RespireRx Pharmaceuticals Inc. Provides Update on Its Development Programs

Glen Rock, N.J., April 22, 2021 /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 provide an update on its therapeutic drug development programs.

EndeavourRx

GABAkines

Scientists associated with the Company have been invited by the prestigious journal, ***Pharmacology and Therapeutics***, to publish a review article describing the preclinical properties of its lead GABAkine compound, KRM-II-81, and its potential clinical therapeutic applications. The multidisciplinary team of authors have been led by Dr. James M. Cook[6,7], Distinguished Professor, University of Wisconsin-Milwaukee and Dr. Jeffrey M. Witkin[1,6,7], both of whom are RespireRx Research Fellows. Authors also include Roc Cerne[1,2,3,4], Arnold Lippa[5], Michael Poe[8], Jodi L. Smith[1], Xiaoming Jin[4], Xingjie Ping[4] and Lalit K. Golani[6]. The paper is undergoing editorial review prior to being published.

KRM-II-81, one of the molecules in RespireRx's EndeavourRx business unit, amplifies inhibitory neurotransmission through selectively potentiating a subset of GABA, particularly $GABA_A$ receptors, to guide its unique efficacy and reduced side-effect profile. Preclinical studies have documented its efficacy in a broad array of animal models of inter-related neurological and psychiatric disorders including epilepsy, chronic pain, anxiety, and depression. KRM-II-81 is the latest GABAkine to begin development in IND-enabling toxicology investigations as a joint program of RespireRx and the University of Wisconsin-Milwaukee. Dr. Jeffrey Witkin, a senior author of the review paper said "The renewed efforts to develop improved GABAkines allows the fine-tuned use of the patient's primary inhibitory neurotransmitter system to help moderate a host of neurological and psychiatric disorders. We are excited about the prospect that this novel GABAkine may give hope to those patients burdened with intractable epilepsy or chronic pain."

Tim Jones, President and Chief Executive Officer said, 'We are honored to have been invited by the esteemed medical journal, ***Pharmacology and Therapeutics***, to author a review paper of our data from KRM-II-81. It is a clear recognition of the significant advancements we are making in our GABAkine programs. I am also very pleased with the progress we are making in drug substance and formulation development across all of our programs'

KRM-II-81 has not yet been tested in humans and there can be no assurance that such tests will be successful.

AMPAkines

The Company has been working with Dr. David Fuller at the University of Florida which has funding from NIH, to evaluate the use of AMPAkines for the treatment of compromised motor function in spinal cord injury ("SCI"). Using rodents that have received spinal hemi-sections, CX717 was observed to increase motor nerve activity bilaterally. The effect on the hemisected side was greater than that measured on the intact side, with the recovery approximating that seen on the intact side prior to administration of AMPAkine. The doses of AMPAkines active in SCI were comparable

to those demonstrating antagonism of opioid induced respiratory depression, indicating target engagement of the AMPA receptors.

Recently, studies done by others in patients with SCI have demonstrated that neural plasticity can be induced to improve motor function. This is based on the ability of spinal circuitry to learn how to adjust spinal and brainstem synaptic strength following repeated hypoxic bouts (short term deprivation of oxygen). Animal studies have demonstrated the ability of AMPAkines to dramatically enhance the effects of acute intermittent hypoxia ("AIH") on motor neuron activity after SCI. Because AMPAkines are known to enhance synaptic plasticity, the potential exists to harness repetitive AIH in combination with AMPAkines as a means of inducing functional recovery of motor function following SCI.

These animal models of motor nerve function following SCI support proof of concept for a new treatment paradigm using AMPAkines to improve motor functions in patients with SCI. With additional funding granted by NIH to Dr. Fuller, the Company is continuing its collaborative preclinical research with him, while it is planning a clinical trial program focused on developing AMPAkines for the restoration of certain motor functions in patients with SCI. The Company is working with researchers at highly regarded clinical sites to finalize a Phase 2 clinical trial protocol. We believe that a clinical study could be initiated within several months of raising sufficient financing (of which no assurance can be provided).

While our AMPAkines have demonstrated positive clinical effects in treating attention deficit hyperactivity disorder (ADHD) and opioid induced respiratory depression, they have not yet been tested in in patients with SCI and there can be no assurance that such tests will be successful.

ResolutionRx

Dronabinol

RespireRx's business unit, ResolutionRx has been utilizing nanotechnological approaches to develop a number of new potential formulations of dronabinol, Δ9-THC. After extensive bench testing, several have been identified for additional testing for selection of lead and secondary formulations, before commencing the required animal pharmacokinetic and pharmacodynamic ("PK/PD") studies that are currently being designed. These formulations are intended to improve the PK/PD profile of dronabinol for an all-night indication such as obstructive sleep apnea, our initial targeted indication.

None of these formulations have yet been tested in humans and there can be no assurance that such tests if conducted, will be successful.

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.

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 the Company 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.

Footnotes:

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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 annual reports on Form 10-K, our quarterly reports on Form 10-Q and our current reports on Form 8-K that we file with or furnish to the SEC.

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