Rockwell Medical Study Demonstrates No Drug-drug Interaction Between Ferric Pyrophosphate Citrate and Unfractionated Heparin

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Findings confirm results from previous population PK study demonstrating safe and effective anticoagulation along with the delivery of Ferric Pyrophosphate Citrate iron

WIXOM, Mich., Nov. 16, 2021 (GLOBE NEWSWIRE) -- Rockwell Medical, Inc. (Nasdaq: RMTI), a biopharmaceutical company dedicated to transforming the treatment of iron deficiency and anemia management and improving outcomes for patients around the world, today announced the publication of results in the *Journal of Bioequivalence & Bioavailability* from a study designed to investigate the co-administration of intravenous (IV) Ferric Pyrophosphate Citrate (FPC, Triferic®) with unfractionated heparin (UFH) as an admixture via the HD-machine syringe pump. The study demonstrated no clinically relevant drug-drug interaction between FPC and UFH on the effects of UFH nor on the ability of FPC to deliver bioavailable iron when these agents are co-administered as a single admixture via an HD-machine syringe pump.

"These findings are significant because they demonstrated no clinically relevant drug-drug interaction between FPC and unfractionated heparin, the latter of which has long been the standard to provide anticoagulation in patients on hemodialysis," said Marc Hoffman, M.D., Chief Medical Officer of Rockwell Medical. "Furthermore, the findings confirm results of a previous study which used a population pharmacokinetic model for anti-Xa activity to confirm the effective anti-coagulation dose of UFH and are consistent with our clinical experience of FPC in the real-world setting, in which more than 1.6mm million doses have been safely administered."

The prospective, single-center, open-label, three-period, crossover trial was conducted to investigate the ability of an FPC/UFH admixture to maintain adequate anticoagulation of the dialyzer circuit and to assess the impact of administration of the admixture on the iron delivery of FPC in patients with Hemodialysis Dependent Chronic Kidney Disease (HDD-CKD). The study investigated three treatment regimens in randomized sequence. Anti-Xa activity, activated prothrombin time (aPTT), Thrombin time (TT) and serum iron parameters were measured. Pharmacokinetics and pharmacodynamics were determined using non-compartmental methods and comparisons of Cmax and AUC were calculated using a standard bio-equivalence approach.

The study found that mean anti-Xa activity, activated prothrombin time (aPTT), Thrombin time (TT) concentrations were comparable across all timepoints at baseline, and throughout the study. The concentration-time profiles for iron and TSAT were the same between the FPC/UFH admixture and FPC/UFH administered by separate routes. FPC and UFH were well tolerated with no reported adverse events.

FPC is FDA-approved in the United States for the replacement of iron to maintain hemoglobin in adult patients with HDD-CKD. FPC may be administered in the dialysate or as a slow continuous IV infusion over three to four hours via the pre dialyzer infusion line, via the post-dialyzer infusion line, or via a separate connection to the venous blood line during hemodialysis. *In vitro* drug-drug interaction studies have demonstrated that FPC can be admixed with unfractionated heparin and retain its pharmacodynamic effect for up to 24 hours.

About Triferic Dialysate and Triferic AVNU

Triferic Dialysate (ferric pyrophosphate citrate) and Triferic AVNU (ferric pyrophosphate citrate injection) are the only FDA-approved therapies in the U.S. indicated to replace iron and maintain hemoglobin in hemodialysis patients during each dialysis treatment. Triferic Dialysate and Triferic AVNU have a unique and differentiated mechanism of action, which has the potential to benefit patients and health care economics. Triferic Dialysate and Triferic AVNU represent a potential innovative medical advancement in hemodialysis patient iron management – with the potential to become the future standard of care.

Triferic Dialysate and Triferic AVNU both deliver approximately 5-7 mg iron with every hemodialysis treatment to replace the ongoing losses to maintain hemoglobin without increasing iron stores. Both formulations donate iron immediately and completely to transferrin (carrier of iron in the body), which is then transported to the bone marrow to be incorporated into hemoglobin. Because of this unique mechanism of action, there is no increase in ferritin (a measure of stored iron). Triferic and Triferic AVNU address a significant medical need in treating functional iron deficiency in end-stage kidney disease patients.

The safety profile of Triferic is similar to placebo in controlled clinical trials in patients with end-stage kidney disease. Since approval, there have been no safety related changes to the product labeling.

IMPORTANT SAFETY INFORMATION FOR TRIFERIC AND TRIFERIC AVNU

INDICATION

TRIFERIC and TRIFERIC AVNU are indicated for the replacement of iron to maintain hemoglobin in adult patients with hemodialysis-dependent chronic kidney disease (HDD-CKD).

Limitations of Use

TRIFERIC and TRIFERIC AVNU are not intended for use in patients receiving peritoneal dialysis. TRIFERIC and TRIFERIC AVNU have not been studied in patients receiving home hemodialysis.

Warnings and Precautions

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in

patients receiving parenteral iron products. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity during and after hemodialysis until clinically stable. Personnel and therapies should be immediately available for the treatment of serious hypersensitivity reactions. Hypersensitivity reactions have been reported in 1 (0.3%) of 292 patients receiving TRIFERIC in two randomized clinical trials.

Iron status should be determined on pre-dialysis blood samples. Post-dialysis serum iron parameters may overestimate serum iron and transferrin saturation.

Adverse Reactions
Most common adverse reactions (incidence ≥3% and at least 1% greater than placebo) in controlled clinical studies include: headache, peripheral edema, asthenia, AV fistula thrombosis, urinary tract infection, AV fistula site hemorrhage, pyrexia, fatigue, procedural hypotension, muscle spasms, pain in extremity, back pain, and dyspnea.

About Rockwell Medical

Rockwell Medical is a commercial-stage biopharmaceutical company developing and commercializing its next-generation parenteral iron technology platform, Ferric Pyrophosphate Citrate (FPC), which has the potential to lead transformative treatments for iron deficiency in multiple disease states, reduce healthcare costs and improve patients' lives. The Company has two FDA-approved therapies indicated for patients undergoing hemodialysis, which are the first two products developed from the FPC platform. Rockwell Medical is also advancing its FPC platform by developing FPC for the treatment of iron deficiency anemia in patients outside of dialysis, who are receiving intravenous medications in the home infusion setting. In addition, Rockwell Medical is one of two major suppliers of life-saving hemodialysis concentrate products to kidney dialysis clinics in the United States. For more information, visit www.RockwellMed.com.

Rockwell Medical Forward-Looking Statements

Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws. Words such as, "may," "might," "will," "should," "believe," "expect," "anticipate," "estimate," "continue," "could," "can," "would," "develop," "plan," "potential," "predict," "forecast," "project," "intend" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward looking statements, including statements relating to the potential benefits of Triferic. While Rockwell Medical believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to us on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in Rockwell Medical's SEC filings), many of which are beyond our control and subject to change. Actual results could be materially different. Risks and uncertainties include, but are not limited to: the impact of the COVID-19 pandemic on Rockwell's business, including any clinical trials, and the FDA's response time, the risks of current treatment patterns in the home infusion setting for iron deficiency anemia and whether the FDA will raise any issues with the IND during its review period; and those risks more fully discussed in the "Risk Factors" section of our Quarterly Report on Form 10-Q for the period ended September 30, 2021 and of our Annual Report on Form 10-K for the year ended December 31, 2020, as such description may be amended or updated in any future reports we file with the SEC. Rockwell Medical expressly disclaims any obligation to update our forward-looking statements, except as may be required by law.

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