AcelRx Pharmaceuticals Announces Publication of Clinical Data Finding Potential Benefits of Nafamostat Compared to Regional Citrate for Anticoagulation of the Dialysis Circuit

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Study results demonstrate that nafamostat had similar efficacy as citrate, while providing lower toxicity and lower costs to the hospital over standard citrate anticoagulation.

HAYWARD, Calif., March 29, 2022 /PRNewswire/ -- AcelRx Pharmaceuticals, Inc. (NASDAQ: ACRX), a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings, today announced the publication of comparative data between two different dialysis circuit anticoagulants in pediatric patients undergoing continuous renal replacement therapy (CRRT). Nafamostat is a commonly used dialysis anticoagulant in South Korea and Japan where it has been approved for this indication for the past few decades, whereas regional citrate anticoagulation (RCA) is commonly used in the EU and US (under an Emergency Use Authorization), since nafamostat is not available commercially. RCA has the risk of citrate toxicity and involves a complex, labor-intensive dosing regimen and therefore there is an interest outside of Korea and Japan to develop nafamostat for dialysis circuit anticoagulation. AcelRx has recently acquired the Lowell Therapeutics nafamostat asset to develop it for use in any extracorporeal circuit, including the dialysis circuit.

The article entitled "Comparison of Nafamostat Mesilate to Citrate Anticoagulation in Pediatric Continuous Kidney Replacement Therapy" was senior authored by Stuart Goldstein, MD, FAAP, FASN, FNKF and published in the journal *Pediatric Nephrology*. Dr. Goldstein holds the Clark D. West Endowed Chair and is Professor and Director of the Center for Acute Care Nephrology at the Cincinnati Children's Hospital Medical Center. While this study focuses on pediatric patients, the standard of care is similar between adult and pediatric populations. The study was a retrospective comparison of pediatric patients undergoing CRRT (also known as CKRT) using nafamostat in a single center in Japan versus citrate in a single center in the US. Outcome measures included dialysis filter lifespan, incidence of bleeding and drug toxicity, and a cost comparison between the two anticoagulation methods was performed.

A total of 158 patients were evaluated at both sites, demonstrating a number of key findings:

- Median filter life was longer for nafamostat but once corrected for key variables, the two groups appeared similar regarding this outcome
- No differences in major or minor bleeding rates were observed
- Citrate toxicity occurred in 14% of patients, whereas no toxicity events with nafamostat occurred
- Citrate anticoagulation is over 3 times the cost of nafamostat

Study limitations include that dialysis protocols varied to some degree between sites, the nafamostat patients on average were younger and smaller, and half the nafamostat patients were concomitantly undergoing plasmapheresis.

"Currently in the US, the safest option for regional anticoagulation in CRRT is the use of citrate," said Dr. Goldstein. "These data demonstrate that both nafamostat and regional citrate can provide acceptable CRRT filter life with a low risk of bleeding events in patients who require CRRT. Nafamostat has the added advantages of a simpler administration regimen for ICU staff, less risk of electrolyte derangement, no dependence on IV calcium or other reversal agents, as well as overall lowered costs to the hospital."

"AcelRx looks forward to the opportunity to develop nafamostat as a regional anticoagulant for CRRT in patients with acute renal failure," stated Dr. Pamela Palmer, AcelRx Chief Medical Officer and co-founder. "Avoiding the risk of citrate toxicity and simplifying the anticoagulation of the dialysis circuit may allow nafamostat to become the preferred method for providing anticoagulation for CRRT once approved for use."

Dr. Mai Miyaji, the study's lead author, was a paid consultant for Lowell Therapeutics but was not compensated for this study. Neither Lowell nor AcelRx provided funding for the conduct of the study, nor did they have any input into the design of the study. Dr. Goldstein is not a paid consultant for Lowell or AcelRx.

About nafamostat mesylate (or mesilate)
Nafamostat is a broad spectrum, synthetic serine protease inhibitor with anticoagulant, anti-inflamatory and potential anti-viral activities. Niyad™ is a lyophilized formulation of nafamostat and is currently being studied under an investigational device exemption, or IDE, as an anticoagulant for the extracorporeal circuit, and has received Breakthrough Device Designation Status from the FDA. LTX-608 is a proprietary nafamostat formulation for direct IV infusion that will be investigated and developed as a potential anti-viral for the treatment of COVID, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) and acute pancreatitis.

About AcelRx Pharmaceuticals, Inc.
AcelRx Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for use in medically supervised settings. AcelRx's proprietary, non-invasive sublingual formulation technology delivers sufentanil with consistent pharmacokinetic profiles. The Company has one approved product in the U.S., DSUVIA® (sufentanil sublingual tablet, 30 mcg), known as DZUVEO® in Europe, indicated for the management of acute pain severe enough to require an opioid analgesic for adult patients in certified medically supervised healthcare settings, and several product candidates. The product candidates include Zalviso® (sufentanil sublingual tablet system, SST system, 15

mcg), an investigational product in the U.S. being developed as an innovatively designed patient-controlled analgesia (PCA) system for reduction of moderate-to-severe acute pain in medically supervised settings, and two pre-filled, ready-to-use syringes of ephedrine and phenylephrine licensed for the U.S. from Aguettant; Niyad™(nafamostat mesylate), a regional anticoagulant for the extracorporeal circuit, and LTX-608, for the potential treatment of COVID-19, disseminated intravascular coagulation, acute respiratory distress syndrome and acute pancreatitis. DZUVEO and Zalviso are both approved products in Europe.

For additional information about AcelRx, please visit www.acelrx.com.

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