Evaluate Vantage

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Roche gets back to business – R&D upgrades and downgrades

Madeleine Armstrong

After a couple of blips Roche is back to doing what it does best: R&D. The company bagged the two biggest upgrades for its phase III assets ocrelizumab and atezolizumab, which are also expected to be the top biological launches this year.

On the flip side, the biggest downgrades went to Ziopharm Oncology's IL-12 gene therapy and OHR Pharmaceutical's eye disease candidate squalamine, which both saw over $1bn wiped off consensus forecasts.

Bish bash Roche

Last year Roche was a surprising entrant on the downgrade list owing to two abandoned projects, bitopertin and onartuzumab (*Roche on the wrong side for once in shifting analyst forecasts, June 5, 2015*).

But this time it was business as usual thanks to the anti-CD20 MAb ocrelizumab for multiple sclerosis and atezolizumab, which is expected to become the first approved anti-PD-L1 MAb this year, likely in non-small cell lung and/or bladder cancer.

Five biggest upgrades to R&D assets over the past 12 months

Project	Company	Status	Therapy subcategory	2020e sales ($bn)	Change ($bn)
Ocrelizumab	Roche	Phase III	MS therapies	2.76	+2.26
Atezolizumab	Roche	Phase III	Anti-neoplastic MAbs	2.49	+1.38
Dupilumab	Sanofi	Phase III	Immunosuppressants	1.87	+1.16
Elagolix	AbbVie	Phase III	Other genito-urinary agents	1.00	+0.52
Ixekizumab	Eli Lilly	Filed	Anti-psoriasis agents	1.03	+0.52

While atezolizumab's launch has been eagerly awaited thanks to the success of the rival anti-PD-1 agents Opdivo and Keytruda, it was edged out by the Rituxan follow-on ocrelizumab, which had a $2bn upgrade after reporting positive phase III results in relapsing-remitting and primary progressive MS.

The rise in the consensus forecast for atezolizumab has been steadier, but Roche will not be complaining – if the sellside is to be believed it will be raking in over $5bn from the two drugs by 2020.

Dupilumab drives Sanofi

Sanofi needs some cheer after sales of its cholesterol-lowering agent Praluent fell well short in its first five months on the market – and this could come in the shape of dupilumab.

Phase III results in atopic dermatitis are due by the end of March, with a filing expected in the third quarter. If all goes to plan dupilumab, like ocrelizumab and atezolizumab, is set to become one of the biggest biological launches of 2016.

And further upgrades might come – bullish Credit Suisse analysts peg peak dupilumab sales at $7.5bn, with $5bn of this coming in dermatitis. However, Sanofi could eventually face competition from other interleukin-targeting antibodies like AstraZeneca's tralokinumab and Roche's lebrikizumab, both in phase II in the skin disorder.

Forecasts for AbbVie/Neurocrine Biosciences' elagolix have grown with increasing visibility. Early last year the phase III Violet Petal study in endometriosis-associated pain met its primary endpoints, and data from another phase III trial are due soon, which could set it up for a regulatory filing this year. Meanwhile, a phase III trial in uterine fibroids is recruiting.

Putting CAR-T before IL-12

The downgrades list was headed by Ziopharm's IL-12 programme, which lost its shine as the company shifted focus to its CAR-T candidates. Analysts had been expecting Ad-RTS-hIL-12 to reach blockbuster status by 2020, but the consensus forecast now stands at a paltry $194m.

Mizuho Securities analysts noted that the IL-12 strategy had fallen out of favour with the advent of CAR-T and other immuno-oncology approaches, and cut the probability of approval of Ad-RTS-hIL-12 from 20% to 15%. But the project is still in phase II trials in breast cancer, and a phase I study in high-grade glioma is also recruiting.

Five biggest downgrades to R&D assets over the past 12 months

Project	Company	Status	Therapy subcategory	2020e sales ($bn)	Change ($bn)
Ad-RTS-hIL-12	Ziopharm Oncology	Phase II	Immunostimulants	0.19	(1.60)
Squalamine	OHR Pharmaceutical	Phase II	Eye/ophthalmic preparations	-	(1.21)
Romosozumab	Amgen	Phase III	Bone calcium regulators	0.22	(0.46)
Pracinostat	MEI Pharma	Phase II	Other cytostatics	0.08	(0.40)
Gevokizumab	Xoma	Phase III	Immunosuppressants	0.13	(0.37)

Meanwhile, OHR is pushing ahead with squalamine, or OHR-102, with a phase III trial of the eyedrop formulation in wet age-related macular degeneration slated to start in the current quarter – despite it failing a phase II study in wet AMD in 2014.

Clinical setbacks also did for MEI Pharma's pracinostat and Xoma's gevokizumab. The former's forecast plunged after it failed in a phase II trial in myelodysplastic syndrome in March, while Xoma discontinued development of gevokizumab in uveitis after the phase III Eyeguard-B study flopped in July (*Reports of Xoma's demise are only slightly exaggerated, July 23, 2015*).

Gevokizumab is still in phase III development for pyoderma gangrenosum, while in December MEI said it planned to start a phase III trial of pracinostat in acute myeloid leukaemia in the second half of 2016. It seems that, in spite of the setbacks and resulting downgrades, companies are ploughing on in the hope of an eventual reward.

To contact the writer of this story email Madeleine Armstrong in London at madeleinea@epvantage.com or follow @medtech_ma on Twitter