

BIOWORLD™ TODAY

THE DAILY BIOPHARMACEUTICAL NEWS SOURCE

Venous inferns: Early work sufficient to attract \$21M for Ilkos' leg ulcers effort

SEPTEMBER 28 , 2016

By Randy Osborne, Staff Writer

“The beauty of this deal is that it’s not just an out-licensing deal from Servier,” CTI Life Sciences partner Jean-François Leprince told BioWorld Today as he explained newly formed Laval, Quebec based Ilkos Therapeutics Inc., which made its debut with a \$21 million three-way investment in equal parts by CTI, the Fonds de solidarité FTQ and Servier Canada.

Ilkos is developing a compound called S42909 for oral, first-line treatment of venous lower limb ulcers. The candidate was deprioritized from Servier’s research and development lineup, but the firm is still “highly interested” in it, Leprince said – interested enough that the company is overseeing phase IIa trials as part of the arrangement with Ilkos. “They remain investors into the newco in Quebec, and the newco is contracting Servier as, I would say, a service provider,” he said. “We will be using the Servier organization to run the phase IIa trials around Europe, Canada and the U.S.” The \$21 million is “more than enough” to finish the dose-ranging trial, which will involve three doses and more than 200 patients, he added.

A nicotinamide adenine dinucleotide phosphate (NADPH) oxidase inhibitor, S42909 “has gone through a very intensive and complete phase Ia trial with more than 200 healthy volunteers,” he said. The outcome turned up data showing S42909 safe and well-tolerated. “We believe, rightly or wrongly – the future will tell – that there is enough de-risking or risk mitigation with this project,” he said. Servier, founded in 1954, is the first French independent pharmaceutical group.

About S42909, Leprince said, “at the very beginning, [venture capital fund CTI] had a little bit of skepticism, because this indication has been the graveyard of many drugs, not to mention the latest cellular therapies. But I must say that the pharmacological properties of the compound have been evidenced by very compelling preclinical results.” Servier, with “global leadership in vein disease” thanks to Daflon (micronized purified flavonoid fraction), makes the ideal partner, in his view. “Would it not have been that way, because of the challenge associated with the indication, we would not have done [the deal]. There is only one company with the kind of expertise in venous insufficiency that can operate a trial like that.”

Specifically, Daflon is indicated for symptoms of venolymphatic insufficiency (heavy legs, pain, restless leg at bedtime) and hemorrhoid attacks.

S42909 “goes one step beyond” Daflon to affect the causes of venous insufficiency, said Leprince. Along with Danny Gagné, manager of the Fonds de solidarité FTQ’s life sciences portfolio, and Frédéric Fasano, Servier Canada’s CEO, he will serve as director of Ilkos. Chairman of the board is Mark Beaudet, co-founder of St. Laurent, Quebec-based Paladin Labs Inc., acquired by Endo International plc, of Dublin, in 2013. (See *BioWorld Today*, Nov. 6, 2013.)

NEUROPATHY . . . AND ALZHEIMER’S?

In the microcirculation damage of venous insufficiency, three mechanisms are implicated: leukocyte additions to the endothelial wall; oxidative stress; and the presence of metalloproteinase-2. S42909 seems to influence all of those, Leprince said. “You will tell me, ‘OK, it’s animals,’ but we believe those animal models are very predictive of what could happen in humans,” he said. Currently, venous lower limb ulcers are treated with compression bandages and “some local, topical products that are used essentially to address the symptoms, i.e., inflammation [and] infections,” he said. “First, we want to demonstrate the efficacy of the compound in venous disease, which [makes up] 70 percent of the total ulcers. Second, maybe the indication we will be targeting is the prevention of recurrence of the venous ulcers. Healing the ulcers is already quite an achievement, but then you run the risk, especially with aged people, to suffer the recurrence. We may [later] contemplate what we call mixed ulcers, which is a combination of venous and arterial, but we are not yet at the level of arterial disease.”

Ilkos takes its name from the Greek for ulcer, “elkos,” with the first vowel changed to suggest illness and thence healing. “The concept is a kind of quasi-virtual company,” Leprince said. Ilkos will contract with Servier and others, intending along with the phase IIa trial to “stake a post in the ground with the beginning of a clinical development program in Japan,” while conducting some preclinical toxicology studies “which are longer-term, 26-week studies on animals,” he said.

A June paper in *Experimental Dermatology* described a two-week preclinical experiment in 24 New Zealand white rabbits. Researchers concluded that “S42909 improved [the] healing process by dampening excessive inflammation and facilitating collagen deposition without wound contraction phenomena,” and said the compound “might be a promising therapy to treat chronic wounds [such] as venous leg ulcers.”

The company is not alone in NADPH oxidase research. At the start of last year, Geneva-based Genkyotex SA raised CHF20 million (then US\$20 million) in a series D round to take forward its pipeline of selective NADPH oxidase inhibitors in a broad range of indications, including diabetic neuropathy. In November 2015, the company gained orphan drug status from the FDA and EMA for GKT137831, its lead drug in the class, targeting systemic sclerosis. Another Swiss firm, Kareus Therapeutics SA, is trying an approach with NADPH in Alzheimer’s disease, though research is early stage. (See *BioWorld Today*, Jan. 7, 2013, and Jan. 8, 2015.) //