Evaluate Vantage

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Snippet roundup: A hit for St. Jude, a knockback for Dynavax and dubious data for Corbus

Edwin Elmhirst

Welcome to your weekly roundup of EP Vantage's snippets – short takes on smaller news items.

This week, November 14-18, 2016, we had thoughts on the following: HeartMate 3 hits for Abbott; Dynavax approval hopes dashed yet again; Corbus's phase II data cut raises hopes and red flags alike; Cardiorentis gets ularitide data out on the third opportunity; SITC – Bristol goes two for three in immuno-oncology combos; PTC's European relief only temporary.

HeartMate 3 hits for Abbott

November 17, 2016

The newest iteration of the HeartMate pump – developed by Thoratec, now owned by St. Jude Medical, and soon to belong to Abbott Laboratories – is odds-on for US approval following a hit in its pivotal US trial. The Momentum 3 trial showed that at six months, 86% of patients on the HeartMate 3 left ventricular assist device (LVAD) survived without disabling stroke or re-operation, compared with 77% of patients given the HeartMate II, the 3's precursor. Perhaps as importantly, there were no cases of blood clots with the HeartMate 3 versus 18 incidents with the II. The HeartMate II is the only LVAD approved for both bridge-to-transplant and destination therapy options in the US; if the 3 can follow this path it could boost sales nicely. That revenue will almost certainly go to Abbott rather than St. Jude; Abbott's $25bn acquisition of the Minnesota company is due to close by the end of this year.

Now St. Jude's, soon to be Abbott's: Thoratec's forecast performance

	2016	2016	2017	2018	2019	2020	2021	2022
WW annual sales ($m)	136	598	674	720	774	846	914	956
Growth per year (%)	-	340%	13%	7%	8%	9%	8%	5%
Change per year ($m)	-	+462	+76	+46	+54	+72	+68	+42

Source: EvaluateMedTech

Dynavax approval hopes dashed yet again

November 15, 2016

Dynavax is clinging on to hope that a second complete response letter for Heplisav-B represents merely another delay, but investors have understandably flocked for the exit. Shares in the company plunged 65% yesterday to an eight-year low. It seems that the FDA has not yet fully assessed the company's new data package, submitted to address concerns raised in a 2013 complete response letter; the company ran a huge 8,400-patient trial to assess the safety and immunogenicity of its project to satisfy the regulator. In a press release it said ongoing areas of interest were specific adverse events – the FDA has previously been concerned about autoimmune disorders – and a numerical imbalance in cardiac events, a new signal that is particularly worrying. Dynavax hopes that the review will be complete in six months, but until the outcome is known any hopes of finding a partner or raising money – both priorities for the group – are dashed. A happy ending to this long-running saga looks less and less likely.

Corbus's phase II data cut raises hopes and red flags alike

November 15, 2016

As a tool to help raise much-needed cash, Corbus's phase II trial of JBT-101 in systemic sclerosis can be considered a success – shares surged 52% yesterday. As a tool to draw rigorous conclusions on the project's potential the data are much less useful. Aside from the standard cautionary statements associated with phase II data such as small sample size, red flags include: the company's decision to de-emphasise 12 week data – on which the primary endpoint is based – in favour of apparently more impressive 16 week data; imbalances in the health of patients and their background medications between the active and placebo arms; the use of a modified intent to treat population; and the use of a novel disease assessment score to generate the results.

On a conference call the trial's lead investigator was not shy with bullish statements about the "breathtaking" results and potential for a short phase III study. However, anything beyond cautious optimism looks unwarranted, particularly when considering that JBT-101's mechanism of action is far from established. Topline results in cystic fibrosis, due in the first quarter of next year, will provide further important insight.

Cardiorentis gets ularitide data out on the third opportunity

November 15, 2016

Cardiorentis has confirmed what was already believed to be the case: its intravenous natriuretic peptide ularitide failed to reduce cardiovascular death in patients with acute decompensated heart failure versus placebo. The removal of the findings of the 2,157-patient True-AHF trial from the American College of Cardiology programme in April hinted at a primary endpoint miss, so when the data finally emerged as a late-breaking clinical trial at the American Heart Association meeting this weekend it came as little surprise. Investigators pointed to short-term biomarker improvements such as a reduction in blood pressure and incidence of worsening heart failure during the infusion period as points for further exploration, but the outcomes data show that this in-hospital treatment has no long-term benefit. Cardiorentis raised SFr60m ($60m) in January to support commercial operations for ularitide, but has not stated its next steps given the negative data.

Global sales outlook for heart failure drugs ($m)

	2016	2017	2018	2019	2020	2021	2022
Entresto	203	636	1,291	2,112	3,001	3,916	4,698
Reasanz	-	56	284	573	932	1,266	1,549
Corlanor	63	163	262	376	461	519	566
Vericiguat	-	-	-	-	83	197	294
Finerenone	-	-	-	-	55	141	252

Source: EvaluatePharma

SITC – Bristol goes two for three in immuno-oncology combos

November 14, 2016

Novel immune checkpoint inhibitors have been slow to emerge, but based on data presented at the SITC meeting over the weekend Bristol-Myers Squibb can boast about adding anti-Kir or anti-Lag3 mechanisms to PD-1 inhibition. No such luck for its anti-CD137 MAb urelumab, which in combination with Opdivo showed little beyond some responses in melanoma. In head and neck cancer Opdivo combined with Innate Pharma's anti-Kir MAb lirilumab showed hints of activity above that of Opdivo monotherapy, and Innate's stock has now risen about 17% in the past three days; lirilumab's all-important monotherapy Effikir trial, in AML, reads out in early 2017. There could also be excitement about Opdivo's combo with the anti-Lag3 MAb BMS-986016, and remarkably the SITC data look like the first clinical results of the anti-Lag3 mechanism. Perhaps for this reason Bristol is cagey: the SITC poster only details three case reports to back efficacy both as monotherapy and in combination. However, a relatively high rate of patient discontinuations due to disease progression in BMS-986016 monotherapy arms hint that combinations might well be the way forward here.

Selected Opdivo combination studies presented at SITC

Combo project	Mechanism	Setting	Data
Lirilumab	Anti-Kir MAb	Squamous head & neck cancer (41 pts, 29 evaluable)	24.1% ORR, driven by PD-L1 positive pts, versus 13.3% ORR for Opdivo alone in Checkmate-141 study (240 pts)
BMS-986016	Anti-Lag3 MAb	Solid tumours (80 pts) & B-cell malignancies (42 pts)	Supports clinical activity, but monotherapy case reports limited to 1 PR in PD-1-refractory NSCLC and 1 CR in B-cell lymphoma
Urelumab	Anti-CD137 MAb	Various (159 pts)	50% ORR in PD-1-naive melanoma, but efficacy over Opdivo monotherapy hard to interpret; some liver enzyme elevation

PTC's European relief only temporary

November 14, 2016

PTC Therapeutics looks set to hold onto the conditional European approval for its Duchenne muscular dystrophy (DMD) therapy Translarna – for now. The project is in limbo, with permanent EU approval, as well as a decision from the FDA, seemingly dependent on new data. Investors pushed PTC's stock up 88% on Friday on the CHMP recommendation for renewal of Translarna's conditional European approval, but it is hard to see that much has changed, with the company now on the hook for a new 18-month study that will not see results until 2021. And, with the previous phase III Act DMD trial failing to meet its primary endpoint, a positive outcome is far from assured. PTC is also facing an uphill battle in the US, where Translarna has received a refuse-to-file letter; the FDA rejected the group's appeal in October. PTC has said it plans to escalate its appeal, and seems to be taking a leaf out of rival Sarepta's book by requesting an advisory committee meeting that would include patient representatives. The FDA, however, might want to avoid another highly charged panel and instead prefer to see more data on Translarna before making its decision.

These snippets were previously published daily via twitter.

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