Armetheon Reaches Agreement with FDA to Conduct a 1000 Patient Single Phase 3 Study Prior to NDA Filing for its Novel Oral Anticoagulant Tecarfarin

Menlo Park, CA, February 9, 2017/ PRNewswire/ – Armetheon, Inc., a specialty pharmaceutical company developing novel small molecule drugs for cardiovascular diseases, today announced it has reached agreement with the U.S. Food and Drug Administration (FDA) for a single 1000 patient final pivotal trial for its drug candidate, tecarfarin (Tecarfarin for AntiCoagulation Trial or TACT) prior to filing an NDA, which is currently projected to occur in 2019. Further, the agency indicated that Armetheon can amend the existing Special Protocol Assessment (SPA) for the 1000 patient TACT study. Tecarfarin is positioned to potentially be, if approved, the oral anticoagulant (OAC) therapy of choice for patients who require anticoagulation with a Vitamin K antagonist (VKA), such as warfarin. This includes patients with prosthetic heart valves (PHV), repeat deep vein thrombosis or patients with chronic kidney disease (CKD) which complicates anticoagulant therapy. The pivotal trial will enroll patients with all indications for anticoagulation, thereby supporting a potential broad label if the product is approved.

Despite warfarin being the standard of care OAC for decades, physicians recognize its limitations related to its metabolism via cytochrome P450 (CYP). Patients who take a CYP interacting drug, have variant CYP2C9 genetics or CKD have significant challenges to achieve stable anticoagulation control with warfarin. The TACT study will specifically enroll patients with these challenges to demonstrate tecarfarin's ability to provide improved anticoagulation control compared to warfarin. There are at least 15 conditions requiring OAC where a VKA such as warfarin is predominantly used, and these represent at least 1.7 million patients in the US alone, with 91% of these patients taking at least one CYP interacting drug.

"To reach agreement with the FDA to conduct a 1000 patient final Phase 3 study prior to a potential NDA filing is unprecedented for an anti-thrombosis/cardiovascular drug", said Armetheon's President & *interim* CEO, M. (Ken) Kengatharan, PhD. "This is because the primary end point for approval is an outcome measure called time in therapeutic range (TTR) of the international normalized ratio (or INR) which indicates how effective anticoagulation is managed in a particular patient."

In a prior interaction with Japan's Pharmaceuticals and Medical Device Agency (PMDA, Armetheon has received regulatory guidance for the development toward the Marketing Authorization Application for tecarfarin in Japan. The PMDA also accepted TTR as a primary end-point for approval.

Tecarfarin has been studied in close to 900 patients in 10 different clinical trials, including a prior pivotal trial and a study in CKD patients where tecarfarin was observed to have potential benefits based on pharmacokinetics when compared to warfarin.

"Tecarfarin is an important therapeutic option in the armamentarium of anticoagulants particularly for patients who can't take a novel oral anticoagulant (or NOAC) and where their only option is warfarin," commented Detlef Albrecht, MD, Armetheon's Chief Medical Officer and Head of Drug Development. "Armetheon is

grateful to the regulatory agencies for accepting our scientific arguments for a trial design enriched with the subjects who have risk factors for poor anticoagulation control and end points that can be used to seek regulatory approval."

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 1,000 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 potential treatment of refractory atrial fibrillation (AF), defined as those patients who have failed at least one first line therapy with anti-arrhythmic drugs or catheter ablation as well as ventricular tachycardia (VT) in patients with implantable cardioverter defibrillators (ICDs). For more information: www.armetheon.com.

Contacts

For Media:

Heather Lake, Director of Corporate Development
+1 650-646-3898, ext. 121
hlake@armetheon.com