Eagle Pharmaceuticals Reports Successful Outcomes from Safety and Efficacy Study of RYANODEX for Exertional Heat Stroke

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Use of RYANODEX with Current Standard of Care (SOC) Showed Substantial Evidence of Increased Effectiveness in Treating EHS than SOC Alone

Favorable Safety Data Shows No Significant Drug-Related Adverse Events in Patients Treated with RYANODEX

Eagle Pharmaceuticals, Inc. (“Eagle” or “the Company”) (Nasdaq:EGRX) today announced positive results from a recently-completed study evaluating the safety and efficacy of RYANODEX® (dantrolene sodium for injectable suspension) for the treatment of exertional heat stroke (“EHS”), an investigational new indication for the product.

“We are very encouraged by the results of this study and are optimistic about the data’s clinically meaningful implications for RYANODEX as a potential treatment for EHS. We believe that the study data successfully supports establishing the safety and efficacy of RYANODEX for the treatment of EHS, potentially expanding the product’s label to include EHS as an authorized second indication,” said Scott Tarriff, President and Chief Executive Officer of Eagle Pharmaceuticals. “We are eager to work with the FDA to make this treatment available to medical practitioners who provide immediate care for EHS patients. We look forward to discussing the data and next steps with the FDA in the near future,” he added.

“RYANODEX, paired with the current standard of care treatment for EHS, substantially increased the percent of patients showing clinically meaningful improvement in their level of consciousness and experiencing improvement in neurological functioning as early as 15 minutes post randomization. RYANODEX, which can be reconstituted and administered in less than one minute, could potentially offer a significant new therapeutic option for EHS, a life threatening condition,” added Dr. Adrian Hepner, Executive Vice President Clinical Research, Regulatory and Medical Affairs.

EHS is the most severe form of heat-related illness, characterized by core body temperature of 104° F (40° C) or greater and significant neurological dysfunction, and carries high rates of morbidity and mortality. The central nervous system is very sensitive to hyperthermia, causing neurologic complications due to involvement of the cerebellum, basal ganglia, anterior horn cells, and cranial and peripheral nerves.

Multiple scientific publications, including Szold *et al.*[1] and Sithinamsuwan *et al.*[2], have reported that despite early diagnosis and aggressive body cooling, EHS remains associated with severe neurological damage.

EHS is one of the leading causes of death in young athletes and non-combat related deaths in the military. There are no drug products on the market today to treat this potentially fatal condition.

Study Design and Outcomes

The first of its kind, Eagle’s study was conducted from September 22-27, 2015, at the Emergency Departments of four hospitals during the Hajj pilgrimage in the Makkah region, Saudi Arabia. Due to the life-threatening, unpredictable and sudden nature of EHS, the study was required to be conducted in an emergency and acute-care medical setting.

The study was primarily designed to assess the change in the level of neurological impairment in subjects suffering from the symptoms of EHS, from baseline to 90 minutes post-randomization, using the Glasgow Coma Scale (“GCS”), a validated and widely used tool among clinicians. In Group A, a greater proportion of patients were restored to a level of minor or no brain injury as compared to Group B.

The use of a validated and well-known instrument to evaluate neurological functioning, such as the Glasgow Coma Scale, provides a reliable assessment of CNS impairment and its progression over time.

The open label study enrolled 34 EHS patients between 18-45 years of age. The Company determined that this patient cohort was a sufficient number of subjects to enable assessment of a clinically meaningful treatment effect of RYANODEX in EHS.

Subjects were randomized 1:1 into two groups to receive either RYANODEX plus Standard of Care (“SOC”), which consists of body cooling by physical methods (e.g. cold water immersion, cold water mist, ice pack application) and supportive measures (Group A, n=17), or SOC alone (Group B, n=17).

Per study protocol, all subjects experienced exertional physical activity within the previous 24 hours, and demonstrated hallmark clinical features of EHS, including:

- Presence of neurological impairment, evaluated using the Glasgow Coma Scale (“GCS”);
- Baseline core body temperature of 104° F (40° C) or greater; and,
- Tachycardia (at least 100 heart beats per minute)

Baseline disease characteristics were comparable between the two groups, including mean GCS score (Group A: 6.1 vs. Group B: 5.9) representing severe impairment, and mean core body temperature (Group A: 106.5° F (41.4° C) vs. Group B: 106.7° F (41.5° C).

Efficacy

Patients were evaluated at baseline and at regular time intervals post-randomization for changes in level of consciousness using GCS, core body temperature and renal, respiratory and cardiac functions. As illustrated by the table below, there was a greater proportion of patients at 90 minutes post-randomization in Group A as compared to Group B showing a GCS score ≥13, which indicates mild to no brain injury.

Cumulative Incidence of Glasgow Coma Scale (GCS) Score ≥13 at 90 Minutes Post-Randomization

Group A (RYANODEX + SOC) (N=17)	Group B (SOC) (N=17)
29.4%	**11.8%**

Furthermore, as shown in the table below, the proportion of patients achieving a GCS score ≥13 increased over time and was greater in Group A as compared to Group B, where the proportion of patients did not show further increase after 15 minutes post-randomization.

Cumulative Incidence of Glasgow Coma Scale (GCS) Score ≥13 Post-Randomization

Time post-randomization	Group A (RYANODEX + SOC) (N=17)	Group B (SOC) (N=17)
0-5 minutes	5.9%	5.9%
15 minutes	17.6%	11.8%
30 minutes	17.6%	11.8%
45 minutes	29.4%	11.8%
60 minutes	29.4%	11.8%
75 minutes	29.4%	11.8%
90 minutes	29.4%	11.8%

Safety

Overall safety findings were comparable between the two study groups, and there were no serious drug-related adverse events. Fewer patients experienced adverse events in Group A (58.8%), as compared to Group B (70.6%), and the overall incidence of serious adverse events (17.6%) in each of the two treatment arms was comparable. In summary, the safety results of the study are consistent with the known, and well characterized, safety profile of RYANODEX.

Next Steps

Eagle believes that these findings further support establishing the safety and efficacy of RYANODEX for the treatment of EHS, and support the expansion of the product's label to include this indication. The Company continues to analyze the study data, and expects to discuss the full data and next steps with the FDA in the near future. Eagle will provide additional information in due course.

About the Glasgow Coma Scale

The Glasgow Coma Scale ("GCS") is a validated tool that functions as a common scoring system among medical practitioners for measuring and describing the varying degrees of consciousness in a person following an acute brain injury.[3]

Widely accepted as reliable and objective, this scoring system is used by trained staff at the site of a potential brain injury, as well as in emergency departments and intensive care units. The GCS was selected for this study as an objective and accurate method to measure the state of mental impairment and the subsequent improvement of test subjects.

The GCS measures three key functions: Eye Opening, Motor Response and Verbal Response.

Eye Opening (E) 4 = spontaneous 3 = to voice 2 = to pain 1 = none	Motor Response (M) 6 = normal 5 = localized to pain 4 = withdraws to pain 3 = decorticate posture (an abnormal posture that can include rigidity, clenched fists, legs held straight out, and arms bent inward toward the body with the wrists and fingers bend and held on the chest) 2 = decerebrate (an abnormal posture that can include rigidity, arms and legs held straight out, toes pointed downward, head and neck arched backwards) 1 = none
Verbal Response (V) 5 = normal conversation 4 = disoriented conversation 3 = words, but not coherent 2 = no words, only sounds 1 = none	

Clinicians use the GCS to assess the eye opening response, the verbal response, and the motor response in patients with an impaired level of consciousness. The total GCS score is the sum of the scores for each of these functions, classified as follows[4]:

Classification	Total Glasgow Coma Scale Score

Severe	3 – 8
Moderate	9 – 12
Mild	13 – 15

About Exertional Heat Stroke

Exertional Heat Stroke ("EHS") is a rare, sudden and unpredictable disorder that constitutes a medical emergency which may result in severe multi-organ dysfunction and death. EHS is more commonly seen in young people undergoing exertional physical activity in a hot weather environment, and is one of the leading causes of death in young athletes. EHS cases are also observed in construction workers, firefighters, military personnel, and farmers. There is no currently approved drug product for the treatment of EHS.

About Ryanodex

RYANODEX (dantrolene sodium) for injectable suspension is indicated for the treatment of malignant hyperthermia ("MH") in conjunction with appropriate supportive measures, and for the prevention of malignant hyperthermia in patients at high risk.

Important Safety Information

RYANODEX is not a substitute for appropriate supportive measures in the treatment of malignant hyperthermia, including:

- Discontinuing triggering anesthetic agents
- Increasing oxygen
- Managing the metabolic acidosis
- Instituting cooling when necessary
- Administering diuretics to prevent late kidney injury due to myoglobinuria (the amount of mannitol in RYANODEX is insufficient to maintain diuresis).

Precautions should be taken when administering RYANODEX preoperatively for the prevention of malignant hyperthermia, including monitoring vital signs, avoiding known triggering agents, and monitoring for early clinical and metabolic signs of malignant hyperthermia that may indicate additional treatment is needed.

The administration of dantrolene sodium is associated with loss of grip strength and weakness in the legs, as well as drowsiness, dizziness, dysphagia, dyspnea, and decreased inspiratory capacity. Patients should not be permitted to ambulate without assistance until they have normal strength and balance. Care must be taken to prevent extravasation of RYANODEX into the surrounding tissue due to the high pH of the reconstituted RYANODEX suspension and potential for tissue necrosis.

In February 2015, RYANODEX was granted seven years of U.S. market exclusivity for the treatment of MH by the U.S. Food and Drug Administration ("FDA").

RYANODEX full Prescribing Information can be found at www.RYANODEX.com

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," "may," "intends," "anticipate(s)," "plan," "enables," "potential," "entitles," "optimistic" "could" "look forward" and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, statements regarding future events including, but not limited to: the safety and efficacy of RYANODEX for the treatment of EHS; FDA approval of the use of RYANODEX for the treatment of EHS; difficulties or delays in manufacturing; the availability and pricing of third party sourced products and materials; successful compliance with FDA and other governmental regulations applicable to manufacturing facilities, products and/or businesses; and other factors that are discussed in Eagle's Annual Report on Form 10-K for the fiscal year ended September 30, 2014, and its other filings with the U.S. Securities and Exchange Commission. All of 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 FDA will ultimately approve RYANODEX for the treatment of EHS; whether our studies will support the safety and efficacy of RYANODEX for the treatment of EHS; 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.

[1] Szold *et al.* Gray–white matter discrimination—a possible marker for brain damage in heat stroke? European Journal of Radiology, Volume 43, Issue 1, July 2002 [2] Sithinamsuwan *et al.* Exertional heatstroke: early recognition and outcome with aggressive combined cooling--a 12-year experience. Mil Med. 2009 May;174(5):496-502.

[3] Teasdale G, Jennett B. (1974). "Assessment of coma and impaired consciousness. A practical scale." Lancet 13 (2): 81–4.

[4] "What Is the Glasgow Coma Scale?" www.brainline.org, n.d. Web. <http://www.brainline.org/content/2010/10/what-is-the-glasgow-coma-scale.html>.

In-Site Communications, Inc.
Lisa M. Wilson, 212-452-2793
President