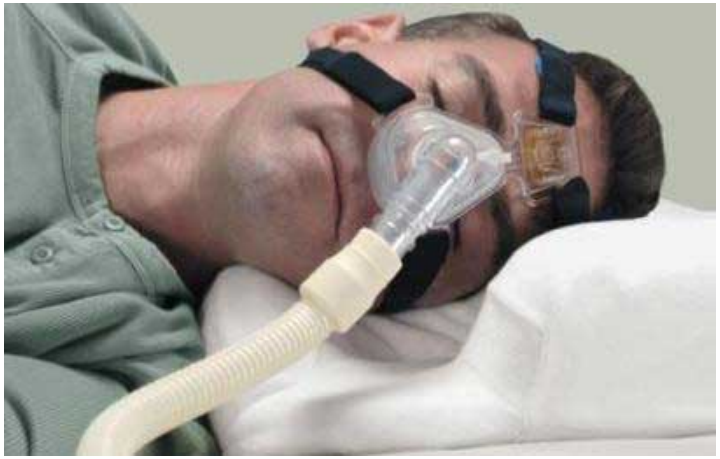
Elmallah *et al*, in press

CX1942: A Soluble AMPA-PAM

- **Mechanism of Action**
  - A Positive Allosteric Modulator of AMPA receptors (AMPA-PAM)
  - Water-soluble for injectable dosage forms
- **Stage of Development**
  - Injectable routes being studied in animal models of respiratory depression
  - Supported by SBIR contract
- **Targeted Indication**
  - Injectable rescue treatment 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**

Sleep Apnea: A Large Market Opportunity

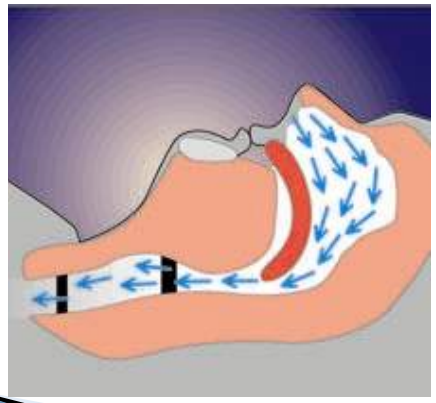
- **Sleep Apnea**
  - Repetitive episodes of airflow cessation (apnea) or reduction (hypopnea) for more than 10s during sleep
  - Three types: Obstructive, Central & Mixed
- **The Sleep Apnea Market is Large**
  - 18 million U.S. adults with moderate or severe sleep apnea
  - Market potential for sleep apnea is $3 - 9 Billion/Year
- **Current Treatments**
  - CPAP device
  - Surgery; dental devices
- **Clear Market Need**
  - Poor compliance with CPAP
  - No drug treatment available



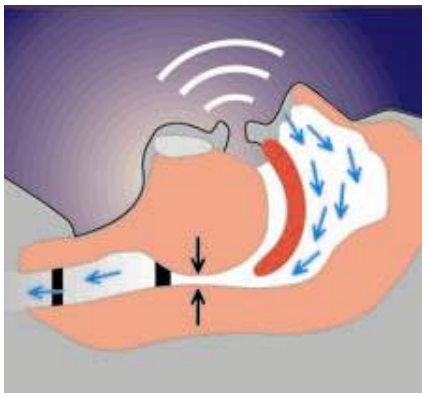
Obstructive Sleep Apnea (OSA)

- **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**

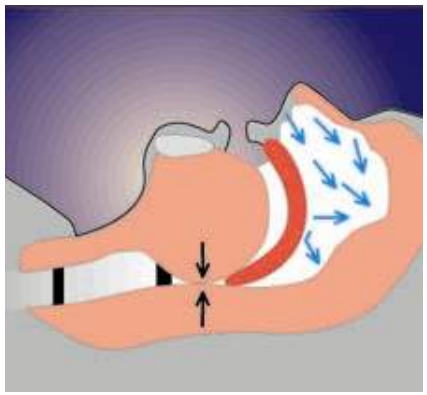
Normal Breathing



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[1-5]	18.0 MM	$75.0 Billion	$ 0
Asthma[6,7]	16.4 MM	$18.3 Billion	$13.5 Billion
Hypertension[8-10]	43.2 MM	$73.4 Billion	$48.5 Billion
Diabetes[11,12]	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
19 Lloyd-Jones, D., et al., Circulation 119(3):e21-181, 2009
10 Acmite Market Intelligence, 2008
11 Arrowhead, Gloabal 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

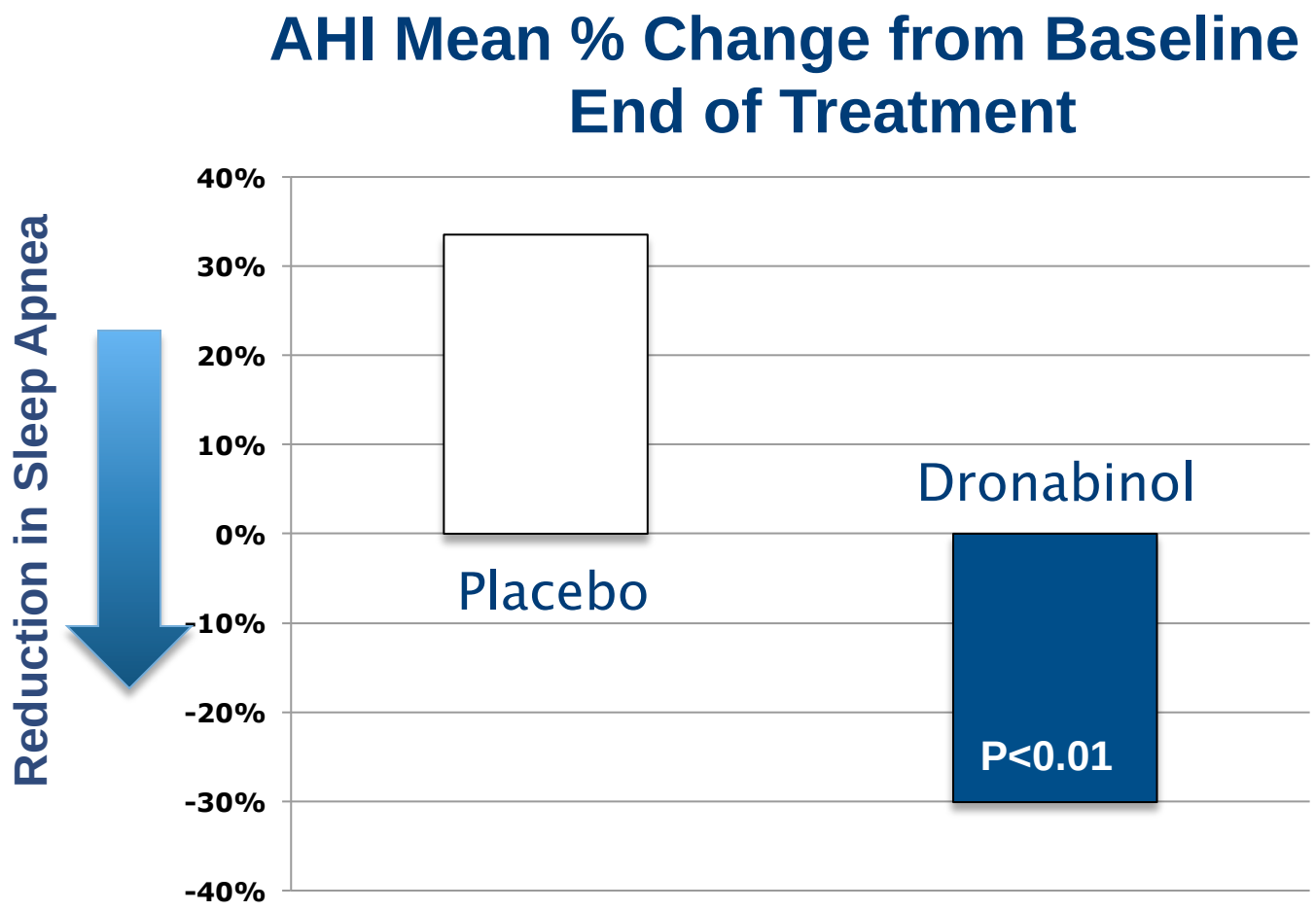
Dronabinol for Treatment of OSA: A Phase 2 Compound

- **Mechanism of Action**
  - Dronabinol is (Δ-9)THC, a cannabinoid agonist
- **Commercial Status**
  - FDA approved for the treatment of anorexia in AIDS patients and nausea and vomiting in cancer patients undergoing chemotherapy
  - Schedule III drug available by prescription, low risk of addiction
- **Stage of Development**
  - Phase 2A data demonstrates statistically significant improvement in OSA
  - Phase 2B study in OSA is in progress with completion in 3Q2015
- **Intellectual Property**
  - 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

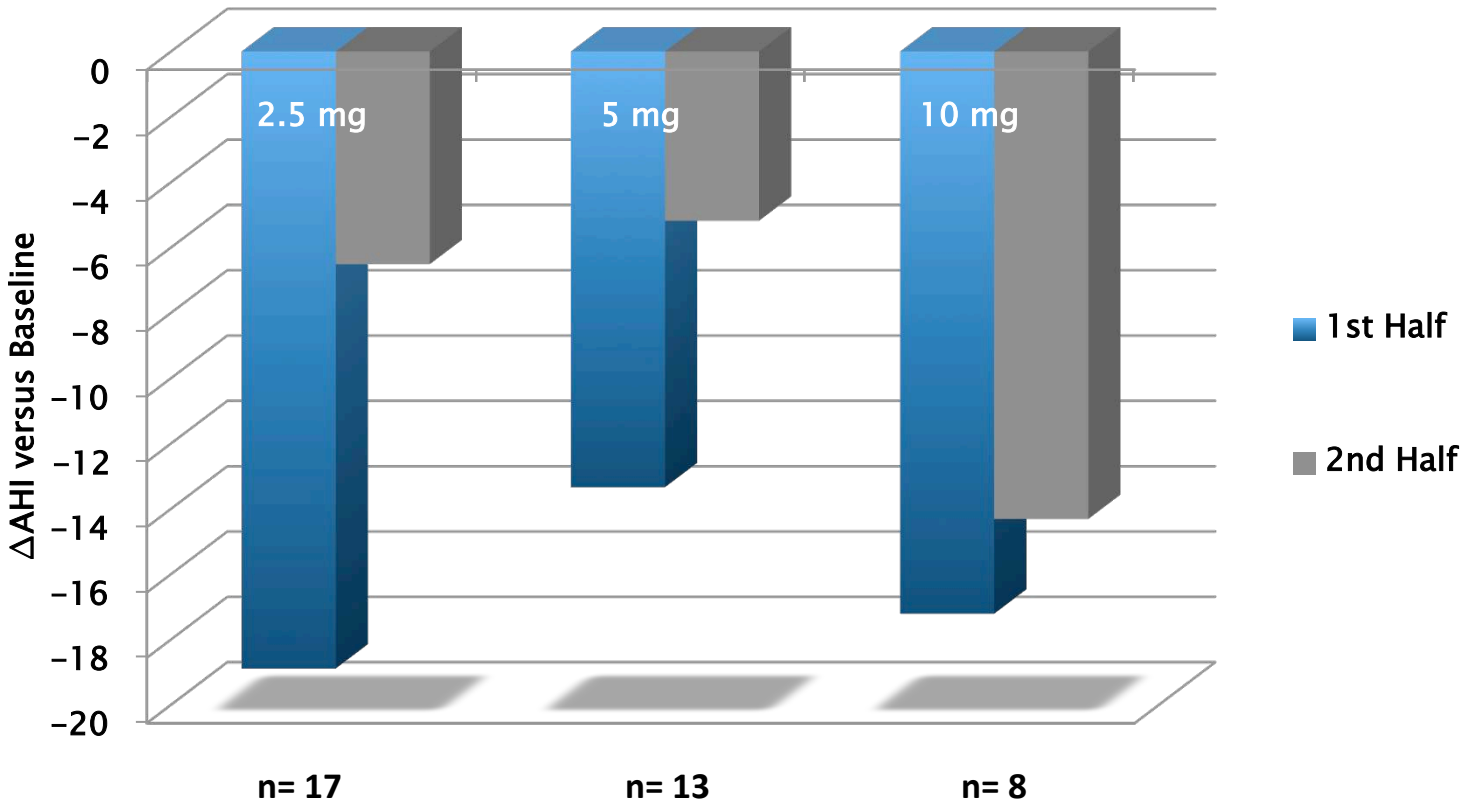
Dronabinol Phase 2A Clinical Study in OSA

- **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 Index (AHI) used to assess OSA efficacy
  - 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 Chronic, Obstructive Sleep Apnea

- **Phase 2B study in progress at University of Illinois**
- **120 subjects (40/group, 6 wks dosing)**
- **Doses: Placebo, 2.5 mg, 10 mg qd**
- **Study costs funded by NIH Grant for $5 MM**
- **Top line data by 3Q2015**

Protecting Dronabinol in the Marketplace

- **Issued Method-of-Use patent for dronabinol and OSA**
  - Expires in 2025
- **Potential proprietary dosage and pulse-dose formulation to provide efficacy over entire night**
  - Pending patent applications
- **US government maintains close oversight on off-label dronabinol sales due to its Schedule III status**
- **Generics and medical marijuana are not covered for this use by third party payers**
  - Off-label prescriptions unlikely

Key Objectives for the Next 12 Months

Compound	Indication	Status	Estimated Start Date	Estimated Completion
Dronabinol	Obstructive Sleep Apnea	Phase IIB	started	3Q2015
CX1739	Opiate-induced RD	Phase IIA	2Q2015	3Q2015
	Propofol-induced RD	Phase IIA	3Q2015	4Q2015
CX1739/ CX717	Pompe Disease	Phase IIA	4Q2015	2Q2016
CX1942	Injectable for RD	Pre-clinical studies	3Q2014	2Q2015