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Pamrevlumab comes off the bench to deliver for Fibrogen

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With Fibrogen investors largely focused on the company's anaemia lead, roxadustat, yesterday's mid-stage success with pamrevlumab probably came as a surprise. At least this is one way to explain the group's 50% share price surge this morning.

The optimism is driven by pamrevlumab's potential in idiopathic pulmonary fibrosis (IPF), a blockbuster disease against which progress is finally being made thanks to Roche's Esbriet and Boehringer Ingelheim's Ofev. Still, IPF is a tough indication, and even Roche has yet to show that its $8.3bn takeover of Intermune, which gave it Esbriet, was worth it.

Remarkably, pamrevlumab barely features in sellside models, and accordingly no reliable consensus forecasts are available. But no doubt Fibrogen investors have cast an eye across to Esbriet and Ofev, which are both shortly expected to become blockbusters in IPF, with 2022 sales hitting $1.2bn and $1.8bn respectively, according to *EvaluatePharma*.

Still, in terms of NPV Esbriet is worth an estimated $3.2bn – a figure well short of the $8.3bn that Roche handed over to Intermune's owners in 2014. On that basis, at least, Fibrogen's $4bn market cap might look reasonable, especially given the additional potential of roxadustat.

Caution

But pamrevlumab still has it all to do in phase III, and it is a well-known fact that small trials in IPF often do not portend a phase III hit (*Therapy Focus – Phase III proves tough for IPF, February 8, 2016*).

And, while the Fibrogen project is said to have hit the primary endpoint in its phase II study – improving 48-week predicted forced vital capacity versus placebo – there are a couple of reasons for caution before full data are presented at the European Respiratory Society conference.

For instance it is clear that, like Esbriet and Ofev, pamrevlumab only slows the course of lung function decline in IPF rather than improving disease, though it cannot be denied that for Fibrogen to demonstrate such a strong effect in a small study is impressive.

Also, the 103-subject study compared pamrevlumab against placebo, not against treatment with approved drugs, which is clearly where it needs to compete in the real world. The study's protocol had been amended last year to add some 60 patients in whom pamrevlumab was combined with either Esbriet or Ofev, but this subset was only used for safety purposes, demonstrating good tolerability, Fibrogen said.

Industry assets targeting CTGF/CCN2			
Project	**Pharmacology class**	**Company**	**Lead indication(s)**
Phase II			
Pamrevlumab	Anti-CTGF MAb	Fibrogen	IPF, pancreatic cancer, DMD
RXI-109	CTGF RNAi therapeutic	RXi Pharmaceuticals	Wound closure, HPV, AMD
Abandoned in phase II			
PF-06473871/EXC 001	CTGF RNAi therapeutic	Pfizer/Ionis	Wound closure
Abandoned in preclinical			
AngioPro	CTGF 2 gene therapy	Transgene	Coronary artery disease
PBI-4419	CTGF inhibitor	Prometic Life Sciences/Allist	Renal fibrosis
sd-rxRNA Anti-Scar Research Program	CTGF RNAi therapeutic	Pantec Biosolutions	Wound closure
Source: EvaluatePharma.			

While the successes of Esbriet and Ofev prompted a surge of interest in IPF, pamrevlumab seems to be the only asset whose mechanism involves antagonising the connective tissue growth factor (CTGF) CCN2. The industry pipeline features a few discontinuations, and the only other clinical project here is RXI Pharmaceuticals' RNAi asset RXI-109, though this is not being studied for IPF.

This indicates the possible breadth of uses for IPF projects against diseases involving fibrosis; Ofev is separately marketed in the EU as Vargatef for non-small cell lung cancer, while one of the most advanced IPF candidates, Roche's lebrikizumab, is also being studied in eczema. Roche today licensed the latter, an anti-IL-13 MAb, to Dermira for just $80m up front.

Pamrevlumab, too, seems to be a jack of all trades, with ongoing phase II trials in pancreatic cancer and non-ambulatory Duchenne muscular dystrophy patients.

In IPF Stifel analysts reckon pamrevlumab can capture 15% of the market against the two current incumbents. For an asset that was until yesterday a virtual non-entity that might be enough.

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