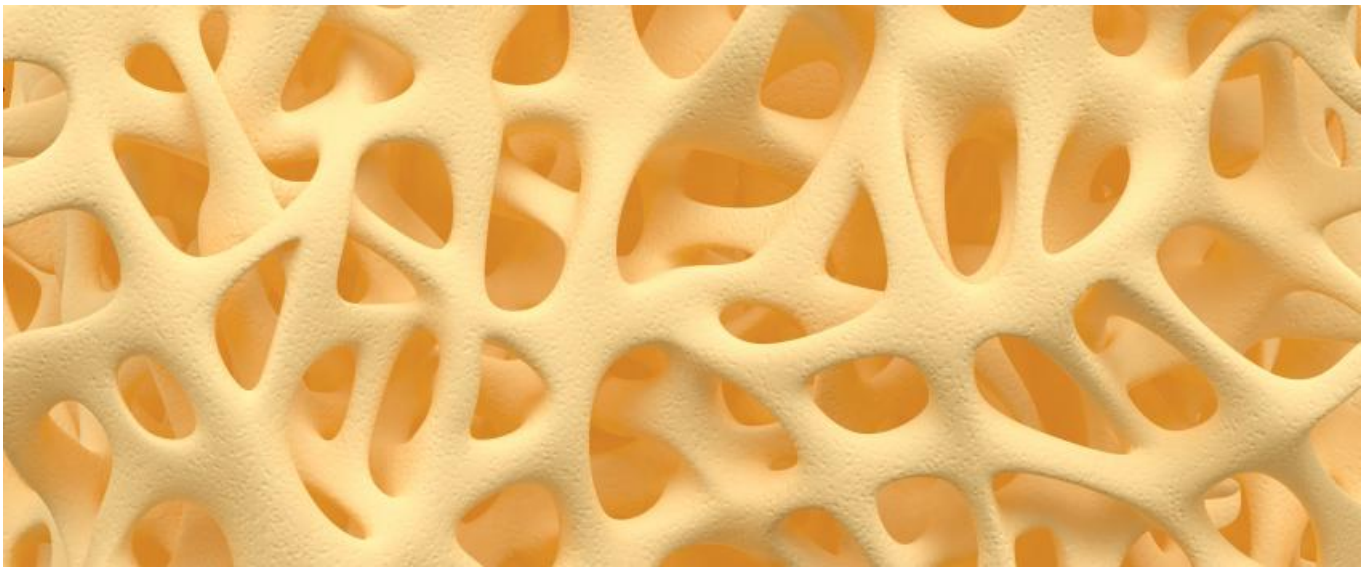
Evaluate Vantage

October 16, 2019

Ipsen doubles down on rare bone disease

Madeleine Armstrong



Today’s deal with Blueprint gives Ipsen two shots at Fop, but makes its takeout of Clementia look even more expensive.

Ipsen clearly wants to be a big deal in the rare bone disease fibrodysplasia ossificans progressiva (Fop). But its move to license BLU-782 from Blueprint Medicines today raises questions about the $1bn it paid for Clementia in February. BLU-782 targets the genetic cause of Fop so could presumably risk making palovarotene, which Ipsen gained through Clementia, redundant.

Ipsen must presumably see room for both therapies. A spokesperson told *Vantage* that the projects’ different mechanisms of action mean that BLU-782 could be given either in combination with palovarotene or after palovarotene monotherapy. However, the company would not give any more details on the rationale behind the deal or its development plans.

BLU-782 is designed to target mutant Alk2; variations in the *Alk2* gene, also known as ACVR1, are known to cause Fop, a condition characterised by abnormal growth of bone in muscles and connective tissues. Meanwhile, palovarotene, a RAR-gamma agonist, is designed to inhibit bone morphogenetic protein signalling that leads to the bone overgrowth seen in Fop.

Ipsen is making a big bet on what could be a very small market. The International Fibrodysplasia Ossificans Progressive Association notes that 800 patients with the disorder have been identified, but estimates that the total number of patients could hit 3,500; Ipsen is predictably more bullish, saying there could be 9,000 Fop patients worldwide.

The sellside is not expecting much, especially in the context of Ipsen's outlay. *EvaluatePharma* consensus predicts 2024 palovarotene sales of $357m; there are currently no forecasts for BLU-782, presumably because of its early stage.

Small up front

At least BLU-782 was a relative bargain in terms of up-front costs: Ipsen is paying $25m initially, and up to $510m in milestones. It is also in line for royalties in the low to mid teens. Ipsen's stock climbed 2% today, suggesting that investors are more positive about the deal than they were about the purchase of Clementia, which sent shares down 6%.

The agreement also like a good result for Blueprint, which has its hands full with targeted cancer therapies and only a small presence in rare diseases. The group’s Fop programme had previously been partnered with

Alexion until the latter canned that deal in 2017. Still, Leerink analysts noted that the deal could hurt speculation about Blueprint as an M&A target, and the group's stock dipped 1% today.

Today's deal also handily takes out one of Ipsen's Fop competitors, although BLU-782 is some way behind palovarotene in development. Blueprint previously said it planned to start a phase II trial by the end of the year, while Ipsen hopes to file palovarotene with the US FDA sometime this half based on mixed results from an uncontrolled phase II trial; a phase III study is ongoing (*Ipsen takes a rare gamble on Clementia, February 25, 2019*).

Palovarotene could also have broader use: it is in phase II development for another rare bone disease, multiple osteochondromas, and could have potential in dry eye disease.

There do not appear to be any other Alk2 inhibitors in the clinic for Fop: Sumitomo Dainippon Pharma's TP-0184 is in phase I, but for solid tumours. Meanwhile, Biocryst has two Alk2 inhibitors in preclinical development, BCX9250 and BCX9499, and according to its website plans to start phase I trials this year.

Still, Ipsen's closest rival – which is also likely to be its fiercest – is Regeneron, whose REGN2477 is in a phase II pivotal study that is set to read out later this year.

Selected projects in development for fibrodysplasia ossificans progressiva

Project	Company	Mechanism	Status	Trial details
Palovarotene	Ipsen	RAR gamma agonist	US filing due H2 2019	Move, NCT03312634
REGN2477	Regeneron	Anti-activin A MAb	Phase II	Lumina-1, NCT03188666
BLU-782	Ipsen/Blueprint	Alk2 inhibitor	Phase I	NCT03858075
BCX9250	Biocryst	Alk2 inhibitor	Preclinical	-
BCX9499	Biocryst	Alk2 inhibitor	Preclinical	-

Source: EvaluatePharma, clinicaltrials.gov.