Evaluate Vantage

October 20, 2017

Snippet roundup: Insulet, Dexcom and Gilead try clever pricing strategies

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

This week, October 16 to 20, 2017, we had thoughts on the following: Insulet and Dexcom make a special offer; Durect feels more pain; Uniqure moves to FIX its haemophilia B gene therapy; Yescarta approval sets up new CAR chase; backing for semaglutide sets up Novo vs Lilly battle; double whammy for J&J's "blockbuster" pipeline; no relief as Probiodrug moves nearer to cash call; Warp Drive accelerates with Roche deal.

These snippets were previously published daily via twitter.

Insulet and Dexcom make a special offer

October 20, 2017

Johnson & Johnson getting out of the insulin pump space earlier this month should have been good for its smaller rivals. But the company opted to guide its ex-customers towards the biggest of all, Medtronic, under a doubtless lucrative partnership agreement. Insulet and Dexcom, finding themselves cut out of the action, have banded together to offer users of J&J's now-unavailable Animas and OneTouch devices a free trial of Insulet's Omnipod pump plus a $200 voucher that can be used towards the purchase of a Dexcom G5 continuous glucose monitor (CGM). This might persuade insured patients with a smallish co-pay, but it probably will not lure those who pay out of pocket: the G5 transmitter and receiver together cost nearly $2,000. In any case the deal between J&J and Medtronic will still probably ensure that most of the 90,000 or so former J&J customers are scooped up by Medtronic. And there might be further shifts to come: J&J is also considering selling or spinning off its Lifescan unit, which makes CGMs. It would not be surprising if a deal of some kind with Medtronic were to materialise here, too.

Insulin pumps: the main players

	WW Sales ($m)		
Company	2016	2022	CAGR
Medtronic	644	1,062	8.7%
Insulet	302	784	17.3%
Johnson & Johnson	308	315	0.4%
Tandem Diabetes Care	62	140	14.4%
Cellnovo	1	29	71.6%

NB: Estimates pre-date J&J leaving the market. Source: EvaluateMedTech.

Durect feels more pain

October 20, 2017

Just when things were looking up for the speciality group Durect a phase III failure has brought it crashing down to earth. Yet again the culprit has been its long-acting bupivacaine formulation Posimir, which failed to beat standard bupivacaine in post-surgical pain, sending the company's stock down 50% in premarket trading today. Were it not for Durect signing up Novartis's Sandoz division as its Posimir partner in May – sparking an impressive run-up into the pivotal readout – the failure would have been less surprising. Durect had crashed in 2014 when the US FDA rejected its Posimir filing citing lack of safety data, and that was two years after the asset failed to show efficacy in a phase III trial in abdominal surgery. The sellside by now seems to have lost patience: today Stifel analysts removed Posimir from their models, and raised doubts about Durect's balance sheet and ability to finance another asset, DUR-928, for primary sclerosing cholangitis. They also expect Sandoz to hand back Posimir rights in the coming days; if this happens Sandoz will join Takeda and Hospira as previous licensees that have decided to ditch Posimir.

Uniqure moves to FIX its haemophilia B gene therapy

October 19, 2017

Uniqure had risked falling behind its haemophilia B gene therapy rival Spark Therapeutics, but will hope that its

latest move will bring it level. Uniqure has ditched its first-generation project AMT-060 in favour of a new contender, AMT-061, which interestingly it insists will inherit the former's US IND and breakthrough therapy designation. AMT-061 could be more effective in triggering factor IX (FIX) activity and give Spark and Pfizer's SPK-9001 a run for its money; the lacklustre efficacy previously seen with AMT-060 was thought to be down to the fact that it encoded wild-type FIX, while SPK-9001 uses a mutated version called Padua FIX. AMT-061 also encodes Padua FIX, and Uniqure believes that the AAV5 vector employed could avoid capsid-related immune responses that have been flagged as a potential problem with SPK-9001. Uniqure's claims will soon be put to the test, with AMT-061 set to begin a pivotal trial next year – the group also said it had just acquired a patent family covering the FIX Padua mutation. Uniqure's stock was up as much as 60% this morning.

DNA/RNA therapeutics in haemophilia B

Phase III		
Fitusiran*	Alnylam Pharmaceuticals	Anti-thrombin III RNAi therapeutic
Phase II		
AMT-061	Uniqure	Factor IX gene therapy
SB-FIX	Sangamo Therapeutics	Factor IX gene therapy
SPK-9001	Spark Therapeutics	Factor IX gene therapy
Haemophilia B Gene Therapy	Freeline Therapeutics	Factor IX gene therapy

*Future uncertain after safety suspension.

Yescarta approval sets up new CAR chase

October 19, 2017

With the second FDA-approved CAR-T therapy, now known as Yescarta, Gilead has undercut its rival Novartis. Yescarta will have a US list price of $373,000, versus $475,000 for Novartis's Kymriah, although there are important differences. For one, Yescarta is approved for adults with relapsed or refractory diffuce large B-cell lymphoma, a much bigger indication than relapsed/refractory paediatric acute lymphoblastic leukaemia, for which Kymriah has the go-ahead. And Gilead does not appear to have followed Novartis's lead in proposing outcomes-based pricing – the latter has pledged not to charge for Kymriah if a patient does not respond after one month. The objective response rate for Yescarta, according to its label, is 72% – below the 82% previously disclosed from the Zuma-1 trial via an investigator-assessed rather than independent review. Yescarta could have an addressable market of nearly $3bn, meaning that the $11.9bn that Gilead spent on its originator, Kite Pharma, might soon begin to pay off.

Yescarta vs Kymriah

	List price per person ($)	Average price incl. refunds ($)	Addressable patient population	Potential market ($m)	2022e sales ($m)
Yescarta	373,000	373,000	7,500	2,798	983
Kymriah	475,000	427,500*	620**	265	945

*Based on estimates that ~10% of Kymriah patients do not respond within one month; **Based on estimates that up to 20% of childhood ALL patients relapse.

Backing for semaglutide sets up Novo vs Lilly battle

October 19, 2017

The unanimous US FDA advisory committee vote backing approval of semaglutide should help Novo Nordisk retain its number-one position in the GLP-1 agonist space. The Danish group's once-daily GLP-1 Victoza is slowly being eclipsed by Lilly's once-weekly product Trulicity, but once-weekly semaglutide gets Novo back on terms with its diabetes rival. The FDA's staff had raised concerns about the increased risk of diabetic retinopathy complications in patients taking semaglutide, but these do not look likely to hold back approval. The adcom discussion centred on the theory that rapid reductions in blood sugar could cause retinopathy complications in the short term, as well as the more common occurrence of complications in those patients with retinopathy at baseline. Should the FDA follow through on approval, semaglutide could be on track for global sales of $2.4bn by 2022, according to *EvaluatePharma* sellside consensus.

Top GLP-1 agonists for diabetes

		WW sales ($m)	
Product	**Company**	**2016**	**2022**
Trulicity	Eli Lilly	926	3,872
Victoza	Novo Nordisk	2,979	3,295
Semaglutide	Novo Nordisk	-	2,422
Bydureon	AstraZeneca	578	711
Semaglutide Oral	Novo Nordisk	-	707

Source: EvaluatePharma

Double whammy for J&J's "blockbuster" pipeline

October 17, 2017

Johnson & Johnson's third-quarter results exceeded analyst expectations – but the group is storing up future problems for its pharma division, ditching two projects it had previously touted as potential blockbusters. One, the Xencor-derived anti-CD123 MAb talacotuzumab, is noteworthy firstly because among the industry's CD123-targeting assets it was the most advanced, and secondly because it was not the one that had caused J&J problems earlier. That dubious distinction belonged to a CD123 bispecific, the Genmab-partnered JNJ-63709178, which spent seven months on clinical hold. Of course, targeting CD123 is known to be problematic

because of off-tumour effects. J&J today said interim phase III results in AML did not support talacotuzumab's benefit/risk ratio, but it has not ruled out continuing development in other indications. Meanwhile, the company's decision to can the rheumatoid arthritis candidate sirukumab, or Plivensia, comes as less of a surprise, after an FDA complete response letter asking for more data – J&J's head of pharma, Joaquin Duato, said the delay had spurred it to focus on other priorities. Plivensia's *EvaluatePharma* consensus forecast has come off since August, but it had still been expected to bring in $875m by 2022.

CD123-targeting projects in development (all for AML)

Project	Company	Mechanism	Notes
Phase III			
Talacotuzumab	Xencor /J&J	MAb	Trial scrapped; J&J evaluating data to determine further steps
Phase II			
SL-401	Stemline Therapeutics	Protein/drug conjugate	Two deaths in BPDCN cohort despite protocol modification
Phase I			
UCART123	Cellectis	Allogeneic CAR-T	2 phase I trials on hold after death of first patient treated
MB-102	Fortress Biotech /Mustang Bio	Autologous CAR-T	
MIH911	Novartis	Autologous CAR-T	Study terminated for "lack of funding"
SGN-CD123A	Seattle Genetics	Antibody-drug conjugate	
Flotetuzumab	Macrogenics	Bispecific MAb	
JNJ-63709178	Genmab /J&J	Bispecific MAb	Put on clinical hold Sep 2016 (lifted Apr 2017); several study sites withdrew
XmAb14045	Xencor	Bispecific MAb	
SQZ622	Novartis	Bispecific MAb	
KHK2823	Kyowa Hakko Kirin	MAb	

Source: EvaluatePharma

No relief as Probiodrug moves nearer to cash call

October 16, 2017

An upbeat statement from Probiodrug, claiming to have initiated the phase IIb stage of its Alzheimer's disease project PQ912, has failed to stem the losses in the group's share price. Perhaps this is because the phase IIb trials in question have not actually started. Rather, all that has happened is that Probiodrug has signed up Julius Clinical, a clinical research organisation, to run the studies whenever the money needed for them to begin is raised; while the likely cost is not spelled out, Probiodrug ended its first half with just €14m in the bank. Its stock crept up 4% today, but still stands off 18% since the first phase II study, Saphir, yielded mixed results in June. While Probiodrug insists that Saphir was positive – there was no safety difference for PQ912 versus placebo, though more active-arm patients discontinued, and an efficacy signal has yet to be seen – the fact that two more confirmatory phase II trials are needed before starting pivotal development shows how slowly PQ912, a glutaminyl cyclase inhibitor, is moving. The latest developments probably do little beyond reminding the markets of Probiodrug's need to raise more money imminently.

Warp Drive accelerates with Roche deal

October 16, 2017

Any worries about the sales potential of new antibiotics do not seem to have affected Warp Drive Bio, which today signed a deal with Roche worth $87m up front. The companies hope to develop novel antibiotics against multidrug-resistant pathogens, but have not given specific details about what targets they are looking at. This appears to be a bit of a gamble by Roche: little is known about the privately held Warp Drive, which claims to harness the "molecules and mechanisms of nature" to discover antibiotic classes that have never been analysed before, mining a database of 135,000 microbial genomes to uncover gene clusters that encode potential new drugs. Roche could shell out another $300m in milestones if the project, which presumably is still at a very early stage, is successful – but there is still a question mark over who might pay for new antibiotics, which could be kept as a last line of defence. Warp Drive already has agreements in place with Glaxosmithkline in oncology and with Sanofi covering aminoglycoside antibiotics. Life remains tough for many antibiotic developers, but Warp Drive has shown that there is money to be made even in this tough sector.

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