RespireRx Pharmaceuticals Inc. Announces Publication of Preclinical Results Supporting the Use of AMPAkines in the Treatment of Human Spinal Cord Injury

Glen Rock, N.J., November 29, 2020 /Globe Newswire – RespireRx Pharmaceuticals Inc. (OTCQB: 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 the publication by Dr. David Fuller (University of Florida) and his colleagues of two new, scientific articles in major, peer-reviewed journals. In these new studies funded by grants from the National Institutes of Health, Dr. Fuller, a long-time RespireRx collaborator, describes the ability of CX1739 and CX717, the Company's lead AMPAkines, to improve motor nerve activity and muscle function in animal models of spinal cord injury (SCI).

The first paper entitled "Spinally delivered ampakine CX717 increases phrenic motor output in adult rats" was published online ahead of print in the journal *Respiratory Physiology and Neurobiology* (https://doi.org/10.1016/j.resp.2021.103814) and describes the ability of direct spinal administration of CX717 to increase the amplitude of motor nerve activity on the side ipsilateral (same side) to that in which a unilateral cervical transection had been made to anesthetized and ventilated rats.

Commenting on these results, Arnold Lippa, Ph.D., Chief Scientific Officer and Executive Chairman of the Board of Directors said, "In combination with prior studies, these new results demonstrate that AMPAkines may potentially have broad effects on both the brain and spinal cord to enhance spinal plasticity and improve motor function in patients with different forms of SCI."

Unlike the above and all prior published articles, the second paper entitled "Ampakines stimulate diaphragm activity after spinal cord injury" was published online ahead of print in the *Journal of Neurotrauma* (http://doi.org/10.1089/neu.2021.0301) and describes research conducted for the first time in awake freely moving rats as late as two weeks after having previously undergone unilateral spinal hemi-transection at the C2 spinal level. For the first time, low dose administration of either CX1739 or CX717 was shown to improve not only motor nerve and muscle activity recorded electrophysiologically from the lesioned side, but to significantly improve actual motor functioning and breathing, even under challenging conditions. The importance of these findings is described in the article by pointing out that the majority of the approximately 500,000 annual SCI cases reported globally involve injuries to the cervical spinal cord and, in severe cases, require the use of mechanical ventilation or direct diaphragm pacing to sustain ventilation. Also, in confirmation of previously reported results in anesthetized animals, the AMPAkines improved, in awake freely moving animals, the motor facilitation produced by an episode of acute intermittent hypoxia (AIH), a treatment currently used in the rehabilitation of SCI patients.

As Dr. Fuller concluded in this paper, "Our study provides evidence that even lower ampakine doses can effectively stimulate breathing and diaphragm muscle activity in a pre-clinical model of

cervical-SCI, with no evidence of adverse effects. Furthermore, ampakine treated animals are capable of increasing respiratory motor drive to a larger degree when challenged, a response often dampened in SCI patients. Lastly, the current data suggest that pairing low-dose and low impact ampakines with even a single brief hypoxia exposure may have value in the context of neurorehabilitation paradigms."

Dr. Lippa said, "As part of our ongoing AMPAkine collaboration with Dr. Fuller, these exciting new research results add considerable support to the concept that AMPAkines might be a new therapeutic alternative for significantly improving clinical recovery from SCI, when given alone or in combination with other types of rehabilitation. As such, they strengthen our intention to translationally extend this work to human clinical trials."

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 treatment options that address conditions affecting millions of people, but for which there are few or poor treatment options, including obstructive sleep apnea ("OSA"), attention deficit hyperactivity disorder ("ADHD"), epilepsy, chronic pain and recovery from spinal cord injury ("SCI"), as well as certain neurological orphan diseases. RespireRx is developing a pipeline of new drug products based on our broad patent portfolios for two drug platforms: (i) pharmaceutical cannabinoids, which include dronabinol, a synthetic form of Δ9-tetrahydrocannabinol ("Δ9-THC") that acts upon the nervous system's endogenous cannabinoid receptors and (ii) neuromodulators, which include AMPAkines and GABAkines, proprietary compounds that positively modulate (positive allosteric modulators or "PAMs") AMPA-type glutamate receptors and $GABA_A$ receptors, respectively.

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.

***ResolutionRx: Pharmaceutical Cannabinoids*.**

Dronabinol. RespireRx 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 to-be-developed new 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 further 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.

EndeavourRx: Neuromodulators

GABAkines. Under a License Agreement with the University of Wisconsin-Milwaukee Research Foundation, Inc. ("UWMRF"), an affiliate of the University of Wisconsin-Milwaukee, RespireRx has licensed rights to certain selectively acting GABAkines that have shown impressive activity in a broad range of animal models of refractory/drug resistant epilepsy and other convulsant disorders, as well as in brain tissue samples obtained from epileptic patients. Epilepsy is a chronic and highly prevalent neurological disorder that affects millions of people world-wide. While many anticonvulsant drugs have been approved to decrease seizure probability, seizures are not well controlled and, in as many as 60-70% of patients, existing drugs are not efficacious at some point in the disease progression. We believe that the medical and patient community are in clear agreement that there is desperate need for improved antiepileptic drugs. In addition, these GABAkines have shown positive activity in animal models of migraine, inflammatory and neuropathic pain, as well as other areas of interest. Because of their GABA receptor subunit specificity, the compounds have a greatly reduced liability to produce sedation, motor incoordination, memory impairments and tolerance, side effects commonly associated with non-specific GABA PAMs, such as Valium® and Xanax®.

AMPAkines. 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 AMPAkines, 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. From our AMPAkine platform, 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. AMPAkines are PAMs of the AMPA glutamate receptor.

AMPAkines 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 adults with ADHD. At present, the major pharmacotherapies available for ADHD are made up of two types of drugs. Stimulants, such as amphetamine, rapidly produce robust effects, but suffer from side effects typical of stimulants, including tolerance, dependence, withdrawal and abuse. For these reasons, stimulants are scheduled by the FDA. Non-stimulants, such as Straterra® (atomoxetine) tend to be less effective than stimulants, with a much longer (approximately 4 – 8 week) latency to onset of action. In a number of animal and human studies, CX717 and other AMPAkines did not display any stimulant properties typically associated with drugs like amphetamine. In the Phase 2 ADHD clinical trial, statistically significant therapeutic effects were observed within one week. Therefore, we believe AMPAkines may represent a novel, non-stimulant treatment for ADHD with a more rapid onset of action than alternative non-stimulant treatment options.

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 and Section 21E of the Securities Exchange Act of 1934 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 products 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.

You should read these risk factors and the other cautionary statements made in the Company's press release and filings with the Securities and Exchange Commission ("SEC") as being applicable to all related forward-looking statements. We cannot assure you that the forward-looking statements in this press release will prove to be accurate and therefore prospective investors are encouraged not to place undue reliance on forward-looking statements. You should read this press release completely, but should also read the Company's recent annual report on Form 10-K in its entirety. 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 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 this press release, our recent annual report on Form 10-K and other filings made with the SEC, as well as other risks and uncertainties 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 this press release and our filings with the SEC. 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 recent annual report on Form 10-K as of December 31, 2020. 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 to consult any further disclosures we may make on related subjects in our most recent annual report on Form 10-K for the year ended December 31, 2020 and any subsequent documents we file with or furnish to the SEC.

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