

SNF472 Mechanism of Action data published in British Journal of Pharmacology

SNF472 selectively inhibits pathological calcification by binding to hydroxyapatite crystals

Palma, Spain and San Diego, USA, 25 June 2020 – Sanifit, a clinical-stage biopharmaceutical company focused on developing treatments for calcification disorders, today announced that data examining the mechanism of action of SNF472, Sanifit’s lead compound in development, has been published in the British Journal of Pharmacology (BJP).

SNF472 is a novel calcification inhibitor for the treatment of cardiovascular calcification (CVC) and the related rare disease calcific uremic arteriolopathy (calciphylaxis) in patients undergoing hemodialysis. SNF472 is currently in a pivotal phase 3 trial for calciphylaxis.

In patients undergoing dialysis, vascular calcification occurs when calcium and phosphate aggregate into hydroxyapatite (HAP) crystals and deposit in arterial walls. HAP crystals block small arteries in skin and soft tissue. SNF472 binds with high affinity to HAP crystals, the final common pathway of CVC, and selectively inhibits their accumulation in arterial walls independently on the etiology of HAP formation.

The studies examined the binding features of SNF472 for HAP crystals across a variety of *in vitro* and *in vivo* models. The binding was found to be fast (80% within 5 minutes) and insurmountable. SNF472 inhibited HAP crystal formation with an EC50 of 3.8 μ M, with complete inhibition at 30.4 μ M. At the lowest concentration tested (1 μ M) in vascular smooth muscle cells, SNF472 inhibited calcification by 67%, with complete inhibition from 30 μ M. Interestingly, the mean plasma concentration in a phase 2 open-label study with SNF472 in patients with calciphylaxis was 28 μ M after 12 weeks of treatment. Improvements in wound healing (primary endpoint), pain and quality of life (secondary endpoints) were observed. Similar concentrations significantly attenuated the progression of coronary artery calcification in a phase 2b double-blind, placebo-controlled phase 2b trial in patients on hemodialysis.

SNF472 showed no deleterious effects on bone mineralization in dogs after 9 months at 25 mg/kg (maximum concentration 384 μ M) and the EC50 for *in vitro* calcium chelation is 539 μ M. Full results can be accessed online [here](#).

The data support continued clinical investigation of SNF472 for the treatment of vascular calcification and calciphylaxis in patients undergoing dialysis.

Joan Perelló, Chief Executive Officer of Sanifit, said: “We welcome the BJP’s publication of these data, which provide valuable insight into SNF472’s mechanism of action and its significant potential as an effective inhibitor of HAP crystallization in the cardiovascular system. With no current approved therapy for vascular calcification or calciphylaxis, which are associated with

Sanifit Therapeutics S.A.

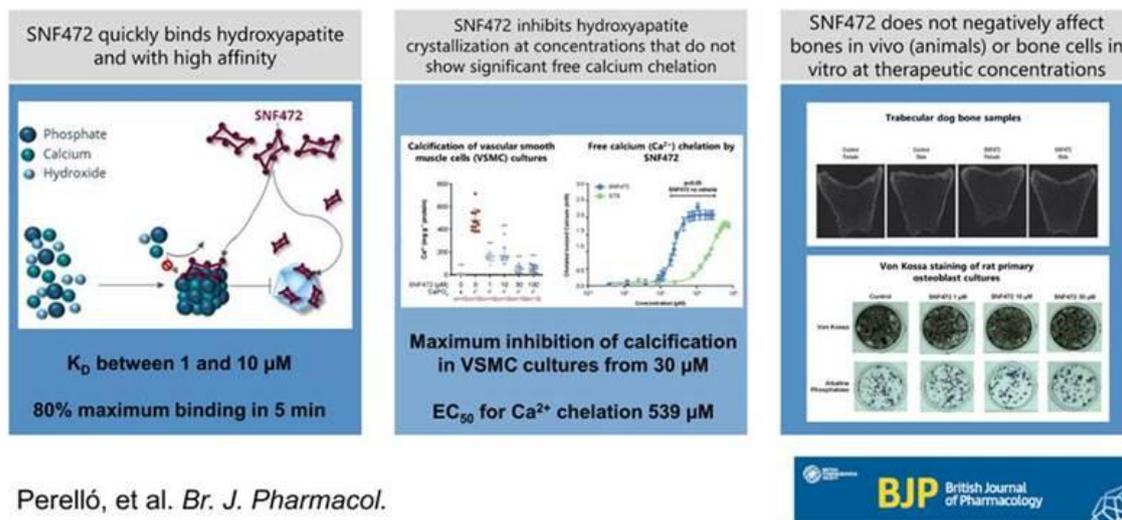
Sanifit Inc.

Phone: +34 971 439 925
PARC BIT. Europa Building. 2nd floor | 07121 Palma. Spain
Phone: +1 858 535 48 44
3655 Nobel Drive Suite #540 | CA 92122 San Diego, USA
info@sanifit.com www.sanifit.com



increased mortality and morbidity in patients undergoing dialysis, we look forward to advancing SNF472 in our clinical development for the patients in need.”

MECHANISM OF ACTION OF SNF472



Perelló, et al. *Br. J. Pharmacol.*

Figure 1: Graphical Abstract from paper: Perelló, J, Ferrer, MD, del Mar Pérez, M, et al. Mechanism of action of SNF472, a novel calcification inhibitor to treat vascular calcification and calciphylaxis. *Br J Pharmacol.* 2020 <https://doi.org/10.1111/bph.15163>

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For further enquiries:

Sanifit

Joan Perelló, CEO

Antonio Jiménez, VP Operations

For media enquiries:

Consilium Strategic Communications

Amber Fennell, Chris Welsh, Nicholas Brown, Sarah Wilson

Tel: +44 (0) 20 3709 5700

Email: sanifit@consilium-comms.com

About Sanifit

Sanifit is a clinical-stage biopharmaceutical company focused on developing treatments for calcification disorders. The company launched in 2007 as a spin-off from the University of the Balearic Islands and expanded its activities to the USA in 2016 with the incorporation of a subsidiary with offices in San Diego, CA. The company's lead asset, SNF472, has successfully completed a Phase 2 proof of concept study in calciphylaxis, and showed a significant reduction in progression of coronary calcification in a Phase 2b

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study among hemodialysis patients. A Phase 3 pivotal study in calciphylaxis is currently underway. Sanifit has raised approximately \$130M, including a 2019 Series D round of \$61.8M (€55.2M) in mid-2019. For more information please visit www.sanifit.com.

About SNF472

SNF472 is an intravenous formulation of myo-inositol hexaphosphate with a novel mechanism of action for the treatment of hemodialysis patients with cardiovascular diseases linked to calcification. SNF472 is in phase 3 development for calciphylaxis, a devastating rare disease which leads to the death of approximately 55% of patients within the first year of diagnosis, with additional indications related to progressive vascular calcification under consideration. SNF472 has been granted orphan drug status for the treatment of calciphylaxis by both the EMA and FDA. SNF472 selectively blocks the progression of pathological cardiovascular calcification, and poses an innovative solution for this unmet medical need.

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