

## Watch out Ibrance - here comes abemaciclib



[Jonathan Gardner](#)

Ibrance is the surprise hit of Pfizer's post-Lipitor era, outperforming early expectations in its first-line breast cancer setting. Now Lilly is looking to muscle into this space with word that it hopes to submit a competitor, abemaciclib, for approval based on phase II data due out in the middle of 2016, pushing up launch by about a year.

This would put Lilly on better footing with Novartis, which has pegged pivotal trials of its own LEE011 to read out about the same time. Pfizer's progress in the oestrogen receptor-positive, Her-negative indication, with blockbuster sales forecast for this year, has kicked a race for second place into high gear.

News that Lilly will take data from abemaciclib's Monarch 1 trial to regulatory authorities, if they are strong enough, took the sector by surprise. A successful bid would not put this project in direct competition with Ibrance yet, but would give it a foot in the door with the HR-positive, Her-negative patients who have progressed on two chemotherapy regimens; patients who have progressed on Ibrance were excluded.

Investors had been expecting Lilly to wait until readout of the phase III programme in 2017 - its Monarch 3 and 2 trials are in first and second-line settings respectively - which would have likely put it in the tough position of third-to-market agent in the cyclin-dependent kinase (CDK) 4 & 6 inhibitor class.

Novartis expects to report data from the Monaleesa-2 trial of LEE011, or ribociclib, around mid-2016; that trial is in first-line treatment of HR-positive, Her2-negative patients in combination with letrozole.

Ribociclib is obviously a more immediate threat to Ibrance's position, but Lilly is bidding to create awareness of its rival before Novartis can become too well established. *EvaluatePharma's* consensus forecasts ribociclib selling \$708m in 2020, versus abemaciclib's \$672m, but look for these numbers to change as more data emerge.

### No cyclin superhighway

Still, Lilly is not in the best competitive position. Thus it might need to show how it can differentiate itself from Ibrance and ribociclib.

Bernstein analyst Tim Anderson wrote earlier this week that Lilly hopes to show that abemaciclib has single-agent activity and a better toxicity profile that will allow continuous dosing, rather than Ibrance's one-week "drug holiday" after three weeks of treatment. Neutropaenia is the major adverse event reported with the Pfizer pill, with reduced dosing also recommended for patients based on toxicity.

Mr Anderson wrote that abemaciclib's gastrointestinal side effects could be an offsetting factor, however.

Ibrance's success has not necessarily been the prelude to clinical expansion in the cyclin inhibition space, however. Since the last time *EP Vantage* examined the pipeline abemaciclib is the only agent to graduate to phase III ([Therapeutic focus - Competitors cycle in palbo's slipstream, April 17, 2014](#)).

Merck & Co and Ligand Pharmaceuticals' dinaciclib appears to have been demoted to phase II trials in solid tumours after completion of a phase III trial comparing it against Arzerra in chronic lymphocytic leukaemia.

### Active phase II/III CDK inhibitors in oncology

	Pharma class	Project	Company	Sales (\$m)		
				2016	2018	2020
<i>Phase III</i>	CDK 4 & 6 inhibitor	Ibrance	Pfizer/Amgen	1,956	3,255	3,311
	CDK 4 & 6 inhibitor	ribociclib (LEE011)	Novartis/Otsuka	-	324	708
	CDK 4 & 6 inhibitor	abemaciclib	Eli Lilly	-	229	672
<i>Phase II</i>	CDK inhibitor	ronaciclib	Bayer	-	-	-
	CDK inhibitor	dinaciclib	Merck & Co/Ligand	-	-	-
	CDK inhibitor	alvocidib	Sanofi/Tolero	-	-	-
	CDK 4 & 6 inhibitor	G1T28-1 (IV)	G1 Therapeutics	-	-	-

Nevertheless, Bayer's roniciclib, which has yet to have specified the CDK on which it acts, has been tested in phase II in small cell lung cancer, and data should be available soon ([Upcoming events - Bayer's lung cancer effort and Apricus and Zealand try again](#), February 5, 2016). Sanofi and Tolero Pharmaceuticals are recruiting patients for an acute myeloid leukaemia study for alvocidib.

These are not immediate threats to the breast cancer space the three leaders appear to have carved out. This year should be a good indicator of whether Novartis and Lilly can command the \$3bn numbers that Ibrance looks on track to earn, or whether they will become also-rans.

Project	Study	Trial ID
abemaciclib	Monarch 1	NCT02102490
ribociclib	Monaleesa-2	NCT01958021

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