RespireRx Pharmaceuticals Inc.
Form 10-K
April 17, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

[X] Annual Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended December 31, 2017

OR

[ ] Transition Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Commission file number 1-16467

RespireRx Pharmaceuticals Inc.

(Exact name of registrant as specified in its charter)

Delaware	**33-0303583**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

126 Valley Road, Suite C

Glen Rock, New Jersey 07452

(Address of principal executive offices, including zip code)

(201) 444-4947

(Registrant's telephone number, including area code)

Securities registered under Section 12(b) of the Act: None

Securities registered under Section 12(g) of the Act:

Common Stock, $0.001 par value

(Title of Class)

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES [ ] NO [X]

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. YES [ ] NO [X]

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act during the preceding 12 months (or for such shorter period that the registrant was required to file such reports); and (2) has been subject to such filing requirements for the past 90 days. YES [X] NO [ ]

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). YES [X] NO [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy

or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [ ]

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer [ ] Accelerated filer [ ] Non-accelerated filer [ ] Smaller reporting company [X] Emerging growth co
(Do not check if a smaller reporting 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. [ ]

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2). YES [ ] NO [X]

The aggregate market value of the voting stock held by non-affiliates as of June 30, 2017 was approximately $3,567,000 (based on the closing sale price of the common stock as reported by the OTC QB) on June 30, 2017.

As of March 31, 2018, there were 3,123,332 shares of the registrant’s common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE: NONE

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In this Annual Report on Form 10-K, the terms “RespireRx,” the “Company,” “we,” “us” and “our” refer to RespireRx Pharmaceuticals Inc. (f/k/a Cortex Pharmaceuticals, Inc.), a Delaware corporation, and, unless the context indicates otherwise, its consolidated subsidiaries.

INTRODUCTORY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K of RespireRx Pharmaceuticals Inc. (“RespireRx” or the “Company”) 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 (the “Exchange Act”) and the Company intends that such forward-looking statements be subject to the safe harbor created thereby. These forward-looking statements are contained principally in the sections entitled “Business,” “Risk Factors,” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” 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 are all forward-looking statements.

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 include, but 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.

For more information about the risks and uncertainties the Company faces, see “Item 1A. Risk Factors” of this Annual Report on 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.

PART I

Item 1. Business

Since its formation in 1987, the Company has engaged in the discovery, development and commercialization of innovative pharmaceuticals for the treatment of neurological and psychiatric disorders. In 2011, however, we conducted a re-evaluation of our strategic focus and determined that clinical development in the area of respiratory disorders, particularly sleep apneas and respiratory depression produced by drugs and neural damage, provided the most cost-effective opportunities for potential rapid development and commercialization of our compounds. As a result of our scientific discoveries and the acquisition of strategic, exclusive license agreements, we believe we are now a leader in the discovery and development of innovative pharmaceuticals for the treatment of respiratory disorders.

There is a substantial unmet need for new drug treatments for breathing disorders. According to a study commissioned by the American Academy of Sleep Medicine, published in August 2016 ("AASM Commissioned Study"), there are approximately 29.4 million adults with obstructive sleep apnea, of whom 5.9 million are diagnosed. Sleep apnea places a considerable burden on society and the health care system because of its association with co-morbidities and adverse events ranging from vehicular (for example: cars, trucks, trains, buses) and industrial accidents, and loss of productivity to increased risk of cardiopulmonary illness and related death. According to the AASM Commissioned Study, the estimated overall cost of obstructive sleep apnea in the United States in 2015 was $162 billion, of which $12.4 billion relates to diagnosis and treatment and the balance relates to all other categories. No drugs currently are approved for the treatment of sleep apnea.

Even in patients without sleep apneas, the use of drugs such as propofol, used as an anesthetic during surgery, and opioid analgesics such as morphine and oxycodone, used during anesthesia and for the treatment of post-surgical and chronic pain, are well known for producing respiratory depression which is a form of apnea. In fact, while respiratory depression is the leading cause of death from the overdose of most classes of abused drugs, it also arises during normal, physician-supervised procedures such as surgical anesthesia, post-operative analgesia and as a result of normal outpatient management of pain.

Although opioid antagonists such as naloxone (Narcan) and nalmefene (Revex) can reverse respiratory depression associated with opioids, they have several major shortcomings. First and foremost, these opioid antagonists do not reverse the respiratory depression produced by other classes of drugs often given/taken either alone or in combination with opioids. Second, while these drugs reverse the serious side effects of the opioids, they also dramatically reduce their analgesic effectiveness. Third, the side effects of opioid antagonists are themselves serious and include seizures, agitation, convulsions, tachycardia, hypotension, nausea, and vomiting.

Furthermore, respiratory depression can arise as a result of a number of other illnesses that involve neural and muscular disorders. For example, certain spinal injuries can interfere with normal neural communication between the brain and the lungs resulting in reduced respiratory capacity. Pompe Disease is an autosomal, recessive, metabolic disorder that damages muscle and nerve cells throughout the body. One of the first symptoms is a progressive decrease in the strength of muscles such as the diaphragm and other muscles required for breathing and respiratory failure is the most common cause of death. In both of these indications, symptomatic treatment for the respiratory depression is severely lacking.

Accordingly, there is a considerable need for pharmaco-therapeutic agents to (i) treat sleep apnea, (ii) prevent and reverse the respiratory depression produced by different classes of drugs, and (iii) relieve the respiratory depression produced in a number of neurological indications, such as spinal injury and Pompe Disease. The Company currently has two drug platforms, each with a clinical stage compound directed at these needs.

Sleep Apnea

Sleep apnea is a serious disorder in which breathing repeatedly stops long enough to disrupt sleep, and temporarily decreases the amount of oxygen and increases the amount of carbon dioxide in the blood. Apnea is defined by more than five periods per hour of ten seconds or longer without breathing. The repetitive cessation of breathing during sleep has substantial impact on the affected individuals. The disorder is associated with major co-morbidities including excessive daytime sleepiness and increased risk of cardiovascular disease (such as hypertension, stroke and heart failure), diabetes and weight gain. Sleep apnea is often made worse by central nervous system depressants such as opioids, benzodiazepines, barbiturates and alcohol. It is therefore important for these patients to seek treatment.

The most common type of sleep apnea is obstructive sleep apnea ("OSA"), which occurs by narrowing or collapse of the pharyngeal airway during sleep. There is currently no approved pharmacotherapy, and the most common treatment is to use continuous positive airway pressure ("CPAP") delivered via a nasal or full-face mask, as long as patients are able to tolerate the treatment. We believe that patient compliance with CPAP devices is extremely low. Alternative treatments include surgical intervention, dental appliances, hypoglossal nerve stimulation (via surgical implant) and other physical interventions. Given the large patient population and the limited treatment options, there is a very large opportunity for pharmacotherapy to treat this disorder.

Central sleep apnea ("CSA"), a less frequently diagnosed type of sleep apnea, is caused by alterations in the brain mechanisms responsible for maintaining normal respiratory drive. CSA is most frequently observed in patients taking chronic opioids and in heart failure patients and is a major correlate for mortality in these patients. There are no therapeutic options for patients with CSA; CPAP is contra-indicated for the treatment of CSA and no drugs are currently approved for this indication.

In addition, many patients present with a pattern of sleep apnea that has both obstructive and central components.

Cannabinoids

RespireRx is developing dronabinol, a synthetic derivative of a naturally occurring substance in the cannabis plant, otherwise known as Δ9-THC or Δ9-tetrahydrocannabinol, for the treatment of OSA which is discussed above. OSA has been linked to increased risk for hypertension, heart failure, depression, and diabetes. There are no approved drug treatments for OSA.

RespireRx holds the exclusive world-wide license to a family of patents for the use of cannabinoids, a family of compounds found naturally in the cannabis plant, including the synthetic cannabinoid dronabinol, in the treatment of sleep disordered breathing from the University of Illinois at Chicago ("UIC"). In addition, RespireRx has several extensions and pending applications that, if issued, will extend patent protection for over a decade. With approximately $5 million in funding from the National Heart, Lung and Blood Institute of the National Institutes of Health, UIC completed a Phase 2B multi-center, double-blind, placebo-controlled clinical trial of dronabinol in patients with OSA. Entitled **P**harmacotherapy of **A**pnea with **C**annabimimetic **E**nhancement ("PACE"), this study replicated an earlier Phase 2A RespireRx sponsored clinical trial and demonstrated statistically significant improvements in respiration, daytime sleepiness, and patient satisfaction after administration of dronabinol and is discussed in more detail below.

RespireRx believes that the most direct route to commercialization is to proceed directly to a Phase 3 pivotal trial using the currently available dronabinol formulation (2.5, 5 and 10 mg gel caps) and to then commercialize a RespireRx branded dronabinol capsule ("RBDC").

The Company also believes that there are numerous opportunities for reformulation of dronabinol to produce a second generation proprietary, branded product for the treatment of OSA with an improved profile. Therefore, simultaneously with its development of the RBDC, RespireRx plans to develop a proprietary dronabinol formulation to optimize the dose and duration of action for treating OSA.

RespireRx initiated its dronabinol program when it acquired 100% of the issued and outstanding equity securities of Pier Pharmaceuticals, Inc. ("Pier") effective August 10, 2012 pursuant to an Agreement and Plan of Merger. Pier was formed in June 2007 (under the name SteadySleep Rx Co.) as a clinical stage pharmaceutical company to develop a pharmacologic treatment for OSA and had been engaged in research and clinical development activities.

Prior to the merger, Pier conducted a 21 day, randomized, double-blind, placebo-controlled, dose escalation Phase 2 clinical study in 22 patients with OSA, in which dronabinol produced a statistically significant reduction in the Apnea-Hypopnea Index, the primary therapeutic end-point, and was observed to be safe and well tolerated.

Through the merger, RespireRx gained access to a 2007 Exclusive License Agreement (as amended, the "Old License") that Pier had entered into with the University of Illinois on October 10, 2007. The Old License covered certain patents and patent applications in the United States and other countries claiming the use of cannabinoids, including dronabinol, for the treatment of sleep-related breathing disorders (including sleep apnea).

Dronabinol is a Schedule III, controlled generic drug with a relatively low abuse potential that is approved by the U.S. Food and Drug Administration (the "FDA") for the treatment of AIDS-related anorexia and chemotherapy-induced emesis. The use of dronabinol for the treatment of OSA is a novel indication for an already approved drug and, as such, the Company believes that it would only require approval by the FDA of a 505(b)(2) new drug application, an efficient regulatory pathway.

The Old License was terminated effective March 21, 2013, due to the Company's failure to make a required payment. Subsequently, current management opened negotiations with the University of Illinois, and as a result, the Company entered into a new license agreement (the "2014 License Agreement") with the University of Illinois on June 27, 2014, the material terms of which were similar to the Old License.

Similar to the Old License, the 2014 License Agreement grants the Company, among other provisions, exclusive rights: (i) to practice certain patents and patent applications, as defined in the 2014 License Agreement, that are held by the University of Illinois; (ii) to identify, develop, make, have made, import, export, lease, sell, have sold or offer for sale any related licensed products; and (iii) to grant sub-licenses of the rights granted in the 2014 License Agreement, subject to the provisions of the 2014 License Agreement. The Company is required under the 2014 License Agreement, among other terms and conditions, to pay the University of Illinois a license fee, royalties, patent costs and certain milestone payments.

On November 30, 2017, the Company announced the publication by the principal investigators, Dr. Phyllis Zee of Northwestern University and Dr. David Carley of the University of Illinois at Chicago, in the peer-reviewed journal SLEEP, the official publication of the Sleep Research Society, of the positive results of the potentially pivotal, PACE (Pharmacotherapy of Apnea by Cannabimimetic Enhancement) Phase 2B OSA clinical trial, that was fully funded by the National Institutes of Health. The results from PACE were published in the journal Sleep Vol. 41. No. 1, 2018. The results of the PACE clinical trial were previously presented by Dr. Carley at the SLEEP 2017 annual meeting in June 2017. In the PACE trial, dronabinol significantly improved 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 recently completed PACE trial was a fully-blinded, two-center, Phase II, randomized placebo-controlled trial of dronabinol in 56 adult patients with moderate to severe OSA. By random assignment, 56 adult subjects with BMI<45, Epworth Sleepiness Scale (ESS)>7 and PSG-documented AHI between 15 and 50 received either placebo (N=17), 2.5mg (N=19) or 10.0mg (N=20) of dronabinol daily, one hour before bedtime for 6 weeks. Repeat in- laboratory PSG followed by maintenance of wakefulness (MWT) testing was completed every 2-weeks during the treatment period. At each visit, the ESS and Treatment Satisfaction Questionnaire for Medications also were completed.

Overall, baseline AHI was 26.0±11.6 (SD) and this was equivalent among all treatment groups. In comparison to placebo, statistically significant end of treatment declines in AHI were observed for both the 2.5 and 10 mg doses (-9.7±4.1, p=0.02 and -13.2±4.0, p=0.001, respectively). Statistically significant declines in ESS were observed for subjects receiving 10 mg dronabinol (-4.0±0.8 units, p=0.001) but not those receiving 2.5 mg or placebo. Subjects receiving 10 mg dronabinol also expressed the greatest overall satisfaction with treatment (p=0.02).

The PACE trial enrolled 73 subjects of which 56 were evaluable 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±11.3, Epworth Sleepiness Scale score (ESS) was 11.45±3.8, maintenance of wakefulness test (MWT) mean latency was 19.2±11.8 min, body mass index (BMI) was 33.4±5.4 kg/m2 and age was 53.6±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±4.4 (p=0.02) and 12.9±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±0.8 points from baseline (p<0.0001) and by -2.3±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±0.6 missed doses/week) were equivalent among all treatment groups.

Drug-induced Respiratory Depression or Drug-induced apnea

Drug-induced respiratory depression ("RD") or drug-induced apnea is a life-threatening condition caused by a variety of depressant drugs, including analgesic, hypnotic, and anesthesia medications. We believe that RD is a leading cause of death from the overdose of some classes of abused drugs, yet it also arises during normal, physician-supervised procedures such as surgical anesthesia and post-operative pain management. For example, in the hospital setting, anesthetics such as propofol are well known for their propensity to produce RD, particularly when combined with opioids. According to data from the National Center for Health Statistics, 48 million surgical inpatient procedures were performed in the United States in 2009. It is notable that, according to the HealthGrades Inc. Patient Safety in American Hospitals Study released in 2011, post-operative respiratory failure produces the third highest number of patient safety events, the fourth highest mortality rate, and the second largest overall excess cost to the Medicare system, when compared to other patient safety indicators. The Company believes that, in these patients, the major risk factor for the appearance of RD is a history of sleep apnea.

In the hospital setting, one of the most serious complications of patient-controlled analgesia is RD and, despite nurses' vigilance, adverse events associated with opioids continue to increase. Drug-induced RD is associated with a high mortality rate relative to other adverse drug events. In post-surgical patients taking opioids for pain management, sleep apnea is a major risk factor for the occurrence of RD. If patients with sleep apnea are receiving combination therapies, they are at even higher risk for complications and extended hospital stays.

Outside the hospital, the primary risk factor for RD is the use of a single opioid in large doses or concomitant use of opioids and sedative agents. Whether due to normal outpatient pain management, or as a result of substance abuse, RD has been reported to be the leading cause of death from drug overdose, with the drug overdose death rate tripling since 1991. In patients chronically consuming opioids, CSA is a major correlate for overdose and most likely represents an early and sensitive form of opioid induced RD. In August 2017, the Centers for Disease Control and Prevention ("CDC") reported that approximately 42,000 people died in 2016 from opioid overdoses, including prescription opioids and illegally made fentanyl and heroin. The CDC reported that the common prescription drugs involved in overdoses were methadone, oxycodone (such as OxyContin®) and hydrocodone (such as Vicodin®). In 2016, the CDC reported that 40% of all US opioid deaths involved a prescription opioid. There were 13,000 heroin deaths in 2015. There are two types of fentanyl, pharmaceutical fentanyl used to manage acute and chronic pain and non-pharmaceutical fentanyl that is illicitly manufactured and is often mixed with heroin or cocaine. The CDC also reported that most of the increases in fentanyl deaths involved the illicit fentanyl and not the pharmaceutical fentanyl.

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Drug Abuse

On January 19, 2016, the Company announced that that it had reached an agreement with the Medications Development Program of the National Institute of Drug Abuse ("NIDA") to conduct research on the Company's ampakine compounds CX717 and CX1739. The agreement was entered into as of October 19, 2015, and on January 14, 2016, the Company and NIDA approved the proposed protocols, allowing research activities to commence. NIDA is evaluating the compounds using pharmacologic, pharmacokinetic and toxicologic protocols to determine the potential effectiveness of the ampakines for the treatment of drug abuse and addiction. The Company retains all intellectual property as well as proprietary and commercialization rights to the Company's compounds. Initial studies focus on cocaine and methamphetamine addiction and abuse and are contracted to outside testing facilities and/or government laboratories, with all costs paid by NIDA. In experiments conducted by NIDA, CX717 antagonized the stimulatory effects of methamphetamine. NIDA is in the process of testing CX717 on the interoceptive effects (determinants of addiction liability) of both cocaine and methamphetamine in models of drug discrimination in rats.

Ampakines

RespireRx is developing a class of proprietary compounds known as ampakines, a term used to designate their actions as positive allosteric modulators of the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid ("AMPA") glutamate receptor. Ampakines are small molecule compounds that enhance the excitatory actions of the neurotransmitter, glutamate at the AMPA receptor complex, which mediates most excitatory transmission in the central nervous system ("CNS"). These drugs do not have agonistic or antagonistic properties but instead modulate the receptor rate constants for transmitter binding, channel opening, and desensitization

Through an extensive translational research effort from the cellular level through Phase 2 clinical trials, the Company has developed a family of ampakines, including CX717, CX1739 and CX1942 that have clinical application in the treatment of CNS-driven respiratory disorders, neurobehavioral disorders, spinal cord injury, neurological diseases, and orphan indications. In particular, we are addressing CNS-driven respiratory disorders that affect millions of people, but for which there are few treatment options and no drug therapies, including opioid induced respiratory disorders, such as apnea (transient cessation of breathing) and hypopnea (transient reduction in breathing). When these symptoms become severe, as in opioid overdose, they are the primary cause of opioid lethality. In addition, we are developing our ampakines for the treatment of disordered breathing and motor impairment resulting from spinal cord injury.

Early preclinical and clinical research suggested that these ampakines might have therapeutic potential for the treatment of memory and cognitive disorders, depression, attention deficit disorder and schizophrenia. Given our current focus on respiratory disorders, we may seek to partner, out-license or sell our rights to the use of ampakine compounds for the treatment of neurological and psychiatric indications, as we focus on the development of our

compounds for the treatment of breathing disorders.

The early ampakines discovered by the Company, Eli Lilly and Company, and others were ultimately abandoned due to the presence of undesirable side effects, particularly convulsive activity. Subsequently, Company scientists discovered a new, chemically distinct series of molecules termed “low impact” as opposed to the “high impact” designation given to the earlier compounds. While these low impact compounds share many pharmacological properties with the high impact compounds, they do not produce convulsive effects in animals. These low impact compounds do not bind to the same molecular site as the high impact compounds and, as a result, do not produce the undesirable electrophysiological and biochemical effects that lead to convulsive activity.

The Company owns patents and patent applications for certain families of chemical compounds that claim the chemical structures, their actions as ampakines and their use in the treatment of various disorders. Patents claiming a family of chemical structures, including CX1739 and CX1942, as well as their use in the treatment of various disorders, extend through at least 2028. Additional patents claiming a family of chemical structures, including CX717, as well as their use in the treatment of various disorders, expired in 2017 in the U.S. and will expire in 2018 internationally. The Company is developing potential market exclusivity strategies for CX717 which may include new patent applications and identifying market opportunities and strategies that may provide exclusivity without patents.

In order to broaden the use of the Company’s ampakine technology into the area of respiratory disorders, on May 8, 2007, the Company entered into a license agreement, as subsequently amended, with the University of Alberta granting the Company exclusive rights to practice patents held by the University of Alberta claiming the use of ampakines for the treatment of various respiratory disorders, including drug induced respiratory depression. These patents extend through at least 2028 and, along with the Company’s own patents claiming chemical structures, comprise the Company’s principal intellectual property supporting the Company’s research and clinical development program in the use of ampakines for the treatment of respiratory disorders.

The Company has obtained preclinical results indicating that several of its low impact ampakines, including CX717, CX1739 and CX1942, were able to antagonize the respiratory depression caused by opioids, barbiturates and anesthetics without offsetting the analgesic effects of the opioid or the sedative effects of the anesthetics. Dr. John Greer, faculty member of the Department of Physiology, Perinatal Research Centre, and Women & Children’s Health Research Institute at the University of Alberta, has shown that these ampakine effects are due to a direct action on neurons in pre-Botzinger’s complex, a brain stem region responsible for regulating respiratory drive.

After several Phase 1 and 2 studies to demonstrate safety and tolerability, the first of these low impact compounds, CX717, was tested in two Phase 2A clinical studies to determine its ability to antagonize the respiratory depressant effects of fentanyl, a potent opioid analgesic. In both of these studies, one of which was published in a peer-reviewed journal, CX717 antagonized the respiratory depression produced by fentanyl without altering the analgesia produced by this drug.

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Despite the loss in 2017 and impending loss in 2018, of U.S. patents and international patents claiming composition-of-matter and certain non-respiratory uses for CX717, the Company believes that CX717 stills retains considerable value as a potential, commercial product, for the following reasons. The Company owns or controls patents claiming the use of CX717 for the treatment of various respiratory disorders that are in effect in the United States and elsewhere at least through 2028, and additional method of treatment patents are planned and are being prepared. Long term preclinical safety studies have been completed and are sufficient to support chronic dosing of CX717 in humans for six months. In nine Phase 1 and Phase 2 clinical studies, CX717 was safe and well tolerated. CX717 has demonstrated the ability to antagonize the respiratory effects of fentanyl, a potent opioid, in two clinical trials, demonstrating target site engagement as well as proof of principle. Promising results also have been observed in clinical trials of attention deficit hyperactivity disorder and cognition. Finally, while CX717 was put on temporary clinical hold by the FDA due to potential neurotoxicity, this hold was completely removed and the Company was allowed to re-initiate clinical trials. This lifting of the clinical hold resulted from the Company obtaining what it believes to be conclusive data showing that the presumed neurotoxicity observed after administration of very high doses of CX717 results from a post-mortem artifact. On December 18, 2017, the Company announced that a paper detailing the neurobiologic safety of CX717 had been accepted for publication by Toxicological Sciences, the Journal of the American Society of Toxicology. The paper, co-authored by RespireRx scientists in conjunction with expert pathologists from around the country who contributed to an extensive neuropathology research program, presents clear scientific evidence that vacuoles that were discovered upon histological evaluation of brain tissue samples from animals treated with high doses of CX717, and which halted the company’s promising CX717 clinical development effort, were actually an artifact of tissue processing rather than a toxic drug effect.

In several Phase 1 clinical studies, the Company’s present lead ampakine, CX1739, has demonstrated good safety and tolerability after single doses up to 1200 mg for seven days, as well as two doses per day of 600 mg each for ten days. Pharmacokinetic results to date from the volunteers who have taken CX1739 show that drug absorption over the range of 50 mg to 1200 mg was linear and predictable, with an approximate half-life of 8 hours.

The Company filed an IND with the FDA in September 2015 to conduct a randomized, double-blind, placebo-controlled, crossover, Phase 2A study of CX1739 (300 mg) versus placebo, followed by dose escalation of CX1739 to 600 and 900 mg, with open-label administration of the IV opioid remifentanil in approximately 18 healthy subjects to assess the ability of CX1739 to antagonize the respiratory depressive effect of remifentanil without altering the analgesic effect of the opioid. The clinical protocol was designed to evaluate the safety and efficacy of CX1739 to antagonize respiratory depression in two models of opioid use and abuse. During REMI-INFUSION, a model of chronic (steady state) opioid use, respiration, pain, pulmometry, and safety were measured during a 30-minute intravenous infusion of remifentanil that produced stable blood levels. During REMI-BOLUS, a model of acute, intravenous opioid overdose, a single, intravenous bolus injection of remifentanil was administered at a dose calculated to achieve significant respiratory depression.

On each study day, REMI-BOLUS was initiated with an intravenous, bolus injection of remifentanil 3 hours after subjects received either placebo or CX1739. Respiration was measured for 20 minutes and then compared to the baseline respiration recorded 5 minutes prior to the bolus injection. REMI-INFUSION was initiated 3.5 hours after placebo or CX1739, with an intravenous infusion protocol designed to maintain stable remifentanil blood levels and

calculated to produce approximately 50% respiratory depression. The ClinicalTrials.gov identifier is NCT02735629.

The commencement of this clinical trial was subject to the resolution of two deficiencies raised by the FDA in its clinical hold letter issued in November 2015, which were satisfactorily resolved in early 2016. As a result, the FDA removed the clinical hold on the Company's IND for CX1739 on February 25, 2016, thus allowing for the initiation of the clinical trial. In March 2016, upon Institutional Review Board approval, the trial was initiated at the Duke Clinical Research Unit, Duke University Medical Center, Durham NC. The dosing and data acquisition phase of the clinical trial was completed in June 2016 and the clinical trial was formally completed on July 11, 2016.

On September 12, 2016, the Company announced preliminary top-line analysis of safety and efficacy data from this clinical trial. On October 3, 2016, the Company discovered an error in the preliminary data reported to it and accordingly, on October 4, 2016, the Company issued a press release retracting the efficacy data contained in the September 12, 2016 press release. On December 15, 2016, the Company announced the corrected results of the trial, and presented the re-analyzed data, as follows.

During REMI-INFUSION, the model of chronic opioid use, CX1739 antagonized the respiratory rate depression produced by remifentanil, with statistically significant effects observed at 300 mg ($p<.005$) and 900 mg ($p<.001$). The antagonism produced by the 600 mg dose did not achieve statistical significance. This lack of a linear, dose response effect is not unusual in early stage clinical trials. During this period, CX1739 did not alter the analgesic and sedative effects of remifentanil. During REMI-BOLUS, the model of IV opioid overdose, CX1739 treatment did not prevent respiratory depression, or improve time to recovery at any of the doses tested.

Overall, CX1739 was found to be safe and well tolerated, both prior to and during administration of remifentanil. Treatment-related adverse events ("AEs") for the various doses of CX1739 were mild, with an incidence comparable to that reported for placebo. The great majority of AEs occurred after remifentanil administration, including nausea and vomiting, which are common side effects associated with opioid administration.

In addition to CX1739, the Company is developing CX1942, a soluble ampakine, as an injectable formulation in a hospital or surgical setting to be used in conjunction with opioids and anesthetics either during or after surgery. Animal studies conducted in collaboration with investigators at the University of Florida and funded by a Small Business Innovation Research contract from the National Institute of Drug Abuse have indicated that CX1942 injected intravenously, intramuscularly or subcutaneously can reverse the respiratory depression produced by fentanyl. Such data will be used to develop an injectable formulation with the flexibility to be administered via different routes.

As part of its preclinical research program, the Company, through Dr. John Greer, Chairman of the RespireRx Scientific Advisory Board, has engaged in research collaborations with a number of academic institutions. As part of its collaborative program with Dr. David Fuller of the University of Florida, studies with RespireRx's ampakines have determined that these compounds improve breathing in animal models of spinal cord injury and Pompe Disease.

Development Goals

To achieve our short-and long-term development goals, as well as to provide for our day-to-day operations, we will need additional capital, the availability of which is subject to uncertainly. Should sufficient financing be available, the Company's short-term development goals consist of the following:

1. The Company intends to have a pre-IND meeting with the FDA in order to identify a Phase 3 plan, a clear pathway for the commercial development of dronabinol for the treatment of OSA, which also may include a request for some form of an accelerated review.

2.

After establishing a clear development strategy, the Company intends to execute a Phase 3 clinical study of dronabinol for the treatment of OSA.

3. The Company intends to initiate a multi-center clinical trial investigating the ability of CX717 or CX1739 to improve breathing in patients with spinal cord injury. Assuming FDA allowance and appropriate approvals by institutional review boards, we intend to have this study conducted at the University of Miami, the University of Florida, the Detroit Medical Center and the Detroit Veterans Administration Hospital.

4. Upon issuance of the final clinical report of the CX1739 Phase 2A trial, the Company intends to seek FDA allowance to conduct a Phase 2 clinical trial investigating the safety and efficacy of CX1739 in chronic opioid patients who have central apnea.

The Company believes that these goals can be achieved in a timely and cost-effective manner. To meaningfully advance any of the above goals, however, the Company must secure sufficient additional financing or enter into one or more arrangements with strategic partner(s). Although the Company is engaged in a number of discussions with potential strategic partners and is periodically involved in financing activities, the Company has not entered into a strategic partnership and does not have sufficient financing resources to pursue these goals, and can provide no assurance that available or future sources of financing or a strategic partner will be secured to enable the Company to pursue or achieve these goals.