Evaluate Vantage

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Snippet roundup: Ash cash rolls in, Voyager boldly goes, but Northwest heads south

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

This week, December 5-9, 2016, we had thoughts on the following: Acelity yanks billion-dollar IPO; Northwest heads for the bulletin boards; Voyager boldly goes into Parkinson's gene therapy; Trump shoots from hip, crushing biotech relief rally; Cures bill set to become law; only happiness around Sage's postpartum depression drug; cash calls are heard as Ash conference doors close; surprise Teva departure ups the ante for crucial February update; Nordic Nanovector: Algeta redux?; good should be enough for GW's Epidiolex; Lilly's sweet Jardiance label win.

Acelity yanks billion-dollar IPO

December 8, 2016

If Convatec can get a £1.47bn ($1.8bn) float away on the London exchange, why can't Acelity manage half that on the NYSE? Acelity announced its intention to float in August 2015, but has now cancelled the offering, which could have fetched $1bn, citing "current public market conditions". Certainly the US exchanges are volatile in the wake of Donald Trump's election as president, but post-Brexit London just played host to the biggest IPO in medtech history. A more likely scenario is that Acelity's private equity backers filed for the float in the hope of flushing out an acquirer. No one bit, and now the woundcare group and its owners must find another way of paying down debt, which includes $1.7bn in 10.5% second-lien senior secured notes that come due in 2018 and $610m 12.5% senior notes due in 2019. The company had total debt of $4.9bn at the end of June 2015.

The five biggest medtech IPOs

Date	Company	Amount raised ($m)	Discount/ premium	Exchange	Focus
October 26, 2016	ConvaTec	1,948	(10%)	LSE	Drug delivery; wound management
July 1, 2015	Natera	180	13%	Nasdaq	In vitro diagnostics
March 14, 2014	Castlight Health	178	14%	NYSE	Healthcare IT
February 3, 2011	Tornier	166	(5%)	Nasdaq	Orthopaedics
October 2, 2015	Novocure	165	(6%)	Nasdaq	Neurology

Source: EvaluateMedtech

Northwest heads for the bulletin boards

December 8, 2016

The lifecycle of Northwest Biotherapeutics is now complete with the Maryland-based company's irrevocable upcoming de-listing from the Nasdaq stock exchange. Northwest said it was removing itself because the exchange refused to accept its plan to comply with Nasdaq rules regarding investor approval for selling shares below market value. Such transactions took place earlier this year. Shares had been below Nasdaq's minimum share price threshold of $1 since May, and have been on a decline since the group, in August 2015, announced its phase III glioblastoma trial of DCVax-L had stopped screening patients. It is an open question whether institutional investors like Woodford Investment Management, which owns a 21% stake, can continue to own Northwest. Shares are down 29% in early trading.

Voyager boldly goes into Parkinson's gene therapy

December 8, 2016

The gene therapy specialist Voyager Therapeutics saw its stock leap 38% post-market after its lead asset, VY-AADC01, posted promising early results in Parkinson's disease. Sentiment has no doubt been helped by the fact that the mainstay of treatment, levodopa, is far from the perfect drug, with efficacy wearing off as the underlying disease worsens. Voyager hopes to combat this by using gene therapy to replace aromatic L-amino acid decarboxylase, the enzyme that converts levodopa into dopamine. The company presented data from the first two dosing cohorts in a phase Ib study up to 12 months after dosing, and found signs that the treatment was having the desired effect – including improvements in measures of motor function, as measured by the UPDRS. Patients on a higher dose performed better than those in cohort one. Voyager plans to complete enrolment in cohort three in early 2017, and is set to report six-month data from this, as well as longer-term data from cohorts one and two, in mid-2017. It also plans another study using a slightly different surgical delivery technique, in the first quarter. A pivotal trial of the Sanofi-partnered project should start in Q4 2017.

Top-five Parkinson's disease products in 2022

Product	Company	Description	Status	2022e sales ($m)
Nuplazid	Acadia Pharmaceuticals	Antipsychotic for Parkinson's-related psychosis	Marketed	1,014
Mirapex ER	Boehringer Ingelheim	Dopamine D3 agonist	Marketed	727
Duopa	Abbvie	Dopamine precursor & dopa decarboxylase inhibitor	Marketed	640
CVT-301	Acorda Therapeutics	Dopamine precursor	Phase III	445
Rytary	Impax Laboratories	Dopamine precursor & dopa decarboxylase inhibitor	Marketed	317

Source: EvaluatePharma

Trump shoots from hip, crushing biotech relief rally

December 8, 2016

Biotech shares slumped Wednesday after President-elect Donald Trump, in an interview with Time magazine, said, "I'm going to bring down drug prices. I don't like what's happened with drug prices." Mr Trump's election had led to a "relief rally" as it was feared that his Democratic rival, Hillary Clinton, would take action to control drug prices. But yesterday the Nasdaq biotechnology index fell 3%, hitting a post-election low, and the S&P Pharmaceuticals index fell 2%. At one point during his presidential campaign, Mr Trump had expressed support for allowing Medicare to directly negotiate drug prices as Ms Clinton had, although his general election campaign only mentioned drug re-importation as a means to control drug prices. Beyond the re-importation proposal and a vague promise to act on drug prices, Mr Trump has said nothing about how he would fulfil his statement. However, that a mere mention of drug prices can shake the faith of biotech investors shows that the issue is still potent. Furthermore, the risks from the repeal of the Affordable Care Act and the potential loss of healthcare coverage for millions of Americans has not been taken into account as much by biopharma investors as it has for those of for-profit hospital companies, which have seen double-digit losses in the last month.

Cures bill set to become law

December 8, 2016

The pro-pharma 21st Century Cures Act cleared its final US legislative hurdle and looks headed toward enactment within days. The US Senate voted 94-5 yesterday, following an overwhelming vote in the House of Representatives last week, and President Barack Obama has said he will sign it into law. The legislation gives the NIH $4.8bn in new spending authority to back the cancer "moonshot" and precision medicine initiatives, creates an accelerated FDA approval pathway for regenerative medicines, and mandates that FDA review trial designs to allow for greater use of biomarker endpoints and novel statistical design. Funding for the programmes will be derived by, over 10 years, stripping $3.5bn from a federal public health fund, $1bn from selling off some of the government's strategic petroleum reserve, and $660m from cutting Medicare reimbursement for drugs delivered via durable medical equipment. The legislation has raised concerns among some lawmakers and industry critics that it would relax FDA drug approval standards at the cost of weakening national efforts on disease prevention, and comes at a time when consumers are angry about the rising costs of drugs.

Only happiness around Sage's postpartum depression drug

December 7, 2016

At one point it had looked as if the readout of data for Sage Therapeutics' lead project in a rare epileptic disorder was going to be a defining moment. Instead news that the FDA could be prepared to allow it to file Sage-547 in postpartum depression using phase II data from ongoing studies has catapulted the also-ran indication into the forefront of investors' minds. The decision from the US regulator has other implications. By avoiding the need for a phase III trial Sage-547 could be launched almost a year early – potentially at the start

of 2019. This is a big win given that it could face generic competition as early as 2024. Luckily the group has a follow-on oral compound in the form of Sage-217, which is also being studied in postpartum depression and Parkinson's disease – and more importantly has patent protection out to 2034. Shares in Sage, which have risen 66% in the past six months, could get another lift in the first half of 2017 when phase III data for '547 read out in super refractory status epilepticus.

Cash calls are heard as Ash conference doors close

December 7, 2016

Two big beneficiaries of advances in haematology moved quickly to capitalise on strong share price gains this week, albeit on different continents. With the Ash conference only just over, it would not be surprising to see more offerings emerge in the coming days. Bluebird Bio, which touched a one-year high this week on the back of impressive early data in multiple myeloma (albeit presented outside the Ash arena) is hoping to raise $250m on Nasdaq. It wants the money to fund further trials of bb2121 and possibly exercise an option to co-develop and co-promote the CAR-T project in the US; partner Celgene has indicated an interest in buying $50m of the new shares. Cash will also be used to take a new anti-BCMA candidate into phase I and fund a phase III trial of its gene therapy, Lentiglobin. In Norway, Nordic Nanovector is seeking $60m; it wants to fund a phase II combination study of its antibody-radionucleotide conjugate Betalutin with Rituxan. The former targets CD37 and the latter CD20, and the company presented encouraging preclinical data at Ash showing a strong synergistic effect of the two approaches in NHL.

Surprise Teva departure ups the ante for crucial February update

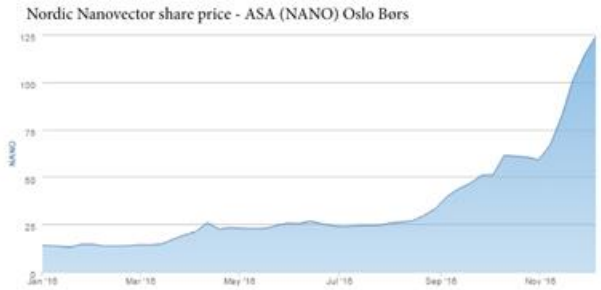
December 7, 2016

For a company struggling to rebuild investor confidence the surprise departure of a well-respected executive will never be taken well. A case in point is Teva, which yesterday saw its stock drop 5.4% on news of the retirement of Siggi Olafsson, head of its huge generics arm and a key architect the $40bn Allergan business buyout. Shareholders are clearly worried that his departure signals more than a desire to spend extra time at the golf club – an understandably pessimistic stance considering that this year Teva shares have slid a disastrous 48% as the company delivered delayed product launches, manufacturing issues and, like its peers, generic drug price erosion. Many remain to be persuaded that Teva did not overpay for the Allergan unit, and what looks like a sprint for the exit by an executive with crucial insight and experience at both his current employer and Actavis, the source of a large part of the generics unit, does nothing to assuage these concerns. The company insists that guidance for 2016 remains intact, but all eyes are on next year and beyond – guidance for 2017 will be updated in February and many already expect numbers to be reined in. With a huge debt pile to service, signs that cash flow is weakening will be even more painfully punished.

Nordic Nanovector: Algeta redux?

December 6, 2016

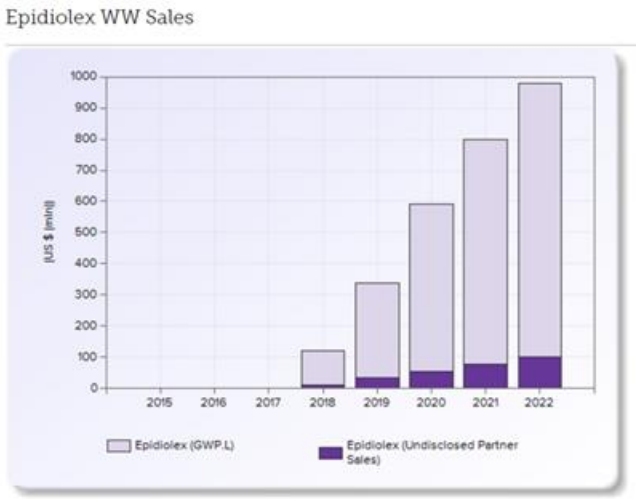
Given that Nordic Nanovector's shares have doubled since Ash abstracts were released at the beginning of November, the group looks to have been a major beneficiary of the huge US haematology conference. However, in reality the rally began several months before, ahead of data from the Lymrit 37-01 study of its lead asset, Betalutin. The antibody-radionucleotide conjugate targets CD37, a cell surface antigen present on B-cell lymphomas. The company revealed highly encouraging data from the ongoing study at Ash this week, with 63% of 35 relapsed follicular lymphoma patients registering a response, and 29% complete remissions. Data from a higher-dose arm will emerge in a couple of months, and if safety remains acceptable all patients will be switched to the new dose, which might also be used in a pivotal phase II study, pencilled in to start next year. NHL is a competitive space but new options are desperately needed for patients that fail to respond to the CD20-targeting agent Rituxan – local retail investors that have been instrumental in driving shares in the Oslo-based company higher are hoping that Betalutin will meet this need. They are also no doubt hoping that the story of Algeta will be re-told – several of Nanovector's executives were formerly with Algeta, which is now owned by Bayer, and indeed the two companies still share the same car park in Oslo.



Good should be enough for GW's Epidiolex

December 5, 2016

After all the enthusiasm some of the gloss was bound to come off GW Pharma's anti-epilepsy project Epidiolex. Results from the phase III trial in Dravet syndrome (DS) showed that the cannabinoid-based asset met its primary endpoint. But to the disappointment of some this was not quite the slam-dunk it scored in Lennox-Gastaut syndrome (LGS), and while showing positive results in cutting the total number of seizures it narrowly missed significance in seizure reduction from baseline. However, with no treatments currently available for DS in the US and Europe, regulators are likely still to be willing to give Epidiolex a chance to get to market. In terms of sales, the LGS population is much bigger than DS, so a hiccup here would have less of an impact. Sales forecasts for Epidiolex stand at $980m in 2022, according to consensus forecasts from *EvaluatePharma*. The only other cloud on the horizon could be the incidence of raised liver enzymes in 20% of patients. GW believes that this could be due to drug-drug interactions with valproate, which is already associated with sever hepatotoxicity.



Lilly's sweet Jardiance label win

December 5, 2016

After the beating Lilly got from the failure of solanezumab it was due some Christmas cheer. Santa, in the form of the FDA, late last week approved a label change for its diabetes drug Jardiance. The SGLT2 is now recommended for use in reducing the risk of cardiovascular death in adults with type 2 diabetes and cardiovascular diseases. The label change, a result of the Empa-Reg Outcome study, will at least for now give Jardiance a significant edge over its SGLT2 rivals, but perhaps not for long – Johnson & Johnson's Canvas

outcomes trial of Invokana is expected to read out next year. And those getting excited about the prospect of a huge uplift in sales from the Jardiance label change should remember one word – Entresto. Despite impressive CV credentials Entresto's roll-out has been slow and torturous. If practitioners are just as cautious about the new label from Jardiance any increase in sales will be a gradual affair. But this does at least show that Lilly has more cards up its sleeve than sola to drive growth.

SGLT2 Inhibitors

			WW sales ($m)		
Product	Generic Name	Company	2015	2022	CAGR
Invokana	canagliflozin	Johnson & Johnson/Mitsubishi Tanabe Pharma	1,313	3,340	14%
Jardiance	empagliflozin	Boehringer Ingelheim	114	3,068	60%
Farxiga	dapagliflozin propanediol	AstraZeneca/Ono Pharmaceutical	528	2,317	23%
Suglat	ipragliflozin L-proline	Astellas Pharma	61	397	31%
Ertugliflozin	ertugliflozin	Pfizer	-	283	n/a
Lusefi	luseogliflozin	Taisho Pharmaceutical Holdings	8	93	43%
Total			**2,024**	**9,498**	**25%**

Source: EvaluatePharma

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