Evaluate Vantage

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Snippet roundup: Transparency for Straumann but a black box for Pfizer

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

This week, August 14 to 18, 2017, we had thoughts on the following: Straumann sees a clear advantage in orthodontics; Besponsa's black box blunts Blincyto challenge; Advair generic substitutability and timing take centre stage again; Teva officially moves into Valeant territory; Ophthotech investors celebrate death of Fovista.

These snippets were previously published daily via twitter.

Straumann sees a clear advantage in orthodontics

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Straumann's decision to buy the clear braces maker Clearcorrect for $150m is, at first glance, rather a leftfield move for a group that specialises in dental implants. But between 30% and 40% of implant patients must have their teeth realigned before the implant procedure can take place, Straumann says, so there is a cross-selling opportunity. The use of clear braces is growing fast: the leading company in this segment, Align, has forecast annual sales growth of 15%, according to *EvaluateMedTech* consensus. Perhaps owing to the dominance of Align, Clearcorrect currently has a very small presence in the US – its market share is around 5% – but Straumann believes it can boost this significantly. Clearcorrect had global sales of $32m in 2016, but analysts from Stifel suggest that this might not grow as fast as Straumann likely hopes, writing that Clearcorrect has a more limited product portfolio than Align. They also point out that Straumann deals principally with dentists rather than orthodontists. Straumann is expanding in other directions too: it has also bought a 38% stake in Geniova Technologies, a Spanish manufacturer of aligners, and increased its stake in Dental Wings from 55% to full ownership for approximately $40m.

Straumann's M&A over the last five years

Date	Target	Target location	Deal type	Value ($m)	Financing Structure
August 17, 2017	Clearcorrect	USA	Company acquisition	150	Cash and shares
August 17, 2017	Dental Wings	Canada	Company acquisition	40	Cash and shares
August 17, 2017	Geniova	Spain	Minority stake	-	Cash and shares
June 14, 2017	Rapid Shape	Germany	Minority stake	-	-
November 30, 2016	Equinox Medical Technologies	The Netherlands	Company acquisition	-	-
April 24, 2015	Neodent	Brazil	Company acquisition	218	Cash
August 13, 2014	Rodo Medical	USA	Minority stake	2	-
December 31, 2013	Medentika	Germany	Minority stake	43	-
December 31, 2013	Createch Medical	Spain	Minority stake	-	-
June 1, 2012	Neodent	Brazil	Minority stake	271	Cash

Source: EvaluateMedTech

Besponsa's black box blunts Blincyto challenge

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Pfizer has bagged approval for its antibody-drug conjugate Besponsa, but a black box warning for liver damage could make it hard to wrestle market share away from Amgen's rival acute lymphoblastic leukaemia therapy Blincyto. Both products target patients with relapsed or refractory B-cell precursor ALL, and both are similarly expensive – Besponsa is said to cost $168,300 for a nine-week treatment course, while Blincyto was launched with a list price of $178,000. Still, Blincyto has its own black box warning for cytokine release syndrome and neurologic toxicities. And Besponsa is more convenient, being given on days 1, 8 and 15, while Blincyto is administered via 28-day continuous infusion. Both drugs could suffer with the entrance of CAR-T therapies, with Novartis's CTL019 expecting approval in paediatric ALL soon – but while remission rates with CAR-T are high these therapies are set to be even pricier. At least there are now more options for patients with ALL – which one comes out on top will likely depend on a mixture of efficacy, safety and cost.

Besponsa vs Blincyto

Product	Company	Mechanism of action	Date approved	Global sales ($m) 2016	2018e	2020e	2022e
Besponsa	Pfizer	Anti-CD22 antibody-drug conjugate	Aug 2017	-	134	255	347
Blincyto	Amgen	Anti-CD19 & CD3 bispecific BiTE MAb	Dec 2014*	115	188	259	308

**Accelerated approval – full approval followed in July 2017; Source: EvaluatePharma.*

Advair generic substitutability and timing take centre stage again

August 17, 2017

The differences in wording might have been subtle, but investors took the hint. Hikma stock slid 9% on what seems to have been a tacit admission that its generic version of Glaxosmithkline's blockbuster Advair might fall behind Mylan's rival. Both companies have been hit by US complete response letters, but until now they were broadly level-pegging. Hikma's partner Vectura has now put the cat among the pigeons, announcing that there were "no material issues regarding the substitutability of the device" – which sounds rather more cautious than Mylan's claim last week regarding its version: "We don't need any more data." For generics players direct substitutability is key to eating Advair's lunch, but this has proved tough owing to the complexities of Glaxo's device. Of course, Mylan might be being unrealistic, and no one knows the scope of any additional "non-material" trials, but Stifel analysts say the caution signals that Hikma and Vectura could slip behind Mylan. And there is another threat: Sandoz's own substitutable generic has been filed and has a second-quarter 2018 US FDA action date.

US contenders with generic versions of Advair

Project	Companies	Status
Airduo Respiclick*	Teva	Approved Jan 2017
Wixela Inhub	Mylan	CRL Mar 2017
Gx Advair	Hikma and Vectura	CRL Mar 2017
OT329	Sandoz (Novartis), via Oriel Therapeutics	Filed Jun 2017; PDUFA date Q2 2018

*Note: *not directly substitutable.*

Teva officially moves into Valeant territory

August 17, 2017

If you live like the debt-fuelled Valeant it is hard to avoid Valeant's fate, as Teva investors are fast learning. Reports from Bloomberg and Reuters suggest that Teva's generics unit Medis, and European oncology and pain assets might now be up for grabs, with Morgan Stanley and Bank of America already tasked with finding buyers for the last two. Thanks largely to the way acquisitions like that of Allergan's generics business, which presumably looked great at the time, were financed Teva now carries over $35bn of gross debt, accounting for a huge 67% of its enterprise value. Still, the problem is neither upcoming repayments nor apparently even covenants – Bernstein's Ronny Gal reckons that "only" $6bn of the total is subject to covenants – but rather the need to live within the new reality of generics pricing pressure and the impending loss of Copaxone, and for more of the company's value to be reflected in its equity. To avoid covenant breach Teva must reduce debt to 4.25x Ebitda – possible through $2bn of divestments and a $2bn improvement in operating cash flow, Mr Gal reckons. No doubt the deal bankers will win again.

Valeantisation: Teva's indebtedness

Maturity	Type of debt	Amount ($m)
2017	Revolving credit & bank facility	155
2017-20	Term loan (USD)	2,500
2018	Term loans (JPY & USD)	3,124
2018	Senior debt (USD & CHF)	2,284
2018	Debentures (USD)	15
2019	Senior debt (EUR & USD)	3,143
2019	Term loan (JPY)	312
2020	Senior debt (EUR & USD)	2,697
2021	Senior debt (USD)	4,208
2022	Senior debt (CHF & USD)	1,233
2022	Term loan (JPY)	521
2023	Senior debt (EUR & USD)	4,468
2024	Senior debt (EUR)	1,704
2025	Senior debt (CHF)	367
2026	Senior debt (USD)	3,491
2026	Convertible debentures*	514
2027	Senior debt (EUR)	798
2028	Senior debt (EUR)	849
2036	Senior debt (USD)	781
2046	Senior debt (USD)	1,984
Total debt at June 30, 2017		***35,148***

*Source: SEC filings; *exercisable at any time.*

Ophthotech investors celebrate death of Fovista

August 14, 2017

Ophthotech investors appear ready to write off nearly a half-billion dollars spent on the failed eye drug Fovista and focus on the next agent up. Shares rose 2% in early trading on the announcement that Fovista's final trial

in combination with Eylea or Avastin had failed to improve the visual acuity of patients with wet age-related macular degeneration (AMD) significantly compared with Eylea or Avastin monotherapy. This follows last year's failure in Lucentis combination trials, which wiped more than $1bn in market capitalisation in a single day. The asset is licensed to Novartis, but the Swiss group's investors likely assumed that it was a bomb when the Lucentis combo flopped. The Eylea/Avastin combo trial failure appears to guarantee that Ophthotech will spend no more of its $196m cash pile on Fovista and will instead use it for Zimura, an anti-complement factor C5a aptamer being tested in dry AMD patients with geographic atrophy and orphan eye diseases.

Ophthotech's Zimura strategy

Status	Indication	Details
Phase II/Phase III	Geographic atrophy secondary to dry AMD	Enrollment: 300 NCT ID: NCT02686658 Primary completion: 01/12/2018
Planned by end of 2017	Stargardt's disease Wet AMD (phase IIa) Idiopathic polypoidal choroidal vasculopathy (phase IIa)	-
Planned in 2018	Uveitis	-

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