Evaluate Vantage

October 17, 2018

Pre-Esmo jitters for Roche

Jacob Plieth

Discontinuations and an unusual revelation about Tecentriq's breast cancer data dominated the R&D part of the company's third-quarter results call.

Roche has long relied on business development to supplement a broad early-stage pipeline, and it would be unrealistic to expect all of its deal-making to work out.

However, in its third-quarter results presentation today the Swiss group revealed the discontinuation of five new molecular entities, no fewer than four of which it had sourced externally: RG6125, acquired through the $105m buyout of Adheron Therapeutics; RG6029, licensed from Xenon Pharmaceuticals; RG7741, derived from a collaboration with Array Biopharma; and RG7990, licensed from Novimmune in 2010.

No specific reasons were cited, but as the company awaits further proof from another acquisition, that of Ignyta, this could raise questions over its biz dev prowess. The discontinuations came after the group recently canned two selective oestrogen receptor degrader (SERD) assets, RG6046 and RG6047, acquired through its $725m takeover of Seragon; a third-generation SERD asset, RG6171, remains in phase I, Roche disclosed in its presentation.

Among in-house projects axed today the most prominent is emactuzumab, an anti-CSF-1R MAb Roche said had proved to be no better in combination than Tecentriq alone. This will be relevant for Five Prime's rival CSF-1R-targeting asset cabiralizumab.

Roche's third-quarter NME discontinuations			
Project	**Mechanism**	**Prior status**	**Source**
RG6125	Anti-cadherin-11 MAb	Phase II	2015 Adheron Therapeutics acquisition, $105m up front
Emactuzumab	Anti-CSF-1R MAb	Phase I	In-house project
RG7990	Anti-IL-13 & IL-17 MAb	Phase I	Licensed from Novimmune in 2010
RG6029	NaV 1.7 sodium channel blocker	Phase I	2011 research collaboration with Xenon Pharmaceuticals
RG7741	Chk 1 inhibitor	Phase I	Licensed from Array Biopharma for $28m up front in 2011
Source: Roche presentation.			

Troubling while this might be, Roche might argue that it is at least failing fast: all of these are all relatively early-stage projects. And Roche investors will be far more worried by another of the group's revelations today, namely that concerning Tecentriq itself.

On an analyst call Roche's head of pharma, Daniel O'Day, said the result of Tecentriq's Impassion-130 study in first-line triple-negative breast cancer was driven by PD-L1-positive patients. The trial is known to have read out positively for progression-free survival, but all other data were being held back for this weekend's Esmo meeting in Munich.

This makes Mr O'Day's disclosure unusual, and perhaps he was trying to rein in analysts' expectations, which are known to be significant. Indeed, some on the sellside expect Impassion-130, scheduled to be presented at Esmo's presidential symposium on Saturday, to be the highlight of the entire conference (*Esmo 2018 preview – Another first-line renal cancer showdown, October 2, 2018*).

The key question now must be the extent to which the Impassion-130 data are driven by PD-L1-positives. If, for instance, virtually no effect is seen in patients whose tumours do not express this biomarker this could seriously cut down Tecentriq's market opportunity in this highly intractable cancer type.

Indeed, Roche had already raised eyebrows when pegging Tecentriq's peak sales here at between SFR500m ($504m) and SFR1bn, a seemingly small amount given the opportunity. If only part of the market is addressable this could explain the conservatism, though Mr O'Day would not be drawn on the matter.

Pressed further, he refused to shed further light on the strength of Impassion-130, but instead pointed to Tecentriq's potential in SCLC and non-squamous NSCLC, and recent readouts in these indications, which he said were equally important.

Investors only have three more days to wait, but with the stock off 3% today the breast cancer revelation will have done little to ease their anxiety levels.