

FORM 8-K

Date of Report (Date of earliest event reported): November 7, 2022

(Exact name of registrant as specified in its charter)

07452
(Zip Code)

(Former name or former address, if changed since last report.)

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- ☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- ☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- ☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
N/A	N/A	N/A

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

RespireRx Pharmaceuticals Inc. (the “Company”) announced today that Dr. Arnold Lippa, Chief Scientific Officer, Executive Chairman of the Board and Interim President and Interim Chief Executive Officer is an invited speaker and panel moderator at the 5th Meridian Drug Discovery Summit, being held November 7th and 8th at the Embassy Suites by Hilton Logan Airport, Boston MA. Dr. Lippa will give his talk, entitled “Translational Approaches to Drug Discovery and Development: A Case Study with AMPAkines,” on November 8 at 12:30 pm, to be followed at 2:30 pm by his panel discussion entitled “Achieving Drug Discovery Diversity Through Actionable Steps.” A copy of the slides from Dr. Lippa’s presentation may be found on the Company’s website.

The related press release is Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The slide deck presented is Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The press release and the slide deck that are Exhibits 99.1 and 99.2 include certain forward-looking information.

The information in this Item 7.01 and the documents attached as Exhibit 99.1 and 99.2 are being furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended (the “Exchange Act”), nor otherwise subject to the liabilities of that section, nor incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits.

Exhibit Number	Exhibit Description
99.1	RespireRx Pharmaceuticals Inc. Press Release dated November 7, 2022
99.2	RespireRx Pharmaceuticals Inc. Slide Deck to be presented at the 5th Meridian Drug Discovery Summit on November 8, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: November 7, 2022

RESPIRERX PHARMACEUTICALS INC.
(Registrant)

By: /s/ Jeff E. Margolis
Jeff E. Margolis
SVP, CFO, Secretary and Treasurer



RespireRx Pharmaceuticals Inc. Announces that Dr. Arnold Lippa Is an Invited Speaker at the 5th Meridian Drug Discovery Summit

Glen Rock, N.J., November 7, 2022 /Globe Newswire – RespireRx Pharmaceuticals Inc. (OTCQ:RSPI) (“RespireRx” or the “Company”), a leader in the discovery and development of innovative and revolutionary treatments to combat diseases caused by disruption of neuronal signaling, is pleased to announce that Dr. Arnold Lippa, Chief Scientific Officer, Executive Chairman of the Board and Interim President and Interim Chief Executive Officer is an invited speaker and panel moderator at the 5th Meridian Drug Discovery Summit, being held November 7th and 8th at the Embassy Suites by Hilton Logan Airport, Boston MA. Dr. Lippa will give his talk, entitled “Translational Approaches to Drug Discovery and Development: A Case Study with AMPAkinines,” on November 8 at 12:30 pm, to be followed at 2:30 pm by his panel discussion entitled “Achieving Drug Discovery Diversity Through Actionable Steps.” A copy of the slides from Dr. Lippa’s presentation may be found on our website.

About RespireRx Pharmaceuticals Inc.

RespireRx Pharmaceuticals Inc. is a leader in the discovery and development of medicines for the treatment of psychiatric and neurological disorders, with a focus on treatments that address conditions affecting millions of people, but for which there are few or poor treatment options, including attention deficit hyperactivity disorder (“ADHD”), epilepsy, pain, recovery from spinal cord injury (“SCI”), certain neurological orphan diseases and obstructive sleep apnea (“OSA”). RespireRx is developing a pipeline of new and re-purposed drug products based on our broad patent portfolios for two drug platforms: (i) neuromodulators, which include AMPAkinines and GABAkinines, proprietary chemical entities that positively modulate (positive allosteric modulators or “PAMs”) AMPA-type glutamate receptors and GABA_A receptors, respectively and (ii) pharmaceutical cannabinoids, which include dronabinol, a synthetic form of Δ9-tetrahydrocannabinol (“Δ9-THC”) that acts upon the nervous system’s endogenous cannabinoid receptors.

The Company holds exclusive licenses and owns patents and patent applications or rights thereto for certain families of chemical compounds that claim the chemical structures and their uses in the treatment of a variety of disorders, as well as claims for novel uses of known drugs.

EndeavourRx: Neuromodulators

AMPAkinines. Through an extensive translational research effort from the cellular level through Phase 2 clinical trials, the Company has developed a family of novel, low impact AMPAkinines, including CX717, CX1739 and CX1942 that may have clinical application in the treatment of CNS-driven neurobehavioral and cognitive disorders, spinal cord injury, neurological diseases, and certain orphan indications. Our lead clinical compounds, CX717 and CX1739, have successfully completed multiple Phase 1 safety trials. Both compounds have also completed Phase 2 proof of concept trials demonstrating target engagement, by antagonizing the ability of opioids to induce respiratory depression.

AMPAkinines have demonstrated positive activity in animal models of ADHD, results that have been extended translationally into statistically significant improvement of symptoms observed in a Phase 2 human clinical trial of CX717 in adult patients with ADHD. Statistically significant therapeutic effects were observed within one week. We believe AMPAkinines may represent a novel, non-stimulant treatment for ADHD with a more rapid onset of action than alternative non-stimulants, such as Strattera[®] (atomoxetine), and without the drawbacks of amphetamine-type stimulants.

In a series of important studies funded by grants from the National Institutes of Health and published in a number of peer reviewed articles, Dr. David Fuller (University of Florida), a long-time RespireRx collaborator, has demonstrated the ability of CX1739 and CX717, the Company’s lead AMPAkinines, to improve motor nerve activity and muscle function in animal models of spinal cord injury (SCI).

GABAkinines. Under a License Agreement with the University of Wisconsin-Milwaukee Research Foundation, Inc. (“UWMRF”) and on behalf of its EndeavourRx business unit, RespireRx has licensed rights to certain selectively acting GABAkinines because of their ability to selectively amplify inhibitory neurotransmission at a highly specific, subset of GABA_A receptors, thus producing a unique efficacy profile with reduced side effects. Preclinical studies have documented their efficacy in a broad array of animal models of interrelated neurological and psychiatric disorders including epilepsy, pain, anxiety, and depression in the absence of or with greatly reduced propensity to produce sedation, motor-impairment, tolerance, dependence and abuse. The Company currently is focusing on developing KRM-II-81 for the treatment of epilepsy and pain.

KRM-II-81 has displayed a high degree of anti-convulsant activity in a broad range of preclinical studies, including in treatment resistant and pharmaco-resistant models. Not only was KRM-II-81 highly effective in these models, but pharmaco-resistance or tolerance did not develop to its anti-convulsant properties. These latter results are particularly important because pharmaco-resistance occurs when medications that once controlled seizures lose efficacy as a result of chronic use and it is a principal reason some epileptic patients require brain surgery to control their seizures. In support of its potential clinical efficacy, translational studies have demonstrated the ability of KRM-II-81 to dramatically reduce epileptiform electrical activity when administered in situ to brain slices excised from treatment resistant epileptic patients undergoing surgery.

In addition, KRM-II-81 has displayed a high degree of analgesic activity in a broad range of preclinical studies. In intact animal models of pain, the analgesic efficacy of KRM-II-81 was comparable to or greater than commonly used analgesics. At the same time, KRM-II-81 did not display side effects such as sedation and motor impairment, but even more importantly, it did not produce tolerance, dependence, respiratory depression or behavioral changes indicative of abuse liability, which are produced by opioid narcotics and are at the heart of the opioid epidemic.

ResolutionRx: Pharmaceutical Cannabinoids.

Dronabinol. RespireRx’s ResolutionRx business unit is developing dronabinol, Δ-9-THC, a synthetic version of the naturally occurring substance in the cannabis plant, for the treatment of OSA, a serious respiratory disorder that impacts an estimated 29.4 million people in the United States according to the American Academy of Sleep Medicine (“AASM”), published in August 2016. OSA has been linked to increased risk for hypertension, heart failure, depression, and diabetes, and has an annual economic cost in the United States of \$162 billion according to the AASM. There are no approved drug treatments for OSA.

Two Phase 2 clinical trials have been completed demonstrating the ability of dronabinol to significantly reduce the symptoms of OSA and, subject to raising sufficient financing (of which no assurance can be provided) and pending the outcome of an intended meeting with the FDA, RespireRx believes that it will be able to commence a pharmacokinetic study for a recently discovered and to-be-developed formulation followed by a Phase 3 clinical study for the treatment of OSA with the new formulation. Because dronabinol is already FDA approved for the treatment of AIDS related anorexia and chemotherapy induced nausea and vomiting, the Company believes that its re-purposing strategy would only require approval by the FDA of a 505(b)(2) new drug application (“NDA”), an efficient regulatory pathway that allows the use of publicly available data.

Additional information about RespireRx and the matters discussed herein can be obtained on the Company’s web-site at www.RespireRx.com or in the Company’s filings with the Securities and Exchange Commission at www.sec.gov.

Not a Securities Offering or Solicitation

This communication shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any sales of securities in any jurisdiction in which such offer, solicitation or sale of securities would be unlawful before registration or qualification under the laws of such jurisdiction.

Cautionary Note Regarding Forward-Looking Statements

This press release contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the “Securities Act”) and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), and the Company intends that such forward-looking statements be subject to the safe harbor created thereby. These might include statements regarding the Company’s future plans, targets, estimates, assumptions, financial position, business strategy and other plans and objectives for future operations, and assumptions and predictions about research and development efforts, including, but not limited to, preclinical and clinical research design, execution, timing, costs and results, future product demand, supply, manufacturing, costs, marketing and pricing factors.

In some cases, forward-looking statements may be identified by words including “assumes,” “could,” “ongoing,” “potential,” “predicts,” “projects,” “should,” “will,” “would,” “anticipates,” “believes,” “intends,” “estimates,” “expects,” “plans,” “contemplates,” “targets,” “continues,” “budgets,” “may,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words, and such statements may include, but are not limited to, statements regarding (i) future research plans, expenditures and results, (ii) potential collaborative arrangements, (iii) the potential utility of the Company’s product candidates, (iv) reorganization plans, and (v) the need for, and availability of, additional financing. Forward-looking statements are based on information available at the time the statements are made and involve known and unknown risks, uncertainties and other factors that may cause our results, levels of activity, performance or achievements to be materially different from the information expressed or implied by the forward-looking statements in this press release.

These factors include but are not limited to, regulatory policies or changes thereto, available cash, research and development results, issuance of patents, competition from other similar businesses, interest of third parties in collaborations with us, and market and general economic factors, and other risk factors disclosed in “Item 1A. Risk Factors” in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on April 15, 2022 (the “2021 Form 10-K”).

You should read these risk factors and the other cautionary statements made in the Company’s filings as being applicable to all related forward-looking statements wherever they appear in this press release. We cannot assure you that the forward-looking statements in this press release will prove to be accurate and therefore prospective investors, as well as potential collaborators and other potential stakeholders, are encouraged not to place undue reliance on forward-looking statements. You should read this press release completely. Other than as required by law, we undertake no obligation to update or revise these forward-looking statements, even though our situation may change in the future.

We caution investors, as well as potential collaborators and other potential stakeholders, not to place undue reliance on any forward-looking statement that speaks only as of the date made and to recognize that forward-looking statements are predictions of future results, which may not occur as anticipated. Actual results could differ materially from those anticipated in the forward-looking statements and from historical results, due to the risks and uncertainties described in the 2021 Form 10-K and in this press release, as well as others that we may consider immaterial or do not anticipate at this time. These forward-looking statements are based on assumptions regarding the Company’s business and technology, which involve judgments with respect to, among other things, future scientific, economic, regulatory and competitive conditions, collaborations with third parties, and future business decisions, all of which are difficult or impossible to predict accurately and many of which are beyond the Company’s control. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we do not know whether our expectations will prove correct. Our expectations reflected in our forward-looking statements can be affected by inaccurate assumptions that we might make or by known or unknown risks and uncertainties, including those described in the 2021 Form 10-K and in this press release. These risks and uncertainties are not exclusive and further information concerning us and our business, including factors that potentially could materially affect our financial results or condition, may emerge from time to time.

For more information about the risks and uncertainties the Company faces, see “Item 1A. Risk Factors” in our 2021 Form 10-K. Forward-looking statements speak only as of the date they are made. The Company does not undertake and specifically declines any obligation to update any forward-looking statements or to publicly announce the results of any revisions to any statements to reflect new information or future events or developments. We advise investors, as well as potential collaborators and other potential stakeholders, to consult any further disclosures we may make on related subjects in our annual reports on Form 10-K and other reports that we file with or furnish to the SEC.

Company Contact:

Jeff Margolis
Senior Vice President, Chief Financial Officer, Treasurer and Secretary
Telephone: (917) 834-7206
E-mail: jmargolis@respirerx.com
RespireRx Pharmaceuticals Inc.
126 Valley Road,
Suite C,
Glen Rock, NJ 07452
www.respirerx.com



OTC QB: RSPI

A Translation Approach to Drug Discovery and Development: A Case Study with AMPAkinés

November 8, 2022

CAUTIONARY NOTES



FORWARD LOOKING STATEMENTS

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These factors include but are not limited to, regulatory policies or changes thereto, available cash, research and development results, issuance of patents, competition from other similar businesses, interest of third parties in collaborations with us, and market and general economic factors, and other risk factors disclosed in “Item 1A. Risk Factors” in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on April 15, 2022 (the “2021 Form 10-K”).

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CAUTIONARY NOTES (cont'd)

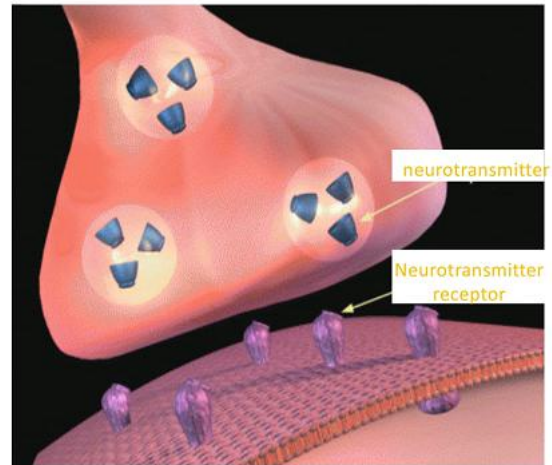


NOT A SECURITIES OFFERING

This presentation is being provided for informational purposes only. This presentation does not constitute an offer to sell, a solicitation of an offer to buy, or a recommendation of any security or any other product or service by RespireRx Pharmaceuticals Inc. (the "Company") or any other third party regardless of whether such security, product or service is referenced in this presentation. Furthermore, nothing in this presentation is intended to provide tax, legal, or investment advice and nothing in this presentation should be construed as a recommendation to buy, sell, or hold any investment or security or to engage in any investment strategy or transaction. We do not represent that the securities, product development opportunities or strategies, or any other features of the Company discussed in this presentation are suitable for any particular investor, collaborator or other stakeholder.

Neuromodulators Can Enhance Synaptic Transmission

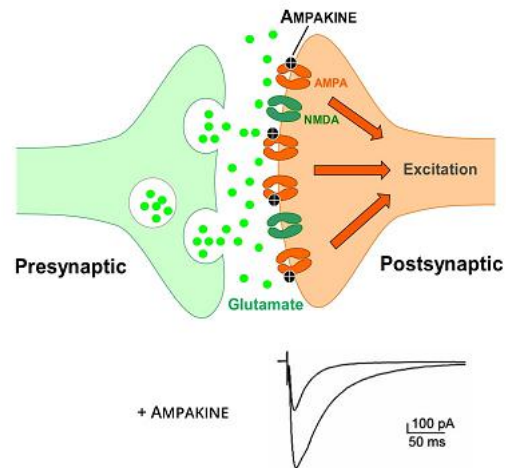
- Neurons communicate by releasing chemical neurotransmitters that bind to specific receptors on the adjacent neuron.
- Glutamate is the major excitatory neurotransmitter and GABA is the major inhibitory neurotransmitter.
- Neuromodulators do not act directly at the neurotransmitter binding site and have no intrinsic activity of their own, but instead act at accessory sites that enhance or reduce the actions of neurotransmitters.
- Neuromodulators offer the possibility of developing “kinder and gentler” neuropharmacological drugs with greater pharmacological specificity and reduced side effects



1. Identify Target

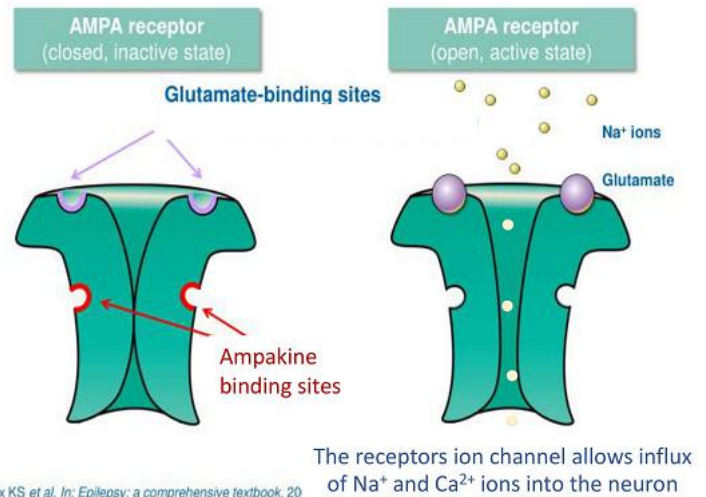
AMPAKINES – A NOVEL CLASS OF DRUGS

- 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

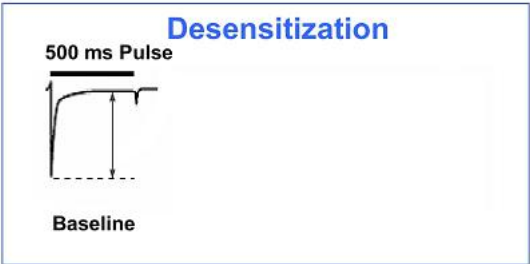
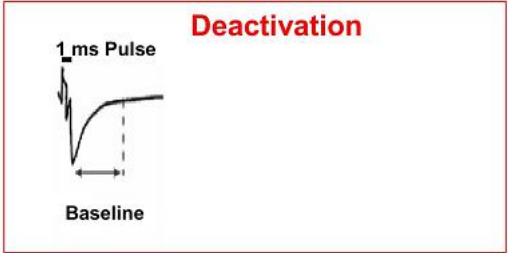


AMPA Glutamate Receptor Structure

- The AMPA receptor is composed of four transmembrane proteins that form a pore, which when activated by glutamate opens and allows positive ions to enter the cell.
- Ampakine binding sites are located adjacent to the glutamate binding sites and increase the normal excitatory response to glutamate.
- As opposed to direct acting agonists that constantly bombard the glutamate binding site in a non-physiological manner, ampakines act by enhancing the natural actions of glutamate.
- *The AMPA receptor proteins are heterogeneous and form various combinations allowing for subtype specificity and neuroanatomical and pharmacological selectivity.*



¹Wilcox KS et al. In: *Epilepsy: a comprehensive textbook*. 20
²Clements JD et al. *J Neurosci* 1998;18:119-121.



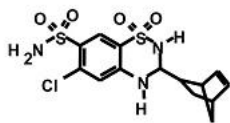
Effects of CX614 and CTZ were examined in patches excised from hippocampal CA1 pyramidal neurons.

- 1. Identify Target**
- 2. Design Drugs**

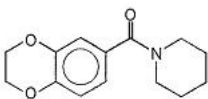
The Lego School of Drug Design



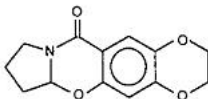
cyclothiazide



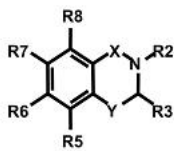
CX546



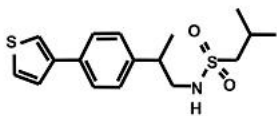
CX614



Neurosearch

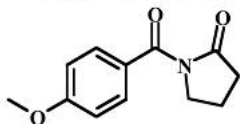


Lilly: LY392098

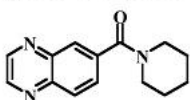


High Impact

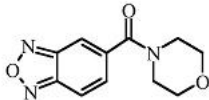
Aniracetam - Roche



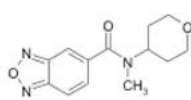
CX516 - Ampalex™



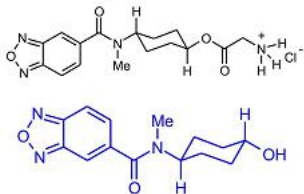
CX717



CX1739

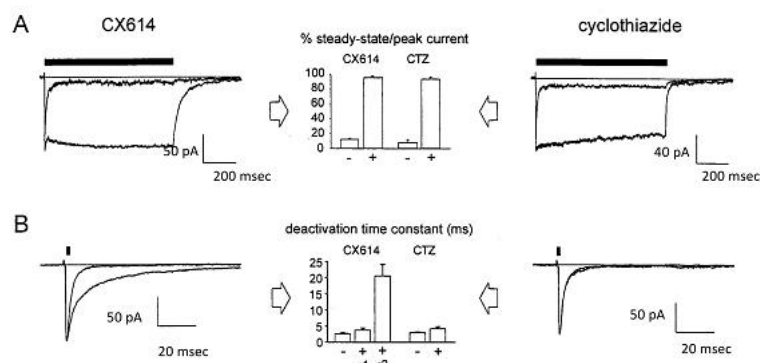


CX1942/CX1763



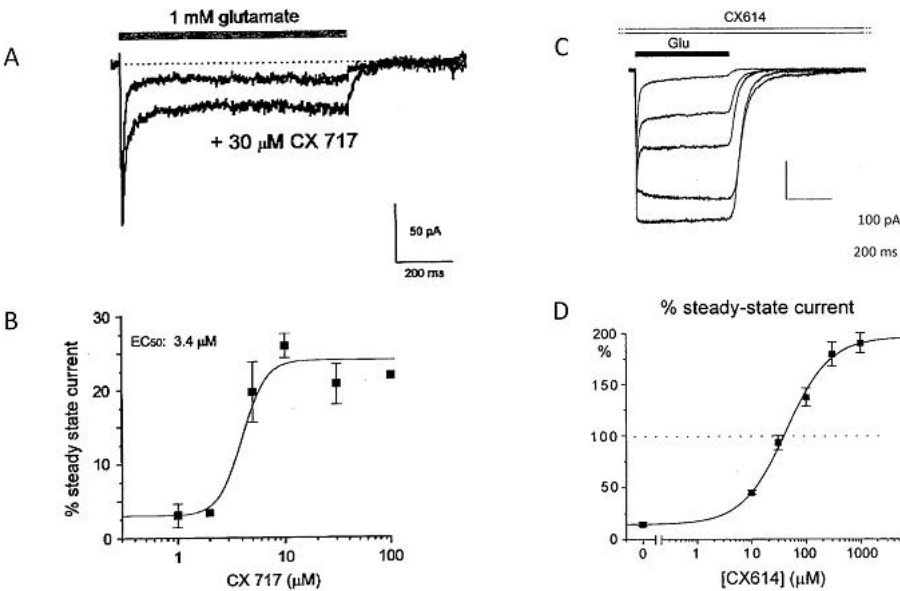
Low Impact

AMPAKINES – High Impact

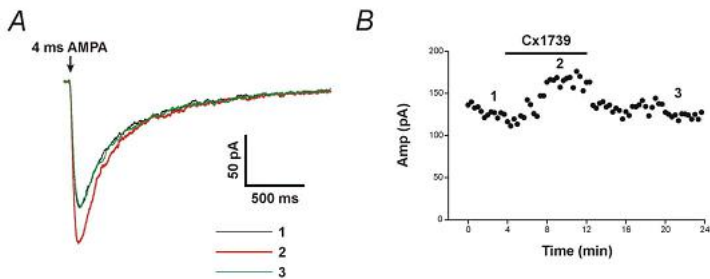


Effects of CX614 and CTZ were examined in patches excised from hippocampal CA1 pyramidal neurons. Patches were equilibrated with the drug before glutamate was applied. A. Effects of CX614 and CTZ on inward currents induced by 100msec application of 10 mM glutamate. Traces were taken from a representative experiment in which both drugs were applied at 100 M to the same patch. The bar graph at the center summarizes the effect of the drugs on the steady-state current as a percentage of the peak current and shows the corresponding control values without drug. Data (mean and S.E.M.) are from 10 (CX614) and 8 patches (CTZ). B. Effects on responses induced by 1-ms application of 10 mM glutamate. The decay phase was fitted with a single-exponential (control and CTZ) or a two-exponential function (CX614). Summarized data are shown at the center. The deactivation time constant in the absence of drug was 2.6 0.3 ms (*n* 8). For CX614, both the fast (τ_1) and the slow (τ_2) component are shown. The effects of the drugs were compared within the same patches (6 pairs).

AMPAKINES – Low Impact

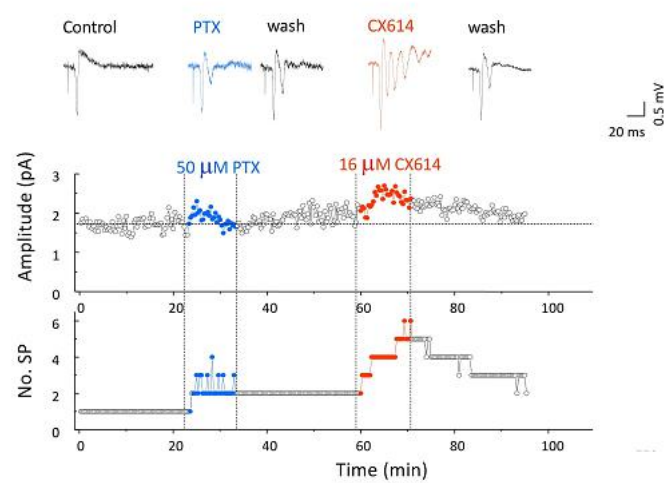


AMPAKINES – Low Impact



Effects of Cx1739 on AMPAR-mediated currents in CA1 pyramidal neurons. *A*, In the presence of TTX (1 μ M), puffing AMPA (0.5 mM, 4 ms pulse, 0.1-0.2 psi) induced a fast current (Black trace and 1) that could be blocked by NBQX (20 μ M, results not shown). Application of Cx1739 (200 μ M) enhanced the amplitude of AMPAR-currents (Red trace and 2), and could be washed out (Green trace and 3). *B*, The time course of Cx1739 effects.

High Impact Ampakines – Tissue Model of Convulsions

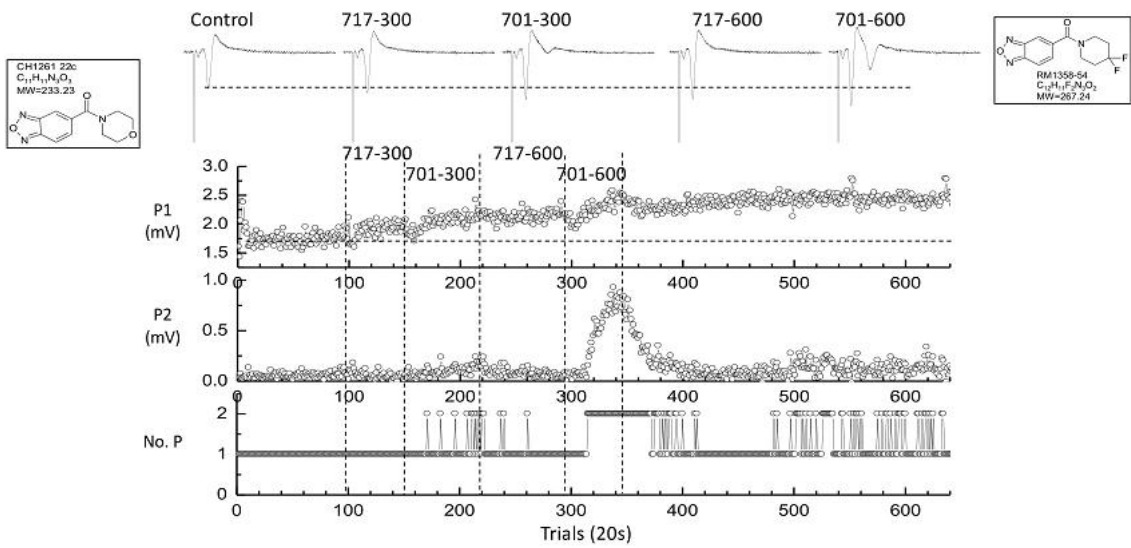


Extracellular field potentials (Population Spikes) from CA1 pyramidal cells were recorded with glass micropipettes after single pulse electrical stimulation of the Schaffer-commissural fiber afferents. The maximal amplitude of PS was determined by increase stimulating intensity until a second spike appeared. Then the intensity was decreased to induce a 50% to 60% of maximal response. The amplitude of PS was measured for each response and plotted against time.

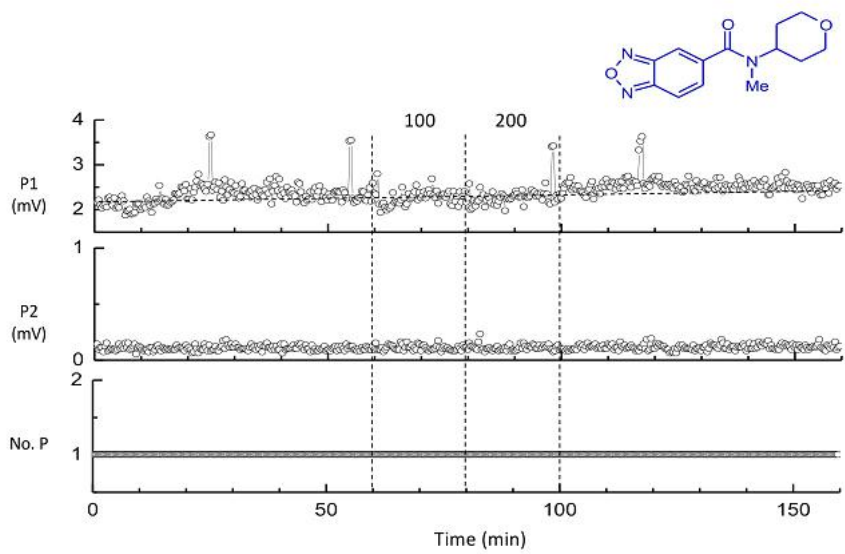
Low Impact Ampakines – Tissue Model of Convulsions

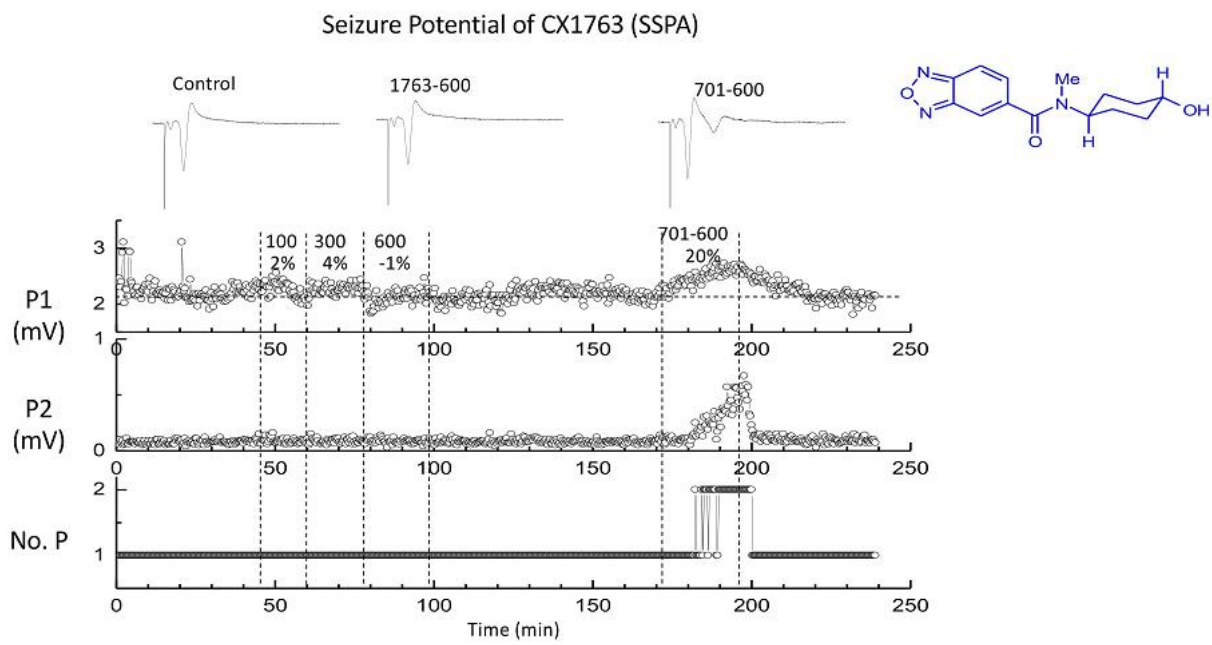


Seizure Potential of CX717-701 (SSPA)



Seizure Potential of CX1739





AMPAKINE Properties



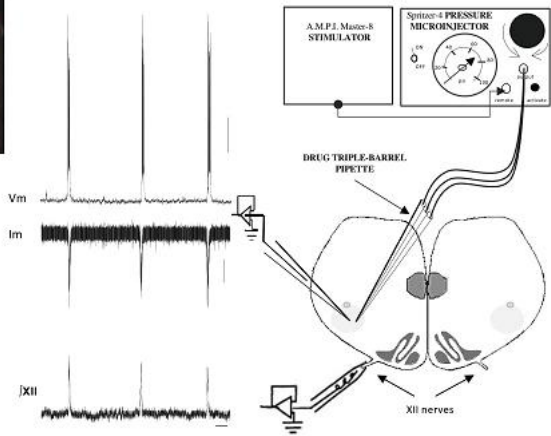
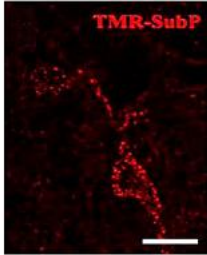
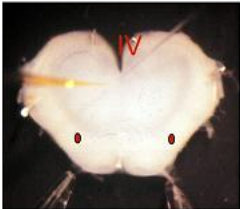
Characteristics of Low Impact and High Impact AMPAKINE® Molecules

Properties	Low Impact	High Impact
Mechanism of action	Increases probability of channel opening	Inhibits desensitization
Bind to cyclothiazide site	No	Yes
Increase EPSP <i>in vivo</i>	Yes	Yes
Increase long term potentiation	Yes	Yes
Effective in cognition tests	Rat/primate	Rat/primate
Increase BDNF	Yes	Yes
Antagonize respiratory depression	Animals/humans	Rats
Rat post-stroke recovery	No	Yes
Huntington's disease model	No	Yes

1. Identify Target
2. Design Drugs
3. Verify Target Site Engagement

- In Vitro Cellular Models
- In Vivo Animal Models
- Clinical Studies

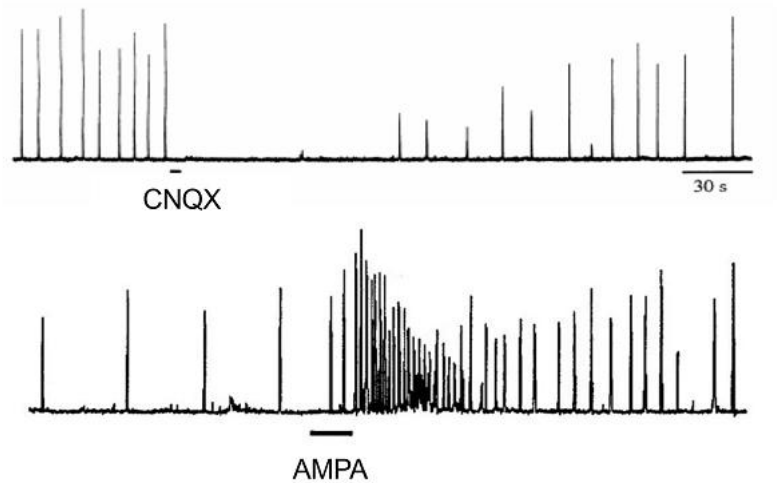
IDENTIFICATION OF KEY RHYTHMOGENIC NEURONS*



Schematic diagram of a rhythmically-active medullary slice (700 μ m) preparation used for recordings of preBötC neurons and XII nerves activity. PreBötC (light grey circles) inspiratory neuron display spontaneous inspiratory depolarizing discharges in current-clamp recording (upper trace; scale bar 10 mV) and input currents in voltage-clamp recording (lower trace, scale bars 100pA and 2sec). Hypoglossal nerve activity is recording at the same time as a reference for inspiratory motor outputs. Drugs can be added to the bath or locally pressure injected via a triple-barrel drug pipette that can each contain up to three different drugs. The pressure injector is controlled by a stimulator. All parameters for the microinjections (duration, intervals, etc.) can be monitored by the stimulator.

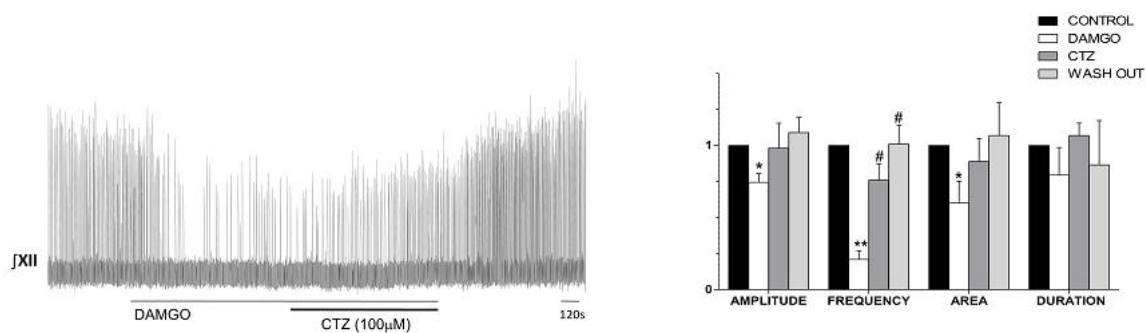
* From Laboratory of Dr. John Greer

RESPIRATORY FREQUENCY IS MODULATED VIA AMPA RECEPTORS



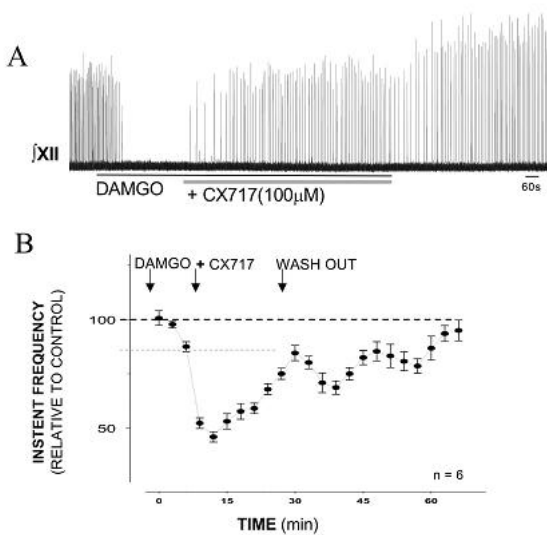
Funk et al. J. Neurophysiology 1997, 78:1414-20

AMPAKINES Antagonize Opioid Induced Respiratory Depression



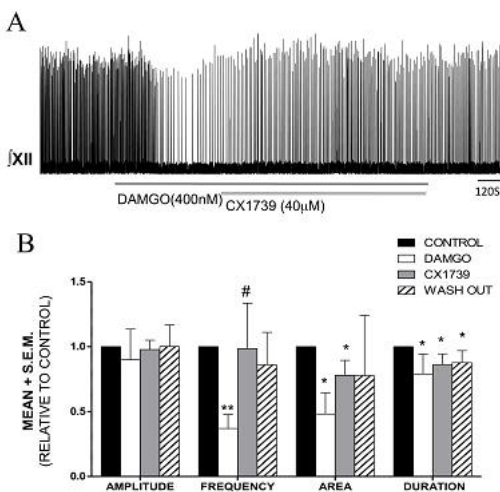
Cyclothiazide reverses DAMGO-induced respiratory drive depression in *in vitro* medullary slice of neonatal rat

AMPAKINES Antagonize Opioid Induced Respiratory Depression



Ampakines Reverse Opioid-Induced Suppression of Respiratory Frequency in a medullary slice preparation. Integrated recordings of XII nerve bursts during bath application of CX717 following 400nM DAMGO bath application.

AMPAKINES Antagonize Opioid Induced Respiratory Depression

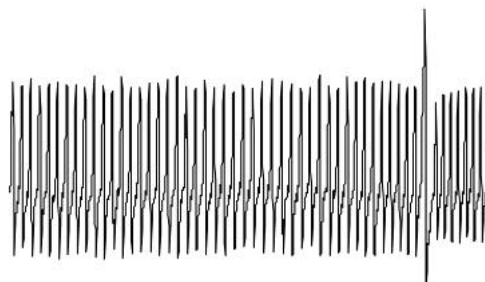
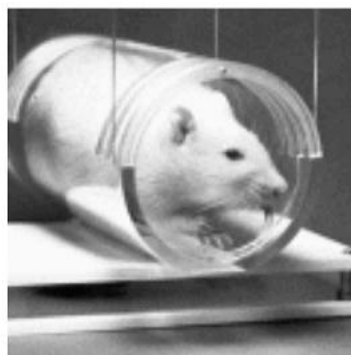


Ampakines Reverse Opioid-Induced Suppression of Respiratory Frequency in a medullary slice preparation. Integrated recordings of XII nerve bursts during bath application of (A) CX1739 following 400nM DAMGO bath application.

AMPAKINES Antagonize Opioid Induced Respiratory Depression

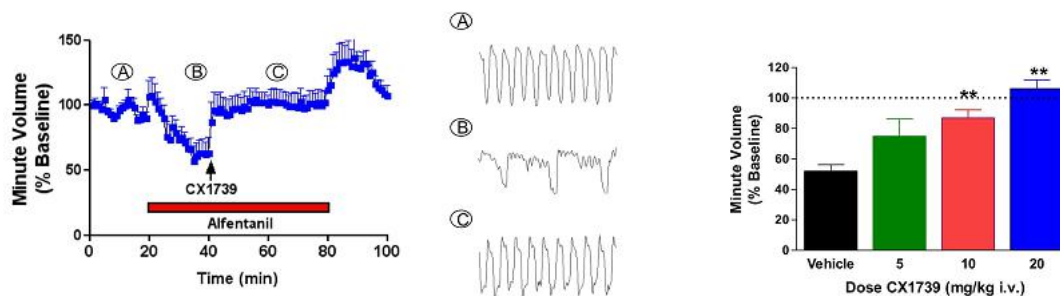


WHOLE-BODY PLETHYSMOGRAPHIC RECORDINGS TAIL INFUSION OF OPIATES AND AMPAKINES



Ren et al. (2006). American Journal of Respiratory and Critical Care Medicine. 174:1384-1391
Ren et al. (2009) Anesthesiology. 110(6):1364-70

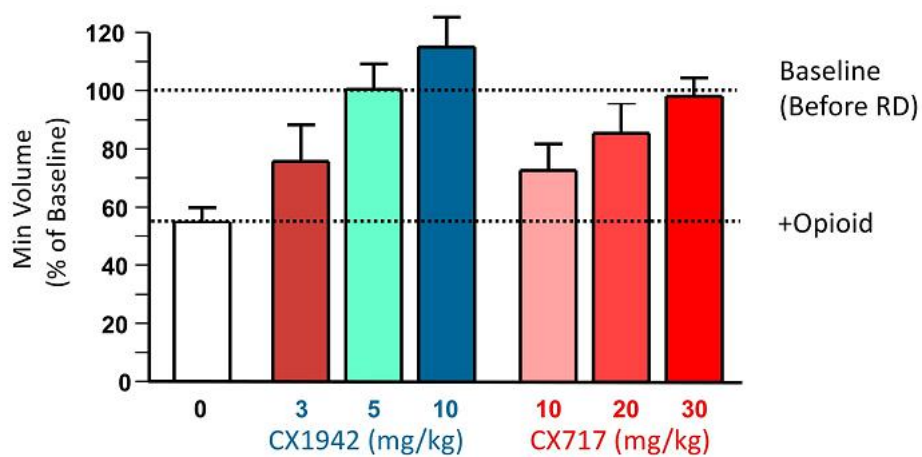
AMPAKINES Antagonize Opioid Induced Respiratory Depression



Effect on Alfentanil-induced Respiratory Depression in Rats

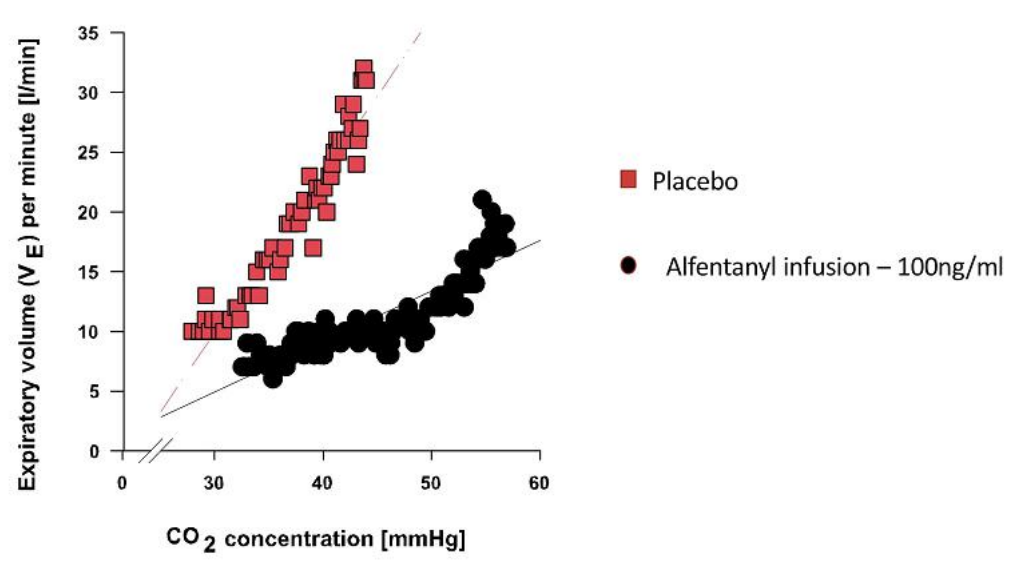
Infusion of alfentanil (250 μ g/kg/20 min) produces respiratory depression in rats. CX1739 administered intravenously at 20 mg/kg rapidly attenuates respiratory depression induced by alfentanil. Data points represent the mean normalized minute volume and standard error of 8 animals. The 5-second traces on the right are taken from time points at baseline (A), during alfentanil infusion (B), and following administration of 20 mg/kg CX1739 (C).

AMPAKINES Antagonize Opioid Induced Respiratory Depression

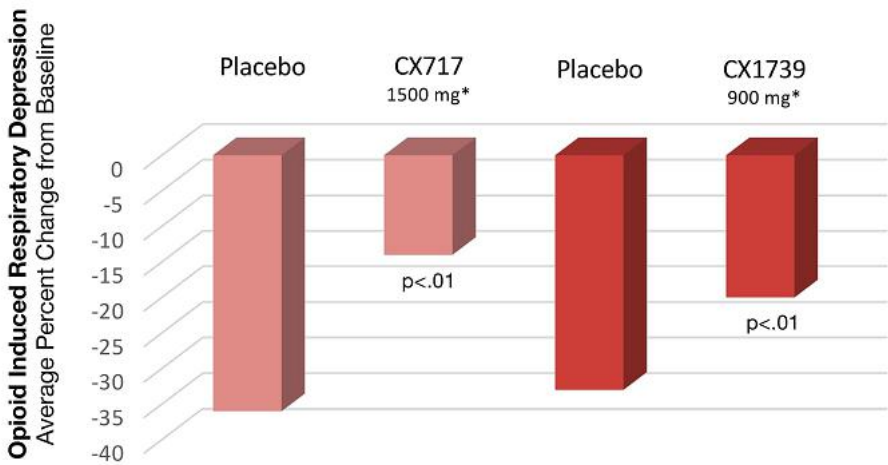


CX1942 and CX717 reverse opioid-induced RD in rats

Alfentanil Induced Respiratory Depression in Humans



Ampakines Reduce Opioid-Induced Respiratory Depression in Phase 2A Clinical Trials



* Approximately 15 and 10 mg/kg on a weight basis, respectively; comparable to animal doses

Validation of Doses for Target Engagement

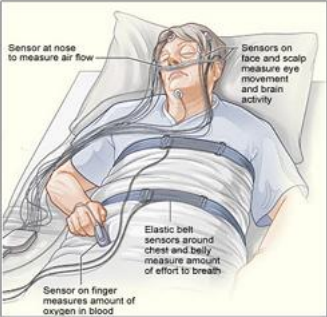
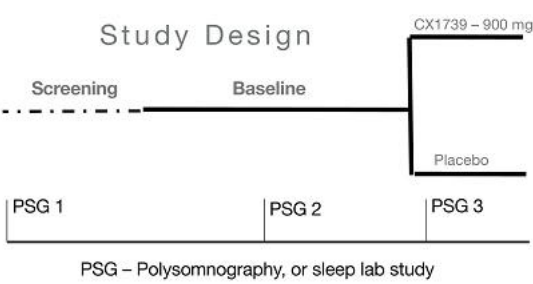
1. Identify Target
2. Design Drugs
3. Verify Target Site Engagement
4. Translational Studies to Demonstrate Efficacy

- Central Sleep Apnea
- ADHD

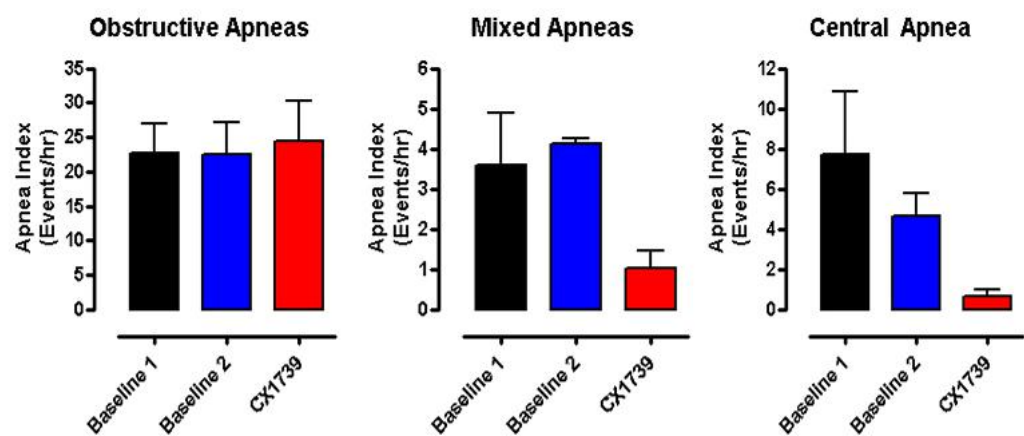
CX1739: Completed Phase 2A in Sleep Apnea – Single Dose



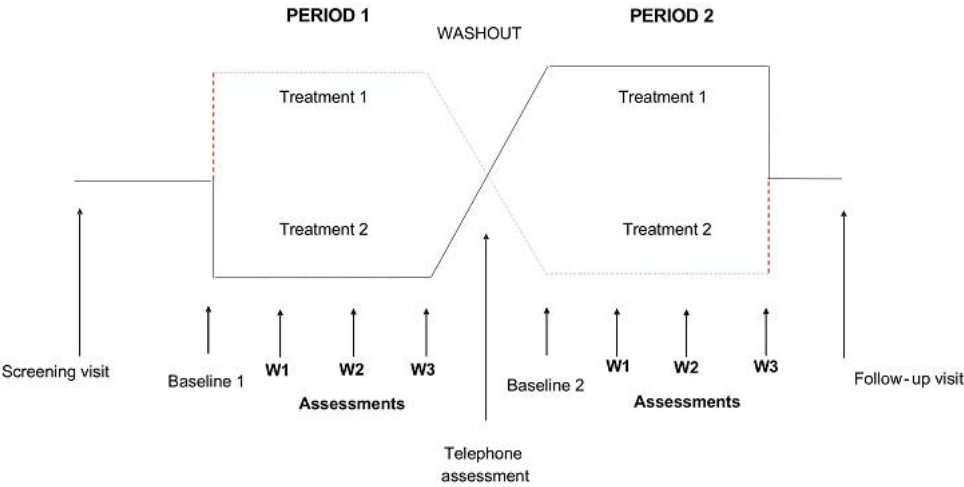
Design	Randomized, double-blind, placebo-controlled study
Population	20 adults with all types of moderate to severe sleep apnea (16 given CX1739; 4 given Placebo)
Dosing	Each subject received either placebo or a <u>single</u> dose of 900mg CX1739 one hour before lights out
Primary Measures	Apnea-Hypopnea measures; Oxygen saturation; Sleep quality, measured by PSG (Apnea: no airflow for >10s; Hypopnea: reduced airflow for >10s)



Patient Selection: CX1739 Was More Effective in Treating Mixed and Central Sleep Apneas



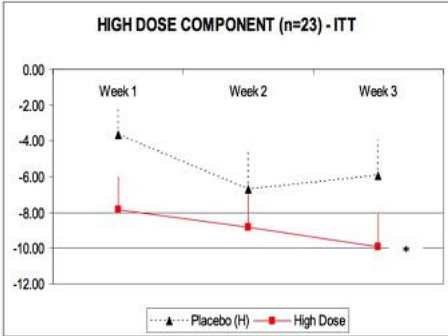
Study Design Schematic



CX717 Shows Significant Improvement in ADHD

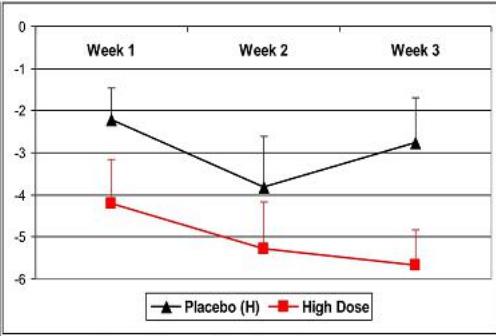


OVERALL ADHR-RS



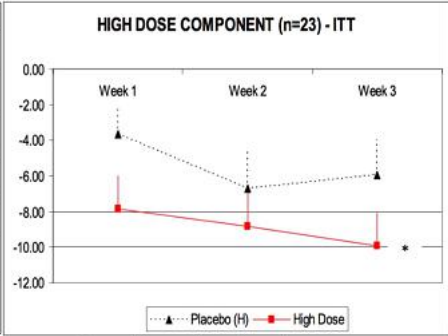
Mean Change from baseline
* Repeated measures analysis , p=0.002

HYPERACTIVITY



Mean Change from baseline
* Repeated measures analysis , p<0.05

INATTENTIVENESS



Mean Change from baseline
* Repeated measures analysis , p<0.04

Phase 2 Study of CX717 in Adult ADHD: Randomized, double-blind, multi-center, 2-period crossover study that compared 2 doses of CX717 (200 or 800 mg BID) with placebo. Statistically significant effects were observed with 800 mg as early as week 1.

CX717 May Be Superior to Strattera® in the Treatment of ADHD: Comparison of ADHD-RS Scores



Strattera® Phase 3 Pivotal Trials

STUDY 1 (LYAA)				
	Placebo (n = 134)	Strattera (n = 133)	Δ	Effect Size
Week 4	-2.4	-4.8	-2.4	0.25
Week 8	-5.6	-9.7	-4.1	0.42
Endpt	-6.0	-9.5	-3.5	0.36

STUDY 2 (LYAO)				
	Placebo (n = 124)	Strattera (n = 124)	Δ	Effect Size
Week 4	-2.8	-6.1	-3.3	0.33
Week 8	-6.9	-12.3	-5.4	0.53
Endpt	-6.7	-10.5	-3.6	0.38

Note: SD change for Placebo = 9.3; Strattera = 10.9
taken from endpoint but assumed for all calculations

Michelson D et al., Biol Psychiatry (2003) Strattera Summary Basis of Approval (2001)

CX 717 Clinical Trial

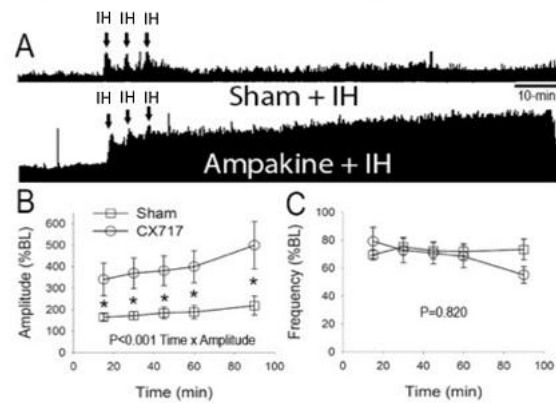
	Placebo (n=23)	CX717 (800mg) (n=23)	Δ	Effect Size
Week 1	-3.8	-8.0	4.2	.44
Week 3	-6	-10.0	4.8	.43

- * CX717 effective as early as 1 week
- * Strattera® takes 4 – 8 weeks to be effective

Next Step: Phase 2 Clinical Trial
CX1739 +/- AIH in the Treatment of SCI



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

Next Step: Phase 2 Clinical Trial CX1739 +/- AIH in the Treatment of SCI



Blinded, Placebo-controlled, Escalating-dose Study of CX1739, With and Without Acute Intermittent Hypoxia, in Patients with Incomplete Spinal Cord Injury

Primary Objectives

1. Evaluate the safety of acute CX1739 treatment at escalating doses in patients with SCI
2. Evaluate the safety of multiple daily doses of CX1739 at escalating doses in patients with SCI
3. Evaluate the safety of CX1739 in Combination with Acute Intermittent Hypoxia in Patients with SCI

Secondary Objectives

1. Evaluate the effect of acute CX1739 treatment at escalating doses on motor function and recovery, with and without acute intermittent hypoxia in patients with SCI
2. Evaluate the effect of multiple BID doses of CX1739 treatment on motor function and recovery, with and without acute intermittent hypoxia in patients with SCI



OTC QB: RSPI

Contact:
Jeff Margolis, CFO
jmargolis@respirerx.com
917-834-7206