



**RespireRx Pharmaceuticals Inc.  
Announces Publication of Phase 2B PACE Study:  
Once per Night Treatment with Dronabinol Provides Statistically Significant Improvement in Clinical  
Measures of Obstructive Sleep Apnea**

Glen Rock, N.J., November 30, 2017/Globe Newswire – RespireRx Pharmaceuticals Inc. (OTCQB: RSPI) (“RespireRx” or the “Company”) announces that the results of the PACE (Pharmacotherapy of Apnea by Cannabimimetic Enhancement) clinical trial have been published by the principal investigators, Dr. Pyllis Zee and Dr. David Carley at Northwestern University and at the University of Illinois at Chicago, respectively. The PACE paper is published in the journal SLEEP, the official publication of the Sleep Research Society, and the leading peer-reviewed journal in sleep and circadian science. The paper can be found at:

<https://academic.oup.com/sleep/advance-article-abstract/doi/10.1093/sleep/zsx184/4600041?redirectedFrom=fulltext>

As previously presented by Dr. Carley at the SLEEP 2017 annual meeting in June, the PACE trial, a randomized, blinded, placebo controlled, Phase 2B study of dronabinol for the treatment of obstructive sleep apnea (“OSA”), clearly demonstrates that dronabinol significantly improves the primary outcome measures of Apnea Hypopnea Index (“AHI”), daytime sleepiness as measured by the Epworth Sleepiness Scale (“ESS”) and overall patient satisfaction as measured by the Treatment Satisfaction Questionnaire for Medications (“TSQM”). The paper reports that in comparison to placebo, dronabinol was associated with lower AHI, improved subjective sleepiness and greater overall treatment satisfaction.

The PACE trial, which was fully funded by a grant of approximately \$5 million from the National Heart Lung and Blood Institute of the National Institutes of Health (“NIH”), enrolled 73 subjects with moderate to severe OSA who met all inclusion and exclusion criteria for the study. At baseline, overall apnea/hypopnea index (AHI) was  $25.9 \pm 11.3$ , Epworth Sleepiness Scale score (ESS) was  $11.45 \pm 3.8$ , maintenance of wakefulness test (MWT) mean latency was  $19.2 \pm 11.8$  min, body mass index (BMI) was  $33.4 \pm 5.4$  kg/m<sup>2</sup> and age was  $53.6 \pm 9.0$  years. Subjects were randomized to receive placebo, 2.5 mg or 10 mg dronabinol. Randomized subjects completed daily self-administration of study drug for 6 weeks, and returned to the laboratory every 2 weeks for overnight polysomnography (PSG), physical examination, and completion of clinical study procedures.

Subjects receiving 10mg/day of dronabinol expressed the highest overall satisfaction with treatment ( $p=0.04$ ). In comparison to placebo, dronabinol dose-dependently reduced AHI by  $10.7 \pm 4.4$  ( $p=0.02$ ) and  $12.9 \pm 4.3$  ( $p=0.003$ ) events/hour at doses of 2.5 and 10 mg/day, respectively. Dronabinol at 10 mg/day reduced ESS score by  $-3.8 \pm 0.8$  points from baseline ( $p<0.0001$ ) and by  $-2.3 \pm 1.2$  points in comparison to placebo ( $p=0.05$ ). Body weights, MWT sleep latencies, gross sleep architecture and overnight oxygenation parameters were unchanged from baseline in any treatment group. The number and severity of adverse events, and treatment adherence ( $0.3 \pm 0.6$  missed doses/week) were equivalent among all treatment groups.

OSA affects approximately 30 million Americans, according to the American Academy of Sleep Medicine. Besides causing next day sleepiness, a major cause of motor vehicle and industrial accidents, OSA is co-morbid with cardiovascular disease, type 2 diabetes and other conditions. Treatment options are limited and the most effective treatment, the CPAP device, has an extremely high non-compliance rate. “There is a tremendous need for effective, new treatments in obstructive sleep apnea,” said Dr. Carley in a press release by the University of Illinois at Chicago.

In the same press release, Dr. Zee commented that, “The CPAP device targets the physical problem but not the cause. The drug targets the brain and nerves that regulate the upper airway muscles. It alters the neurotransmitters from the brain that communicate with the muscles.”



Dr. David Rapoport, MD, Professor of Medicine at the Ichan School of Medicine at Mount Sinai and a member of the RespireRx Clinical Research Advisory Panel, who was not an investigator in the PACE trial, offers his views on the clinical impact of the research, “The PACE Trial demonstrates that dronabinol is effective in lowering AHI in patients with moderate obstructive sleep apnea. There is a growing recognition that mild to moderate OSA is a very prevalent condition and may affect not only quality of life but also long term cardiovascular and cerebrovascular health. Recent work also suggests a link of the AHI to memory loss and progression of Alzheimer Disease biomarkers. These data point to the possibility of a benefit of treating even asymptomatic individuals with elevated AHI. Treatment with positive airway pressure is not always tolerated by patients, particularly when they are minimally symptomatic. The results of the PACE trial are among the first to show sustained effect of a drug therapy targeting the behavior of the upper airway. Dronabinol is easy to take, appears to have a low side effect profile and now has been shown to be effective. It may therefore help address the significant medical need for alternative treatments for OSA. These promising early results should encourage the medical community of sleep specialists to explore this alternative therapy with appropriate patients.”

Arnold Lipka, Ph.D., Chief Scientific Officer and Executive Chairman of RespireRx stated, “The PACE study results validate our previous Phase 2A clinical trial as well as our business focus on developing new treatments for respiratory disorders for which there are no available drug therapies. OSA is a major medical disorder with detrimental impacts on daily function and performance, cardiovascular health, memory, cognition, and long-term outcomes. We look forward to working with our key opinion leaders and the FDA to advance the approval and commercial introduction of dronabinol for the treatment of OSA.”

## **Background**

Obstructive Sleep Apnea is the most common form of sleep apnea and affects 29.4 million Americans according to the American Academy of Sleep Medicine. 5.9 million adults are diagnosed (23.5 million are undiagnosed). Besides causing next day sleepiness, a major cause of motor vehicle and industrial accidents, OSA is co-morbid with cardiovascular disease, type 2 diabetes and other conditions. Treatment options are limited and the most effective treatment, the CPAP device has an extremely high non-compliance rate. The overall cost to the U.S. economy of the diagnosed and undiagnosed portions of the OSA market is estimated to be \$12.4 billion and \$149.6 billion respectively for a total cost of \$162.0 billion in 2015. There is no drug therapy approved for OSA. While certain stimulants such as modafinil and methylphenidate are FDA approved for next day sleepiness in certain OSA patients, they do not treat OSA itself. Dronabinol, currently formulated as a capsule, is believed to be much more user-friendly than the current devices, should have a higher patient compliance rate and should work well in the moderate to mild patient segment, which represents approximately 60% of the overall OSA patient population, and may result in more of the currently undiagnosed patient population getting diagnosed.

Dronabinol is synthetic  $\Delta^9$ -THC (delta 9-tetrahydrocannabinol), one of the active cannabinoids found in marijuana. Dronabinol is approved in the United States in 2.5mg, 5mg and 10mg capsules for the treatment of anorexia associated with AIDS and chemo-therapy induced nausea and vomiting. It is a schedule III drug, meaning there is a low abuse potential, but it is monitored by the United States DEA (drug enforcement agency). It is Medicare part B reimbursed for its current approved indications. Use of dronabinol for the treatment of OSA is novel.

## **About RespireRx Pharmaceuticals Inc.**

RespireRx Pharmaceuticals Inc. is a leader in the development of medicines for respiratory disorders, with a focus on sleep apneas and drug-induced respiratory depression. 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.

RespireRx has a pipeline of medicines in Phase 2 clinical development focused on pharmaceutical treatments for a variety of breathing disorders. Clinical development in the area of respiratory disorders, particularly drug-induced



respiratory depression and sleep apnea, has created opportunities for the development and commercialization of the Company's compounds.

**Cannabinoids.** One platform being developed by RespireRx is the class of compounds known as cannabinoids, including dronabinol. Under a license agreement with the University of Illinois, the Company has rights to patents claiming the use of cannabinoids for the treatment of sleep-related breathing disorders.

**Ampakines.** The other platform of proprietary medicines being developed by RespireRx are ampakines, which act to enhance the actions of the excitatory neurotransmitter glutamate at AMPA glutamate receptors. Several ampakines, in both oral and injectable forms, are being developed by the Company for the treatment of a variety of breathing disorders. In clinical studies, select ampakines have shown preliminary efficacy in central sleep apnea and in the control of respiratory depression produced by opioids, without altering the opioid analgesic effects. In animal models of orphan disorders, such as Pompe Disease, spinal cord injury and perinatal respiratory distress, it has been demonstrated that certain ampakines improve breathing function. The Company's compounds belong to a new class that does not display the undesirable side effects previously reported for other ampakines.

Additional information about the Company and the matters discussed herein can be obtained on the Company's website at [www.RespireRx.com](http://www.RespireRx.com) or in the Company's filings with the Securities and Exchange Commission at [www.sec.gov](http://www.sec.gov).

#### **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 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 are all forward-looking statements.*

*In some cases, forward-looking statements may be identified by words including "anticipates," "believes," "intends," "estimates," "expects," "plans," and similar expressions 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, and (iv) 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 and competitive conditions, 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, and market and general economic factors. This discussion should be read in conjunction with the condensed consolidated financial statements (unaudited) and notes thereto included in Item 1 of the Company's current Quarterly Report on Form 10-Q as of and for the periods ending September 30, 2017 and the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2016, including the section entitled "Item 1A. Risk Factors." The Company does not intend to update or revise any forward-looking statements to reflect new information, future events or otherwise.*



Company Contact:

Jeff Margolis  
Senior VicePresident, Chief Financial Officer, Treasurer and Secretary  
Telephone: (917) 834-7206  
E-mail: [jmargolis@respirerx.com](mailto:jmargolis@respirerx.com)