Eagle Pharmaceuticals Announces Positive Results of a Study Conducted in Partnership with the U.S. Military to Evaluate Neuroprotective Effects of RYANODEX for the Treatment of Nerve Agent Exposure

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-- Statistically significant lower incidence of brain damage compared to control group, demonstrating neuroprotective properties of RYANODEX in treating nerve agent exposure --

-- Statistically significant robust p-values of 0.04 or less were determined in six cortical areas of the brain --

WOODCLIFF LAKE, N.J.--(BUSINESS WIRE)--Eagle Pharmaceuticals, Inc. (Nasdaq: EGRX) (“Eagle” or the “Company”) today announced positive results of its study to evaluate the neuroprotective effects of RYANODEX® (dantrolene sodium) secondary to nerve agent (NA) exposure, conducted with the United States Army Medical Research Institute of Chemical Defense (USAMRICD), the nation's leading science and technology laboratory in the area of medical chemical countermeasures research and development.

The study results show a p-value of 0.04 or less compared to the control group in six critical areas of the brain. We believe these results demonstrate the neuroprotective effects of RYANODEX. It has been hypothesized that nerve agent poisoning triggers intracellular calcium release in the body. The study data supports the proposed mechanism of action of RYANODEX, which modulates intracellular calcium in different organs including the brain.

“We are very pleased that the results of our study support the use of RYANODEX as a neuroprotective therapy in nerve agent exposure. Current treatment options do not protect the brain from neurological damage in the event of exposure. If approved, RYANODEX would represent the first of its kind agent as a neuroprotective treatment for nerve agent exposure, serving as an important treatment option for U.S. military personnel, as part of the U.S. strategic national stockpile for civilian use, and for our allies abroad,” said Scott Tarriff, Chief Executive Officer of Eagle.

“We intend to meet with the U.S. Food and Drug Administration (FDA) to discuss next steps as soon as possible. Given the life-threatening nature of NA exposure, we believe this indication would be evaluated under the FDA’s Animal Rule. If approved, this would be an additional indication for RYANODEX, as we continue to develop additional potential indications and an intramuscular formulation of the drug,” added Tarriff.

Study Design

Eagle conducted an initial study in 2017 to evaluate the neuroprotective effects of RYANODEX in a rodent model of NA-induced brain damage. Positive results of this study led to this GLP study to evaluate the efficacy of RYANODEX to reduce neuropathology in catheterized rats exposed to the nerve agent soman. The study was conducted with the USAMRICD, at their laboratories in Aberdeen, Maryland, under a Cooperative Research and Development Agreement (CRADA), a written agreement that allows government laboratories to partner with private industries or academia on research and development projects.

The animal study was conducted in a rat model of acute nerve agent (soman) exposure. Animals were randomized into each of the six study groups, including a positive control and a negative control group. Five groups received standard treatment with HI-6, atropine and midazolam. Four of the groups also received RYANODEX. Surviving animals were evaluated for neuropathology 24 hours post-soman exposure to assess the neuroprotective effects of RYANODEX in this well-established animal model.

“We believe the study shows that RYANODEX treatment after soman exposure decreases free intracellular calcium concentrations, thus lowering calcium elevations as a result of organophosphate induced status epilepticus, and, therefore, mitigates neuropathology resulting from these continuous seizures. The topline results of this GLP study are strong and confirm our belief in the neuroprotective effects of RYANODEX,” stated Adrian Hepner, Chief Medical Officer of Eagle.

Mechanism of Action

Scientific evidence indicates that elevated intracellular calcium levels may have a role in seizure-related brain damage resulting from induced seizures and status epilepticus secondary to NA exposure. As in other conditions, including acute hyperthermic and hypermetabolic disorders, intracellular calcium overload leads to severe brain and other organ damage. RYANODEX (dantrolene sodium) is a well-characterized ryanodine receptor antagonist that inhibits intracellular calcium overload secondary to different triggers. Ryanodine receptors are widely distributed in the body, including skeletal muscle, heart and brain tissues. The active ingredient in RYANODEX is the only approved drug that inhibits the ryanodine receptors, modulating the intracellular calcium levels.

About Nerve Agents

NAs were first widely used in World War II (WWII); their impact became a significant public health issue thereafter. NAs acquired their name because they affect the transmission of nerve impulses in the nervous system. NAs include compounds such as sarin, VX and soman.

NAs, whether gas, aerosol or liquid, are extremely toxic and have a very rapid effect. The NA enters the body through inhalation or through the skin. Poisoning may also occur through consumption of liquids or foods contaminated with NAs. NA survivors will likely experience severe symptoms, including neurologic consequences.

NAs produce seizures and seizure-related brain damage. The seizures quickly develop into status epilepticus and usually become refractory to standard antiepileptic therapy.

At present, antidotes for nerve agent exposure provide limited protection, and current treatments do not fully reduce nerve-agent-induced seizures and subsequent brain injury. Additionally, medical care for NA casualties is likely to be delayed beyond the therapeutic window of opportunity to terminate

NA-induced seizures, resulting in seizure-related brain damage that continues along the pathological cascade. Thus, there is a need for adjunct drug therapy that is capable of interrupting the pathologic cascade and augmenting neuroprotection when administered in combination with antiepileptic drugs during the refractory phase of NA-induced seizures.

Scientific evidence supports a pivotal role of elevated intracellular calcium levels in seizure-related brain damage resulting from induced seizures and status epilepticus secondary to NA exposure. In addition, there are several reports that a neuroprotective approach, aimed at attenuating delayed calcium overload, combined with antiepileptic treatment, may lead to greater protection against seizure-related brain damage than anti-epileptics alone.

About Eagle Pharmaceuticals, Inc.

Eagle is a specialty pharmaceutical company focused on developing and commercializing injectable products that address the shortcomings, as identified by physicians, pharmacists and other stakeholders, of existing commercially successful injectable products. Eagle's strategy is to utilize the FDA's 505(b)(2) regulatory pathway. Additional information is available on the Company's website at www.eagleus.com.

Forward-Looking Statements

This press release contains forward-looking information within the meaning of the Private Securities Litigation Reform Act of 1995, as amended and other securities laws. Forward-looking statements are statements that are not historical facts. Words and phrases such as "will," "expected," "we believe," "committed," "plan," "promise," "may," "enables," "potential," and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, statements regarding future events, including: the Company's ability to advance RYANODEX, including with USAMRICD or other parties, in the treatment of nerve agent exposure; the Company's and USAMRICD's ability and willingness to perform their respective obligations under the Cooperative Research and Development Agreement; the success of the Company's commercial relationship with USAMRICD; successful compliance with the FDA; and the commercial success of the Company's commercial portfolio, including RYANODEX, if and when launched. All such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond Eagle's control, that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. Such risks include, but are not limited to: whether the Company can successfully advance RYANODEX in the treatment of nerve agent exposure; whether the FDA will ultimately approve RYANODEX for the treatment of nerve agent exposure and/or other indications; whether Eagle's studies will support the safety and efficacy of RYANODEX for the treatment of nerve agent exposure; whether Eagle will maintain successful compliance with the FDA and other governmental regulations; whether the Company will incur unforeseen expenses or liabilities or other market factors; the effect of competitive factors and Eagle's reactions to those factors; the pace and extent of market adoption of Eagle's products and technologies; uncertainty in the process of obtaining regulatory approval or clearance for Eagle's products; the success of Eagle's growth strategies; timing and achievement of product development milestones; the outcome of ongoing or future litigation; the impact and benefits of market development; Eagle's ability to protect its intellectual property; dependence upon third parties; unexpected new data, safety and technical issues; market conditions; other risks inherent to drug development and commercialization; and other risks described in Eagle's filings with the U.S. Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

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