SNF472 is a molecule with the potential to inhibit cardiovascular calcification in end-stage renal disease patients on hemodialysis.

**INTRODUCTION**

SNF472 is an intravenous (i.v.) formulation of myo-inositol hexaphosphate (Fig. 1), a small and highly water-soluble molecule that inhibits calcification by binding to the growing sites of the hydroxyapatite (HAP) crystal, the main component of calcification in arteries. SNF472 is being developed for preventing cardiovascular calcification in end-stage renal disease (ESRD) patients undergoing hemodialysis (HD).

**AIM**

To assess the potential of SNF472 to inhibit cardiovascular calcification (CVC) in vivo in an animal model and ex vivo in HAP crystallization on HD patient samples.

**PRECLINICAL EFFICACY STUDY**

- Performed in 50 Sprague-Dawley rats with CVC induced by 75,000 IU/kg vitamin D.
- Five groups of 10 animals receiving: 0, 3, 10, 30, 100 mg/kg SNF472.

**FIRST-TIME-IN-HUMAN CLINICAL TRIAL**

- Performed in eight hemodialysis patients.
- One single i.v. dose of 9 mg/kg SNF472 through dialysis tubing during the 4 hours of dialysis.
- No systemic adverse events nor effects in safety parameters.
- Pharmacokinetic measurements revealed a low SNF472 clearance through the dialysis membrane.

**CONCLUSIONS**

1. SNF472 inhibits CVC in animal models.
2. SNF472 inhibits HAP crystallization in human plasma, so it has the potential to inhibit calcification.
3. These results suggest a favorable benefit/risk ratio of SNF472 and support further studies in dialysis patients.