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# Big Changes At Bayer With Animal Health Exit And 12,000 Jobs Cut

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**Bayer AG** has unveiled a huge restructuring program which includes the expected loss of 12,000 jobs and an exit from the animal health market.

Rumors have swirled around the animal health pillar of Bayer's operations for years and on a conference call, chairman Werner Baumann said that it is a unit that was "well positioned in an attractive industry which will continue to grow." However, he added that the "necessary investments to further develop this business are not available within Bayer given the priorities with our core areas," namely pharmaceuticals, consumer health and crop science.

Because of these priorities, Baumann said, "we are convinced that Bayer is no longer the best owner for animal health." A sale would appear to be the most likely option but the company limited itself to saying it is assessing available options for the exit.

The sweeping changes are not only affecting the animal health business and Baumann noted that having recently divested its prescription dermatology products to **Leo Pharma**, Bayer was "evaluating an exit" for its sun screen range Coppertone and Dr Scholl's foot care products. The company is also in conversations regarding the sale of its 60% stake in German site services provider Currenta. *(Also see "Deal Watch: LEO Pharma Expands Market Reach Through Bayer Dermatology Deal" - Scrip, 31 Jul, 2018.)*

## 900 PHARMA R&D JOBS TO GO

As for pharma, Baumann noted that there was going to be a restructuring of internal R&D and the resources freed up from the cuts will be put to "strengthening our investment into collaborative research models and external innovations." Some 900 jobs in pharma R&D will go and he added that "our future innovation model in pharmaceuticals will follow a simple principle: where an innovation comes from is less important than how we turn it into benefit for customers and patients."

He cited this week's FDA approval of Bayer and **Loxo Oncology Inc.**'s *Vitrakvi* (larotrectinib) as "a great example of how successful innovation can come about through external collaboration. That's exactly how we want to move forward." *(Also see "FDA Nod For Loxo/Bayer Tissue Agnostic Drug Marks Paradigm Shift In Cancer " - Scrip, 27 Nov, 2018.)*

Also, just a day after celebrating the European approval of its new hemophilia drug *Jivi*, Baumann noted that the area had "a significant increase in competition" of late and "to remain competitive in this segment," Bayer has decided not to utilize the Factor VIII facility it has built in Wuppertal, Germany, a move which will see 350 jobs go, and will focus all recombinant Factor VIII production in Berkeley in the US. *(Also see "Bayer's Hemophilia A Portfolio Boosted by Jivi's EU Approval " - Scrip, 28 Nov, 2018.)*

In total, the measures Bayer is taking will result in almost 10% of its 118,200-strong workforce being cut by the end of 2021, with a significant number of the jobs being lost in Germany. Of the 12,000 figure, 5,500-6,000 jobs in corporate functions, business services and country platforms will be slashed.

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## from the editor

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The latest company to announce restructuring, Bayer (see cover story), is following a trend in big pharma to reduce diversification of business areas. Others that have exited animal health include Elan and Pfizer, while Novartis this year took the decision to divest its Alcon eye care business. Like others, Bayer is also rationalizing its R&D, with the intention of sourcing more innovation from outside its own walls. The German major is no stranger to procuring external pipeline assets; indeed the TRK inhibitor it bought into via a 2017 deal with Loxo Oncology has just won US approval (see p8).

With the expanding scope and complexity of avenues to explore revealing exciting new possibilities in R&D, big pharma is having to change its business models. Now more than ever it needs to be selective about where it puts its R&D dollars, seeking to excel in a narrower range rather than spreading its bets widely. And having doubled down, companies need to reach out across the wider biopharma universe to identify the most relevant cutting edge science and access it. Bayer is not the only one that needs to sign new deals: it's a constant imperative across big pharma.

Fragmentation is both a weakness and a strength for this sector. The rich ecosystem of different entities engaged in R&D is a defense against tunnel vision and dead ends. But as big companies shuffle and prune their packs, new combinations will begin to make commercial sense. Companies bulking up through M&A in their chosen therapeutic areas will enable more efficient exploitation of end markets.

Scrip

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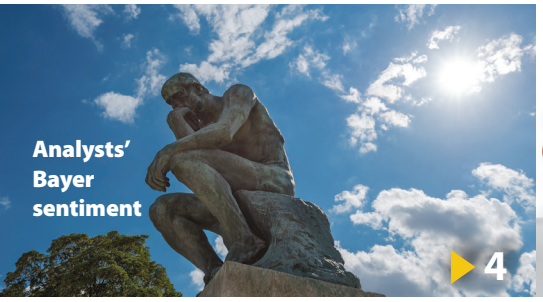




## exclusive online content

**Novartis's Blockbuster Gilenya Cleared For Children And Adolescents In Europe**
https://bit.ly/2Qb2sqd
Novartis's blockbuster MS drug is now approved for children and adolescent use in the EU as well as the US, as the big pharma continues to build its MS franchise in advance of the start of generic competition to Gilenya, expected sometime after mid-2019.

**Vertex's CF Three-Drug Combo Excels In Phase III, But Filing Depends On Second Regimen's Results**
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**Is Alkermes' Schizophrenia Data Enough To Drive Demand?**
https://bit.ly/2PgJ9Xj
Alkermes showed that combo pill ALKS 3831 offers a better weight gain profile compared to olanzapine in schizophrenia patients, but analysts differed on whether the benefit would be great enough to drive demand against entrenched generics.

**What's Keeping Korea From Becoming A Digital Healthcare Power?**
https://bit.ly/2Ed4UpN
While digital healthcare start-ups are increasingly being established in South Korea, strict regulations and a limited market environment are keeping them from adopting innovative ideas and technologies to rapidly catch up with global competitors. A recent report on digital healthcare suggests what issues need to be resolved to improve the situation.

**European Loan Funds F2G's Late-Stage Novel Antifungal**
https://bit.ly/2QAoWAz
€24m loan from the European Investment Bank with match funding will progress Phase IIb antifungal Olorofim in invasive aspergillosis. CFO Ralf Schmid goes into details with *Scrip*.

**Deal Watch: PDS And Edge Merge To Progress HPV-Linked Cancer Immunotherapy**
https://bit.ly/2KAJiEq
Immunotherapy firms Edge and PDS announce planned merger, while Telix advances its prostate cancer strategy by acquiring ANMI. Kyowa Hakko Kirin is signed up to distribute GlaxoSmithKline's Phase III CKD-associated anemia product daprodustat in Japan.

# inside:



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These changes "are necessary and lay the foundation for Bayer to enhance its performance and agility. With these measures, we aim to take full advantage of the growth potential for our businesses," said Baumann. He added that "we are aware of the gravity of these decisions for our employees. As in the past, we will implement the planned measures in a fair and responsible way."

'Through the end of 2022 alone, we aim to invest a total of around €35bn in our company's future, with R&D accounting for over two-thirds of this figure,' – Werner Baumann, Bayer chairman

## SYNERGIES

Baumann stressed that the decisions were not made necessary by the recent controversial acquisition of seeds giant Monsanto "and certainly not by glyphosate litigation in the US", referring to closely watched legal cases involving cancer claims about use of Monsanto's weedkiller *Roundup*. He went on to say the restructuring moves "extend beyond the commitments we've made as part of the integration. They represent the right step for our company and they position us for the future, as a leader across all of our core life science businesses."

Including the synergies expected from the acquisition of Monsanto, Bayer expects the restructuring to be worth around €2.6bn a year from 2022. "Through the end of 2022 alone, we aim to invest a total of around €35bn in our company's future, with R&D accounting for over two-thirds of this figure," Baumann added.

More details will be unveiled at what promises to be a keenly-anticipated capital markets day in London next week (Dec. 5).

*Published online 29 November 2018*

# Analysts Weigh Up Benefits Of Big Bayer Restructuring

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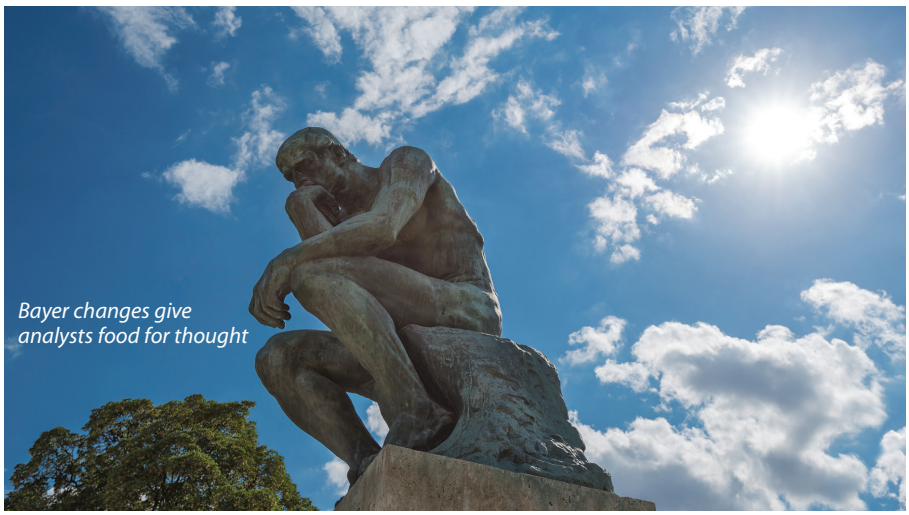
**Bayer AG**'s announcement about significant restructuring measures and potential disposals took observers by surprise, especially as it came just a week before its capital markets day in London (Dec. 5), but analysts have been weighing up the implications for the Germany-based major.

Arguably the least surprising news to come out of Leverkusen yesterday (Nov. 29) was that Bayer has decided to pull out of the animal health market. Chairman Werner Baumann said that it was a unit that was "well positioned in an attractive industry which will continue to grow" and analysts at Credit Suisse agreed, issuing a note to remind investors that with 2017 revenues of €1.5bn, the division is the fifth largest global animal health player, behind Zoetis, **Boehringer Ingelheim GMBH**, **Merck & Co. Inc.** and Elanco, "with robust industry fundamentals across both companion and production animal segments."



*Bayer changes give analysts food for thought*

While Bayer said it was assessing available options for the exit, a sale would appear to be the most likely option and there are going to be a number of players interested. The Credit Suisse team noted that "we continue to view animal health as an attractive alternative healthcare play, with inherent advantages over human healthcare with more efficient R&D operations, more sustainable product portfolios, limited generic threats and essentially no direct exposure to payer reimbursement cuts, elections, or healthcare reform."

Analysts at Deutsche Bank, who said that Bayer's measures would provide "a much-needed shake-up and slimming down of the organisation," claimed that the divestment of animal health "makes sense as asset prices are high and we see no clear evidence why Bayer should own it, given limited overlap with the large core divisions."

As to how much the division could be sold for, analysts at Bernstein, using Zoetis and Elanco as references, believe the Bayer unit is worth around €7-€7.5bn, but argued that €6-€6.5bn "seems fair, particularly given the recent weak third quarter."

They added that "there is a clear appetite for animal health, so either sale or spin would work." This, along with initiatives for Bayer's consumer health division that could see the sale of sun-screen range Coppertone and Dr Scholl's foot care products, could generate €7bn, Bernstein added. *(Also see "Coppertone, Dr. Scholl's On The Block As Bayer Narrows Consumer Health Focus" - Pink Sheet, 29 Nov, 2018.)*

The various measures put forward by Bayer, which will involve headcount reductions of 12,000 by the end of 2021 (around 10% of its current workforce), should result in total cost savings of €2.6bn by 2022, al-

though the moves will involve one-time costs of over €4bn. Now the speculation has started about how much of that will be invested in the core pharma business.

Baumann said on a conference call announcing the measures that the emphasis now would be on "collaborative research models and external innovations" rather than internal R&D where 900 jobs will be cut. The Bernstein team argued that with the asset sales and cost-cutting, Bayer should be "in a much stronger position to license and bolt-on pipeline assets over the next 12-24 months."

> The decision to mothball the Wuppertal plant is being seen as a sensible option by analysts and the Bernstein team stated that 'hemophilia was never going to be a growth driver'

The broker said it has highlighted a need for more external deals for a while as it believes "Bayer's pipeline does not come close" to offsetting the patent cliff it will soon on its two biggest earners – the anticoagulant *Xarelto* (rivaroxaban) and eye drug *Eylea* (aflibercept ). The Bernstein analysts are keen to hear more details at the London presentation next week but said that "our initial read is positive" about more partnering in deals similar to the one Bayer has with **Loxo Oncology Inc.** on the just-approved tissue agnostic cancer drug *Vitrakvi* (larotrectinib). *(Also see "FDA Nod For Loxo/Bayer Tissue Agnostic Drug Marks Paradigm Shift In Cancer " - Scrip, 27 Nov, 2018.)*

Baumann also announced that Bayer had decided not to utilize the Factor VIII facility it has built in Wuppertal, Germany, a move which will see 350 jobs go, and will focus all recombinant FVIII production in Berkeley in the US. The decision to mothball the Wuppertal plant is being seen as a sensible option by analysts and the Bernstein team stated that "hemophilia was never going to be a growth driver."

Only a few days before, Bayer added another key market for its longer-acting FVIIII hemophilia A therapy *Jivi*, winning approval in the EU soon after being authorized in Japan in September and by the FDA in August. However the Bernstein analysts argued that Jivi faces a lot of competition from products marketed by **Sanofi**, **Shire PLC** and **Novo Nordisk AS**, as well as from **Roche**'s much-vaunted *Hemlibra* (emicizumab), "so we can see the logic here."

As for the analysts at Deutsche Bank, they concluded that "the value of Bayer's actions to shareholders ultimately comes down to an assessment of whether the savings required are achievable and whether reinvestment into R&D will yield longer-term rewards." All in all, they see the divestments as "sensible, i.e.generating cash, but not materially changing the structure of the company" and for now these measures are likely to appease more vocal stockholders. However, "achievement of targets and ongoing business performance is likely required to limit risks of a call for a more radical breakup of the conglomerate structure."

*Published online 30 November 2018*

# Novartis UK Moves To London To Seek Its Life Sciences Digital Fortune

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Swiss firm **Novartis**'s UK headquarters are set to move to London from its current base in Frimley, Surrey, by January 2020. The company will relocate to The WestWorks, a 1.9 million sq ft campus in White City, which is emerging as a new life sciences and technology cluster in the west of the capital city.

The decision fits with Novartis's strategic direction under new CEO Vas Narasimhan to become a "data-centric, digitally enabled organization." *(Also see "New Dawn At Novartis As Narasimhan Demands Breakthroughs" - Scrip, 24 Jan, 2018.)*

The company brought on board its first chief digital officer Bertrand Bodson in January who was swiftly appointed onto its executive committee in a clear indication of how seriously Novartis is taking its digital ambitions. Bodson came with impressive experience of implementing digital innovation and culture change in large non-pharma businesses such as Sainsbury's Argos, EMI and Amazon. *(Also see "Digital Gets Top Billing As Novartis CEO Wields Management Broom " - Scrip, 12 Mar, 2018.)*

Novartis said the "bold move" to London was a multi-million pound investment in UK life sciences. The company employs about 1,500 people in the country. The WestWorks houses a number of technology and innovation companies as well as Imperial College London's major new research and innovation campus. It co-locates multidisciplinary research with global businesses, new start-ups and fast-growth technology companies.

"The nature of healthcare and medicine is changing and as we pivot towards becoming a focused medicines company, powered by digital and data, we want to be closer to our customers and partners, and become better networked in the healthcare and life science ecosystem." said Haseeb Ahmad, Novartis UK country president. He added that The WestWorks campus complemented how the company was working to deliver on its "strategy to reimagine medicine."

*London: Where The Streets Are Paved With (Digital) Gold*

David Gann, vice president of innovation at Imperial College London, said that the co-location of academic research and businesses was central to driving innovation and economic growth. "Novartis is a natural fit for White City's booming life sciences ecosystem, and we hope that this move will pave the way to new collaborations and partnerships to enhance our work in this area," he said.

Despite **AstraZeneca PLC**'s decision five years ago to leave London for Cambridge, Novartis is not alone in its desire to move to the UK capital: late in 2017, **MSD** announced its intention to build a new innovation hub in the city. *(Also see "Merck's UK Proposal: What's Attracting The US Giant To London For Innovation?" - Scrip, 27 Nov, 2017.)*

*Published online 3 December 2018*

# BMS SCLC Chances Dive After Opdivo, Yervoy Combo Flunks CheckMate-451

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**Bristol-Myers Squibb Co.**'s prospects in small cell lung cancer (SCLC) now look doubtful after the US group reported disappointing Phase III data from CheckMate-451 in which *Opdivo* (nivolumab) combined with *Yervoy* (ipilimumab) missed the primary endpoint of overall survival, analysts say.

The miss comes shortly after BMS's Phase III CheckMate-331 in relapsed small cell lung cancer using Opdivo failed to meet an overall survival endpoint compared to standard-of-care chemotherapy.

Although CheckMate-331's failure in October was disappointing, many analysts at the time forecast that – due to a lack of treatment options for patients – BMS's PD-1 inhibitor would keep the third-line SCLC indication. *(Also see "Bristol's Checkmate-331 Failure Not Likely To Endanger SCLC Labeling For Opdivo" - Scrip, 12 Oct, 2018.)*

That view seems to be changing after the failure of CheckMate-451.

Analysts at Evercore said Opdivo's failure in CheckMate-431, which evaluated the drug along with Yervoy as maintenance therapy in extensive-stage SCLC after completion of platinum-based chemotherapy, "means that the small cell lung cancer indication is in jeopardy."

BMO Capital Markets agreed, saying in a reaction note that "following the failures of CheckMate-331 and CheckMate-451, Bristol will likely not be competitive in SCLC.

Opdivo, although a blockbuster, has fallen behind **Merck & Co. Inc.**'s rival *Keytruda* (pembrolizumab) in terms of sales. Keytruda boosted that lead by winning approval in first-line non-small cell lung cancer, where Opdivo has been unable to produce convincing results.

In August, Opdivo won accelerated approval to treat metastatic SCLC in patients who have progressed after chemotherapy and at least one other therapeutic regimen, which was the first new SCLC approval in two decades. Response rate data from the early-phase CheckMate-032 trial had allowed Opdivo to gain that status.

Evercore noted that the FDA had approved the extensive-stage small cell lung cancer indication for Opdivo "based on a smaller trial, and the Phase III CheckMate-331 in relapsed small cell lung cancer was supposed to be confirmatory. A few weeks ago, that trial didn't work. However, there was an expectation that if first-line CheckMate-451 works, it could act as confirmatory. It didn't."

## ROCHE SEEN BENEFITING FROM BMS WOES

BMS's disappointment should be good news to **Roche**.

The Swiss group's Phase III IMpower133 trial testing its anti-PD-L1 *Tecentriq* (atezolizumab) with chemotherapy recently demonstrated PFS and OS benefits in first-line small cell lung cancer and the combination has been submitted to the FDA. *(Also see "Tecentriq's Small-Cell Lung Cancer Success Takes Edge Off Roche's IO Position" - Scrip, 25 Sep, 2018.)*

Even if Opdivo maintains its approval for third-line patients, the failure of these trials highly restricts the drug's potential in an indication where there is a huge unmet need, said Datamonitor Healthcare analyst Hardik Patel.

"In comparison, Tecentriq in combination with chemotherapy has already demonstrated an overall survival benefit in first-line SCLC patients in the Phase III IMpower133 trial, and Roche previously stated that the company intends on filing for approval in 2018," he said.

**AstraZeneca PLC** is also testing its PD-L1 checkpoint inhibitor *Imfinzi* (durvalumab) in combination with chemotherapy or chemotherapy and tremelimumab in first-line SCLC patients in the Phase III CASPIAN trial with hopes of filing for approval in 2019 if data are positive.

'Following the failures of CheckMate-331 and CheckMate-451, Bristol will likely not be competitive in SCLC.'
– BMO Capital Markets

Similarly, Keytruda in combination with chemotherapy is being tested in the first-line setting in the Phase III KEYNOTE-604 trial, which has a primary completion date of January 2019, Patel said.

The failure of CheckMate-331 and CheckMate-451 could have broader implications on sentiment for BMS, some analysts say.

"This [CheckMate-451 failure] is another IO setback that will likely increase uncertainty about R&D execution. Given Bristol's dependence on IO, it is difficult to get constructive without improved R&D execution," BMO Capital Markets said.

Morningstar analysts said while the drug combination of Opdivo and Yervoy "continues to look well positioned in melanoma and renal cancer, the failure to show a survival benefit in SCLC reduces our peak sales for Bristol's immuno-oncology drugs to just over $10bn, down by close to $800m annually."

*Published online 28 November 2018*

# Severe Asthma Proves Too Much Of A Challenge For Vectura

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**Vectura Group PLC** is staying positive despite having decided to stop development of a drug-device combination to treat severe uncontrolled asthma after a late-stage study failure.

The Phase III trial of VR475, which consists of budesonide delivered by the UK company's proprietary nebulizer inhalation system, did not meet its primary endpoint, with the study failing to achieve statistical significance versus placebo. Vectura has decided to terminate development of VR475 immediately and principal investigator Tim Harrison at the University of Nottingham said in a statement that the results suggested that in severe asthma, "nebulized budesonide is not an appropriate treatment alternative to biologic therapy." The open label arm with conventional nebulizer also failed to reach statistical significance against placebo.

He added that while the outcome is a disappointment, "the primary endpoint in this difficult-to-treat patient population presented a high hurdle from the outset," a point echoed on a conference call Nov. 26 by Vectura CEO James Ward-Lilley. He said that the miss was "clearly disappointing but not one that is completely surprising," given the "challenging endpoint we set."

Ward-Lilley noted that this was the first major Phase III trial Vectura had undertaken on its own – the study involved 713 uncontrolled asthmatics and cost about £35m – claiming that the findings at least showed the quality of the study "and we were pleased with the design." Also despite the failure, an initial review showed certain secondary endpoints achieving statistically significant and clinically meaningful differences between VR475 and placebo and versus conventionally nebulized budesonide, notably in terms of lung function.

Gonzalo de Miquel, Vectura's chief medical officer, added that the firm remained confident about the potential of its technology, claiming that the results "reinforce the differential characteristics of our guided inhalation system versus conventional nebulization."

However there is no doubt that the end of the road for VR475 is a blow, not least on the financial front. The failure will have a negative impact on the group's loss before tax of £40m, or £29m after tax.

How big a blow it is to the fortunes of Vectura, which merged with fellow UK biotech SkyePharma in 2016, is debatable and while the stock sank more than 13% after the VR475 news was announced, it recovered later in the day. The performance of drugs such as **Mundipharma International Corp. Ltd.** and **Kyorin Pharmaceutical Co. Ltd.**'s *Flutiform* (fluticasone/formoterol) and **Novartis AG**'s *Ultibro Breezhaler* (indacaterol/glycopyrronium) for which Vectura receives royalties, represents much of analysts' focus on the company.

Ward-Lilley acknowledged that "we had flagged that this was a riskier study" but said now that VR475 (acquired through the purchase of Germany's Activaero in March 2014) had been terminated, the company would focus on VR647. The latter is also a nebulized budesonide product which is being positioned as an alternative treatment for asthma in children in the US market.

In August this year, the company successfully concluded two pediatric studies to support the use of the drug/device combo as a more convenient treatment option for children, potentially reducing treatment times and the steroid burden, without compromising exposure or safety. De Miguel noted on the call that the failure of VR475 "will have no effect on the likelihood of success" for VR647 as the latter represents "a very different proposition."

The next step will be to outline plans for the Phase III program with the FDA, he added, and if all goes well, VR647 could start late-stage development by the end of next year or the beginning of 2020. Discussions with possible partners have already been initiated but de Miquel noted that no deal was likely to be signed off until the Phase III design had been agreed with the FDA.

Next year should also see a US re-submission by Vectura and partner **Hikma Pharmaceuticals PLC** for VR315, a generic version of **GlaxoSmithKline PLC**'s inhaled asthma blockbuster *Advair* (fluticasone/salmeterol). The firms received a complete response letter from the FDA in May 2017 but decided to progress a dispute resolution process against the agency regarding the interpretation of the results from their pivotal study.

That bid ended in failure and in March this year, the FDA upheld its original decision and included a request that Hikma complete an additional clinical endpoint study. That trial has started and Vectura is hopeful of a potential approval and launch during 2020.

Vectura and Hikma are also going after another GSK respiratory franchise, having inked an agreement earlier this month to develop generic versions of the UK major's portfolio of products that use the *Ellipta* inhaler. First up, they are planning to test a copy of GSK's *Breo/Relvar* (fluticasone furoate/vilanterol trifenatate). *(Also see "Watch Out GSK: Vectura And Hikma Target Ellipta Portfolio" - Scrip, 8 Nov, 2018.)*

*Published online 26 November 2018*

# FDA Nod For Vitrakvi Marks Paradigm Shift In Cancer

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In a momentous move for precision medicine, the FDA has granted accelerated approval to **Loxo Oncology Inc.** and **Bayer AG**'s cancer treatment *Vitrakvi* (larotrectinib) based on a common biomarker rather than the location in the body where the tumor originated.

Vitrakvi has got the thumbs-up for the treatment of both adult and children with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion, without a known acquired resistance mutation that are either metastatic or where surgical resection will likely result in severe morbidity, and have no satisfactory alternative treatments or have progressed following therapy. Examples of tumor types with an NTRK fusion that have been shown to respond to the drug, a tropomyosin receptor kinase inhibitor, include soft tissue sarcoma, salivary gland cancer, infantile fibrosarcoma, thyroid cancer and lung cancer.

The likelihood of approval increased after updated Phase III data were presented at the ESMO meeting in Munich in October which revealed an overall response rate (ORR) of 80% including 18% complete responses in patients that comprised the primary dataset submitted to the FDA (n=55), as well as a supplementary cohort (n=67). In an interview with *Scrip* at ESMO, Robert LaCaze, head of Bayer's oncology strategic business unit, also highlighted the impressive safety profile seen in the 176 patients across three studies.

The FDA is clearly convinced about the potential of Vitrakvi, saying in a statement that "the approval marks a new paradigm in the development of cancer drugs that are tissue agnostic." In an unusual step, the agency's commissioner Scott Gottlieb also commented, noting that the green light "reflects advances in the use of biomarkers to guide drug development and the more targeted delivery of medicine. We now have the ability to make sure that the right patients get the right treatment at the right time." The Vitrakvi thumbs-up is actually the second tumor site-agnostic approval of a drug targeting a key genetic driver of cancer. In May 2017, **Merck & Co. Inc.** got accelerated approval from the FDA for *Keytruda* (pembrolizumab) to treat microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, although the already-established blockbuster immunotherapy had already chalked up several approvals for a range of cancers by then. *(Also see "Biomarker-Led Claim Is Small Step For Merck's Keytruda, Giant Leap For Cancer Indications" - Pink Sheet, 23 May, 2017.)* Vitrakvi is considered the first FDA approved cancer drug to gain a tissue agnostic indication initially.

## TESTING IS KEY

The pathway to commercial success for Vitrakvi is less clear, however, and with the US approval in the bag, the challenge facing Bayer, which is leading the commercialization, is to identify the patients who have the fusion that the drug treats; there are estimated to be 2,000-3,000 people a year in the US who develop NTRK-related cancers. And a big challenge is that the already rare cancer can present across varying tumor sites.

At present next-generation sequence (NGS) testing is limited and largely conducted only at major medical centers. Loxo's management has talked openly about the testing challenge confronting the launch of Vitrakvi. Loxo formed a partnership in April with **Illumina Inc.** to develop a companion diagnostic that will use sequencing to identify whether patients' tumors carry a broad range of genomic signatures. Loxo did not provide an update on the status of the Illumina companion diagnostic. LaCaze told *Scrip* in Munich that Bayer was involved in discussions with several companies to produce a specific Vitrakvi test.

**Roche** separately announced Nov. 27 that it will launch a Ventana pan-TRK assay, the first automated in vitro diagnostic immunohistochemistry assay to detect TRK proteins in cancer.

Loxo, during its third quarter sales and earnings call Nov. 8, said it believed the Ventana test would be used as an adjunct screening tool by labs that would prefer to pre-identify patients with certain cancer types for referral to a molecular panel.

Another factor that could impact the launch is price. The wholesale acquisition cost will be $32,800 for a 30-day supply of 100 mg capsules for adults, while the price for the liquid formulation for children and some adults will start at $11,000 per month.

However, Bayer estimates that monthly out-of-pocket costs for the majority of patients will be in the region of $20 or less, saying that is committed to ensuring that patients in the US who are prescribed Vitrakvi "are able to access the medication and receive the support they may need."

The German major is introducing a program that will refund the cost of Vitrakvi to payers, patients and third-party organizations paying on behalf of patients, if the latter do not experience clinical benefit within 90 days of treatment initiation. It also cited the Bayer US Patient Assistance Foundation, a charity that helps eligible patients get access to the company's prescription medicines at no cost.

The initiatives went down well with pharmacy benefit manager **Express Scripts Holding Co.** and its chief medical officer Steve Miller said his company "applauds Bayer for its thoughtful approach to patient access," adding that "the Vitrakvi Commitment Program represents a significant advance."

Analysts are also upbeat about the approval. Matthew Harrison at Morgan Stanley issued an investor note saying that the price was higher than forecast and "using an assumed real-world ORR of around 70%, we estimate net annualized pricing of $300,000 per patient, 50% above our expectations and we would expect a similar amount above consensus expectations."

> "The FDA is clearly convinced about the potential of Vitrakvi, saying in a statement that 'the approval marks a new paradigm in the development of cancer drugs that are tissue agnostic.'

He expects the launch to be limited by initial availability of genetic testing, as do analysts at JMP Securities. They noted that Loxo has also guided toward "a somewhat tepid commercial launch...noting the difficulty in identifying NTRK fusions that occur at a very low rate across a variety of cancer types and the need to increase utilization of diagnostics that can detect the fusions."

## COMMERCIAL POTENTIAL

However, the broker added that "we maintain a high degree of optimism for the longer-term commercial potential of the larotrectinib franchise given the impressive durability data recently presented at ESMO and Bayer's involvement… when it comes to operations and key decision-making on issues, such as spending, strategy and pricing." The JMP analysts concluded by saying the success of Vitrakvi is "a crucial step in the paradigm shift we see occurring in the treatment landscape for oncology toward biomarker-driven drug development" and they view the FDA's support, through its accelerated approval pathways,"as signaling the agency's commitment to market and the ushering in a new era of targeted medicines in oncology."

The Vitrakvi green light marks the first drug for Loxo to reach the market. The company stands to receive a big financial boost. Under the deal signed a year ago, Loxo is eligible to receive $450m in milestone payments from Bayer for approvals and first commercial sales in certain major markets. The drug was filed in Europe in August. *(Also see "Loxo's Tissue-Agnostic Approach Brings $400m Upfront From Bayer" - Scrip, 14 Nov, 2017.)(Also see "Bayer Files Larotrectinib In EU As LOXO-292 Hurtles Towards The Market " - Scrip, 29 Aug, 2018.)*

Loxo will co-commercialize the Vitrakvi in the US, with the companies sharing commercial costs and profits evenly.

*Published online 27 November 2018*

# Bayer's Hemophilia A Portfolio Boosted By Jivi's EU Approval

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**Bayer AG** has added another key market for its hemophilia A therapy, *Jivi*, winning approval in the EU soon after being authorized in Japan in September and by the US FDA in August.

Formerly known as BAY94-9027, Jivi was approved by the European Commission on Nov. 27 for the treatment and prophylaxis of bleeding in previously treated patients 12 years of age or older with hemophilia A.

The EU marketing authorization follows the therapy's recommendation in September by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency, and is based on the Phase III multi-centered PROTECT VIII trial that showed bleed protection and safety for up to a median of 1.9 years, with a range of 0-2.6 years, involving 126 patients.

## LONGER-ACTING FACTOR VIII THERAPY

Jivi is a longer-acting Factor VIII therapy designed to cut the number of infusions needed to prevent bleeds in patients with hemophilia A. FVIII replacement therapy is the standard of care to stop or prevent bleeding. Hemophilia is mainly an inherited disorder affecting about 400,000 people around the world.

The approvals and consequent market launches in the US, Japan and now Europe complement Bayer's existing Factor VIII treatments, *Kogenate* and its successor *Kovaltry* (octocog alfa), which had combined sales of €967m in 2017, down 17.1% from 2016. But Bayer says Jivi is not a replacement for Kogenate/Kovaltry, but rather it is an addition to the drug maker's offering that brings flexible dosing and an extended half-life option to the table.

## COMES AMID RISING HEMOPHILIA A ACTION

Jivi's arrival coincides with rising activity within the hemophilia A therapeutic space.

Early 2018 saw Paris-based **Sanofi** take over hemophilia specialist **Bioverativ Inc.** for $11.6bn. That **Biogen Inc.** spinoff was formed with two profitable products, the extended half-life therapies *Eloctate* (efmoroctocog alfa) and *Alprolix* (eftrenonacog alfa) to treat hemophilia A and B, respectively, plus a pipeline of candidates in hemophilia and rare blood diseases.

In October, **Roche**'s *Hemlibra* (emicizumab-kxwh) received an expanded indication from the FDA to prevent or reduce bleeding episodes in adults and children with hemophilia A without factor VIII inhibitors, boosting the drug's commercial prospects.

There is also rising excitement around gene therapy for hemophilia A, due to it being a disease with a clear genetic cause.

For example, **Spark Therapeutics Inc.** and partner **Pfizer Inc.**. with their SPK-9001 for hemophilia B, and **BioMarin Pharmaceutical Inc.** with its valoctocogene roxaparvovec (BMN 270) for hemophilia A, are seen as potential early beneficiaries of accelerated approval for gene therapy in hemophilia.

Whether payers would be willing to pay for expensive hemophilia gene therapies remains to be seen.

*Published online 28 November 2018*

# Breast Cancer, HIV Drugs May Face Tougher Part D Climate Under Protected Class Proposal

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The Medicare Part D formulary reforms proposed by the US Centers for Medicare and Medicaid Services will impact some biopharma sponsors more than others, with the cyclin-dependent kinase (CDK) 4 and 6 inhibitors for breast cancer and the integrase inhibitors for HIV among the high-profile branded drugs that could be impacted by the policy changes for protected classes.

The CDK 4/6 class includes **Pfizer Inc.**'s *Ibrance* (palbociclib), **Novartis AG**'s *Kisqali* (ribociclib), and **Eli Lilly & Co.**'s *Verzenio* (abemaciclib). The integrase inhibitors include **ViiV Healthcare**'s *Tivicay* (dolutegravir), **Gilead Sciences Inc.**'s *Biktarvy* (bictegravir/emtricitabine/TAF) and **Merck & Co. Inc.**'s *Isentress* (raltegravir).

CMS wants to allow Part D plans to exclude any single-source drug in the protected classes from coverage if their list price increases faster than inflation relative to the price in a baseline month and year. The rate of inflation would be calculated using the Consumer Price Index for all Urban Consumers. *(Also see "Part D Protected Class Management Tools To Save Medicare $1.85bn" - Pink Sheet, 26 Nov, 2018.)*

The protected classes policy requires Part D plans to cover all or substantially all drugs in six classes: oral cancer drugs, HIV/AIDS treatments, anti-psychotics, antidepressants, anti-convulsants, and immunosuppressants.

The requirement has limited plans' leverage in negotiating rebates with manufac-

turers, which has led to higher prices for drugs in those classes, CMS notes. The proposed rule, announced Nov. 26, includes a number of policies aimed at driving down prices in the Part D and Medicare Advantage markets.

The price increase provision is one of three modifications to the protected classes policy in the proposed rule and could present the biggest threat to manufacturers if implemented as described.

The other two modifications include allowing broader use of prior authorization and step therapy management and allowing plans to exclude a new formulation of a protected class drug from coverage even if the original version is no longer on the market. CMS did not opt to eliminate some protected classes altogether in the proposal, which some stakeholders had anticipated.

Two realities of the protected classes world will influence how the proposed changes could affect branded drugs. First, four of the classes are now mainly generic (anti-psychotics, anti-depressants, anti-convulsants, and immunosuppressants), and plans do not have to cover the brand when a generic is available. That suggests the biggest changes for brands may be seen in the oral cancer and HIV/AIDS drug sectors.

Second, the number of brands that can be impacted would depend on the number of drugs available in a class because of the overarching Part D requirement that plans must cover at least two drugs per class. As a result, only drugs in a class with at least three competitors, such as the CDK 4/6 group or the integrase inhibitors, may be subject to threats of exclusion.

"A product like **AbbVie Inc.**'s *Imbruvica* would remain unphased … [because] it is one of only two approved drugs in the [Bruton tyrosine kinase inhibitor] class," a Nov. 26 note by Wolfe Research analysts Tim Anderson et al. points out.

However, products like Ibrance and Tivicay "could be more at risk because they reside in classes where there are more than two drugs currently approved."

The analysts point out that "a quick examination of list price increases for drugs in the oral cancer and HIV drug categories shows they have clearly exceeded the CPI-U, usually by around 2-3x (i.e., in the 5%-9% range annually) over the last few years."

Therefore, "if today's new rules were to come into effect without modification, it could compel manufacturers of these products to take fewer prices increases going forward, which would naturally moderate sales growth."

## PRICE POLICY EXPECTED TO ENCOURAGE REBATES, NOT EXCLUSIONS

CMS is expecting the price increase policy will lead to tougher negotiations and compel manufacturers to concede more in the way of rebates. The agency sought to downplay concerns that it would result in formulary exclusions.

"It is our expectation that this exception policy would benefit the program and beneficiaries by encouraging manufacturers to work with Part D sponsors to ensure formulary inclusion and favorable access (for instance, better cost sharing, more competitive negotiated prices, etc.) for Part D enrollees, rather than a loss of formulary inclusion for drugs in the protected classes," the proposal states.

"Even if a protected class drug could be excluded from a Part D formulary under this proposed policy, Part D sponsors are not required to do so," it emphasizes.

Bernstein analyst Ronny Gal suggested the proposal is not likely to lead to major disruption in access to cancer and HIV drugs based on the experience in commercial insurance markets.

With regard to cancer drugs, "there are multiple unique mechanisms and even within the same mechanisms, observed clinical differences," he noted in an email. However, "there is almost no blocking of these drugs in commercial prescribing, beyond making sure they are prescribed to [National Comprehensive Cancer Network] guidelines."

For treatments for HIV, "payers so far have not attempted to sequence drug use (and in our discussions with them have limited appetite to do so)."

Nevertheless, early reactions by stakeholders sound the alarm on the proposal's potential to create access restrictions.

"The protections in Part D were put in place to protect access for the most vulnerable patients and ensure insurance design did not discriminate based on disease," the Pharmaceutical Research and Manufacturers of America said in a statement.

"Letting plans restrict access to the medicines that patients rely on, particularly for those with serious and complex health conditions like HIV/AIDS, cancer and mental illness, reduces adherence to those medicines, jeopardizing their health, increasing their need for inpatient care and resulting in poorer health outcomes for seniors and higher costs for taxpayers."

CMS seeks public input on a number of different aspects of the price increase policy, including whether an alternative pricing threshold should be considered and whether an increase in a price other than wholesale acquisition cost, such as a negotiated price or average wholesale price, should be used. Comments are due Jan. 25.

*Published online 28 November 2018*

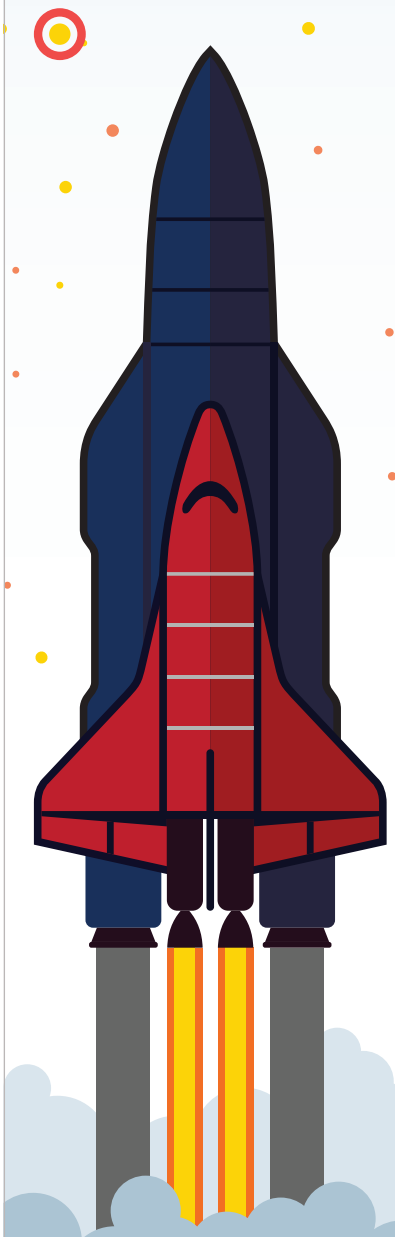
# US Biopharma IPOs Surge

**Initial public offerings in the US by biopharmaceutical firms surged in the first 10 months of 2018 even in October when the Nasdaq Biotechnology Index fell 14%.**

**61**
IPOs in 2018 through October 31

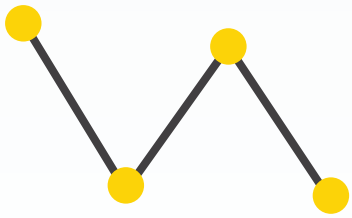
Average return was
**0.3%**
as of October 31[1]

For the 54 IPOs launched in the first nine months of 2018, the average return was **13.6%** at the end of September[1]



Largest IPO was **Allogene Therapeutics Inc.** in October[1]

**$372.6m**



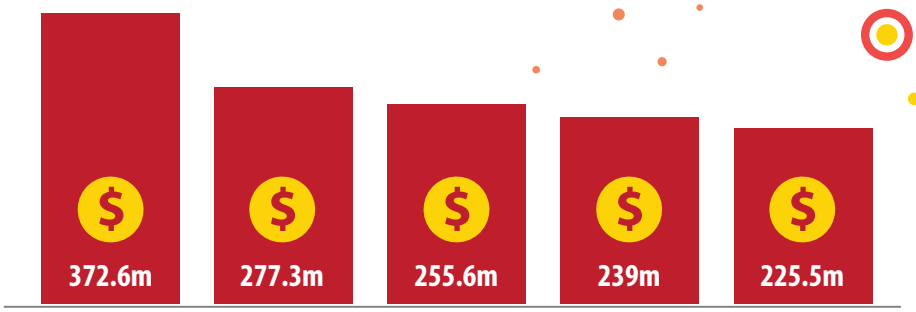
Smallest IPO was **Genprex Inc.**, in March[1]

**$6.4m**

**$25.04**
The biggest IPO launch price was for **MorphoSys AG** in March[1]

**$4**
The smallest IPO launch price was for **Provention Bio Inc.** in July[1]

## Top five IPOs by gross proceeds[1]




Source: [1]Scrip, [2]Leerink

## Number of IPOs by month[1]

| 6 | 2 | 5 | 2 | 6 | 14 | 9 | 2 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|
| January | February | March | April | May | June | July | August | September | October |

**$48.35**
The highest stock price as of October 31 was for **Allakos Inc.**

**$1.65**
the lowest stock price was for **Genprex Inc.**[1]

**Biggest return versus IPO price:**

**194.1%**
for **Armo Biosciences Inc.***[1]

**Biggest loss versus IPO price:**

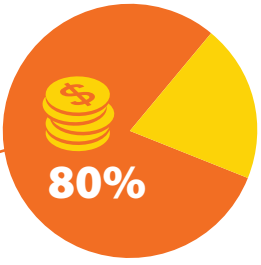
**-64.1%**
for **Menlo Therapeutics Inc.** as of October 31[1]

**Armo was acquired by Eli Lilly & Co. for $1.6bn or $50 per share in May*[1]

**269** biopharma IPOs in the US between January 2013 and September 2018 raised **$24.1bn**[2]

**44%** of biopharmas that went public in that time had a positive return as of September 30[2]

**20%** of biopharmas that went public in that period generated more than 80% of the returns[2]




There was an average of six IPOs per month in 2018 raising **$104m** per offering[1,2]

**<4** biopharmas went public per month between January 2013 and September 2018 with an average IPO size of $89.6m

# No, It's Not Just Out-Of-Pocket Costs That Are A Problem, John Arnold Tells Pharma

**JESSICA MERRILL** jessica.merrill@informa.com

Billionaire philanthropist John Arnold confronted industry at the Forbes Healthcare Summit Nov. 29, pushing back on some of the drug industry's long-standing arguments when it comes to the debate around drug prices.

Arnold is considered something of an industry adversary because his foundation – the Laura and John Arnold Foundation – is focused on drug pricing among other priorities, including criminal justice reform and education. The foundation has been a big financial supporter of the increasingly influential Institute for Clinical and Economic Review (ICER) and the patient advocacy group Patients for Affordable Drugs.


"A lot of people in the industry talk about out-of-pocket expense. I'm looking at this from all of society," said Arnold, a former hedge fund manager who started out energy trading at Enron. "For me, it doesn't matter whether the money is coming from the government, from the employer, or from the individual. That is society's money. That is society's resources."

Indeed, that is one of the underpinnings of the LJAF's work when it comes to the issue of drug pricing – that the price of a drug should be linked to value and the value should be weighed against the value of other societal priorities.

## COST TO THE SYSTEM MATTERS TOO

Pinpointing out-of-pocket costs as the drug pricing culprit suggests the cost is okay if the government is paying for it or an employer, he added.

"It all filters back down to the person, so whether the person is the direct payer of that or not is an issue," Arnold said. "We need to make sure that we increase access, that we make it easier for people who need these drugs to get them, but we also have to consider what is the total cost to the system. Just shifting money from the individual to the government or the individual to the employers is not a solution." Industry is generally quick to highlight patient affordability and a willingness to take steps to lower out-of-pocket costs when it comes to confrontations around drug pricing. In fact, Arnold's comments on the topic of out-of-pocket costs came after BIO CEO Jim Greenwood, in the audience, defended industry and particularly highlighted its willingness to come to the table with policy makers on the issue of out-of-pocket spending. The problem, from Arnold's point of view, is that there are a lot of societal problems that can be solved with money, but the resources are finite. The federal government is running up a trillion dollar deficit, he pointed out.

> 'The lobbyists for pharma have the easiest job because they just advocate for something that Congress is really good at, which is do nothing,' John Arnold said

"That's my biggest frustration when we have these debates and people say you are against the free market, you are against capitalism. No, you have to understand the trade-offs."

LJAF landed on drug pricing as an issue to tackle as part of a broader investment review, evaluating areas where the foundation could have a meaningful impact by helping to find solutions where market failures and political failures exist. The foundation is interested in healthcare more generally but focused in on drug pricing initially, in part because of the political climate surrounding this issue..

"We had to start with small ambitions in this huge space of healthcare," Arnold said. "We were able to postulate that this political window of drug price reform...[would] open and it did. We've proven to be right on that."

When it comes to drug pricing regulation, Arnold said he supports more regulation around pharmaceutical pricing. "We are not advocating for utility-style regulation, but we are advocating for something greater than zero regulations."

Arnold called ICER one of the foundation's "success stories" over the last five years. The foundation contributed a three-year, $13.9m grant to help fund ICER in October 2017, following an initial two-year, $5.2m award in 2015.

ICER is an independent value assessment organization that measures the value of drugs on a Quality Adjusted Life Year (QALY) basis. It has been gaining some influence in the US, which does not have any signifi-

cant government-funded value assessment organization as some other countries do. Industry, which increasingly says it supports linking the price of a drug to value, generally works with ICER while also taking issue with the way the organization assesses value.

Arnold said he would prefer a government-funded independent entity to assess the value of drugs. "ICER is the next best thing until we get to that," he said. As for HHS' latest proposal to use an international pricing benchmark for some drugs under Medicare Part B, Arnold said the US should rely on its own system. "I think it's better if the United States has its own model," he said. "There are issues with relying on what France does, what Germany does, what Japan does."

HHS proposed using a target price derived from an index of drug prices in other countries for some single-source drugs reimbursed under Medicare Part B in October, along with other Part B proposals. Despite a lot of proposals coming out of President Trump's blueprint on drug pricing, there are still a lot of uncertainty about what will be implemented in terms of policy and when.

Arnold also defended his foundation's investment in Patients for Affordable Drugs, a non-profit patient advocacy group founded by cancer patient David Mitchell and focused on policy changes to lower the price of prescription drugs. The group has gotten under the industry's skin with emotionally-charged campaigns highlighting cases of what it calls pharmaceutical greed, and recently held a vote to determine the "most hated pharma CEO of the year."

But Arnold pointed to the pharmaceutical industry's own lobbying initiatives, speculating the industry likely spent around $1bn on lobbying in 2018 between trade organizations and independent company donations.

"They are not going to spend $1bn on politics unless it's getting them something," Arnold said. "The lobbyists for pharma have the easiest job because they just advocate for something that Congress is really good at, which is do nothing," he said. "The system works really well for pharma."

Matching that level of spending from a patient advocacy side would be hard to do, but Arnold applauded Mitchell for activating angry voters and targeting obstructionist politicians. He said the foundation would continue to keep up its support. "If our politicians are active obstructionists in trying to fix the system, then we're going to call it out."

*Published online 29 November 2018*

# Teva Launches Generic EpiPen At Same Price As Mylan's Generic

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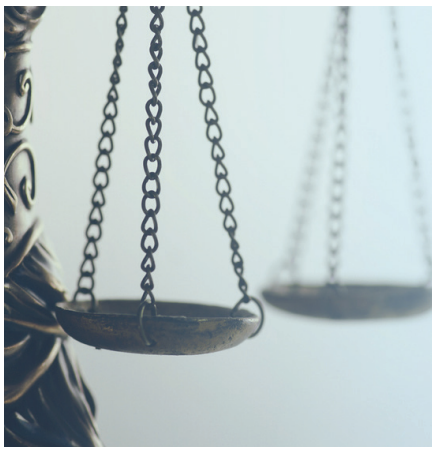
**Teva Pharmaceutical Industries Ltd.** is launching the first alternative version of the emergency allergy medicine *EpiPen* (epinephrine) outside of **Mylan**'s brand and authorized generics, but the cost will be the same. The wholesale acquisition cost of Teva's generic is $300 for a two-pack, the same WAC as Mylan's authorized generic.



It looks like it might take more competition on the market to lower the price, or perhaps competitive rebating, though rebates don't necessarily help the patient buying out-of-pocket at the point of sale.

## SUPPLY AND DEMAND

For now, the supply of EpiPen and generics is limited, which also impacts demand and price. Teva is only able to supply limited doses of the 0.3 mg auto injector in the US for now, but expects additional supply to be available in 2019, along with doses of a version of the 0.15 mg EpiPen Jr.

"Once we received FDA approval, we began preparations for release, as it is a complex drug-device combination," Teva said. "All available product has been released." No additional details on the quantity of the supply are being disclosed.

FDA cleared Teva's generic version of EpiPen in August after a lengthy review. The approval was viewed as a positive check off FDA's to-do list, part of a commitment by the agency to get more complex generics to market faster. *(Also see "Teva To Launch First Generic EpiPen In 'Coming Months'; FDA Heralds Approval Of Complex Product" - Pink Sheet, 16 Aug, 2018.)* The launch was delayed three months as Teva built up supply of the product.

The development of a generic version of the complex drug-device combination of EpiPen has been challenging. FDA initially issued a complete response letter to Teva in 2016, citing deficiencies in the ANDA. The agency took steps to help sponsors, publishing three draft and final guidances beginning in 2009.

EpiPen specifically has been notable because Mylan has had a monopoly on this category of medicines. As a result, Mylan was able to continuously raise the price of EpiPen unfettered until 2016, when the price of EpiPen tipped over $600, sparking a pricing scandal. Patients finally pushed back on the price hikes, outraged over the cost many were having to pay out-of-pocket to get the life-saving drug. EpiPen eventually became the center point of a Congressional probe.

Mylan responded to the crisis by launching an authorized generic version of EpiPen at half the cost, or $300.

> The development of a generic version of the complex drug-device combination of EpiPen has been challenging

Now Teva's decision to launch a generic at the same price as Mylan's generic might be viewed as a disappointment to some, including patients.

FDA Commissioner Scott Gottlieb made a big deal about how the first generic could lower the cost of epinephrine back when the approval was announced. "This approval means patients living with severe allergies who require constant access to life-saving epinephrine should have a lower-cost option," he said in a statement at the time.

*Published online 27 November 2018*

# China Researcher's CCR5 Knockout Babies Shock World Into New Gene Editing Debate

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A graduate of Rice University with a one-year postdoc from Stanford University in the US, He Jiankui appears to be a typical Chinese "returnee" with years of western education under his belt. But He also has things that few of his peers can match. During the seven years since he has returned to China, the scientist has also quietly acquired controlling stakes in as many as seven companies, including Direct Genomics, a major gene sequencing firm in Shenzhen.

The most startling announcement from He however - and the thing that has thrust him into the global spotlight - is that he claims to have created the world's first gene-edited babies, capturing worldwide headlines. The news is sparking renewed debate on the ethics and role of such work as a tool to engineer the genome in relation to health, but significant doubts remain over the work and its prior approval.

After a year of post-doctoral research on molecular medical diagnostics at Stanford, where he attempted to use high-throughput DNA sequencing to monitor human responses to vaccines, He returned to Shenzhen in southern China bordering Hong Kong, and became a board director at local firm Direct Genomics. Meanwhile, he also taught at Shenzhen's China Southern University of Science and Technology.

On Nov. 26, on the eve of an International Human Genome Editing Conference in Hong Kong, He stunningly announced the birth of the world's first gene-edited babies, twins that had been modified at the post-in vitro fertilization embryonic stage to be more resistant to HIV infection by knocking out the CCR5 gene, which normally allows the virus to enter cells.

The fathers in all the seven couples reportedly involved in the CCR5 gene editing work were HIV-positive, and the babies were born to one of the couples. The C-C chemokine receptor type 5 is expressed on the surface of white blood cells such as T-cells and macrophages, and acts a receptor for HIV cell entry. Individuals with mutant CCR5 were already known to be naturally resistant to HIV infection.

The news has since stirred up worldwide controversy and an outpouring of questions about the study's ethical approval process, the risks associated with it, and its potential consequences, along with issues around the previously little-known researcher.

## CHINA GENE, CELL THERAPY DEVELOPMENT

Although China approved its first gene therapy *Jinyousheng*, a P53 adeno vector injection for cancers, back in 2003, this has not been widely used. But several hospitals are now rushing to get new gene therapies to patients.

Chenghu-based Western China (Huaxi) Hospital, for one, started treating lung cancer patients using similar CRISPR-cas9 gene editing technology used by He. The primary investigator, Lu You, obtained the hospital's ethics board clearance and started a human trial in July.

One year ago, Huang Junjiu, a researcher at Guangzhou-based Sun Yet-sun University in 2015, announced the completion of the first human embryo stage gene editing research, again using CRISPR-cas9 technology.

Meanwhile, multiple Chinese companies are venturing into CAR-T cell therapies in the immuno-oncology space, with one, Nanjing Legend, striking a multi-million deal with **Johnson & Johnson**. However, the firm was hit by recent allegations that it "cherry-picked" the clinical trial data to present at the last American Society of Clinical Oncology annual meeting. *(Also see "China CAR-T Front-Runner Allegations Reveal Soft Underbelly Of Development Race" - Scrip, 28 Sep, 2018.).*

## DENY, DENOUNCE

In the wake of the global outcry over He's as yet independently unverified embryo gene editing work, the municipal government of Shenzhen, where China Southern University is located, released a statement denying it had sponsored He's controversial study.

The Shenzhen Technology Innovation Committee, under the Shenzhen Science and Technology Board, also said that reports that the gene edited baby project was financially backed by the government were untrue. The government stressed that it has never sponsored any CCR5 gene editing or the safety assessment of any HIV gene editing projects.

Although the gene editing approach has been increasingly common among researchers looking to cure disease-related gene mutation deficiencies, gene-editing at the human embryo stage has long been considered an ethical red line that could lead to "designer babies", and also because it would lead to the engineered traits being inherited by descendants.

Many leading researchers in the CRISPR gene editing field, including technique inventor Professor Zhang Feng of Broad Institute and Prof Jennifer Duodena of the University of California, Berkeley, have called for thorough prior assessment and appropriate safety measures prior to any gene editing work on human embryos. Zhang denounced the latest CCR5 research by He and his team, calling it "risky"

and unnecessary and calling into question its actual utility. "The risks of editing embryos to knock out CCR5 seem to outweigh the potential benefits, not to mention that knocking out CCR5 will likely render a person much more susceptible to West Nile Virus. Just as important, there are already common and highly-effective methods to prevent transmission of HIV from a parent to an unborn child," Zhang said in a statement to MIT Technology Review.

Medical researchers specialized in HIV/AIDS echoed this view. Tsinghua Professor and director of its Global Infectious Diseases and HIV Prevention Center Zhang Linqi labelled He's study "imprudent" and potentially unethical. "Gene-editing CCR5 can't guarantee HIV infection won't occur from another virus. And ethically, unless it's 100% safe, CCR5 gene editing should never be allowed to be used on humans," Zhang said in an interview with Chinese internet portal Netease.

## CALL FOR HALT

The birth of the gene-edited baby twins, named Lulu and Nana, could mark the end of an era during which researchers have carefully avoided applying the technology at the human embryo stage and avoided tampering with the human genetic "blueprint", with some dubbing its potential ramifications "unimaginable" and "irreversible".

Up to now, worldwide genetic researchers have been following an ethics agreement reached in 2015 that calls for thoughtful assessment of the appropriateness prior to any gene editing of human embryos.

The latest announcement could "fundamentally alter the integrity of human genomes and could lead to unthinkable consequences," warned Tsinghua's Zhang. "Today you can alter this gene, and another gene tomorrow, which could be the beginning of self-destruction."

Leading researchers like Broad Institute's Zhang called for an immediate halt to He's work. "Given the current state of the technology, I'm in favor of a moratorium on implantation of edited embryos, which seems to be the intention of the CCR5 trial, until we have come up with a thoughtful set of safety requirements first."

## SHROUD OF SECRECY

What's also concerning other global researchers in the field is the lack of transparency surrounding the newly disclosed study. So far, the fundamental question of whether it was actually cleared by an ethics committee has not yet been answered.

China Southern University of Science and Technology has said the study was conducted outside the university, and that He had left the institution to work on his own projects since this February. "The project was conducted out of the school and has not been reported to the school or its biology department, we have no knowledge," the university stressed in a statement posted on its website.

"Regarding the gene editing on human embryos by associate Prof. He, the Biology Academic Committee believes it severely violates ethnics and academic regulations," the management added, and it is now planning to launch a formal investigation.

Finding himself at the center of a growing global storm, He said he would make a clarification statement on Nov. 28.

*Published online 28 November 2018*

(With contributions from Ian Haydock in Tokyo.)

*From the editors of PharmAsia News.*

# AI-Driven Drug Development Seen Blossoming In Korea As Government Lends Support

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The South Korean pharma industry has welcomed the parliament's passage of a revision to a special act to support and nurture the sector, which includes plans to support artificial intelligence (AI)-driven new drug development.

Although details of the plans have not been determined yet, one major industry association hopes the move will sharply reduce the time and cost required for the discovery of new drug substances. "The new act is significant as it has established a systemic base to enable companies to secure global competitiveness by preemptively dealing with the new paradigm in new drug development," the Korea Pharmaceutical and Bio-Pharma Manufacturers Association (KPBMA) said in a statement. South Korea has been seen as relatively slow in adopting digital healthcare tools, including AI-driven new drug development, but the government and industry appear to be stepping up efforts so as not to fall further behind emerging global trends.


*Korea Moves To Support AI-Driven New Drug Development*

## SCIENCE MINISTRY TO BUILD AI PLATFORM FOR INDUSTRY

With a goal to bring forward development of innovative drugs using AI and big data, the Ministry of Science and ICT (Information and Communications Technology) began to build a platform earlier this year by establishing a research team. This will develop big data and AI systems that predict the relationship between drugs and their targets, and drug mechanisms. These platforms will be fully unveiled next year so that researchers and companies will be able to use them freely.

Usage of AI in the discovery process is expected to as much as halve the total time and cost required for new drug development, while the ministry notes the market for AI-driven new drug development is expected to grow by an average of 40% annually to reach $4bn in 2024.

Once the platform project is successfully completed, the science ministry expects to slash the time required to develop candidates from five years on average to as little as one year.

As demand for the technology will mostly come from the pharma industry and hospitals, the ministry aims to form an expert consultation group among pharma firms and hospitals. The ministry is also seeking a project to apply AI, biotechnology and robotic technology to medical devices to develop new concept breakthroughs in this area.

Meanwhile, the KPBMA has also set up a task force to establish a center to support new drug development using AI. Its member pharma and biotech companies are increasingly attempting to apply this technology to new drug development via collaborations with relevant companies or development of their own expertise.

## YUHAN LINKS WITH SYNTEKABIO

Against this background, a number of companies are moving to establish partnerships. **Yuhan Corp.** has reached a new drug development collaboration with Korean bioinformatics venture Syntekabio Inc., under which the two have agreed to collaborate and co-research applications of AI and genome analysis technology to new drug development, as well as to explore anticancer active substances using AI and to explore biomarkers via the genome analysis of clinical trial patients.

Syntekabio, which aims to grow into an AI-based new drug development firm, has a platform that predicts anticancer response via application of deep learning technology, and has also developed an algorithm that discovers biomarkers involved in drug reactions via the integration of genomic big data and AI technology.

The company also owns Personal Genome Map Technology (PMAP), an "in silico" genomics research institute which uses big data algorithms. Syntekabio manages genome analysis and big data using a supercomputer.

Based on this collaboration, Yuhan and Syntekabio plan to expand the application of AI from the development of substance candidates to all cycles of clinical development, such as prediction of drug metabolism and adverse effects. Meanwhile, another South Korean firm, **SK Biopharmaceuticals Co. Ltd.**, has completed the development of an AI-based drug design platform, comprising an AI model (prediction of drug characteristics/drug design), chemical compound data storage, and AI model storage.

The AI model was developed via machine and deep learning methods at SK C&C (another SK group company), and is made up of a "drug design" model that designs and recommends new chemical compounds by understanding the drug's hidden patterns and properties from data using a prediction model for the compound's absorption, distribution, metabolism and excretion profile and mode of action.

Drug characteristic prediction systems are already widely available in South Korea, but SK Biopharmaceuticals is the sole owner in the country of the platform that can design completely novel compounds that can be filed for substance patents.

Using the AI-based drug design platform and SK Biopharmaceuticals' discovery portal, company researchers will be able to efficiently explore and design new drug substance candidates and suggest research hypotheses.

There have been a number of other recent collaborations in the AI field in South Korea, indicating the field's steady emergence. CJ Healthcare has also linked with Syntekabio to develop immuno-oncology drugs using AI, in a partnership under which Syntekabio will handle the early stages of drug development, while CJ Healthcare will proceed with clinical trials.

**Daewoong Pharmaceutical Co. Ltd.** has meanwhile reached a co-research agreement with the Ulsan National Institute of Science and Technology (UNIST) on new drug development using AI.

Last year, the Korean company Standigm launched the AI-driven drug discovery services *Expander* and *Hunter* to help pharma firms minimize costs and risks. Expander enables pharma companies to quickly identify novel clinical uses for their existing drugs, while Hunter identifies repositioned lead compounds tailored to customers' needs.

Hunter, which is based on Standigm's AI technology, searches for potential drugs and protein targets related to specific diseases, and other collaborative partners for the system include Korean drug discovery company **CrystalGenomics Inc.**

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*From the editors of PharmAsia News.*

# Pharma CEO Pay Up In India, Ratio Versus Employee Earnings Glaring

**ANJU GHANGURDE** anju.ghangurde@informa.com

Business pressures and earnings bumps notwithstanding, CEOs of most leading domestic and foreign firms in India saw good gains in their remuneration in 2017-18 over the previous year, data compiled by *Scrip* indicate. The co-chair and CEO of Dr Reddy's is the only executive on the list who drew a lower salary in 2017-18 versus the previous year.

CEOs/managing directors at the Indian firms reviewed continued to earn much more than bosses of foreign firms' Indian operations, though some domestic firms are led by founding family members and a comparison of their remuneration with their peers at multinational corporations (MNCs) may not be completely appropriate. Many of the Indian founding groups are known to have invested their life earnings in building their firms from scratch. *(Also see "India CEO Pay: Local Firms Still Way Ahead Of Foreign Peers" - Scrip, 3 Oct, 2017.)*

Cadila Healthcare managing director, Dr Sharvil Patel, topped the earnings chart by a significant margin over his peers, while GSK In-

*Pharma CEOs in India received higher remuneration in 2017-18*

dia managing director, Annaswamy Vaidheesh, was the top earner among foreign firms reviewed by *Scrip*. All CEOs on the list drew higher remuneration in 2017-18, except GV Prasad, the Dr Reddy's co-chair and CEO, who took home a lower salary compared with the previous year.

## CEOS 'NOT OVERPAID'

Some experts said that an "upward trend" in CEO salaries is expected, but conceded that in most Indian pharma companies the founder/promoter CEOs earn "way above" their professional counterparts. And most foreign firms have their global HR guidance on CEO compensation, which also takes into consideration factors such as the country's tax rate, inflation and cost of living, they added.

Dr Ajit Dangi, president and CEO of Danssen Consulting and also a former president and executive director of Johnson & Johnson India, explained that CEO compensation is often based on availability of leadership talent, competition, and size and complexity of the business. Pharma is also one of the most highly regulated businesses in India with rigid price controls, intense competition, weak enforcement of IPR (intellectual property rights) laws and other regulatory issues, he noted.

"A pharma CEO therefore has to navigate through these multiple challenges and give reasonable returns to the investor. Additionally, the concept of 'triple bottom line' [financial, social and environmental] is gaining ground in reputed companies. Considering these factors, I don't think pharma CEOs are overpaid," Dangi told *Scrip*, adding that corporate India is "loosening its purse strings" to attract the best talent.

Other experts added that salaries of top bosses at Indian firms aren't high even on a regional basis.

Salil Kallianpur, a former executive vice president at GlaxoSmithKline India, now running a digital health consultancy, said that research by the global advisory firm, Willis Towers Watson, shows annual base salaries in India are the lowest in the Asia Pacific region and significantly lower than China.

"While this is not specific to India, it shows that at senior management levels, India offers the lowest average annual base salary across the region, which is almost half that of China," Kallianpur told *Scrip*.

## CADILA MD TOP EARNER

Specifics on the CEO earnings data indicate that Dr Sharvil Patel, who took over Cadila Healthcare's reigns last year from his father and Cadila's founder Pankaj Patel, earned INR250m ($3.5m) in 2017-18. Patel junior earned over 38% more than his father had in the previous year; Pankaj Patel was managing director up to July 11, 2017.

Peer Lupin, also led by a member of the founding family and managing director Nilesh Gupta, saw the scion draw remuneration of INR90.66m in 2017-18, while Cipla MD and global CEO, Umang Vohra, the only CEO who is not part of a founding family on the list of India firms covered by *Scrip*, earned a cool INR146.7m.

Vohra's earnings dwarfed that of Dilip Shanghvi, founder and managing director of India's top-ranked firm Sun Pharma. Shanghvi's remuneration stood at INR30m for 2017-18. Shanghvi, though, is, entitled to a remuneration of INR39.3m (excluding specific perquisites which are to be taken at actuals) for FY 2017-18 as approved by the board of directors.

However, details in the firm's annual report explained that in view of "absence of profits" for the year under review, the company paid remuneration for the FY 2017-18 up to the permissible ceiling limits. Sun has, however, made an application to the Central Government for approval of payment of remuneration to Shanghvi and another executive for FY2017-18 as per their entitlement and the approval is awaited, the company said in its annual report submitted to the Bombay Stock Exchange on Oct 1.

## FOREIGN FIRMS

On the MNCs side, where there has been a string of top level management changes over the recent past, GSK India's boss led the earnings list, with remuneration of INR60m for the year ended March 2018, followed closely by Abbott India managing director Ambati Venu who had earnings of INR58.5m.

| COMPANY | MD/CEO | 2016-17 REMUNERATION IN INR MILLION | 2017-18 REMUNERATION IN INR MILLION |
|---|---|---|---|
| Cadila Healthcare | Pankaj Patel (up to July 11,2017)/ Dr Sharvil Patel | 180 | 250 |
| Cipla | Umang Vohra | 136.6 | 146.7 |
| Dr Reddy's | GV Prasad | 97.7 | ~77.4 |
| Lupin | Nilesh Gupta | 81.7 | 90.66 |
| Sun Pharma | Dilip Shanghvi | 28.4# | ~30 |
| Abbott India | Ambati Venu | ~26.4 (Sept. 29, 2016 to March 2017) | ~58.5 |
| GSK India | A Vaidheesh | ~39.2 | 60.1 |
| Novartis India | Ranjit Shahani*/ Jawed Zia** | ~37.6* | 53.1*/3.2** |
| Pfizer India | S Sridhar | ~27 | ~34.2 |
| Sanofi India | Dr S Ayyangar | ~16.1 (year ended Dec'16) | 27.7 (year ended Dec '17) |

# Sun's 2017-18 annual report notes that during the year, the company received an Order from the Ministry of Corporate Affairs for approval of remuneration of INR20.23m to Mr Shanghvi for the financial year 2016-17 and a balance remuneration amount of INR9,147,601 has been refunded by the executive to the company.

Abbott India said that it does not have any stock option plan for its employees but the managing director is entitled to restricted stock units of Abbott Laboratories US under its Incentive Stock Option Program. The executive is also eligible to purchase shares of Abbott Labs US under its Affiliate Employee Stock Purchase Plan the perquisite value of which is included in the remuneration figure, details in the Abbott India's 2017-18 annual report specified.

Outgoing Novartis India vice chair and managing director Ranjit Shahani earned INR53.1m, while incoming head Jawed Zia had INR3.2m, though Zia has since moved on to Abbott. Shahani had resigned with effect from Feb. 28, 2018, and Zia was appointed effective March 1, 2018, but left soon after to join Abbott India as vice president (established pharmaceuticals). Milan Paleja, currently leads Novartis India as country president and country head (pharmaceuticals).

Sanofi India too saw top level changes with long-serving managing director Dr Shailesh Ayyangar moving on to a new role in the Sanofi Asia region though he still remains a Non-Executive Director on Sanofi India's board effective Jan 1, 2018. Rajaram Narayanan took over as the managing director of Sanofi India Limited with effect from January 1, 2018.

As of Dec. 2017, when he was whole-time director, Narayanan's remuneration stood at INR43.8m as against INR27.7m paid out to Ayyangar during 2017-18.

*Scrip*'s review, however, does not include the big boys - Merck & Co, Eli Lilly, Johnson & Johnson and Roche - whose operating firms are unlisted in India.

## HUGE DIFFERENTIAL 'NOT ACCEPTABLE'

Although rising pharma CEO pay in India doesn't seem unusual, experts generally disapproved of the sharp pay differentials at some companies, both Indian and foreign, when compared with average employee pay.

While the ratio of the remuneration of the top management to the median remuneration of the employees of their respective companies was varied, these were generally high across the board. In the case of the managing director of Cadila Healthcare the ratio was 641.03, while at Lupin it was 225, Cipla 587, GSK India 61.59, Abbott India 85.7 and Pfizer India 45.76. Ex-GSK India executive Kallianpur said that while CEOs must receive remuneration according to the role, responsibility and status of the positions they hold, the huge differentials in CEO to median remunerations is "not acceptable".

He noted that an article in Forbes last year listed the salaries of CEOs of blue-chip firms in India across sectors and the difference that has with median pay in their firms - "it is nauseating," he commented.

Kallianpur reiterated that while one may rationalize that CEO salaries are influenced by global levels while salaries in lower ranks are influenced more by local conditions, reports show that British and American CEOs earn 331 times that of median salaries in their organizations. Public sector firms in India, on the other side, represent another extreme where CEO salaries are three to four times that of median salaries, though it's unclear if perks form part of the remuneration.

Kallianpur had previously underscored that the idea is to strike a "balance between adequate CEO remuneration and glaring inequalities".

Danssen's Dangi mirrored similar views noting that the gap between CEO salaries and median employee pay is rather high in India and not a healthy trend; however, so is the case in most developed areas like Europe and the US.

"What is unacceptable however is the gap between male and female CEO compensation which exists even in the US to an extent of 15-20% and must be bridged if one is committed to gender parity in compensation," Dangi added.

Earlier this year, Teva indicated that the annualized total compensation of its President and CEO, Kåre Schultz, who came on board in 2017, was $19.37m and that the ratio of his annualized total compensation to the estimated median of the annual total compensation of employees was 302:1.

"We believe this pay ratio is a reasonable estimate calculated in a manner consistent with SEC rules," Teva said in Feb. 2018, adding that a substantial portion of Schultz's compensation for 2017 was the "sign-on equity awards" he received in accordance with his employment agreement, which had a grant date fair value of approximately $10.2m. Excluding the sign-on equity awards, the ratio would have been 143 to 1.

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# Sun To Trim US Manufacturing, Over 90 Jobs At Stake

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**Sun Pharmaceutical Industries Ltd.** is streamlining manufacturing in the US, with an eye on pruning costs and improving efficiencies. Operations at two US sites – New Brunswick and Cranbury – will now be combined, with more than 90 jobs likely to be hit.

India's top-ranked drug firm has issued a notice under the WARN [Worker Adjustment and Retraining Notification] Act indicating that 96 positions could likely be affected at its Cranbury facility. It comes with an effective date of Jan. 31, 2019, as per details on the website of the New Jersey state department of labor and workforce development. WARN typically offers protection to workers, their families and communities by requiring employers to provide notice 60 days in advance of covered plant closings/ mass layoffs.

Sun told *Scrip* that it was "consolidating" its manufacturing operations at New Brunswick and Cranbury into the one location.

"As part of this process the operations at Cranbury including inventory, products, manufacturing and lab equipment are being transferred to New Brunswick. The restructuring is aimed at optimizing our manufacturing operations and improving cost efficiencies in the increasingly competitive US market," Sun said.

The Indian firm expects to offer full support to the employees at Cranbury and is assisting them with "internal reallocations and outplacement services." Sun, with an estimated 40 plus manufacturing units across six continents, has been rationalizing its manu-

CONTINUED ON PAGE 23

# Novo Nordisk May Use Priority Review Voucher To Speed Oral Semaglutide To Market

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The last of **Novo Nordisk AS**'s 10 PIONEER clinical development program trials - PIONEER 6 - has read out early with good results, allowing the Danish diabetes fighter to file its oral GLP-1 semaglutide in the first-half of the new year, earlier than previously expected, chief science officer Mads Krogsgaard Thomsen told *Scrip*.

*Novo Nordisk chief science officer Mads Krogsgaard Thomsen*

Thomsen, who has been with the Danish group for more than 25 years, also said Novo Nordisk may use a priority review voucher to hasten the regulatory approval process and thus get the oral therapy to patients more quickly.

"Originally we said we would submit a filing for semaglutide in the US around mid-2019," he said in an interview.

"The PIONEER 6 readout has occurred sooner than we had originally anticipated, so we are hoping to wrap up the semglutide application as soon as possible so aiming for the first half of next year and the regulatory process would typically be 10 months in the US unless you use a priority review voucher, in which the review would be reduced to 6 months."

"We have not yet communicated whether we would use such a voucher, but that is clearly an option," he said.

## PIONEER 6 MESSAGE

The CSO was speaking after the release of topline data from PIONEER 6, a Phase IIIa pre-approval cardiovascular outcomes trial showing that its once-daily oral therapy semaglutide hit the primary endpoint of non-inferiority of major adverse cardiovascular events (MACE) versus placebo in patients with type 2 diabetes at high risk of cardiovascular events.

The trial showed significant reduction in cardiovascular death and all-cause mortality in people with type 2 diabetes.

Patients who received semaglutide in tablet form along with the standard regimen suffered 21% fewer major heart complications than those who got a placebo. While that wasn't enough to show that the drug was safer than standard care, it hit the goal of showing it's at least as safe, and also demonstrated significant reductions in cardiovascular-related and overall deaths.

"This was the tenth and last of the PIONEER trials and also the most exciting one because it's not every day that you reduce all-cause of mortality significantly by 49% with only 3,000 patients with an average follow-up of only 16 months, and a highly significant P Value of only 0.008," Thomsen said.

He said Novo Nordisk will now discuss the data with FDA and attempt to use PIONEER 6 and SUSTAIN 6 to gain a potential CV claim for injectable *Ozempic*, without the need for a CV superiority study.

In the SUSTAIN-6 study, Ozempic demonstrated a 26% reduction in major adverse cardiovascular events, but the company said at the time the data were released that it would need a larger, longer outcomes study post-approval in order to get a claim for a cardiovascular benefit.

"The maths of PIONEER 6 and SUSTAIN 6 show the strengths of semaglutide and that if you add together findings from those two trials you'll find there is a 25% cardiovascular risk reduction that's driven by all three components – mortality, myocardial infarction and strokes," he said. And Thomsen played down the fact the 21% reduction in MACE in favor of oral semaglutide seen in PIONEER 6 did not reach statistical significance.

> 'The ultimate goal – namely mortality – is actually reduced significantly by 51% in a trial that wasn't powered to show any significance. So we view these results very positively and as being confirmatory of the notion that semaglutide as a molecule is cardio protective'

"The numerical reduction of 21% would also have been statistically significant if the study had had the same amount of MACE events as SUSTAIN 6."

"This [PIONEER 6] is simply a safety trial - but it shows the hazard ratio is in the ball park of what we saw for semaglutide in SUSTAIN 6 and corroborates and solidifies the view that semaglutide has a stronger cardio protective action than for instance *Victoza* (liraglutide) and GLP-2 inhibitors that typically are in the 13% to 14% MACE reduction range as seen in their trials." He said the reduction in cardiovascular mortality seen in PIONEER 6 was very significant. "The ultimate goal – namely mortality – is actually reduced significantly by 51% in a trial that wasn't powered to show any significance. So we view these results very positively and as being confirmatory of the notion that semaglutide as a molecule is cardio protective," Thomsen told *Scrip*.

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# Phase III

| Event Stage | Lead Company/Partner | Drug Name | Indication | Comments | Change To LOA (%) | LOA (%) |
|---|---|---|---|---|---|---|
| Phase III Trial Suspension | Vectura Group plc | VR475 (budesonide) nebuliser | Severe Uncontrolled Asthma | Missed Primary Endpoint | -12 | 0 |
| Phase III Published Results | Shire Pharmaceuticals | Takhzyro (lanadelumab) | Hereditary Angioedema | HELP; In JAMA, Nov. 27, 2018 | 0 | 100 |
| Phase III Interim/Top-Line Results | Bristol-Myers Squibb | Opdivo (nivolumab) Plus Yervoy (ipilimumab) | Small Cell Lung Cancer | CheckMate-451 (Maintenance); Missed OS Primary Endpoint | 0 | 100 |
| Phase III Interim/Top-Line Results | Novo Nordisk A/S | Oral semaglutide | Diabetes Type II | PIONEER 6 (CV Safety); Met Primary Endpoint | 0 | 76 |
| Phase III Interim/Top-Line Results | Merck KGaA | Erbitux (cetuximab), Plus Chemo | Head and Neck Cancer, First-Line | CHANGE 2; Safe And Effective In Chinese Patients | 0 | 100 |
| Phase III Interim/Top-Line Results | GW Pharmaceuticals plc | Epidiolex (cannabidiol) | Dravet Syndrome | Gwpcare2; Achieved Primary Endpoint, Reduced Seizures | 0 | 100 |
| Phase III Interim/Top-Line Results | Vertex Pharmaceuticals Inc. | VX-659 | Cystic Fibrosis | Safe And Effective In A Triple Combo | 5 | 80 |
| Phase III Interim/Top-Line Results | Eisai Co., Ltd. | Fycompa (perampanel) | Partial Seizures | Study 342 (Japan); Met Primary Endpoint | 0 | 100 |
| Phase III Interim/Top-Line Results | Alkermes plc | ALKS 3831 (olanzapine/samidorphan) | Schizophrenia | ENLIGHTEN-2; Positive Results, Met Co-Primary Endpoints | 0 | 55 |
| Phase III Trial Initiation | ObsEva SA | OBE001 (nolasiban) | Assisted Fertility | IMPLANT 4; An Oxytocin Antagonist | 0 | 68 |
| Phase III Trial Initiation | Jazz Pharmaceuticals plc | JZP-258 (oxybate mixed salts) | Idiopathic Hypersomnia | In Centers In The US And EU | 0 | 52 |
| Phase III Trial Initiation | Principia Biopharma, Inc. | PRN1008 | Pemphigus Vulgaris | PEGASUS; In Moderate-To-Severe Disease | 39 | 59 |
| Phase II/III Trial Announcement | Tocagen, Inc. | Toca 511 (vocimagene amiretrorepvec) | Brain Cancer | Nrg-Bn006; In Newly Diagnosed Disease | 0 | 37 |

**Source: Biomedtracker | Informa, 2018**

CONTINUED FROM PAGE 20

facturing operations in the US. In 2016, Sun sold two oral solid dosage manufacturing facilities located at Philadelphia, PA, and Aurora, IL in the US, along with 15 related pharmaceutical products to Frontida BioPharm, Inc, as part of efforts to consolidate manufacturing there.

Sun's founder and managing director Dilip Shanghvi has reiterated recently that the company is continuing to pursue efforts to control costs and improving efficiencies. "These steps are necessary to ensure that we continue to earn reasonable returns in the current competitive state of the US generic market," Shanghvi said on the firm's earning call Nov. 13.

> Sun's founder and managing director Dilip Shanghvi has reiterated recently that the company is continuing to pursue efforts to control costs and improving efficiencies

Besides, with significant initial expenses anticipated in 2018-19 as Sun seeks to establish its recently launched products *Yonsa* (abiraterone acetate) and *Ilumya* (tildrakizumab) in the US, the Indian firm is generally expected to keep a hawk eye on costs. *(Also see "As AbbVie's Risankizumab Looms, Sun Pushes To 'Maximize Time' Of Ilumya" - Scrip, 16 Nov, 2018.)*

*Sun Pharma is consolidating manufacturing in the US*

Some of Sun's Indian peers too have been recalibrating their US business in view of the competition and pricing pressures – **Cipla Ltd.** for instance has fine-tuned its US product portfolio with an eye on margins and the "relative burden" on its manufacturing and supply chain infrastructure. *(Also see "Cipla Evaluates US Portfolio Tucks, Generic Advair Studies Progress" - Scrip, 8 Feb, 2018.)* More recently, **Glenmark Pharmaceuticals Ltd.** said it was no longer pursuing development of four in-licensed complex generic assets as the overall business case for these products had "significantly weakened" due to the intensely competitive landscape in the US.

*Published online 29 November 2018*

## APPOINTMENTS

| Executive | To Company | New Role | From Company | Previous Role | Effective Date |
|---|---|---|---|---|---|
| Vipin K. Garg | Altimmune Inc | Chief Executive Officer and President | Neos Therapeutics | Chief Executive Officer and President | 30-Nov-18 |
| Steven Lydeamore | Anatara Lifesciences Ltd | Chief Executive Officer | Apotex | President | 3-Dec-18 |
| Matt Wiley | Foamix Pharmaceuticals | Chief Commercial Officer | Jazz Pharmaceuticals | Vice President, Marketing and Business Unit Lead | 27-Nov-18 |
| Dashyant Dhanak | Incyte Corp | Chief Scientific Officer and Executive Vice President | Janssen Research and Development | Global Head, Discovery Sciences | 10-Dec-18 |
| Dirk Huebner | Mersana Therapeutics | Chief Medical Officer | Boston Biomedical | Vice President, Head, Development | 27-Nov-18 |
| Samson Tom | Osiris Therapeutics Inc | Chief Executive Officer | Bioventus LLC | Vice President, Research and Development | 26-Nov-18 |
| Daniel Schneider | Photocure ASA | Chief Executive Officer and President | Ablynx NV | General Manager | 1-Nov-18 |

**Click here for all appointments: https://bit.ly/2oHWRYn**

*Source: Medtrack | Informa, 2018*

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