Evaluate Vantage

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Orion’s cancer reset bears fruit

[Jacob Plieth]

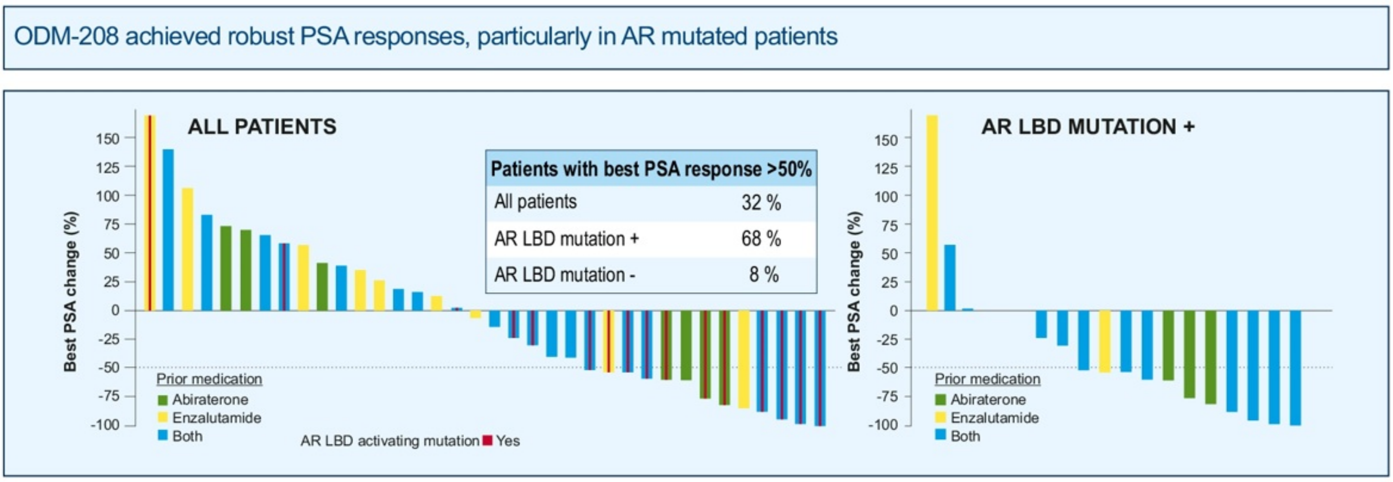
Already boasting the marketed Nubeqa, Orion licenses its next-biggest prostate cancer hope to Merck & Co.

Just four months after cutting back R&D to focus on cancer and pain, Finland’s Orion has reaped the benefit. Today’s licensing deal with Merck & Co covering ODM-208, a mid-stage prostate cancer project, is this year’s second biggest by up-front value.

The tie-up shows Merck getting further into prostate cancer – the US group already boasts a mutation-defined label for Lynparza here – while the less well-known Orion builds on Nubeqa, a Bayer-partnered drug sold for non-metastatic disease. It is likely that the trigger for the $290m deal, beyond Orion flagging ODM-208 in its R&D overhaul, was data revealed at February’s Asco-GU conference.

This meeting featured results of [Cypides, a first-in-human study] of ODM-208, in 44 metastatic castration-resistant prostate cancer patients, all of whom had progressed on Zytiga and/or Xtandi. 32% achieved a PSA decrease of 50% or more, a number that rose to 68% in a subgroup with a mutation in the androgen receptor ligand-binding domain.

Best PSA change from baseline (%) by prior medication



Source: Professor Karim Fizazi & Asco-GU.

ODM-208 acts by inhibiting cytochrome P450 11A1, an enzyme involved in steroid production. It is thought that in prostate cancer the androgen receptor axis remains open even after Zytiga or Xtandi treatment, and it can become reactivated by non-androgenic steroid hormones.

ODM-208 is said to shut down steroid biosynthesis entirely, thus inhibiting prostate cancer progression. *Evaluate Pharma* reveals no other oncology work on CYP11A1 inhibition. Angion Pharma is active in cytochrome P450 inhibition, and had looked preclinically at the CYP17 inhibitor ANG-3279 in prostate cancer, but this is now discontinued; Angion is now developing CYP11B2 inhibitors, though not for cancer.

Merck buys in

Either way, Merck has clearly been persuaded of the potential of the anti-steroid approach. It has given Orion $290m for co-development rights to ODM-208 and other CYP11A1 inhibitors, and retains an option to take out a global, exclusive licence.

Merck/Astrazeneca’s Lynparza is already carving out a place in castrate-resistant prostate cancer, thanks to its unusually broad US label allowing use in second-line patients with any HRR mutation. However, a Lynparza/Keytruda combo failed the Keylynk-010 prostate cancer study in March.

Merck clearly sees prostate as the place to be, however, and Orion had signalled its intention to build a presence here when it cut back investments in neuroscience and inhaled drug delivery, to focus on cancer and pain. The Finnish group cited Nubeqa and ODM-208 as reasons for optimism.

The former drug, licensed to Bayer, is approved for non-metastatic, castrate-resistant prostate cancer, and a second niche, hormone-sensitive prostate cancer, has opened up thanks to positive data from the Arasens trial published in the NEJM this year.

True, Zytiga is already available in the latter setting, and Xtandi in both, but the sellside still expects Nubeqa to become a blockbuster by 2026, according to *Evaluate Pharma* consensus. ODM-208 does not yet feature in most analysts’ models, a fact both companies will hope changes soon.

Top 10 licensing deals of 2022 so far*			
Licenser	**Deal partner**	**Up-front value**	**Details**
Gilead	Dragonfly	$300m	Gilead to develop DF7001, a 5T4-targeting NK cell engager for solid tumours, plus options on additional programmes
Merck & Co	Orion	$290m	Co-development of Orion's ODM-208 and other CYP11A1 inhibitors, plus option to convert to a full exclusive licence
Bristol Myers Squibb	Evotec	$200m	Extension of 2018 deal to develop molecular glue degraders
Novartis	Molecular Partners	$162m (Sfr150m)	Novartis to develop ensovibep as Covid therapy
Sanofi	IGM Biosciences	$150m	Collaboration on IgM antibody agonists against 3 oncology targets and 3 immunology/inflammation targets
Menarini	Newamsterdam	$143m (€143m)	Menarini to commercialise obicetrapib, a once-daily CETP inhibitor, in Europe
Roche	Repare Therapeutics	$125m	Roche to develop camonsertib, ATR inhibitor, in cancer
Bristol Myers Squibb	Century Therapeutics	$100m (plus $50m equity)	Collaboration on up to 4 iPSC-derived NK/T-cell programmes in cancer
Sanofi	Exscientia	$100m	Collaboration on 15 novel small molecules for cancer/immunology using Exscientia's AI tech
Bristol Myers Squibb	Bridgebio	$90m	Bristol to develop BBP-398, a Shp2 inhibitor, in cancer

**As at 13 Jul 2022; Source: Evaluate Pharma & company announcements.*

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