Evaluate Vantage

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Pharma news over the Christmas period

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If the recent performance of biotech stocks prompted you to pull down the shutters until the New Year celebrations subsided here's what you might have missed.

Considering how much pain biotech investors suffered in the last three months of 2018, the fact that the Ishares Nasdaq biotechnology index lost only 10% over the whole year might be seen as a blessing.

As the new year gets under way many will be seeking out reasons for optimism, one of which is the continuing readiness of regulators to approve new drugs. Last week the Chinese FDA greenlit the country's second checkpoint MAb in the space of 10 days, for instance, while its US counterpart handed Portola a late present, enabling the group to celebrate New Year's Eve with a 14% stock increase.

December 31

Portola's approval related to the factor Xa inhibitor antidote Andexxa, whose solo US launch in June preceded a share price collapse. Monday's green light concerned a second-generation manufacturing process that Portola says will allow broad commercial launch, though specific plans will not be announced until January 8.

It was almost exactly a year ago that the US FDA delayed Andexxa's accelerated approval decision by three months, having already rejected the project once. Clearly things are looking up, though Portola could find that securing broad approval is only half the battle.

December 27

More good news also came two days earlier, with Harpoon Therapeutics flying in the face of negative biotech sentiment by filing to raise $86m in a Nasdaq IPO. The group's focus is on bispecific MAbs – a hot theme – though it is still unclear how much benefit its Fc domain-less constructs bring to the table.

As for the increasingly important Chinese market, the local FDA has its foot firmly on the accelerator. The day after Boxing Day the agency approved Innovent's anti-PD-1 MAb, sintilimab, having greenlit Shanghai Junshi's toripalimab on December 17.

Innovent has a broad alliance with Lilly, while Shanghai Junshi completed an IPO on the Hong Kong stock exchange, on the back of toripalimab and a follow-on PD-L1 inhibitor, JS003, on December 21. The moves mean that China suddenly has four approved anti-PD-(L)1s, with two more waiting in the wings.

Anti-PD-1/PD-L1 MAbs in China			
Drug	**Company**	**Indication**	**Status**
Opdivo (nivolumab)	BMS/Ono	2L NSCLC	Approved 15 Jun 2018
Keytruda (pembrolizumab)	Merck & Co/Taiho	2L melanoma	Approved 26 Jul 2018
Tuoyi (toripalimab)	Shanghai Junshi	2L melanoma	Approved 17 Dec 2018
Tyvyt (sintilimab)	Innovent Biologics	3L classical Hodgkin's lymphoma	Approved 27 Dec 2018
Camrelizumab	Jiangsu Hengrui	Classical Hodgkin's lymphoma	Awaiting approval
Tislelizumab	Beigene	Classical Hodgkin's lymphoma	Awaiting approval
Tecentriq (atezolizumab)	Chugai (Roche)	Various	Phase III
Imfinzi (durvalumab)	Astrazeneca	NSCLC, liver & urothelial cancers	Phase III
Bavencio (avelumab)	Pfizer/Merck KGaA	Head & neck cancer	Phase III
KN035	3D Medicines	Biliary tract cancer	Phase III
CS1001	Cstone Pharmaceuticals	NSCLC	Phase III
KL-A167	Harbour Biomed/Kelun	Classical Hodgkin's lymphoma	Phase II
TQB2450	Chiatiai Tianqing	Not disclosed	Phase II
ZKAB001	Lee's Pharmaceutical	Osteosarcoma	Phase I/II
JS003	Shanghai Junshi	Solid tumours	Preclinical
Source: Shanghai Junshi IPO document & EvaluatePharma.			

Less positive news was in store for Ziopharm, whose share price collapse forced it to issue an explanatory statement. The company is best known for teaming up with Intrexon to buy MD Anderson's Sleeping Beauty-based CAR-T technology for $100m, and then benefiting from Intrexon licensing this on to Merck KGaA; but in the subsequent four years negligible progress has been made.

Matters came to a head in October, when a management shake-up followed replacement of the Ziopharm/Intrexon tie-up with a new deal. The new arrangement gives Ziopharm rights to T cell receptor-based therapeutics and two CAR-T assets, including one against CD19, while Intrexon is to focus on other CAR applications of Sleeping Beauty.

On December 20 Merck KGaA pulled out of its end of the alliance, in return for $150m in Intrexon stock. As for clinical progress, investors are still waiting (*Ziopharm stalls its CAR yet again, June 19, 2018*). Even including a much-needed $50m private placement Ziopharm's pro forma cash stands at around $80m.

December 21

Earlier, several companies celebrated what looked like the US FDA's effort to tidy up its in tray: Acorda's inhaled levodopa, Inbrija, got the thumbs up, as did Stemline's much-maligned anti-CD123 construct, Elzonris, albeit only in the rare condition blastic plasmacytoid dendritic cell neoplasm (*Stemline patient death becomes secondary investors' problem, February 3, 2017*).

No such luck for Jazz, whose excessive sleepiness project solriamfetol is to be reviewed by March 20 after the FDA on December 21 deemed additional data to amount to a major amendment warranting a three-month delay. The asset, Jazz's pipeline lead, is expected to generate $489m of revenue in 2024, according to *EvaluatePharma's* sellside consensus.

On the same day Aimmune filed for US approval of its own lead, the peanut allergy project AR101, taking full advantage of the disaster unfolding at its competitor DBV Therapeutics, which two weeks ago pulled its US filing for Viaskin Peanut.

As the JP Morgan conference gets under way next week investors will look for more guidance from these and many other companies. The meeting tends to set the upcoming year’s tone for the sector, which in 2019 looks to be in particular need of good news.