Armetheon Announces Positive Results of Pharmacokinetics Study of Tecarfarin versus Warfarin

Clinical data show promise of tecarfarin in chronic kidney disease patients requiring anticoagulation

MILPITAS, Calif., Aug. 25, 2016 /PRNewswire/ -- Armetheon, Inc., a specialty pharmaceutical company developing novel small molecule drugs for cardiovascular diseases, today announced results from its Phase 1 clinical trial evaluating the effect of severe chronic kidney disease on the pharmacokinetics (PK) of tecarfarin, Armetheon's lead candidate, and of warfarin, the current standard of care in anticoagulation. Tecarfarin's pharmacokinetics (renal clearance and plasma half-life) were not significantly affected by severe renal impairment, whereas warfarin clearance was substantially reduced and a large increase in half-life was seen.

Despite warfarin being the treatment of choice for decades for patients requiring anticoagulation, physicians have also recognized the limitations of warfarin, which can result in a significant portion of patients being poorly controlled. Armetheon's pharmacokinetics study provides clinically relevant insights demonstrating that warfarin metabolism and clearance are markedly affected by renal function. Based on these positive findings, Armetheon plans to enroll chronic kidney disease (CKD) patients in its upcoming Phase 3 Tecarfarin for AntiCoagulation Trial (TACT). The Company also plans to report the results of its Phase 1 study in a peer-reviewed journal.

Dr. Mintu Turakhia, a cardiologist at Stanford University and an investigator on the study, commented, "For patients with chronic kidney disease, anticoagulation is a challenge, and warfarin is still widely used. Unfortunately, kidney disease complicates management with warfarin, and these patients tend to have more unstable anticoagulation with warfarin, which increases risk of stroke and bleeding. The current study provides clear pharmacological evidence why warfarin works poorly in the presence of kidney disease, while tecarfarin was not really affected. This could have huge promise for the many patients with advanced kidney disease that presently do not have good treatment options."

The Company's Phase 1 trial was a US multi-center, double-blind, randomized, crossover study designed to evaluate the safety, tolerability, and pharmacokinetics of tecarfarin and of warfarin in 12 subjects with CKD Stage 4 and 10 matched healthy volunteers. Study endpoints included primary PK parameters of tecarfarin and warfarin, incidence and severity of adverse events (AEs), and changes in clinical laboratory parameters, including renal clearance and plasma half-life.

"We are greatly encouraged by the results of this Phase 1 study in CKD patients, which suggest that tecarfarin holds promise as an improved option for anticoagulation in these patients," said Detlef Albrecht, MD, Armetheon's Chief Medical Officer and Head of Drug Development. "The safety and pharmacokinetics findings support the broadening of our enrollment plan for TACT to include patients with severe renal impairment, which represent a growing subgroup among anticoagulated patients and who are often excluded from pivotal Phase 3 cardiovascular studies of novel anticoagulant therapies."

About Tecarfarin
Tecarfarin is being investigated for use as an oral, once-daily anticoagulant that inhibits Vitamin K epoxide reductase (VKOR), an important enzyme in the coagulation system, and avoids CYP450 metabolism and renal elimination. In Phase 2 and Phase 2/3 (EMBRACE-AC) clinical testing, tecarfarin improved time in therapeutic range (TTR) in chronically anticoagulated patients. The effect of tecarfarin on TTR will be further investigated in the Company's upcoming pivotal clinical trial, TACT (Tecarfarin for AntiCoagulation Trial), which will be conducted under a Special Protocol Assessment agreed upon with the FDA. TACT is an open-label trial expected to enroll 3,000 patients with any indication for anticoagulation, including prosthetic heart valve (PHV) patients. TTR was chosen as the primary endpoint for TACT on the basis of evidence suggesting that better anticoagulation control (as measured by higher TTR) can protect patients from severe or even fatal adverse events. Tecarfarin is monitored using INR (International Normalized Ratio) and is being investigated for use without the need for CYP2C9 genotyping since tecarfarin is not metabolized via the CYP450 system. In preclinical and early clinical studies, the anticoagulant effect of tecarfarin was reversed by existing and readily available antidotes for Vitamin K Antagonists.

About Armetheon
Armetheon, Inc., is a privately held, specialty pharmaceutical company developing and commercializing innovative medicines addressing major unmet needs in cardiovascular disease, initially in thrombosis and cardiac arrhythmias. Armetheon focuses on improved therapies with the goal of increased efficacy, safety, and utility, targeting specialty markets with clearly defined regulatory pathways. Armetheon's lead candidate, tecarfarin, is being investigated for use as a Vitamin K Antagonist and is currently in Phase 3 development for the prevention and management of thrombosis. Armetheon is also developing its anti-arrhythmic drug candidate, budiodarone, for the treatment of ventricular tachycardia (VT) in patients with implantable cardioverter defibrillators (ICDs). For more information: www.armetheon.com.

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