RespireRx Pharmaceuticals Inc. CEO Issues Progress and Status Report

Glen Rock, N.J., February 12, 2020 /Globe Newswire – RespireRx Pharmaceuticals Inc. (OTCQB: RSPI), a leader in the development of medicines for respiratory disorders and central nervous system ("CNS") indications, with a focus on obstructive sleep apnea, attention deficit hyperactivity disorder ("ADHD"), spinal cord injury and other neurological conditions, today provides a progress and status report to its stockholders, stakeholders, strategic partners as well as other interested parties.

Dear Stockholders, Stakeholders, Strategic Partners and Other Interested Parties:

In conjunction with the start of a new year, we would like to provide you with this open letter summarizing where we are now and our goals for the immediate future. Of course, we can provide no assurance that we will achieve these goals (see cautionary note about forward-looking statements near the end of this letter), but we believe that they are based on realistic assumptions and are reasonably achievable. We will certainly work hard on your behalf to try to achieve what we lay out here.

RespireRx Pharmaceuticals Inc. ("RespireRx," the "Company," "we" or "our") is developing a pipeline of new drug products based on our broad patent portfolios for two drug platforms: cannabinoids, including dronabinol, an FDA approved synthetically manufactured form of Δ9-tetrahydrocannabinol ("THC"), and neuromodulators, currently ampakines, which are proprietary compounds that positively modulate AMPA-type glutamate receptors to promote neuronal function. To build out the neuromodulator program, we are considering the addition of non-ampakine neuromodulators to the platform.

As part of the cannabinoid platform, two Phase 2 clinical trials have been completed demonstrating the ability of dronabinol to significantly reduce the symptoms of obstructive sleep apnea ("OSA"), a sleep-related breathing disorder that involves an episodic decrease or complete halt in airflow despite an ongoing effort to breathe during sleep. OSA afflicts an estimated 30 million people in the United States and a comparable number in Germany and the United Kingdom combined. Continuous Positive Airway Pressure ("CPAP"), the most common treatment for OSA, is cumbersome and difficult for many patients to tolerate. The true benefits of CPAP are seen with complete adherence to patients' treatment programs. Unfortunately, studies report that most patients either refuse to initiate or completely discontinue CPAP use within the first several months and that most patients who continue to use the device do so only intermittently. With no approved drug treatments for OSA, we believe a clear need exists for a safe, effective pharmaceutical alternative.

We initially believed that the most direct route to commercialization was to proceed directly to a Phase 3 pivotal clinical trial using the currently available, FDA approved (for other indications), generically available dronabinol gel cap formulation and to commercialize, within the present RespireRx public corporate structure, a RespireRx branded dronabinol capsule under a 505(b)(2) FDA regulatory pathway in the US. We planned to follow this product with a proprietary formulation. However, several recent developments have caused us to re-evaluate this approach and to consider accelerating the development of a new proprietary formulation, as well as implementing an internal restructuring plan that contemplates spinning out the cannabinoid platform into what initially would be a wholly-owned subsidiary of RespireRx ("Newco", official name not yet determined) for the purpose of developing pharmaceutical cannabinoids. Newco's initial primary focus will be the re-purposing of dronabinol for the treatment of OSA, using a new proprietary formulation.

Below are some of the recent developments that have led to this re-evaluation.

1. ***Pharmaceutical Cannabinoids*** – While the liberalization of state laws regulating the use and sales of marijuana has created a major industry based on the commercialization of marijuana for both medical and recreational use, the U.S. Food and Drug Administration ("FDA") has not recognized or approved the marijuana plant as medicine nor is it federally legal to sell products that contain cannabinoids, the pharmacologically active substances found within marijuana, as drugs, dietary supplements or foods (edibles) without its approval. In parallel with the widespread public attention given to the growth of the cannabis industry, an alternate approach has focused on the development of cannabinoids as pharmaceutical products. The term "pharmaceutical cannabinoids" refers to the development of cannabinoids according to the FDA accepted regulatory pathway by which a company receives FDA approval to market and sell a new drug. Scientific study has focused on the two major cannabinoids, THC and cannabidiol ("CBD"), although additional cannabinoids are gaining attention.

To date, the FDA has approved three cannabinoids: (1) dronabinol (proprietary names Marinol® and Syndros®), synthetically manufactured THC, approved for the treatment of AIDS related anorexia and chemotherapy induced nausea and vomiting, (2) Epidiolex®, an oral formulation of purified CBD, approved for seizures associated with Lennox-Gastaut syndrome or Dravet syndrome, and (3) nabilone (Cesamet®), a synthetic analogue of THC, approved for chemotherapy induced nausea and vomiting. Sativex®, an oral solution containing a complex botanical mixture of THC and CBD for the treatment of spasticity due to multiple sclerosis, is sold in Europe and over 23 other countries, but is not approved in the U.S. We believe that the commercialization of these pharmaceutical cannabinoids has opened the door to a potentially large, expanding pharmaceutical cannabinoid market opportunity.

RespireRx has capitalized upon this opportunity by emphasizing its development of dronabinol for the treatment of obstructive sleep apnea ("OSA"). Within the last 15 months, senior members of RespireRx have accepted invitations to be major speakers at three international pharmaceutical cannabinoid conferences, one of which will be taking place in London, UK in May 2020. Within this context, we have had discussions with a number of

potential cannabinoid investors and strategic partners who have expressed interest, mostly in the development of a new, proprietary formulation with extended patent life, with essentially no interest in the ampakine platform. Our assessment is that such potential investors or strategic partners, while apparently willing to accept the risks of a cannabinoid platform, are not interested in subjecting their cannabinoid investment or efforts to the risks of the neuromodulator platform. Alternatively, other potential investors and strategic partners might be interested in the neuromodulators independent of the cannabinoid platform.

2. ***Intellectual Property*** – RespireRx has exclusive rights to issued and pending patents claiming cannabinoid compositions and methods for treating cannabinoid-sensitive disorders, including sleep apnea, pain, glaucoma, muscular spasticity, anorexia and other conditions. We recently filed a continuation-in-part for our pending patent that describes and claims novel doses, controlled release compositions and methods of use for cannabinoids, as well as a new U.S. provisional patent application further disclosing novel dosage and controlled release compositions and methods of use for cannabinoids, alone or in combination, including with non-cannabinoid molecules. Specific claims describe low dosage strengths and controlled release formulations for attaining a therapeutic window of cannabinoid blood levels that produce the desired therapeutic effect(s) for a controlled period of time, while minimizing undesirable side effects. As previously disclosed, the original patents were filed by RespireRx and are now included in an exclusive license agreement with the University of Illinois. While no assurance can be provided that the claims in this continuation-in-part or the U.S. provisional patent application will be allowed in whole or in part, or that the patents will ultimately issue, we believe that these new filings, if allowed, will provide market protections through at least 2031.

New technologies, including nano- and micro-emulsions and thin films, have been shown to bypass the normal route of absorption and liver metabolism of cannabinoids, thus dramatically increasing blood levels and allowing for the use of low doses. Similarly, technologies may be used to achieve a controlled release of dronabinol. New cannabinoid formulation technology clearly is headed in the direction of enhanced absorption and controlled release. However, we believe that our pending patent priority relating back to 2010 predates the efforts of others seeking to develop low-dose or extended release formulations of cannabinoids. To the extent that new technologies result in lower doses and/or controlled release formulations, we believe they would infringe on our pending patents once issued, not only for use in the treatment of OSA but potentially a wide variety of other indications as well. For these reasons, we believe our new and continuing intellectual property initiatives may afford expanding strategic options and market exclusivity in the burgeoning pharmaceutical cannabinoid business sector.

3. ***Formulation Issues*** – In its present form as a soft gelatin capsule, dronabinol as currently marketed suffers from several major deficiencies:

a) Poor and erratic absorption – THC is not water soluble and so commercial dronabinol is currently formulated as a sesame oil-based liquid within a soft gelatin capsule. The absorption of dronabinol after oral administration is poor and highly variable with some patients achieving very high levels and others achieving very low levels. This

erratic absorption may be responsible for the variable therapeutic responses observed in dronabinol clinical trials.

b) Rapid and extensive metabolism – Dronabinol is rapidly and extensively (approximately 80%) metabolized upon first pass through the liver, resulting in low blood levels. In addition, dronabinol has a relatively short half-life (approximately 3 – 4 hours) and, in its present formulation, is not optimally suited for therapeutic indications requiring blood levels to be sustained for 6 hours or longer.

c) Undesirable side effects from high dosage strength – In order to achieve sustained, therapeutic blood levels, we have found it necessary to use higher doses of dronabinol in our OSA clinical trials. For example, over an 8-hour period, the 2.5 and 10 mg doses produced therapeutically equivalent effects during the first 4 hours, but only the 10 mg dose produced therapeutic effects during the second 4 hours (see below for details). Unfortunately, the 10 mg dose produces a higher occurrence of side effects than the 2.5 mg dose (see Marinol® package insert). We anticipate focusing on new formulations that would achieve the blood levels produced by the lower doses for a sustained time period, resulting in the desired therapeutic effect(s) while minimizing undesirable side effects.

Data from our Phase 2 clinical trials has allowed us to design new proprietary formulations of dronabinol, disclosed in our patents and optimized for the treatment of not only OSA, but other indications as well. Within the past 6 to 12 months, new formulation technology has emerged potentially allowing for the creation of a proprietary dronabinol formulation with optimized dose and duration of action for treating OSA. We have discussions in progress with a number of companies that have existing cannabinoid formulation technologies, expertise, and licensure capabilities, which may lead to the development of a proprietary formulation of dronabinol for RespireRx based on RespireRx's pending patents for low-dose and extended release dronabinol. While no assurance can be provided that any of the formulation technologies that we are currently analyzing will result in viable products or that formulation agreements will be consummated on terms acceptable to us, if successful, we believe that the development of a novel, proprietary formulation of dronabinol would only extend time to market entry by approximately 12 months compared to the currently available generic soft gel capsules, but would dramatically extend market exclusivity.

4. ***Recent Developments Regarding OSA*** – OSA is a serious public health issue with established links to important co-morbidities, including hypertension, type II diabetes, obesity, stroke, congestive heart failure, coronary artery disease, cardiac arrhythmias, and even early mortality. The estimated economic burden of OSA in the United States is approximately $162 billion annually. While it is estimated that 30 million people in the U.S. suffer from OSA, only approximately 20% are diagnosed. The consequences of undiagnosed and untreated OSA are medically serious and economically costly.

The important need for diagnosing and treating OSA has recently been highlighted by the FDA clearance of several sleep apnea home test kits that are now third party reimbursed. Further highlighting this need, CVS Health Corporation (NYSE: CVS) recently has announced the

implementation of a program to diagnose and treat OSA initially within their own in-store, walk-in MinuteClinics. If implemented throughout their HealthHUB store network, the number of people diagnosed with sleep apnea and eligible for treatment should increase dramatically. Fitbit (NYSE: FIT), the health oriented smart watch company is seeking clearance from the FDA to diagnose sleep apnea. We believe that the combination of more efficient and patient friendly diagnostic procedures and, ultimately, pharmaceutical treatments such as those we are developing will encourage more patients to seek diagnosis and treatment.

5. ***Possible Corporate Re-structuring*** – Our major challenge has been to raise substantial equity or equity-linked financing to support research and development programs for our two drug platforms, while minimizing the dilutive effect to pre-existing stockholders. At present, we believe that we are hindered primarily by our public corporate structure, our OTCQB listing, limited float and low market capitalization as a result of our low stock price. A number of potential cannabinoid investors and strategic partners with whom we have had discussions have expressed interest only in the development of a new, proprietary formulation with extended patent life.

For this reason, RespireRx is considering an internal restructuring plan that contemplates spinning out the cannabinoid platform into what initially would be a wholly-owned private subsidiary of RespireRx ("Newco", official name not yet determined) with its own management team and board of directors. We have identified and are in discussions with an individual highly experienced in the cannabinoid industry to potentially serve as the chief executive officer, as well as key opinion leaders to sit on Newco's scientific advisory board ("SAB"). However, we cannot provide assurance that this individual or the SAB candidates will join us. A detailed business plan with *pro forma* budgets has been prepared, which describes our strategy and plans for developing and commercializing the dronabinol platform for the treatment of OSA, including a review of the market opportunity, clinical development and regulatory pathway. A joint development and supply agreement is already in place with Purisys LLC ("Purisys"), a subsidiary of Noramco, Inc., a leading dronabinol manufacturer, in which Purisys will provide in-kind funding for API manufacturing and supply costs prior to NDA approval and into early commercialization. This agreement along with our license with the University of Illinois at Chicago, will need to be transferred or otherwise made available to Newco. While Newco's initial, primary focus will be on re-purposing dronabinol for the treatment of OSA, we believe that our broad enabling patents and a new proprietary formulation may provide a framework for expanding into the larger burgeoning pharmaceutical cannabinoid industry.

We believe that by creating Newco, it may be possible, through separate finance channels, to optimize the asset value not only of the cannabinoid platform, but our neuromodulation platform as well.

6. ***Neuromodulator Platform*** - We currently are creating a business plan specific to developing drugs that act as neuromodulators at certain neurotransmitter receptors, with an initial focus on AMPA glutamate receptors. 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. Our lead clinical compounds, CX717 and CX1739, have successfully completed multiple Phase 1 safety trials and Phase 2 efficacy trials demonstrating target engagement. CX717 has successfully completed a Phase 2 trial demonstrating the ability to significantly reduce the symptoms of adult ADHD. In an early Phase 2 study, CX1739 improved breathing in patients with central sleep apnea. Preclinical studies have highlighted the potential ability of these ampakines to improve motor function in animals with spinal injury. Subject to raising sufficient financing, of which no assurance can be provided, we believe that we will be able to rapidly initiate a human Phase 2 study with either CX1739 or CX717 in patients with spinal cord injury and a human Phase 2B study in patients with ADHD with either CX717 or CX1739.

I would like to acknowledge and thank my colleagues, Jeff Margolis, our CFO, Richard Purcell, our Senior VP of Research and Development, and our Board of Directors as well as patent and general counsel, for all of their energy in advancing the Company and its promising drug candidates. And, to our investors, other stakeholders and strategic partners, we thank you and look forward to and rely upon your continued support.

Arnold Lippa, Ph.D.
Executive Chairman, Board of Directors
Interim Chief Executive Officer
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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 progress report 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 "anticipates,"

"believes," "intends," "estimates," "expects," "plans," "contemplates," "targets," "continues," "budgets," "may," and similar expressions 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 proposed products, (iv) reorganization plans, and (v) the need for, and availability of, additional financing. The forward-looking statements included herein are based on current expectations that involve a number of risks and uncertainties. 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 the Company believes that the assumptions underlying the forward-looking statements are reasonable, actual results may differ materially from those set forth in the forward- looking statements. In light of the significant uncertainties inherent in the forward-looking information included herein, the inclusion of such information should not be regarded as a representation by the Company or any other person that the Company's objectives or plans will be achieved. Factors that could cause or contribute to such differences include, but are not limited to, regulatory policies or changes thereto, available cash, research and development results, competition from other similar businesses, interest of third parties in collaborations with us, and market and general economic factors. For more information about the risks and uncertainties the Company faces, see "Item 1A. Risk Factors" of the RespireRx Pharmaceuticals Inc. Annual Report on Form 10-K as of December 31, 2018. For more current information about the Company, see the Company's Quarterly Report on Form 10-Q as of September 30, 2019. 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-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.

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