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Palbo puts cyclin back on the agenda

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It is ironic that on the same day the US FDA approved Pfizer's palbociclib, resurrecting the investment case for cyclin-dependent kinase inhibition, Onconova stock lost 36% in the wake of Baxter pulling the plug on the group's lead project.

Onconova has a phase I asset that also targets cyclin-dependent kinase, and the group might well have to look early in its pipeline to generate investor interest. Palbo's unusually fast approval certainly renews hope for this once popular drug class and a second down-and-out player, Cyclacel, showed a flicker of life on the news.

There had been doubts for palbo after Pfizer reported mixed phase II data from the Paloma-1 breast cancer trial, whose interim analysis was insufficiently mature to show an effect on overall survival, and then said it would file without waiting for phase III data.

Next the FDA said there would be no advisory panel meeting, prompting the market to assume that it was moving to delay the filing. In the event, however, the green light did come – and no less than two months before the agency's action date: palbo has been approved, as Ibrance, for first-line treatment of oestrogen receptor-positive/Her2-negative metastatic breast cancer.

Consensus forecasts, as compiled by *EvaluatePharma*, are for 2020 palbo sales to hit $3.1bn; Amgen, which through Onyx Pharmaceuticals acquired the originator's interest in the molecule, is owed an 8% royalty.

First in class

With palbo, the first-in-class cyclin-dependent kinase (CDK) 4/6 inhibitor on the market, attention turns to the next representatives of this class: Novartis's LEE011 and Lilly's abemaciclib are in phase III trials for breast, and breast and lung cancers, respectively (*Therapeutic focus – Competitors cycle in palbo's slipstream, April 17, 2014*).

Merck & Co's dinaciclib, which inhibits the CDK1/2/5/9 isoforms, has completed a phase III trial in chronic lymphocytic leukaemia, and is in phase II for solid tumour indications. Cyclacel, meanwhile, has a portfolio focused on cell cycle inhibition, but has been crushed by the failure of its lead asset, sapacitabine.

Cyclacel does boast the CDK2/7/9 inhibitor seliciclib in phase II, but this relies on the same technology as sapacitabine. The market thus assumes that Cyclacel is to all intents and purposes dead, valuing it at just $13m; the stock rose 5% in early trading today.

Onconova's dire straits might not be quite as bad, though the comparison only damns it with faint praise. Its market cap sunk to $55m after Baxter said it would not pursue rigosertib, Onconova's lead asset, in low-risk myelodysplastic syndromes, wiping out a milestone payment that would have otherwise been due.

This came a year after the project flopped in high-risk MDS – an indication with which Onconova now says it plans to plough on in a second phase III study; it will surely need to go back to investors for more cash.
It was already pretty clear that Onconova was going nowhere fast, so Baxter's decision simply underlined the young US biotech's 2013 flotation as one of the bull market's biggest flops (*Onconova loses IPO shine with trial failure, February 20, 2014*).

In terms of exciting investors it is a long shot but the group has briciclib, a CDK4/cyclin D1 inhibitor, in phase I, and ON 123300, a CDK4/Ark5 inhibitor, in preclinical development; and, technically at least, its Baxter deal is still in effect. Cyclacel, meanwhile, is left having to fund a study that is doomed to fail.

Palbo's surprise approval is unlikely to rescue either of these companies, but given their valuations the opportunity to cash in on short-term share price swings is considerable.

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