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Ipsen takes a rare gamble on Clementia

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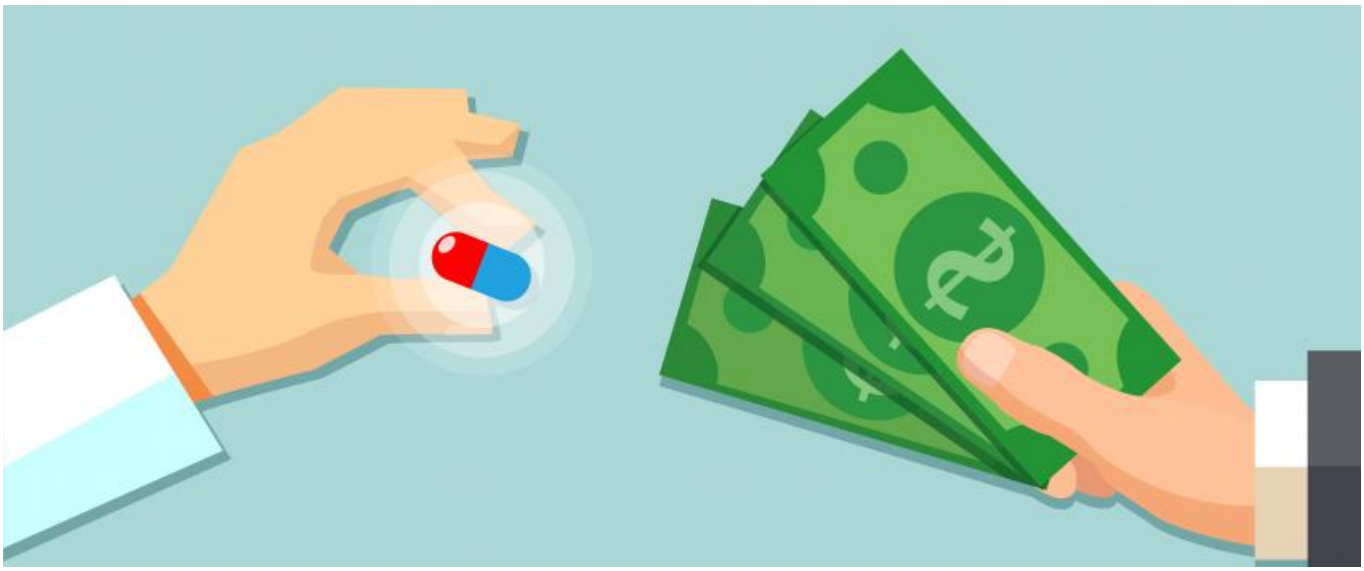

In placing a $1bn bet on the rare disease player Clementia, Ipsen is banking on a lenient US regulator.

Mixed phase II results have not stopped Clementia trying to get a quick approval for its rare bone disease project palovarotene. And they have also not stood in the way of the Canadian group becoming a takeout target, with Ipsen picking up Clementia for $1.04bn today.

The move might reflect desperation on Ipsen's part: the company's pipeline is underwhelming and it has made no secret of its need for deals. But with an approval decision and more data on palovarotene due next year, Ipsen must feel it worth taking a risk on Clementia while it is still a relative bargain.

At a 100% probability of success *EvaluatePharma* sellside consensus puts palovarotene's net present value at $1.1bn. How much economic interest remains in palovarotene is a separate question as Ipsen stands to pay the project's originator, Roche, low-teens royalties. The French company's shareholders' were unimpressed, sending its stock down 6% today.

Derisked?

On an analyst call today Ipsen's chief executive, David Meek, described palovarotene as a "largely derisked asset".

And in a call with *Vantage* the French group's chief commercial officer, Harout Semerjian, highlighted Clementia's "close interactions" with the FDA. He added that palovarotene already had orphan, fast-track, breakthrough therapy and rare paediatric disease designations.

Of course, those are not a guarantee of approval. Palovarotene's lead indication is fibrodysplasia ossificans progressiva (FOP), a condition characterised by abnormal growth of bone in muscles and connective tissues, known as heterotopic ossification.

Palovarotene, a small-molecule retinoic acid receptor gamma agonist, is designed to inhibit bone morphogenetic protein signalling, which results in an overgrowth of bone and cartilage.

Within FOP, Clementia has been developing palovarotene for episodic and chronic treatment. Approval could come first in the former, with a filing with the FDA planned in the second half of this year. In the chronic setting Clementia is carrying out the open-label phase III Move trial, with an interim analysis due this year.

Ipsen estimates that palovarotene could bring in peak sales of $400m in the chronic and episodic FOP uses,

and further sales could come from another rare bone disease, multiple osteochondromas, where the project is in a potentially registrational phase II trial. The French company is on the hook for another $263m if the FDA accepts a filing for this additional use.

Clementia has also been developing the project for dry eye disease, where it recently began a phase I trial. A priority review voucher, should palovarotene be approved, is also something to take into consideration, although the value of these is not what it used to be.

Flare-up farrago

Still, all this might not be plain sailing given the results of the open-label phase II trial, which evaluated various dosing regimens of palovarotene. In part A the project was only given in the event of a flare-up, at 20mg followed by a 10mg dose that will soon be evaluated by the FDA.

Part B, meanwhile, saw patients receive 5mg of palovarotene per day, which could be increased in the event of a flare-up. However, part B results were disappointing: the primary endpoint, change in new heterotopic ossification volume, was reduced by 28% by palovarotene – well off the 65% benchmark that analysts had hoped for.

Clementia blamed this on one patient who had multiple flare-ups yet did not meet the requirements for flare-up treatment. But it also said nearly half of the patients in part B had flare-ups that were not treated because they did not meet the trial criteria.

The company has relaxed the criteria in the phase III Move trial so patients only need to have one flare-up symptom to receive higher-dose therapy, and Ipsen will hope that this translates into a better result in this setting.

Notwithstanding the caveats Ipsen has obviously seen enough to think that it can be first to market, and Mr Meek said he did not see any near-term competitive threats to palovarotene.

Regeneron has REGN2477, an anti-activin A MAb, in development for FOP, but Mr Meek maintained that this was in the very early stages of development despite it being in a phase II trial, Lumina-1. Unlike Clementia's trial, which is due to complete this year, this includes a placebo arm.

Palovarotene might well get the go-ahead in episodic FOP, but there are still plenty of questions for Ipsen to answer.