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Interview – F2G's novel antifungal brings in the bucks

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Antifungal drugs have been unloved for some time. But now with fungi, as with bacteria, the threat of resistance is rearing its head and companies in the space are getting more attention. One, the UK group F2G, has just raised an impressive $60m that should take its lead compound through phase III and to registration.

"We have a novel class of drug for an unmet medical need," F2G's chief executive, Ian Nicholson, tells *EP Vantage*. "That's what it comes down to in terms of our ability to raise capital in what is otherwise a very difficult financing environment." F2G does not quite make it into the top five biopharma fundraisings of 2016, but it is not far off in a year that has yet to reach the dizzy heights of 2015 (see table below).

Top five pharma and biotech VC fundraisings Jan 1-Jun 20, 2016

Company	Amount ($m)	Sector	Country	Round
DalCor Pharmaceuticals	100	Cardiovascular	Canada	Series B
Mission Therapeutics	86	Oncology	UK	Series C
Forty Seven	75	Oncology	US	Series A
C4 Therapeutics	73	Oncology & others	US	Series A
Kala Pharmaceuticals	68	Ophthalmology	US	Series C

While many of the other big fundraisers are active in oncology, F2G's lead candidate, F901318, is being developed for invasive aspergillosis and other serious rare mould infections. Because its mechanism differs from other antifungals F901318 might sidestep the problem of resistance, the company believes.

There is only one class of approved antifungals that are given both intravenously and orally, according to Mr Nicholson: azole drugs such as voriconazole. "However, in certain parts of Europe significant resistance to these drugs is building," he says, adding that resistance rates of 20-25% are being reported in the Netherlands.

Different class

F901318 works in a different way from the azoles, inhibiting fungal dihydrooratate dehydrogenase (DDOH), a key mitochondrial enzyme. "We believe it's the only agent of its type in the clinic or in development that targets this enzyme," Mr Nicholson says.

He claims that so far, F901318 has not shown any resistance in trials and the company has not been able to induce resistance via serial passage, a method of growing bacteria in a lab that can be used to study the development of resistance. The project has also not been linked with any serious adverse reactions during use in around 100 healthy volunteers, the chief exec says.

F2G will need to carry out a 40-patient pharmacokinetic study, slated to start in September, "just to ensure the pharmacokinetics we've seen in healthy volunteers is the same as in the at-risk patient population".

Then the group can begin a global pivotal trial, scheduled for the second quarter of 2017, which will enrol around 200 patients and have a primary endpoint of six-week mortality.

The company is developing both an intravenous and oral formulation of F901318, and both will be used in the phase III study. "Our proposed approach is to treat patients on IV for up to about two weeks and then step them down to oral therapy, which could last as long as two to three months," Mr Nicholson says.

Accelerated approval?

F2G expects topline data from the pivotal study in 2019, which it plans to use as the basis for regulatory filings in the US and Europe shortly afterwards. This small study should be enough as the FDA and EMA have both agreed to an accelerated approval process, according to Mr Nicholson, contingent on the company carrying out a larger post-market study.

If successful, F901318 will likely be used initially in patients who cannot tolerate existing therapies, which can be up to 10-30%, he estimates. “And it will certainly be used where there’s a high risk of resistance – in Northern Europe for example – and in settings where others drugs are not used such as solid organ transplantation and, potentially, in prophylaxis.”

The chief exec believes that F901318 could have peak sales of over $500m – a big stretch in a market controlled by Pfizer and Merck & Co that has already seen generic entrants. Still, this sector is seeing an increase in the number of immuno-compromised people, such as those receiving stem cell or bone marrow transplants, or chemotherapy.

There is limited competition from new agents: last year Basilea’s Cresemba became the first new antifungal in nearly a decade, but is forecast to be selling only $157m in 2022, according to sellside consensus; the clinical pipeline effectively comprises F901318 and Scynexis’s SCY-078, in phase II (*Basilea pins future on speciality business and US float, November 30, 2015*).

F2G has projects in preclinical development including an anti-Candida agent that also targets the DDOH enzyme, as well as a broad-spectrum agent that does not.

When asked if the company would seek a partner if phase III results with F901318 are positive, Mr Nicholson replies: “We’re going to be opportunistic. We have the potential to go either way – through the partnership route or via an IPO. We’re keeping our options open.”

First, the company has to show that F901318 lives up to its promise.

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