



Armetheon Announces European Medicines Agency's Support for 1000 Patient Single Phase 3 Study prior to MAA Filing for its Novel Oral Anticoagulant Tecarfarin

Potential for Harmonization of Development Plan for Tecarfarin in the US and EU

Menlo Park, CA, February 14, 2017/ PRNewswire/ – Armetheon, Inc., a specialty pharmaceutical company developing novel small molecule drugs for cardiovascular diseases, today announced it has received advice from the European Medicines Agency (EMA) Scientific Advice Working Group (SAWG) for the development of its novel oral anticoagulant tecarfarin. The SAWG advised that Armetheon can conduct a single 1000 patient pivotal study prior to filing the Market Authorization Application (MAA) for tecarfarin. If approved, tecarfarin is positioned to potentially be 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. This 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 face significant challenges achieving stable anticoagulation control with warfarin. The planned 1000 patient Phase 3 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 therapy where a VKA such as warfarin is predominantly used.

"The advice received from the EMA-SAWG for the conduct of a single 1000 patient final Phase 3 study prior to a potential MAA filing allows for a global harmonization of our development plan for tecarfarin", said Armetheon's President & *interim* CEO, M. (Ken) Kengatharan, PhD. "The primary end point for approval is time in therapeutic range (TTR) of the international normalized ratio (or INR), an outcome measure, which indicates how effectively anticoagulation is managed in a particular patient receiving a VKA and has now been accepted by the EMA, FDA and the PMDA."

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 for patients with indications requiring an oral anticoagulant where only warfarin can be used and who can't take a novel oral anticoagulant (NOAC) such as a Factor Xa or a thrombin inhibitor," commented Detlef Albrecht, MD, Armetheon's Chief Medical Officer and Head of Drug Development. "We are grateful to the major regulatory agencies, US FDA, Japan's PMDA and now the EMA 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 without the need for clinical outcome studies.”

Armetheon also announced that an article entitled “Pharmacokinetics and pharmacodynamics of tecarfarin, a novel vitamin K antagonist oral anticoagulant” has just been published electronically ahead of print in the medical journal “*Thrombosis and Haemostasis*”

(<https://th.schattauer.de/contents/archive/issue/special/manuscript/27138.html>)

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, budiardone, 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.

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