Inositecâ€™s INS-3001 Significantly Reduces Vascular Calcification Data Presented at Kidney Week 2018 Indicates

Inositec, a pioneer in the development of life-saving small molecule drugs based on myo-inositol hexaphosphate (IP6), announced today that INS-3001, a novel vascular calcification inhibitor, demonstrated the ability to significantly inhibit the calcification process in preclinical studies. The build-up of calcium deposits in arterial walls and cardiac valves lead to an increase in cardiac events, particularly in patients with chronic kidney disease. Data was presented in three abstracts at the American Society of Nephrologyâ€™s Annual Meeting Kidney Week 2018 (23-28 October).

â€œAt present, there is no approved treatment for vascular calcification and affected individuals are left at great risk of experiencing cardiovascular events and death. The data we presented at Kidney Week shows that our novel vascular calcification inhibitor, INS-3001, possesses superior potency and pharmacokinetics to the natural IP6 molecule in terms of inhibiting vascular calcification. This suggests that INS-3001 could provide significant patient benefit if confirmed in clinical studies,â€• stated Dr. Mattias Ivarsson, CEO of Inositec. â€œWe are now conducting our IND-enabling studies, with first-in-human studies scheduled to begin in 2019.â€•

Data Presented at Kidney Week

To develop a new class of inhibitors of vascular calcification, Inositec conducted multi-step syntheses, starting from protected myo-inositol species, involving selective PEGylation, phosphorylation or sulfation to build a library of novel IP6 analogs with improved drug-like properties. IP6 has previously been shown to be a potent inhibitor of calcification. Data presented from in vitro experiments showed that INS-3001 was superior to natural IP6 with regard to efficacy and stability in a serum calcification propensity assay. INS-3001 also had efficacy superior to IP6 in cell culture studies performed on primary human vascular smooth muscle cells treated with either calciprotein particles or calcification medium to induce formation of calcified deposits.

In rats, INS-3001 administration significantly blunted carotid calcification following vitamin D overdose, reducing the amount of calcium in tissues by a factor of two compared to controls while a numerical decrease was observed at the level of abdominal aorta. INS-3001 also showed a beneficial effect on the renal function of animals in this model.

The effect of INS-3001 was further evaluated in vitamin D-warfarin induced calcification in rats. In the abdominal aorta, significantly lower total calcium content was measured in the INS-3001 groups compared to the vehicle group following bolus subcutaneous dosing. The von Kossa positivity (area% of stained tissue representing the extent of calcification) of the abdominal aorta was also significantly lower in the INS-3001 groups compared to the vehicle group. The effects on both the total calcium and the von Kossa positivity were dose-dependent, and correlated with mortality. Similar reductions in total calcium content and area% von Kossa positivity were seen in the thoracic aorta, and the femoral and carotid arteries.

The uremic state appeared to significantly influence the rat plasma pharmacokinetics of INS-3001 after subcutaneous and intravenous administration, suggesting that uremia extended plasma exposure of INS-3001 without increasing peak plasma levels.

About Inositec

Inositec is pioneering the development of life-saving small molecule drugs based on inositol phosphate, a natural facilitator of diverse cellular functions. Using its broadly applicable Inosituneâ„¢ technology to adjust the chemical and physical properties of inositol phosphate analogs, Inositec is developing a novel class of drugs currently focusing on high-unmet medical needs related to calcification disorders. Inositec was founded in December 2015 based on the award-winning research of Dr Mattias Ivarsson, Prof Jean-Christophe Leroux and Prof Bastien Castagner at ETH Zurich, Switzerland. Further information can be found at www.inositec.com.

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