Press Release

Crossject elaborates on ZEPIZURE® potential in light of landmark RAMPART study and its own, recently published, bioequivalence study

- Landmark RAMPART study established midazolam intramuscular (IM) injection as a standard of care in the pre-hospital emergency management of epilepsy crises compared to traditional benzodiazepine intravenous (IV)
- Crossject's bioequivalence study, recently published in *Neurology and Therapy*, remarkably consistent with RAMPART's findings and authors' views

Dijon, France 26 June, 2024, 07:30 CET -- Crossject (ISIN: FR0011716265; Euronext: ALCJ), a specialty pharma company in advanced phases of development and registration for ZEPIZURE®, its emergency treatment for the management of epileptic crises based on its award-winning needle-free auto-injector ZENEO®, provides additional, clinically meaningful perspectives on ZEPIZURE® in light of its recently published bioequivalence study results and of the conclusions and hints by the authors of the RAMPART (**R**apid **A**nticonvulsant **M**edication **P**rior to **AR**rival **T**rial) study[1], a landmark double-blind randomized clinical trial comparing the efficacy of IM midazolam vs. IV lorazepam in the pre-hospital treatment of status epilepticus by paramedics. Status epilepticus is defined as a seizure lasting more than 5 minutes.

RAMPART unequivocally raised IM midazolam to the status of standard-of-care in the pre-hospital emergency management of status epilepticus by demonstrating its non-inferiority vs. IV lorazepam, as its primary endpoint. Moreover, IM midazolam demonstrated statistically significant superiority (p value<0.001) on the percentage of patients arriving in hospital seizure-free, which was 10% higher when using IM midazolam (329 out of 448 patients or 73.4% vs. 63.4% in the IV lorazepam 445-patient arm). These results underscored the importance of the speed of IM administration of midazolam, as an easy to store and pre-prepared medication for use by paramedics, features that were likely critical in driving efficacy in controlling seizures by the time of arrival in emergency departments. RAMPART was one of the largest studies every conducted in emergency settings, involving 4,314 paramedics, 33 EMS (Emergency Medical Services) units and 79 hospital ER (Emergency Room) departments across the U.S. It was supported by the National Institute of Health (NIH) and by the Biomedical Advanced Research and Development Authority (BARDA). The RAMPART study publication can be found here.

Crossject's study, recently published in the peer-reviewed journal *Neurology and Therapy*, positively echoed the benefits implied from RAMPART and is remarkably consistent with certain hints put

[1] *Silbergleit et al. New England Journal of Medicine, February 2012. Clinicaltrials.gov NCT05026567*

forward by the authors in the RAMPART study. In Crossject's study, ZEPIZURE® was equivalent to the IM injection from a syringe equipped with a 30mm needle (Dormicum®), and results also suggested a 2-fold lower variability as compared to that usually observed for routes of administration such as intranasal.

With some vision and based on their experience then, RAMPART authors had highlighted a number of issues regarding intranasal solutions in epileptic seizures in general, and their prediction of the likely dominance of the IM route for the future. Today, no intranasal solution is approved for the management of status epilepticus. According to RAMPART's authors, the upfront minutes were critical factors in driving the 10% superiority of IM midazolam, administered through traditional manual vial-form injectable, in positive clinical outcome by ER arrival. ZEPIZURE®, as an ultra-rapid two-step injection, strongly resonates in this practical interventional reality and is likely to further improve the speed of action by healthcare professionals and reliability in injecting a full dose of midazolam. Furthermore, in Crossject's study, ZEPIZURE® enhanced the midazolam absorption during the very first few minutes post-injection, possibly resulting from the needle-free 50 milliseconds injection compared to manual IM and suggesting that seizure treatment may be efficient even sooner.

Patrick Alexandre, CEO of Crossject added: "*Beyond the 505(b)(2) regulatory and market gate for ZEPIZURE® into the arsenal available to healthcare professionals in status epilepticus episodes, as potentially the most rapid-to-use and lowest variability tool for the delivery of a complete midazolam dose pre-hospital, our product presents additional upside. ZEPIZURE®'s rapid and easy two-step application should potentially require limited training compared to traditional injectables, and its consistency in administering an effective dose would confer a key advantage. ZEPIZURE® is therefore poised to provide all patients, and their relatives or caregivers, with the professional standard-of-pre-hospital-care solution anytime and anywhere. Our team in Europe and the U.S. is now executing our development strategy to materialize these broad prospects, aiming to position ZEPIZURE® from a productivity contribution to healthcare professionals toward a high impact solution for all patients and families at risk of a broad range of epilepsy seizures.*"

About Crossject

Crossject SA (Euronext: ALCJ; www.crossject.com) is an emerging specialty pharmaceuticals company developing medicines for emergency situations harnessing its award-winning needle-free auto-injector ZENEO® platform. Crossject is in advanced regulatory development for ZEPIZURE®, an epileptic rescue therapy, for which it has a $60 million contract* with the U.S. Biomedical Advanced Research and Development Authority (BARDA). The Company's versatile ZENEO® platform is designed to enable patients or untrained caregivers to easily and instantly deliver a broad range of emergency medicines via intramuscular injection on bare skin or even through clothing. The Company's other products in development include mainly solutions for allergic shocks and adrenal insufficiencies, as well as therapies and other emergency indications.

* *Contract no: 75A50122C00031 with the Department of Health and Human Services; Administration for Strategic Preparedness and Response; Biomedical Research and Development Authority*

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