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EP Vantage Interview – Genkyotex pockets SFr25m to NOX out diabetic nephropathy

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The SFr25m ($26m) just raised by the private Swiss company Genkyotex would be welcome by any European start-up, but it is especially remarkable given that investors had already sunk SFr27m into the business, whose sole clinical-stage project has yet to show any signs of efficacy in humans.

The cash will fund a phase II study next year of Genkyotex's lead agent in diabetic nephropathy, with the aim of generating proof-of-concept data by the end of 2013. Not only will this give the first indication as to whether the lead works in humans, "it could provide proof of concept for the whole platform", the firm's CEO, Dr Ursula Ney, tells *EP Vantage*. Perhaps this goes some way to explaining private backers' willingness to endorse Genkyotex so strongly.

The Swiss company's focus is on inhibition of NADPH oxidases, also known as NOXs, which it hopes can target a broad set of diseases characterised by oxidative stress-mediated tissue damage. This is based on studies of the relevance of pathways through which NOX inhibitors prevent the generation of radical oxygen species, carried out by the company's scientific founders at the universities of Geneva, Kyoto and Texas. These universities are responsible for Genkyotex's somewhat unwieldy name.

"[The founders] realised that the pathway was unexplored therapeutically," says Dr Ney, adding that more established approaches had focused further down the pathway to mop up reactive oxygen species, using antioxidants or free radical scavengers – a relatively unspecific approach.

As such, Dr Ney claims that Genkyotex's GKT137831 is a first-in-class project. This is borne out by *EvaluatePharma* data, which show only two other NOX-inhibitors in development: the US biotech company Alimera Sciences is studying this approach at the preclinical stage as a possible treatment for dry acute macular degeneration, while ProNoxis, a private Swedish firm, is investigating the activation of NOX2 for treating autoimmune disease.

Lead focus

Genkyotex chose diabetic nephropathy, a progressive disease of the kidneys that results from longstanding diabetes, as the first indication as much through pragmatism as because of efficacy seen in preclinical models, Dr Ney says.

A convenient three-month treatment period, a grant from the Juvenile Diabetes Research Fund that had led to '831 being tested in diabetes models, and the promise of a blockbuster therapy area combined to make this a no-brainer.

Big pharma interest in diabetes – most recently evidenced by Bristol-Myers Squibb and AstraZeneca's joint $7bn buyout of Amylin Pharmaceuticals – is expanding to looking at diabetes-related conditions. "20-40% of diabetics will get nephropathy," says Dr Ney. "Whichever way you cut the data, it's a $2bn market."

Diabetic nephropathy currently tends to be treated using off-patent drugs, mainly ACE-inhibitors, which represents a symptomatic approach targeting early stages of the disease. It does not stop patients progressing, says Dr Ney, and many lose kidney function and develop end-stage renal disease. Signs from animal models are that '831 actually stops disease progression, she adds.

EvaluatePharma data reveal a range of pharmacological approaches to diabetic nephropathy in development, with one phase III project – Alfa Wassermann's thrombin inhibitor sulodexide; 16 in phase II and six in phase I studies. There is some big pharma involvement in R&D, with phase II projects from Boehringer Ingelheim, Lilly, GSK and Abbott Laboratories.

Clearly, Genkyotex will be hoping that big pharma is poised to jump on its project to in-license should the data back it up. There is evidence of prior interest: Reata Pharmaceuticals' bardoxolone methyl, in phase III for treating chronic kidney disease and phase II specifically for diabetic nephropathy, was licensed to Abbott in 2010 for a combined $450m, and last December Abbott picked up Reata's second-generation oral antioxidant inflammation modulators for $400m up front.

Dr Ney says the funds just raised should also allow Genkyotex to start a second clinical trial in a different indication – perhaps idiopathic pulmonary fibrosis – as well as advancing the early-stage pipeline. Fibrosis could also be of interest to partners; Bristol-Myers Squibb's $325m acquisition of Amira Pharmaceuticals was driven by the biotech firm's fibrosis programme.

Selective inhibition

'831 selectively targets NOX 1 and 4, and has undergone a small phase I trial that showed good safety and tolerability. A multiple ascending-dose portion of the trial should finish late this quarter, and Genkyotex hopes to be in phase II by the year end.

Phase II would be a placebo-controlled European/US trial in around 150 patients, with the same primary endpoint – decrease in proteinuria – as used in animal models. According to Dr Ney, Genkyotex's ability to assay for NOXs - which are complex, transmembrane enzymes - could serve as an important barrier to competitor entry.

Dr Ney, the former chief operating officer of Antisoma, now commutes between her UK home and Genkyotex's headquarters in Geneva. She joined the fledgling company in 2011, a year after leaving Antisoma as the UK company was in its death throes following clinical trial failures.

The collapse of Antisoma, once seen as the standard bearer for the UK's biotech sector, typified the binary risk of investing in biotech. Dr Ney will be hoping that for Genkyotex the coin lands the other side up.