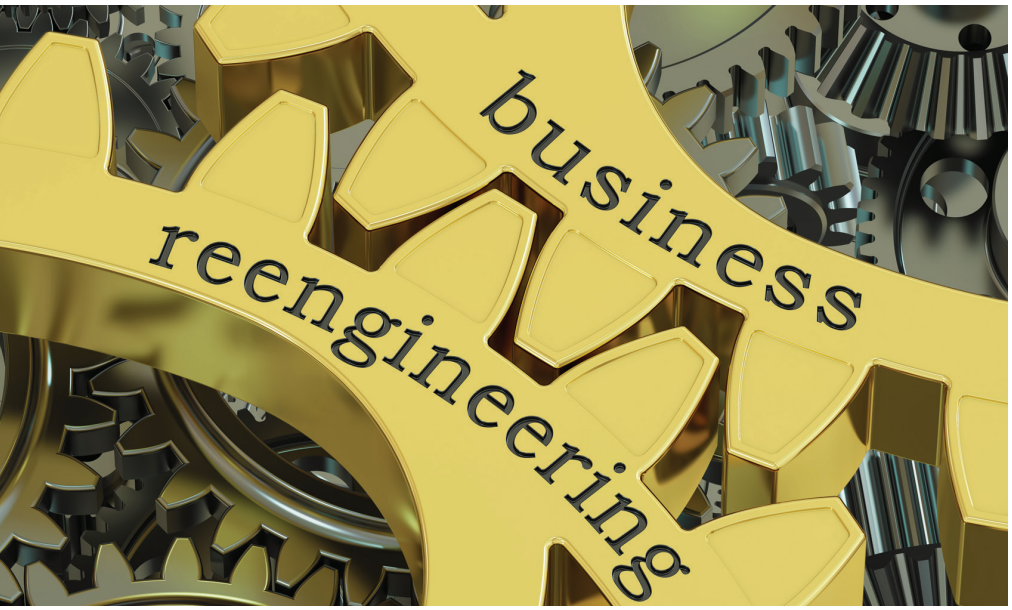
Scrip
21 September 2018
No. 3923
scrip.pharmaintelligence.informa.com
Pharma intelligence | informa



Deerfield To Go As Takeda Plans Realignment Of Post-Shire US Ops

IAN HAYDOCK ian.haydock@informa.com

Takeda Pharmaceutical Co. Ltd. is to close down one of its main sites in the US, relocating and rationalizing most functions, as it continues to implement restructuring around its planned $62.4bn acquisition of **Shire PLC**.

Activities at the Deerfield, Illinois site, which acts as the major Japanese firm's main US headquarters and currently employs nearly 1,000 people across three large buildings, will gradually be relocated to Boston, Massachusetts, potentially beginning within next year.

Takeda in Japan confirmed the move to *Scrip*, saying in a statement that: "Takeda has made the decision to close the Deerfield site post-closing [of the Shire deal].

"The work currently performed at Takeda's Deerfield location will progressively consolidate from Deerfield into the greater Boston area following a successful closing of the Shire acquisition."

The deal remains subject to final regulatory and shareholder approval, but Takeda anticipates closing of the massive planned acquisition of its larger quarry within the calendar first half of next year, in what would be the biggest ever overseas M&A transaction by any Japanese company.

Those at Deerfield are expected to learn if their jobs will go within six months of the buy-out's closure.

A progressive shift and consolidation of functions to greater Boston away from Deerfield - home to **Takeda Pharmaceuticals USA Inc.** (TPUSA) - is something that the company has already hinted would happen in US restructuring around the Shire deal.

Takeda has already relocated much of its global R&D activities to the area last year, and the $5.2bn acquisition of Cambridge, MA-based **Ariad Pharmaceuticals Inc.** early in 2017 further added to Takeda's presence there. *(Also see "Takeda Acquires Ariad In $5.2bn Deal – US Infrastructure A Key Component?" - Scrip, 9 Jan, 2017.)*

Shire also already has a major presence in the northeastern state through its sites in Cambridge.

In all, Takeda has around 5,000 employees in the US, its biggest single market globally by sales, and TPUSA was founded in 1998 as the firm's largest commercial business unit outside of Japan, contributing close to a third of group sales.

Takeda US spokeswomen Julia Ellwanger told local media that an unspecified number of those working at Deerfield would be provided with relocation opportunities or other internal job offers, and that the closure would not affect the field force based at the site.

Elsewhere in Illinois, Takeda also has a site at Bannockburn near Deerfield, but it is not yet clear how this may be affected.

"The [Deerfield] move, while difficult, will allow closer collaboration across Takeda to best position our future pipeline for success. It will also simplify our existing Takeda U.S. operations," Ellwanger was quoted as saying in the *Chicago Tribune*.

WIDER MOVES

Takeda has already been taking steps elsewhere to trim its property holdings, including relocating its Tokyo main office and

CONTINUED ON PAGE 4

from the editor

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Congratulations to Roche and Biogen for topping this year's Dow Jones Sustainability Index in the pharmaceuticals and biotechnology industries, respectively. Now in its twentieth year, the index analyses companies on more than 100 environmental, social and corporate governance (ESG) criteria, factors which are widely recognized by investors as playing a part in determining the strength of individual companies' investment propositions.

It wasn't always thus, but consideration of these factors is now incorporated into the fiduciary duties of company custodians. They no longer merely depict a company's level of altruism or desire to do good as a separate side show from their main business of turning a profit. It's become quite mainstream to view good ESG practice as an integral part of protecting the longer-term interests and sustainability of the company, not just its profile as a "good" corporate citizen in global society.

The biopharma industry can naturally claim strong credentials overall in comparison with most other industries when it comes to contributing to health outcomes. But there are other areas where there is still room for improvement. For example, exerting political influence: the healthcare industry spends more of its revenue on lobbying than other industries, which is perhaps unsurprising given that it is so highly regulated. However, powerful but narrowly self-interested lobbying by its members may ultimately hurt an industry. US drug pricing is an area where the healthiest approach is to collaborate with other stakeholders as a decent partner to find a way to balance patient access with fair returns, rather than lobbying for industry protection.

Scrip

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Boehringer Ingelheim Is Getting Bets In Early In I-O Space
https://bit.ly/2PFQQXy

The head of the German family-owned firm's venture fund tells *Scrip* that investing very early in promising start-ups gives Boehringer Ingelheim "a little bit of a head start" on rival pharma companies in identifying technologies that could translate into therapies five years down the line .

Roivant's New Respiratory-Focused Vant Adds Chronic Cough Candidate To The Portfolio
https://bit.ly/2pjiJcS

Respivant will be Roivant's 13th "vant," focused on developing what was Patara Pharma's mast cell stimulator for chronic cough in patients with idiopathic pulmonary fibrosis. Former Patara CEO Bill Gerhart will lead the firm.

Assessing Artios: $83m Series B, Big-Name Investors, Nothing In The Clinic
https://bit.ly/2QD6NPL

Cambridge, UK-based Artios Pharma attracted several new investors for its over-subscribed series B round in August 2018, but the company is yet to enter the clinic with its DNA repair drug portfolio and has many hurdles ahead to validate its technology. *Scrip* speaks to investors from LSP and Arix about why preclinical-stage biotechs are getting more attention in 2018.

REPAIR Is Trying To Fix The Antibiotic Gap Left By Industry
https://bit.ly/2xteYoW

As large biopharmaceutical companies continue to exit antibacterial R&D, investments by Novo Holding's REPAIR Impact Fund and grants from CARB-X can push forward novel therapies for drug-resistant microbial infections.

Deal Watch: Cigna Acquisition Of Express Scripts OKed By US Justice Dept.
https://bit.ly/2PKAsFj

It remains unclear what impact the consolidation within the drug-distribution sector may have on pricing. Pfizer partners with France's Cytoo for its new gene therapy approach to DMD, while Gilead teams with Precision BioSciences for its goal to cure HBV.

Finance Watch: Opko's Stock Halted As Nasdaq Awaits An Explanation For SEC Pump-And-Dump Lawsuit
https://bit.ly/2MIxWxA

Public Company Edition: An SEC complaint alleges that the company, Opko CEO Frost and co-defendants bought penny stocks, pumped up their value, then dumped shares for sizeable profits. Also, Pfizer and Retrophin float debt offerings, while Zealand sells royalties and milestone fees to raise cash.

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CONTINUED FROM FRONT COVER

divesting the old building, as it seeks to maximize income ahead of the Shire move.

There have also been some media reports in Japan that its Osaka headquarters may be sold off, but as yet there has been no confirmation from the company on such a plan.

At the time the Shire acquisition was first announced, there were estimates that up to 6-7% of the combined Takeda/Shire global workforce of around 53,000 could be cut in post-merger rationalization; Takeda has already projected annual pre-tax cost synergies of at least $1.4bn per annum.

The company has said that just over half of these projected savings will come from reduced selling, general and administrative expenses - mainly sales and marketing efficiencies - and the consolidation of overlapping office locations, with much of the remainder deriving from R&D rationalization. *(Also see "Takeda Feels Need For Speed In Approaching Shire Integration " - Scrip, 10 May, 2018.)*

In total, Takeda is planning to unlock around $1.74bn in cash in the current fiscal year to next March 31 through a variety of asset disposals, as it aims to minimize its reliance on loan financing for the Shire move. *(Also see "Takeda To Unlock More Cash As It Preps For Shire" - Scrip, 14 May, 2018.)*

VOCAL OPPOSITION TO SHIRE DEAL

Meanwhile, the Japanese company is continuing to face increasingly vocal opposition in Japan to the planned transaction from a group of conservative activist shareholders including Kazu Takeda, part of the company's founding family.

He has warned of "disastrous" consequences if the deal goes ahead, and that it goes against the corporate philosophy of "Takeda-ism", the founding principles of the 237 year-old company that include integrity, fairness, honesty and perseverance.

Apparently aiming to take his views to a wider global audience, "We understand that scaling up is necessary, but Takeda management has to think about the traditional corporate culture and the health of the company," the family investor told the UK's *The Times* newspaper.

The scion is a key member of a group of around 130 investors (with a combined holding of roughly 1%) that have dubbed themselves "Thinking About Takeda's Bright Future", and have retained a former equity analyst to help build support for their concerns.

One outcome may be a possible motion to halt the effective merger with Shire, which if successful would result in existing Takeda investors holding only 50% of the combined entity.

The group proposed a motion at Takeda's late June annual general meeting that would have required senior management to seek investor approval of any large M&A deals worth more than JPY1tn (around $9.2bn).

In the event, the proposal did not receive wide support and was not passed.

Takeda's CEO, Frenchman Christophe Weber, has repeatedly stated that the Shire deal would provide multiple benefits as the group seeks true global scale and competitiveness, and that the values of "Takeda-ism" would be fully respected as part of the transaction.

Published 12 September 2018
From the editors of PharmAsia News.

Mixed Views On Hong Kong Market's Role Despite IPOs Lining Up

JULES QUARTLY

Four months on from the biggest revamp in a quarter of a century for Hong Kong Exchanges and Clearing (HKEX), and the dawn of a touted new era is still breaking.

Chinese biotech valuations have taken a hit since the exchange's new rules for the listing of pre-revenue biotech venture were introduced on April 30. The Shanghai composite market continues its slide of nearly 20% over the past year, dragged down by US trade war fears and a slowing economy, while a fake vaccine scandal in mainland China further depressed pharmaceutical stocks in July.

Meanwhile, the US stock market and the Nasdaq in particular is hitting all-time highs, prompting some commentators to declare that Hong Kong's expected IPO takeoff has crashed and the city no longer looks like a biotech listings hub to rival New York.

However, this pessimistic view is decidedly not that of industry insiders, analysts and investors in Hong Kong, who describe the new and planned IPOs as a "good start" and counsel patience. Furthermore, they insist the HKEX is a "must-have market for China biotech" and the future of "innovation with Chinese characteristics."

MIXED PERFORMANCES SO FAR

In reality, the situation has been mixed since HKEX CEO and Executive Director Charles Li rang the regulatory changes and declared them the "dawn of a new era," giving the green light to biotech companies without revenues or profits, in addition to those with dual-class share structures, to go public in the territory.

On the one hand is the example of **Ascletis Pharma Inc.**, the Chinese early-stage developer of hepatitis C and HIV drugs. It was the first to list at the end of July, with a generous $2bn valuation, but it's share price has since halved, plummeting from HKD14 ($1.78) to HKD7.3. *(Also see "Finance Watch: Ascletis First Biotech To List Under New Hong Kong Rules, BeiGene Joins In" - Scrip, 3 Aug, 2018.)*

BeiGene Ltd. was up next. The Beijing-based company focuses on innovative drugs to treat cancer and was the first early-stage Chinese biotech to be listed on the Nasdaq Global Select Market in the US. Its HKEX debut raked in $903m but its performance since then has been lackluster, and was trading in early September slightly lower than its high of HKD106.2. *(Also see "A Safe Harbor For Biotechs? Ascletis, BeiGene Mark Early Wins For HK Exchange" - Scrip, 9 Aug, 2018.)*

On the other hand, it is still early days for the HKEX. In the buildup to the new listing regime, Li made it abundantly clear that this was a five-year project and that quick gains were "unlikely." The bigger picture of siphoning trade from Nasdaq by giving Chinese investors the opportunity to bypass China's partially closed capital markets but still list closer to home in Hong Kong is still expected to an attractive option. *(Also see "Hong Kong Ushers in 'New Era' For Bioventures As Listing Rules Eased" - Scrip, 1 May, 2018.)*

Product familiarity and proximity, plus potentially better valuations for Chinese biotech companies, are among the reasons for optimism about Hong Kong listings. Time zone, language and cultural advantages are other pluses. From a macro perspective, a huge and ageing population of 1.4 billion people in China, plus sustained economic growth in this market, hold out the promise of mega profits for drug makers.

This is especially true given the "normalization" of the market due to ongoing regulatory reforms that include an overhaul of the China National Medical Products Administration (NMPA, formerly the CFDA or CDA). Among the changes, it is fast-tracking drug reviews for unmet needs, relaxing rules on clinical trials, and speeding up drug approvals, in addition to expanding the country's national insurance scheme for medicines.

10 IPOS PLANNED AS HK TOUTS BENEFITS

Though China stock markets have been lagging, the good news for Hong Kong is that it has regained its position as the world's biggest IPO fundraising destination in general, registering $38.1bn over the past year, partly due to the new relaxed listing rules it has instituted.

Furthermore, the success and failure of companies on the HKEX are not predicated on where the listing is made. Arguably, BeiGene is a "five-star hotel" or best in class company - meaning it is truly innovative and sound - whereas Ascletis could be considered more of a "me too" rather than a "me better" company and was possibly overvalued - hence the market correction since its listing.

A HKEX spokesperson commenting to *Scrip* said 10 companies have so far lined up to make their IPO pitch in Hong Kong. "Listings and applications so far suggest we're off to a good start as we work to broaden our market with the addition of a thriving biotech sector".

"Our objective was to update our rules, to align them with today's economy and position our market for the future – and we are confident we did what we set out to do."

The spokesperson added that the new rules have enabled a much wider range of local, mainland and international biotech, pharmaceutical and life science companies to list in Hong Kong.

"In addition to providing funds at the IPO stage, listing in Hong Kong - a free market which has abundant liquidity - gives companies great flexibility in subsequent fundraising in the secondary market. Moreover, with Stock Connect [a system allowing mutual remote trading in the Hong Kong, Shanghai and Shenzhen exchanges through either three], we offer the unique benefits of the only access to a diverse pool of mainland and international investors.

"For the foreseeable future, we believe Hong Kong will continue to provide a one-of-a-kind bridge between a fast-growing but not fully open mainland economy and the rest of the world that sets us apart from other markets."

As for the negatives, such as Forex restrictions and the policies of the US and Chinese governments, the HKEX spokesperson said: "All stock sectors in Hong Kong have been affected by less positive market sentiment compared with the beginning of the year, or last year, when Hong Kong blue chips gained 36%. They've also been affected by geopolitical developments that have reduced optimism about economic growth around the world and the outlook for capital markets globally.

> HKEX CEO Li made it abundantly clear that the new listing regime was a five-year project and quick gains were 'unlikely.'

"From our perspective, the listing rules for pre-revenue biotech companies that we introduced in the second quarter of this year are a long-term initiative and should be viewed in that context. Most if not all pre-revenue biotech companies almost certainly share our view. As early stage companies, they cannot focus on the short term."

'TEST LAB' ROLE

Frank Yu, founder and CEO of Ally Bridge Group (ABG), a Hong Kong-based healthcare investment group, was in Taipei for talks and set aside time for a wide-ranging discussion with *Scrip* about the newfound role of the HKEX and its position as a listings exchange for innovation vis-à-vis New York.

Yu pointed out that his company had a "3 by 3" strategy of investing in the three key geographies of China, the US and Europe, with a focus on innovation, buyouts and hedge funds. The company was one of four cornerstone investors sweeping up 19.8 million shares in the BeiGene IPO offering.

"The HKEX is a kind of test lab for the China biotech market. It is common knowledge that one of the main reasons for much of the cutting-edge innovation landscape is the role of the Nasdaq [in the US], which funds many thousands of IT or life sciences companies without revenue," Yu said.

"The advantages of Hong Kong are that it has common law jurisdiction, which makes it good for financial markets and innovation because it's flexible. It is a thriving international financial center, combined with being a free market." As such it will be a magnet for investment in an Asian biotech market that is still in its infancy. In time, it will also be able to draw on the experience of the Nasdaq and life science industry to attract specialist investors and analysts.

"There will be a learning curve and I would expect the Hong Kong market to develop and become more sophisticated in a financial and industry context. It should provide a key alternative to the Nasdaq for companies and especially those that are not suitable to list on the Nasdaq," Yu predicted.

STILL EARLY FOR PIVOT

The HKEX also provides flexibility and possibly better valuations. That said, Yu does not see the balance of power shifting significantly in the near future as the Nasdaq will "continue to be the mecca for technology, biotech and innovation stocks".

"Sooner or later companies will go to the Nasdaq. Time and again it has generated global superstars in these industries. China has a lot of liquidity but whether this can generate world-class superstars is another matter." However, "Hong Kong is a bridge from China to the world and it promotes for the first time a public market for Chinese investors and others to invest in pre-revenue biotech companies from China."

Yu concluded: "This [Hong Kong] is a must-have market for China biotech. If you don't have this market then China will be handicapped in the development of its homegrown innovation. This is really important for China and what I call 'innovation with Chinese characteristics.'"

Published online 12 September 2018
From the editors of PharmAsia News.

HHS Secretary Alex Azar Talks Rebate Changes, But Not Eliminating Discounts Altogether

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HHS Secretary Alex Azar reaffirmed that drug rebate changes are coming, during an address at the FT Pharma Pricing and Value Summit Sept. 13, but he did not mention eliminating discounts altogether.

The pharmaceutical industry is in a whirlwind about rebates, preparing for a future that is expected to include big changes to the long-standing practice industry relies on to negotiate market access for drugs with US payers. As part of the Trump Administration's blueprint on drug pricing released in May, the government is expected to implement rebate reform that will change the way discounts on net drug prices are negotiated – or perhaps eliminate them altogether.

While industry is generally receptive to changing its rebating practices, eliminating them altogether would be a major disrupter to the current drug distribution model and greatly shift the competitive dynamics. HHS' Office of Inspector General is preparing a proposed rule that could remove the safe harbor that allows negotiated rebates from the anti-kickback statute, but what will ultimately come out of the ongoing process remains to be seen. *(Also see "HHS Advancing Attack On Rebates With Proposal To Revoke Safe Harbor" - Pink Sheet, 24 Jul, 2018.)*

HHS Secretary Alex Azar discussing drug pricing.

Source: FT Live

In comments at the FT summit, Azar did not discuss the elimination of rebates altogether or mention the safe harbor provision, but talked instead about discounts that could be handed down to patients at the point of sale, something some insurers have already announced they will begin doing in 2019.

"If we were to rethink the rebate system and instead, for instance, have a system where negotiated discounts are done, brought forward at the point of sale, to the benefit of the patient at point of sale, I believe you would have a radical change in the incentive system from pharmas to actually reduce their list price and reduce what those in the industry call the gross-to-net spread that has been increasing every more," Azar said.

The Trump Administration's blueprint endorses point-of-sale rebates but only if the policy is implemented as part of a package

of Part D reforms, some of which would produce savings to offset what is expected to be increased costs of such a policy.

The Congressional Budget Office projected redirecting drug rebates to offset Part D beneficiary cost sharing at point-of-sale would increase government spending $43bn over 10 years. While industry has advocated in favor of handing the rebate to consumers at point-of-sale, payers have argued that money saved from rebates goes to offset higher insurance premiums. Critics argue that payers are incentivized to contract for higher list price drugs on which they receive a bigger rebate.

"The rebate system that we have is a constant incentive to higher list prices," Azar said in his most recent comments. "Every player in the system makes more money off higher list prices because they are all getting compensated as a percent off the list price."

A BEAR VIEW OF VALUE-BASED REIMBURSEMENT CONTRACTS

How any rebate reform might impact industry's move toward value-based reimbursement contracts has also been a concern of stakeholders in the industry. Drug makers have shown increasing willingness to work with payers to offer value-based contracts that allow for steeper rebates if a drug fails to help a patient as it is meant to. Value-based contracts, however, inherently rely on some kind of discounted payment model.

Azar said he wants to keep value-based pricing options on the table, but sounded skeptical of the ability of such contracts to deliver big savings when it comes to drug spending.

"We certainly don't want government standing in the way of private arrangements that reliably deliver lower costs," he said. "But I want to be very clear: value-based contracts are not going to be the main answer to the high prices faced by American patients." The Centers for Medicare and Medicaid Services recently opted not to move forward with a value-based contracting program for **Novartis AG**'s CAR-T therapy *Kymriah*, noting that it isn't practical for all medications. Implementing value-based contracts for most drugs is simply not realistic, he said, so value-based options will be part of a multi-factor solution to a complex problem.

'I want to be very clear: value-based contracts are not going to be the main answer to the high prices faced by American patients.'

"If a pharma company wants to put their money where their mouth is, money-back guarantees, I want to make sure that pathway is open," he said. "But that is not going to be the case for the thousands of drugs out there. For those of us who have worked in that world, the transaction costs are just too high."

The US Center for Medicare and Medicaid Innovation will include value-based models as it experiments with alternative reimbursement models for drugs. Industry, which has led many early experiments with value-based contracting, had pushed for more government experimentation with these payment models.

BE WARY OF ANNUAL INCREASES

As for the annual drug price increases on marketed drugs that have come under fire recently, including from President Trump's Twitter handle, Azar warned drug makers to be cautious as the new year approaches.

"I suspect there are not many companies out there that are planning on net price increases in their internal business plan and modeling," he said. "The smarter companies are going to skate to where the puck is going and that is not an environment built around ongoing list price increases."

"We are going to be in a world of price deflation, lower gross-to-net and tougher negotiation against government programs, and if you don't build your business plans around that, you are going to be surprised."

Published online 13 September 2018

J&J Well Positioned For US Drug Pricing Changes Regardless Of Timing Or Form, Duato Says

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Biopharmaceutical companies can't talk business strategy with investors for long these days without addressing the issue of US drug pricing and healthcare reform. That was the case during **Johnson & Johnson**'s commercial overview presentation Sept. 13, where Vice Chairman Joaquin Duato assured investors the diversified pharma is well positioned to absorb changes, whatever shape they take.

J&J executives stressed that the company derives all of its growth from volume, not from price increases. Duato boasted of a compound annual growth rate (CAGR) of 8.6% from 2010 to 2017 for J&J, double the 4.3% rate posted by the industry at large for global branded drug revenue over that span – and said the pharma is set to continue on a similar trajectory.

"We operate in a challenging environment," Duato noted. "There is growing pressure by public and private payers to reduce overall health care costs. In the US, the current administration is focused in particular on reducing drug prices, and we are also facing accelerating competition from biosimilars. These are the dynamics we'll continue to navigate as we remain confident in Johnson's proven business model to help us drive sustainable success."

Illustrating J&J's business model and its results, Duato pointed out that the $8.4bn it invested in R&D last year "is unmatched in our industry" and that it has obtained 14 new product approvals since 2014. Further, its portfolio includes 14 products currently achieving blockbuster sales or projected to do so near-term, cutting across all six of its priority therapeutic areas – cardiovascular and metabolic disease; immunology; infectious disease/vaccines; neuroscience; oncology; and pulmonary hypertension.

J&J added the sixth area of focus with its $30bn acquisition of **Actelion Pharmaceuticals Ltd.**, finalized midway through 2017, which brought in approved drugs *Tracleer* (bosentan) and *Opsumit* (macitentan).

J&J Vice Chairman Joaquin Duato

> 'Since we do not rely on price to drive revenue growth, we are able to weather short-term challenges more effectively than many of our peers.'

Duato asserted that J&J's model enables it to succeed in a challenging business climate that has taken a toll on some rivals.

"Our growth comes exclusively from volume," he said. "Since we do not rely on price to drive revenue growth, we are able to weather short-term challenges more effectively than many of our peers. We believe our approach gives us a significant competitive advantage in a very complex market. In fact, our proven business model has helped us deliver growth that is nearly double that of the global branded market, with seven consecutive years of growth, and we are confident this model will help us to continue to deliver sustainable above-market growth."

EXPECTING SLOW PACE TO US PRICING CHANGES

During the pharma's full-year 2016 earnings call in January 2017, CEO Alex Gorsky announced a business transparency plan including a pledge for "responsible pricing" of its products. This followed a White House meeting between newly elected President Trump and a host of business leaders, including Gorsky. One of Trump's campaign issues – although never clearly detailed – focused on reining in prescription drug prices.

In late February of that year, J&J issued its first drug pricing report, in which it claimed it had held increases to average list prices below 10% during the prior five years, resulting in average net price increases – after rebates and discounts – ranging from 2.5% to 5.2%. One year later, in its second pricing report, J&J said the effect of rebates and discounts had resulted in a 4.6% reduction in net prices for its products, although as with other industry transparency reports, the figures cut across the portfolio, which means price increases for some newer growth drivers were higher.

During J&J's second quarter earnings call in July, Chief Financial Officer Joseph Wolk advised investors to expect 4%-6% net pricing impact on the pharma's products for full-year 2018. Also during that call, Gorsky urged that any changes to drug pricing structure in the US be implemented slowly, in order to avoid unintended consequences.

J&J Vice Chairman Joaquin DuatoDuring the Sept. 13 investor presentation, Duato spoke as if a slow process for reworking drug pricing was a virtual certainty.

"We understand there's more to do and we also share the administration's goals of trying to reduce healthcare costs while improving quality of care and patient access," he said. "In that context, it's also important to consider aligning incentives across the supply chain. So, when we think about those goals, we think it's appropriate … to talk about the role of the rebates and to work constructively to see what role they play with the goal of reducing healthcare costs and improving patient access."

"That said, when I think about the impact or when we think about the impact on the timing, there's not still enough information to comment on this proposal and what the business impact would be," Duato continued. "We're still preliminary so we don't have still enough information to comment on it. And in any case, given the process required for major policy changes, we would expect any change in that area to be gradual … it will take some time to be implemented."

GETTING READY FOR REMICADE EROSION

Meanwhile, in offsetting the commercial impact of biosimilars, Worldwide Chairman, Pharmaceuticals Jennifer Taubert told the call that in immunology, products such as *Stelara* (ustekinumab), *Simponi/ Simponi Aria* (golimumab) and recently launched *Tremfya* (guselkumab) are expected to help to mitigate the sales erosion for *Remicade* (infliximab).

Biosimilar competition to Remicade from **Pfizer Inc.**'s *Inflectra* and **Merck & Co. Inc.**'s *Renflexis* haven't taken a big bite so far, however, as J&J reported in July that Remicade has retained a 94% market share among infliximab products.

Duato attributed this mainly to physician and patient loyalty to J&J's branded product, as well as the lack of biosimilar interchangeability. "The strength of Remicade on how it is performing is based on physician and patient preference and the fact that we have a much broader set of indications and data than the biosimilars," he noted. "So, given the fact that biosimilars today are not interchangeable with the original product, the physician and patient preference does matter in that context."

At the same time, the company has implemented an effective rebating program for Remicade, one that Pfizer has alleged is anti-competitive in a lawsuit. J&J has also talked at length about its defensive contracting strategy for Remicade, which benefits, in part, because of the high volume associated with the brand drug versus new-to-market biosimilars.

Among the many proposals under consideration from the Trump Administration's drug pricing blueprint are changes to the US rebate structure – or the elimination of rebates altogether. Such a move would have a big impact on the way drug manufacturers negotiate market access with payers and could potentially impact the leverage that high-volume, mature brands like Remicade have over new entrants, including biosimilars.

Asked about the potential impact of rebate reform on Remicade, Duato said he doesn't expect any major impact in 2019. In addition, he noted, much of Remicade's durability is due to physician and patient preference and the fact that biosimilars are not interchangeable.

"Remicade and Remicade strength is not based on rebates," he declared.

Published online 13 September 2018

Allergan Buys Bonti, Releases New Data In Defense Of 'Iconic' Botox Brand

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Allergan PLC will pay $195m up front to buy the fast-acting, short duration neurotoxin maker **Bonti Inc.**, but the acquisition doesn't bring in a competitor to its blockbuster *Botox Cosmetic* (onabotulinumtoxinA). Instead, the company sees Bonti's EB-001 as a sort of gateway drug – one that lets patients test drive treatment with a wrinkle-reducing toxin before committing to Botox.

The deal was one of multiple defensive moves Allergan revealed on Sept. 14 during an investor event in New York City to showcase its medical aesthetics business, which generated $3.8bn in global sales in 2017 and is expected double to $7bn-$8bn by 2025. It was repeatedly noted that Botox is an "iconic" brand in the medical aesthetics market, but the company is under pressure from current competitors and new neurotoxins that could hit the market during the next few years.

In particular, **ReVance Therapeutics Inc.** plans to submit a biologic license application in 2019 for its neurotoxin candidate RT002 (daxibotulinumtoxinA) and will seek a label indicating efficacy for up to six months, versus Botox's three months. *(Also see "Revance's Long-Acting RT002 Will Have Slow-Moving Impact On Allergan" - Scrip, 5 Dec, 2017.)*

Allergan has attempted to throw doubt on its competitor's six-month efficacy claim, since only a third or less of patients treated with RT002 had no or few forehead wrinkles at 26 weeks in two Phase III studies. Even so, there has been speculation that Allergan would buy Revance to get its hands on a long-acting toxin, but the company revealed the deal for a shorter-acting agent instead.

Allergan also announced results on Sept. 14 from a 233-patient clinical study for higher doses of Botox, which seemed to show it doesn't need to buy Revance to acquire a longer-acting neurotoxin. The company tested its Botox Cosmetic 20-unit dose versus 40, 60 and 80-unit doses to see how many patients would be considered responders at 24 weeks (six months). The percentage of responders was 16% for 20 units, 32% for 40 units, 30.6% for 60 units and 38.5% for 80 units.

Allergan has not determined whether it will pursue a long-acting claim for Botox; it would need to conduct a Phase III study to seek additional approvals.

But when questioned about buying Revance to gain a longer-acting product, Allergan CEO Brent Saunders noted that the company would not invest in a product that helped only one-third of patients when physicians want something that helps at least 80%.

Revance's stock fell as low as $22.25 on Sept. 14 based on the lack of an Allergan deal, but closed down just 1.1% at $25.68.

However, Allergan investors lost enthusiasm for the company's medical aesthetics growth story as its six-plus hour presentation wore on: its stock traded as high as $191, but closed down 1% at $188.22.

BONTI TOXIN COULD TURN BOTOX CONSIDERERS INTO USERS

The Bonti deal was announced early in Allergan's medical aesthetics investor event. Bonti, founded as Endurance Biotech, launched in 2015 with $8.9m in Series A venture capital; as Bonti it raised an $11.7m Series B round in April 2017. *(Also see "Venture Funding Deals: Cell Medica Raises $73.2m, Tango Dances In With $55m" - Scrip, 16 May, 2017.)* Bonti closed a $15.5m Series C in February of this year. Four of the biotechnology firm's five co-founders are former Allergan research and development, manufacturing, commercial and business development executives.

Bonti has two botulinum neurotoxin serotype E (BoNT/E) programs in Phase II, including EB-001A for aesthetic indications and EB-001T for therapeutic indications. Saunders said the company is buying the start-up based on EB-001's aesthetic indications, but therapeutic indications may be pursued if data from ongoing studies supports that type of investment.

More than half of Allergan's $1.75bn in Botox revenue during the first half of 2018 came from its therapeutic indications, including chronic migraine headache prevention, overactive bladder and spasticity.

EB-001's active ingredient BoNT/E has a rapid onset of action within 24 hours of administration with a short two- to four-week duration of treatment effect, which were confirmed in recent Phase II top-line results for EB-001A in the reduction of glabellar lines, otherwise known as forehead wrinkles.

Allergan will pay Bonti and its investors undisclosed fees on top of its $195m upfront payment based on the achievement of undisclosed commercial milestones. Chief Commercial Officer Bill Meury noted during Allergan's medical aesthetics event that the company already is evaluating commercial opportunities for EB-001A, including a package deal that could turn people who are on the fence about aesthetic treatments into Botox users.

Bonti has two botulinum neurotoxin serotype programs in Phase II, one for aesthetic indications and one for therapeutic indications.

Meury said EB-001A's rapid onset and short duration could be attractive to people who want to try a neurotoxin without a long-term commitment to its effects. If they like the results, they could take advantage of Botox for a discount under a package deal with their EB-001A purchase.

He noted that EB-001A could be marketed as both a "starter toxin" for new medical aesthetics patients and an "event toxin" for individuals that want a fast-acting, "on-demand" beauty boost before a high-profile personal or professional event.

MULTIPLE INVESTMENTS IN BOTOX'S DEFENSE

Allergan described multiple investments in medical aesthetics on top of the Bonti buyout during its investor event to grow and defend the business and its flagship brand Botox, including a nearly three-fold increase in its annual direct-to-consumer (DTC) spending from an average of $55m between 2015 and 2017 to an average of $150m per year between 2018 and 2020.

Meury noted during the company's second quarter earnings call on July 26 that DTC spending usually pays off within six months. The investment for 2018 already is well under way with the launch of an unbranded website called The Spotlyte that's designed to answer consumer questions about medical aesthetics and direct them to dermatologists or plastic surgeons that offer treatment.

R&D also is a major ongoing investment, with Allergan planning to spend $1bn on medical aesthetics programs through 2025 to deliver more than 25 new products or new indications for existing products, including Botox and EB-001A. One to two product launches are expected each year.

The company intends to win US FDA approval for a pre-filled syringe Botox product – versus the current product that has to be reconstituted before injection – in 2022. A liquid formulation in a vial of the follow-on product nivobotulinumtoxinA also is expected to be approved in 2022. New Botox indications to contour the neck, define the jaw line and smooth skin are expected to launch between 2023 and 2025. EB-001A approval for glabellar lines is expected in 2024.

Earlier-stage investments include a topical neurotoxin delivered by microneedle technology and a long-acting injection that shows treatment effects without an increased dose of toxin.

Allergan also is investing internationally with the expectation that its ex-US business will triple by 2025, driven in large part by China, which grew 54% in 2017.

Published online 14 September 2018

Scrip has published a three-part series taking a closer look at the medical aesthetics market. Go online for these articles:

Medical Aesthetics: Key Players In A Largely Untapped Market: **https://bit.ly/2xsgY0D**

Medical Aesthetics: A Rising Tide Lifts All Ships In A Booming Market With Room For Growth: **https://bit.ly/2NmmmNQ**

Medical Aesthetics: Sales Rise For Popular Products, But Unmet Needs Remain: **https://bit.ly/2xsiu2P**

Rheumatoid Arthritis Data Position Filgotinib Ahead Of Competition, But It's Playing Catch-Up

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More evidence supporting **Gilead Sciences Inc.** and its partner **Galapagos NV**'s jointly developed JAK1 selective kinase inhibitor has come in the form of positive results from filgotinib's first pivotal trial in rheumatoid arthritis - results that analysts say effectively de-risk the investigational therapy.

Filgotinib, which is being developed for multiple indications, achieved the primary endpoint in the FINCH 2 late-stage study evaluating it in doses of 100 mg and 200 mg versus placebo in adults with moderately to severely active rheumatoid arthritis who had failed treatment with biologics.

FINCH 2 TOPLINE DATA

The pivotal trial achieved its primary endpoint in the proportion of patients achieving an American College of Rheumatology 20% response rate (ACR20) at week 12.

For the secondary endpoints of ACR50 and ACR70, both the high and low doses of filgotinib achieved statistical significance compared to placebo.

Both doses also achieved statistical significance versus placebo at week 24 and achieved statistical significance for low disease activity and disease remission.

Detailed findings from the FINCH 2 study will be submitted for presentation at a future, unidentified scientific conference, the companies said.

Importantly, according to analysts, at week 24 the rates of high response levels (ACR70) and disease remission rose significantly in the two active arms but did not change materially in the placebo arm. At the highest dose, 31% of patients achieved disease remission at week 24, and 32% of patients achieved ACR70, which are the most stringent levels of efficacy included in the study and disclosed in the press release

The positive top-line data follow close on the heels of promising mid-stage clinical data for filgotinib in another inflammatory disease, ankylosing spondylitis. *(Also see "Gilead/Galapagos' Trailing JAK1 Filgotinib Boosted By AS Trial" - Scrip, 6 Sep, 2018.)*

ANALYSTS APPLAUD

Analysts were particularly impressed with FINCH 2's message on the drug's safety profile as filgotinib showed itself to be generally well-tolerated, with no new safety signals compared to those reported in previous studies of the JAK1 inhibitor.

Under a reaction note subtitled 'Filgotinib De-Risked… Potential for Best-in-Class Label', analysts at Leerink said that while filgotinib was widely expected to succeed given the precedents of other JAK inhibitor trials, "the details of the efficacy and safety are important to the product's competitive positioning against **Pfizer Inc.**'s *Xeljanz* (tofacitinib), **Eli Lilly & Co.**'s *Olumiant* (baricitinib) and **AbbVie Inc.**'s upadacitinib ... filgotinib does indeed appear to be the most JAK1 selective of this class and was therefore destined to have the cleanest safety profile."

Credit Suisse agreed, saying "overall, the safety data looks to be best in class while the efficacy is close to that of AbbVie's upadacitinib but looks better than Pfizer's Xeljanz and Lilly's Olumiant."

If this quality is borne out in subsequent data releases then "filgotinib, while it may not be the first of these drugs to market – it is likely to be the last - might be the best," Leerink concluded. Analysts at Baird Equity research weighed in, saying the FINCH 2 data "is as good as it could reasonably be, with strong efficacy outcomes and no red flags on safety."

Gilead chief scientific officer John McHutchison said in a statement that the FINCH 2 data "are particularly encouraging as we look ahead to Phase III results from the ongoing FINCH 1 and FINCH 3 trials, which are exploring filgotinib in other populations of patients with rheumatoid arthritis."

Analysts at Jefferies said that "the FINCH 2 success also de-risks the ongoing FINCH 1 and FINCH 3 trials, and provides positive read-through to ongoing Phase III inflammatory bowel disease studies, cementing confidence in multi-blockbuster potential."

APPROVAL CHANCES SEEN RAISED

The top line FINCH 2 data are thus seen as having improved the drug's chances of regulatory approval.

Leerink now sees the probability of filgotinib being okayed in rheumatoid arthritis and inflammatory bowel disease at 80%, up from 65% before the release of the FINCH 2 data.

Analysts at Bernstein said the good safety performance shown in FINCH 2 means "filgotinib should be differentiated in light of it, but the market is tough. JAKs will continue to penetrate in RA, reaching 25% of the market in 2030, and there is appetite to use the class earlier in the paradigm."

They said that the landscape in IBD looked "mixed" with higher unmet need but added that alternative orals exist for that indication representing an estimated 20% market share. "We expect filgotinib, driven by safety, to be considered best in class but not enough for dominance," they concluded.

Credit Suisse summarized the FINCH 2 message by saying: "Assuming similar results from FINCH 1 and 3, the biggest challenge for filgotinib may be the time to market as we assume a 2021 US launch and expect Pfizer's Xeljanz to go generic in the US by the end of 2025. We assume peak probability-adjusted sales of $2.5bn."

Published online 12 September 2018

TRANSFORMING CLINICAL TRIALS: The Path To A Successful Digital Trial

By Marie Mc Carthy, Senior Director Product Innovation, ICON & Chen Admati, Head of Intel® Pharma Analytics Platform, Intel

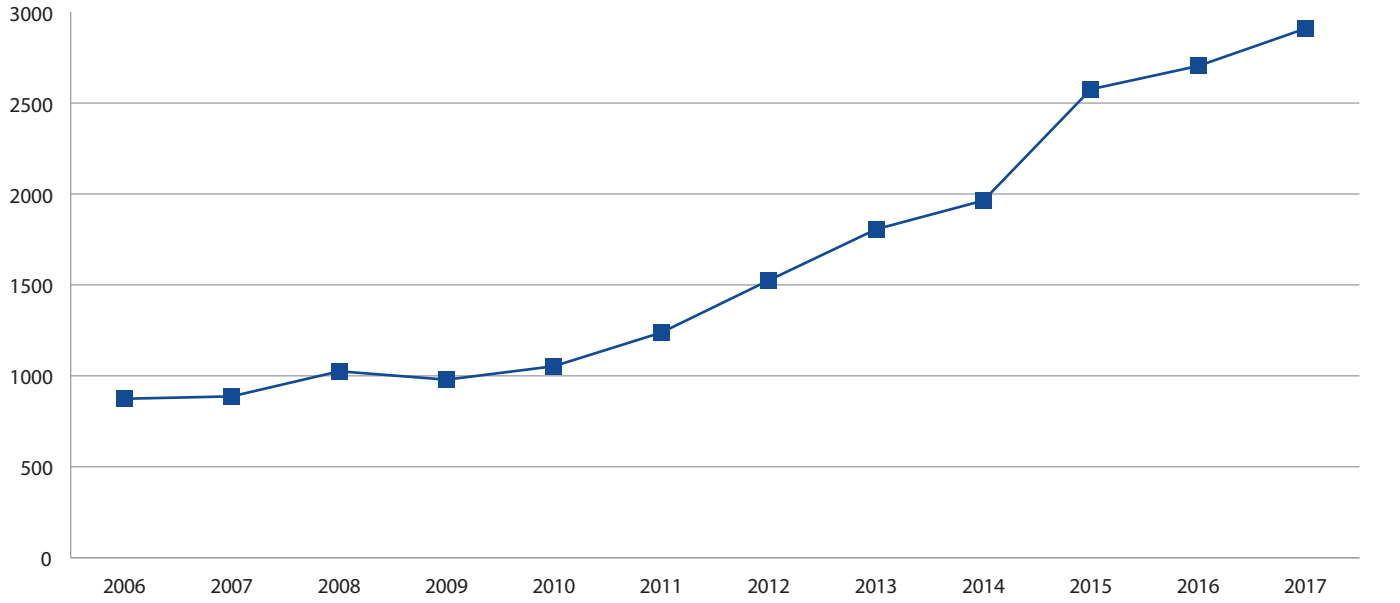
Over the last number of years the use of mHealth technologies has been increasingly embraced by patients, healthcare providers and payers. Connected health ecosystems have been evolving at a rapid pace and it is now believed that the IoHT (Internet of Healthcare Things) market will be worth $163bn by 2020[1]. It has been estimated that over 7.1m patients worldwide benefit from remote monitoring and the use of connected medical devices as part of their care regimen[2], to better inform and educate themselves about their disease and to share their knowledge with each other. This patient empowerment is reflected by the estimate that 1 in 20 Google searches is healthcare related[3]. mHealth device technology has evolved to the point where it is now possible to collect a vast array of physiological data including vital-signs such as heart rate, respiration rate, oxygen saturation, continuous glucose monitoring, sleep and activity data, and using advanced analytics to monitor patients in their own home outside the hospital environment. There is a growing awareness in the healthcare sector of the benefit and value of a mHealth approach to healthcare. As early as 2013 as a way of maximising healthcare spending, sleep apnoea patients in France have been monitored remotely to ensure they are compliant in the use of their CPAP (continuous positive airway pressure) devices. This has led to new care models in mobile health, for example, University of California, Los Angeles actively promote their remote patient monitoring program as having positive values for patients and their primary healthcare teams to manage their health "from the comfort of your own home" and to reduce hospital admissions and emergency room visits[4]. However the penetration and use of wearables and devices in the pharmaceutical industry is still limited. But interest in mHealth/digital technology is apparent with nearly 3000 articles published in peer reviewed journals in 2017 (PubMed), an almost 100% increase on the number published five years earlier. The value of the technology is clear—in a recent industry survey for the ICON whitepaper 'Improving Pharma R&D Efficiency' respondents cited big data, predictive analytics, smartphones and wearables & sensors as amongst the top disruptive technology trends which will have the greatest impact on clinical trial operations.

So the question remains, in the context of drug development studies, why has the use of this technology been limited to a relatively small number of pilots? It is clear that concerns still remain about implementation of this technology in a clinical trial. These concerns focus on a number of key areas: Patient Acceptance, Device Suitability, Data Complexity and Insight Generation, Operationalisation, Privacy and Security Issues, and Regulatory Acceptance.

How To Implement Successful Digital Clinical Trials

#Patient Acceptance. Patient recruitment and retention are key issues for clinical trials. While it is generally accepted that the use of devices and sensors can help create more patient centric studies, if not carefully managed digital technology can add additional burden for the patient. This is a critical factor when integrating devices and sensors into a study; ensuring your study design has a 'maximum passiveness' approach is key. Data collection should be as seamless as possible with minimal

Figure 1. Number of mHealth Articles (PubMed)



actions required from the patient. Selection of a low-burden device that is simple to use with an attractive form-factor is another important aspect for increasing patient engagement. The device should, where possible, support both iOS and Android operating systems to allow for a BYOD (bring your own device) model. A single study app, that acts as the interface between the individual and the trial and includes features to support the patient in his/her day-to-day life, must also reflect the disease specific characteristics. These apps need to be designed with the user experience in mind and should add value to the patient experience while part of the study. Lastly, compliance monitoring has proven to be a significant contributor to the success of digital trials. Proactively flagging non-compliance and utilising a multi-faceted approach to engage with patients; from app to SMS notifications to direct contacts contacting patients, can help drive greater compliance and ensure optimal data generation and capture.

 # Device Selection. New devices are launched almost every day and selecting the right device is a challenging task and poses a number of critical questions; so how to choose? Should we use single or multiple devices? Medical grade devices or consumer technology? Unfortunately there are no simple answers, and certainly there is no one device that can be used in all studies. There are some publications that provide guidelines[5] and can support the selection process. Of primary importance is the selection of a device that can generate the data required to meet the study needs. The device itself must be fit for purpose: have high usability such as long battery life, be form factor appropriate for the study population, and

While it is generally accepted that the use of devices and sensors can help create more patient centric studies, if not carefully managed the use of digital technology can add additional burden for the patient.

facilitate the collection and transfer of the required data. The trial design will guide the device(s) selection process, if a device is being selected to support an endpoint, ensuring there is sufficient scientific evidence to support the use of that device is critical. If a device is being used to track trending and changes, or is used in late phase studies, greater choice exists in terms of the devices being selected for use.

 # Data Complexity and Insight Generation. Existing clinical studies rely to a large extent on results from monthly outcome assessments carried out in a clinic. The potential to generate new insights from continuous measures captured as patients go about their lives is significant. If we take as an example a typical Phase II clinical trial in CNS: a few dozen patients, participating in a trial for a few months to a year. Let's assume we would like to capture objective insights and provide these patients with a wrist-worn device equipped with a 50Hz accelerometer and gyroscope sensors. The use of such a device will generate nearly 1 billion data points per day. Combining these data with ePRO (electronic patient-reported outcomes) methods, along with other physiological data such as heart and respiration rates can create a big, complex dataset that is beyond the capacity of standard electronic data capture (EDC). Therefore, when selecting a digital platform, the ability to scale and ingest high frequency datasets is important. In order to generate insights and digital biomarkers, skilled experts in advanced analytics, data scientists, are needed. The platform should enable the data scientists' work by exposing the appropriate tools to process the data and run machine learning algorithms.

 # Operationalisation. The art of simplicity is a puzzle of complexity. When running a successful digital trial, there are multiple stakeholders and processes involved. Device selection, device purchasing, application setup, device distribution and reconciliation after the study, IRB submission, patient and site training, and patient support are some of the challenges facing the study team. Establishing and structuring data sourced from diverse systems can also be technically daunting. An experienced study team with a strong patient engagement element and a reliable, robust digital framework is required to ensure delivery of an end-to-end solution out-of-the-box with full integration.

 # Privacy and Security. With increasing concerns on data privacy and security, these issues must impact the selection of the digital platforms as well as the trial design. A chosen platform must meet industry standards such as HIPPA, GDPR, and ISO 270001. Decisions on where to locate the trial globally may introduce new data privacy requirements. When collecting and storing the data, all data need to be pseudonymised in accordance with local regulations. Patients need to be appropriately consented, particularly with regards to the use of the data. This will become even more significant as the value of the collected data lies not only in the study for which it has been collected, but also in its potential value for meta-analysis and the testing of new and yet unidentified algorithms.

 # Regulatory Acceptance. As with all trials, the recommendation is that early engagement with the regulators is required. There are a number of roadmaps and recommendations from both the Clinical Trials Transformation Initiative (CTTI)[6] and the ePRO Consortium[7] that can be used as reference when considering the integration of digital technologies in trial design. Regulators are also striving to support the use of digital technologies in clinical trials. The US Food and Drug Administration (FDA) in particular, is actively participating with stakeholders to be in a position to offer guidance on the use of digital and mHealth technology and have recently launched a digital technology website[8] and a Digital Health Innovation Action Plan[9].

Summary

Declining research and development (R&D) efficiency is one of the biggest challenges the pharmaceutical industry is facing today. The traditional approach of three discrete, fixed trial phases designed for testing mass-market drugs often is not viable in today's increasingly competitive, value-based therapeutic markets. It lacks the flexibility, analytic power and speed required to develop complex new therapies targeting smaller and often heterogeneous patient populations. As a consequence, clinical trials are changing. Digital disruption in the form of new wearables, sensors and medical devices enable pharmaceutical and medical device companies to generate new types of datasets. Artificial intelligence and machine learning can generate new insights and digital biomarkers that have the potential to be more clinically responsive to change. However, to run a successful remote/digital trial, a complete end-to-end solution is required. Carefully selected technology, combined with the right trial design and operational excellence, will increase the likelihood for success.

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CEO Interview: Roche Pharma Head Daniel O'Day On R&D Strategy

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Armed with data and analytics and a focus on personalized healthcare, **Roche** will be able to drive future innovation and overcome the challenge of biosimilar competition to mainstay products, its pharma CEO has said. Bolt-on acquisitions will also play a role driving growth that Daniel O'Day is confident of despite biosimilar threats.

Roche Pharmaceuticals CEO Daniel O'Day

Roche used a virtual pipeline presentation on Sept. 13 to update investors on its overall pharma strategy and flag the fact its late-stage pipeline is at a record high as measured in new molecular entities (NMEs) and line extensions. The total number of NMEs at a pivotal stage currently stands at 38, up from 31 a year ago.

'GETTING PERSONAL' WITH DATA

The event was chaired by O'Day, who stressed that data and analytics lie at the center of Roche's strategy and will impact all parts of the business.

Speaking to *Scrip,* O'Day emphasized the importance that personalized healthcare will have in transforming R&D at Roche and how patients are treated.

He said there would be an increased focus on diagnostics and biomarkers with a goal of understanding the science to determine the best combos. This effort would be driven in part by acquisitions like **Flatiron Health Inc.** and **Foundation Medicine Inc.** (FMI) and their overlaps.

"In addition to these acquisitions we have lots of partnerships because what you need to do is bring new disciplines into your equations, so we have machine-learning partnerships, we have partnerships for data sources, and these are empowering our journey towards personalized healthcare - and sometimes we'll see an external therapy that we think we can accelerate by investing in it," O'Day said.

He said the world could expect more M&A from the world's biggest cancer drug maker. *(Also see "'Watch This Space' Roche Execs Say, Outlining RWE Rationale For Flatiron Buy " - Scrip, 26 Apr, 2018.)*

"We're constantly looking for great science outside the group; these will tend to be earlier stage bolt-on asset acquisitions that can add more value, and that's what we'll continue to do."

Meanwhile the use of real world data will transform how Roche and other pharma companies do drug discovery and development. *(Also see "Roche Pushes Personalization With $2.4bn Foundation Buy-Out" - Scrip, 19 Jun, 2018.)*

"The approach using real world data is going to transform the way that we look for new medicines as well as the relationship we have with patients and the physician communities through the journey of studying the medicine and it is going to create efficiencies, bringing a higher probability of success with the medicines and we'll also be able to move them faster."

He pointed to clinical trials as an example.

"Rather than screening 100 patients to find one for your trial, which is very time-consuming, if you have a robust real time, realworld data source where you can say 'let's go into the data source and find out where these patients are being first diagnosed and then offer them the opportunity to enter the clinical trial,' then that's a much more efficient way for patients - and also for us."

The executive said real world data could also be used to supplement clinical trials.

"It's a long process to recruit people in a standard of care control arm; but if you could supplement data – with regulatory authorities – with real world data and either reduce or in some cases even eliminate a control arm, for instance in rare cancer types, that's going to both accelerate the clinical trial plus it's just more patient-friendly; if you can go to a patient and say 'would you like to be on an experimental medicine?' versus going to the patient and saying 'you're going to be randomly assigned to an arm of a trial which is either standard of care or this new medicine,' then it's more patient-friendly at the end of the day," O'Day said.

He said the abundant supply of cancer biomarkers will ensure there's enough to feed the R&D appetites of big companies focused on oncology for years to come.

"One needs only to look at the research pipeline of pharma companies or academics to see how many targeted medicines there are and it still represents the vast majority or market potential in cancer today and probably will be in five years' time."

He said cancer immunotherapy would also become personalized over time.

"We're at the early stages where we're moving from treating all patients with a drug but getting different results per patient over to an environment where we'll be able to have biomarker tests that allow us to determine which cancer immunotherapy - or which combination - is going to give a particular patient the best hope for a cure, the best hope for a sustained response."

PROGRESSING POLATUZUMAB

Among its many late-stage assets, Roche highlighted promising prospects for polatuzumab, which was recently advanced to Phase III with the POLARIX study in first-line diffuse large B cell lymphoma (DLBCL). Polatuzumab vedotin, developed in collaboration with **Seattle Genetics Inc.**, is an antibody drug conjugate that targets CD79, and brings a toxin to the lymphoma. The Phase II (combination) results were presented at this year's ASH. *(Also see "ASH In Review: Roche Refreshes Hematology Portfolio With Robust New Drugs" - Scrip, 15 Dec, 2017.)*

> 'We're constantly looking for great science outside the group; these will tend to be earlier stage bolt-on asset acquisitions that can add more value, and that's what we'll continue to do.'

The company has yet to file polatuzumab with regulators. O'Day said Roche intended to do so in the second half of the year based on the Phase II data.

"It has taken half a year or so to catch up with these extraordinary results," O'Day said. "We were not expecting to see such extraordinary results in that Phase II trial which was really intended to look at dosing schedules and safety when in fact we saw some really significant survival benefits."

"Normally you would have a plan to produce commercial supply, and then you also have a plan for your discussions with regulators but after these results we immediately starting working with regulatory authorities and also looking at how fast we can move from what is a clinical trial supply to a kind of routine patient supply."

O'Day said Roche shouldn't be criticized for not yet having made a regulatory submission for polatuzumab - which won FDA Breakthrough Therapy designation and PRIME designation from the EMA on the basis of the Phase II data.

"One shouldn't look at it as a delay in the filing; rather one should look at it as a multi-year acceleration to get this medicine in the hands of patients with blood cancer," he said.

Published online 14 September 2018

Is Quarterly Dosing For Teva's Ajovy Enough To Differentiate It From Other CGRP Inhibitors?

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Teva Pharmaceutical Industries Ltd. won an important US FDA approval for *Ajovy* (fremanezumab) in the prevention of migraine headache and is the first CGRP inhibitor approved for monthly and quarterly doses, but its biggest competitor from **Amgen Inc./Novartis AG** has a four-month head start and Ajovy could hit the market at the same time as **Eli Lilly & Co.**'s third-in-class product.

Teva believes that the option for quarterly treatment with Ajovy, which will launch at the same price as Amgen/Novartis' *Aimovig* (erenumab), is an important differentiator. But while analysts agreed, they also pointed out several factors that could make it the third-largest selling CGRP inhibitor despite being the second product approved in the competitive drug class, including the fact that it's available only in a pre-filled syringe and not an autoinjector, and it has a much higher rate of injection site reactions.

And since Teva said it will be another two weeks past the Sept. 14 approval date before Ajovy is available through retail and specialty pharmacies, the biologic could hit the market at or very close to the launch of Lilly's *Emgality* (galcanezumab), which the FDA is expected to approve by the end of September.

Even so, the FDA decision came earlier than some investors may have anticipated, since the agency previously delayed its decision due to concerns at the biologic's manufacturer **Celltrion Inc.** *(Also see "Teva Pushes CGRP Timeline Back To End Of 2018" - Scrip, 3 May, 2018.)*

Teva's stock closed 2.5% higher on Sept. 17 at $23.43 per share, while its two main competitors held steady; Amgen increased 0.1% to $200.81 and Lilly dipped less than 1% to $105.72. *(Also see "Best-In-Class Or First-In-Class: CGRP Inhibitors Line Up To Win The Migraine Market" - Scrip, 8 May, 2017.)*

Alder Biopharmaceuticals Inc., developing the CGRP inhibitor eptinezumab as a quarterly intravenous therapy, fell 6.3% to $17.05. Developers of oral CGRP inhibitors include **Allergan PLC** and **Bio-**

haven Pharmaceuticals Holding Co. Ltd. Allergan, which also markets the neuromodulator *Botox* (onabotulinumtoxinA) for chronic migraine prevention and other indications, closed down 2.1% at $184.29. Biohaven declined 2.5% to $35.86.

PRICING: THE UNKNOWN DIFFERENTIATOR

Pricing could be a big differentiator across the CGRP inhibitor class, but it remains to be seen how much lower Lilly will be able to go to than its competitors and still capture an acceptable return on its investment, since Teva's Ajovy pricing matches Amgen/Novartis' $6,900 per year wholesale acquisition cost (WAC) for Aimovig. That price already is far below the expectations of market observers, payers and the Institute for Clinical and Economic Review (ICER).

Teva Executive Vice President for North America Commercial Brendan O'Grady noted in an interview with *Scrip* that about a year ago the widely expected pricing for CGRP inhibitors was in the $10,000-$12,000 range.

> Pricing could be a big differentiator across the CGRP inhibitor class, but it remains to be seen how much lower Lilly will be able to go to than its competitors and still capture an acceptable ROI.

But after "a lot of market research, a lot of discussions with payers as well as physicians, manufacturers – such as us and such as Amgen – listened to the market and came in with a much more modest price," O'Grady said. "We believe that given the high unmet need, given the appropriate pricing, that hopefully payers will see that as well and give relatively broad access to this much-needed class of medications."

Ajovy will cost $575 for each 225 mg monthly dose and $1,725 for each 675 mg quarterly dose before payer discounts. Teva's patient assistance program will offer co-pay assistance, down to $0 per month, for eligible patients covered by commercial health plans.

Ajovy's WAC matches Aimovig's list price of $575 per month for both the 70 mg and 140 mg dose. It's unknown what kind of discounts either drug's manufacturers are giving to payers to improve reimbursement, but ICER estimated the net cost for Aimovig after rebates and discounts will be about $5,000 annually. *(Also see "ICER Says Amgen/Novartis Migraine Drug Aimovig Is Cost Effective At $5,000 Net Price" - Scrip, 1 Jun, 2018.)*

Price doesn't seem to be a barrier for Aimovig, which analysts note has seen significant early interest and rapidly rising numbers of prescriptions based on unmet need for preventative migraine therapies and the availability of free product for patients' first few months of treatment. Analysts estimated that as much as 70% of Aimovig prescriptions to date are patients trying the drug for free.

Amgen noted when it reported second quarter earnings on July 26 that most of the initial sales could be attributed to two-month free trials of Aimovig that were being offered to patients while the company and Novartis continued to negotiate with payers. Contracts were in place with payers representing about 30% of US patient lives as of late July. Those agreements generally allowed for treatment with Aimovig after patients tried generic oral medicines, but before Allergan's Botox. *(Also see "Harper, Hooper Exit As Amgen Revenues Rise" - Scrip, 26 Jul, 2018.)*

REASONABLE FORMULARY PLACEMENT EXPECTED

O'Grady said Ajovy also is likely to be placed on payer formularies after migraine patients do not see relief from at least one oral generic drug, including triptans.

"We don't necessarily see that as problematic, because many of those patients have used or are on those products anyway. I think whether it's one or whether it's two prior medications, most patients that are candidates for the anti-CGRP products have exhausted that therapy already, so we really don't see that as much of an obstacle," O'Grady said.

Payers also have not required patients to try Botox before Ajovy, he added, noting that the Allergan biologic is a physician-administered buy-and-bill product, which makes it a potentially more expensive prophylactic treatment for migraine sufferers.

Teva's Josh Cohen, senior director and therapeutic area lead for migraine and headache, also pointed out in the same interview with *Scrip* that "Botox is only indicated for chronic migraine, which is 15 or more headaches per months, whereas we're indicated for migraine broadly. We've shown in our clinical trials efficacy in both episodic and chronic migraine."

Episodic migraine is defined as 14 or fewer headaches per month. Cohen, who treated patients as a headache specialist for more than a decade before working in the biopharmaceutical industry, said that in the eyes of payers it probably would not be viewed as appropriate for migraine patients to have to try Botox before a CGRP inhibitor.

"There's a high unmet need here and there is a lot of pent up demand," O'Grady said. "Amgen coming to market early has obviously benefitted from some of that, but I think there's still many, many patients – hundreds of thousands or millions – out there that have not sought out treatment as yet, so we think there's room for numerous products in this category."

ANALYSTS NOTE AJOVY'S LIMITATIONS

Analysts see CGRP inhibitors for migraine as a multibillion-dollar market, but with wide-ranging estimates for Ajovy's second- or third-place position based on various factors, including Amgen/Novartis' first-in-class Aimovig launch. Amgen executives previously have noted that the biologic also is different from other CGRP inhibitors because of its mechanism of action targeting the CGRP receptor rather than – like Ajovy – targeting CGRP itself. *(Also see "As Amgen Looks To Aimovig's Launch, It May Learn From Repatha's Past" - Scrip, 25 Apr, 2018.)*

"Our prior work estimates that Ajovy will achieve mid-single digit percent market share by the end of 2018 and ~20% share of the CGRP antibody class longer term," Leerink analyst Geoffrey Porges wrote in a Sept. 15 note to Amgen investors. "Aimovig prescription data continues to be robust, suggesting there is plenty of room for multiple entrants in this space, and we continue to see this as a $5bn-$6bn drug class globally by the mid-2020s."

He estimated that Aimovig will capture about 38% of the $5.5bn market for monoclonal antibodies targeting CGRP in 2025, followed by Lilly's Emgality with 24%, Ajovy with 20% and Alder's eptinezumab with 19%.

Leerink analyst Ami Fadia noted in a Sept. 15 report to Teva investors that the company has said in the past that, like Amgen and Novartis, it also plans to offer free doses of Ajovy early in the product's launch and its earnings guidance for this year does not assume any revenue from the CGRP inhibitor, though Leerink estimates $3m in 2018 sales.

BTIG analysts were more optimistic about Ajovy sales in a Sept. 16 report, forecasting $25m in 2018, $200m in 2019 and $500m in 2020 with the drug reaching blockbuster status at about $1bn in sales by 2022. Jefferies analysts estimated in a Sept. 17 note that Teva's biologic is a $500m-plus product.

Leerink expects US Ajovy sales to total $108m in 2019, growing to $629m in 2023, hindered by the drug's lack of an autoinjector and the Teva's product's higher rate of injection site reactions – 43%-45% in Phase III studies versus 5%-6% for Aimovig.

"We believe Ajovy with initial availability only as a [pre-filled syringe (PFS)] will be less preferred versus autoinjectors from Amgen and Lilly and we await launch of an autoinjector, which is expected in" the second half of 2019," Fadia wrote. "MEDACorp physicians we spoke with believe that not having an autoinjector will be a limiting factor, as the physicians believe patients may not feel as comfortable self-administering with a PFS compared to an autoinjector."

"Physicians also were skeptical that the quarterly administration at the physician's office would be enough of an incremental advantage over monthly autoinjector administration to choose Ajovy," Fadia continued, "and physicians also indicated that for quarterly dosing in the future, Alder's eptinezumab may be preferred as they believe it has slightly faster onset of action and better efficacy."

BTIG also noted that Ajovy's lack of an autoinjector and higher rate of injection site reactions "could put it at a disadvantage to its peers."

NEVERTHELESS, AJOVY APPROVAL IS A WELCOME WIN FOR TEVA

Despite the challenges for Ajovy, Credit Suisse analyst Vamil Divan highlighted the "clearly significant" demand for CGRP inhibitors that should make it an important revenue generator for Teva. The company needs all the help it can get as it deals with competition from *Copaxone* generics, lower-than-expected sales for its own US generics business, and massive debt. *(Also see "Teva Braces For A Bigger Hit As Price Competition Intensifies For Copaxone" - Scrip, 2 Aug, 2018.)*

Commercialization of Ajovy apparently will not require a massive new investment in sales representatives, however, since Teva plans to market the product with existing neurology and respiratory teams, O'Grady explained.

"It fits real well within the neurology team that we currently have," he said. "Our Teva Neuroscience sales force is calling on neurologists with a high overlap with neurologists that treat headaches. We feel that that force is intact and then we have a specialty sales force that was selling some of our respiratory products and we've redirected some of their efforts to call on some of the non-neurologist headache specialists in the marketplace whether they are primary care or whatever they may be."

O'Grady said the company will reevaluate Ajovy performance later in 2019 or in 2020 to determine if any sales team changes are needed.

Published online 17 September 2018

Interview: Korea's Enzychem Eyes Global Expansion Via Nature-Inspired Drug

JUNG WON SHIN jungwon.shin@informa.com

It all began with curiosity about the effect that a traditional medicine extract from deer antler had on improving fatigue. A specific substance in the extract called PLAG was first discovered in the 1990s by two professors at South Korea's Asan Medical Center during their research on its hematopoietic effect.

After researching this natural substance for decades, **Enzychem Lifesciences Corp.** is now moving closer to the development of a derived first-in-class immune modulator that the company believes has the potential to be effective across a wide variety of clinical indications.

"There must be a reason that our ancestors have been taking deer antler as medicine. We have developed this compound inspired by a natural source. It is a synthetic compound, but only Koreans could have thought of this," declared Ki Young Sohn, Chairman and CEO of Enzychem, in an interview with *Scrip* in Seoul.

As PLAG (1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol) is present at just 0.002% in the traditional deer antler extract, a way had to be found to synthesize it artificially, and the company began to mass synthesize the substance as EC-18 in 2011, and then to proceed with new drug development based around its activity.

Using this synthetic monoacetyldiglyceride molecule, Enzychem first launched the functional health food *Rockpid* with immunomodulation effect in South Korea in 2014, and subsequently moved on to develop related prescription drugs for a range of possible indications in oncology, inflammatory and pulmonary diseases.

The South Korean biotech's pharmaceutical business centers on EC-18 as a first-in-class, proprietary drug molecule platform which modulates neutrophils and macrophages via cytokines and chemokines, and transcription factor STAT3/STAT6.

"As [China's] Professor Youyou Tu earned the 2015 Nobel Prize for the discovery of artemisinin in treating malaria, the answer could be in the conventional wisdom. This is why our immune modulator is quite unique. It is oral, lipid-based, has a first-in-class mode of action and an excellent safety profile," Sohn said.

The company is initially focusing on progressing EC-18's possible oncology indications - chemotherapy-induced neutropenia (CIN),

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Enzychem Lifesciences Chairman and CEO Ki Young Sohn

chemo-radiation induced oral mucositis (CRIOM), and acute radiation syndrome (ARS) - in the US to develop new therapies that are exclusive and can be rapidly launched in the market.

Neutropenia is a common side-effect of chemotherapy and associated with a higher risk of serious infections. G-CSF is currently commonly used for the treatment of CIN but can cause various adverse events such as injection site discomfort, fever, malaise and influenza-like symptoms. Bone pain, the most common side effect, develops in 10-30% of patients receiving G-CSF.

Studies have shown EC-18 regulates circulating neutrophils from exaggerated extravasation and augments pegfilgrastim's therapeutic effect by inhibiting neutrophil transmigration through CXCL2/CXCL8 modulation.

Enzychem is aiming to complete global Phase II clinical trials for these initial three indications by the end of 2019, and has already received US FDA fast-track designation for its product in CRIOM and orphan drug designation in ARS.

UNMET NEEDS

The company is trying to bring to market a compound where patients truly have unmet needs. "There is nothing on the market for these patients. The only potential drug that is used to treat neutropenia has a completely different mechanism of action and is still delivered as an injection, so we really see this [EC-18] as a first-in-class medicine. And we also see this as a platform technology that we can use to launch not only for these first three indications, but also for many other indications," said Jeff Clark MD, JD, Enzychem's Chief Licensing Officer and Director of IP, in the interview.

The company has high expectations for the compound as it can potentially be used widely in a manner similar to Bayer Aspirin, which is applied for pain/inflammation as well as in blood clots and cancer management. This is in line with the global trend for pharma companies to develop their key drugs across multiple indications, the checkpoint inhibitors in cancer being one example.

"First, it [EC-18] will be used as a cancer supportive care treatment. And once its effect is proven, it could potentially be used in combination therapy for all cancer therapies. At present, the problem of cancer drugs is dose-limiting toxicity. If this is resolved, we can more effectively treat cancer and guarantee better quality of life to patients," said Sohn.

"Going forward, the global trend of drugs will focus on safety, while in the past, there was a trade-off between safety and efficacy."

After moving on to indications in inflammatory disorders such as rheumatoid arthritis, sepsis, atopic dermatitis and psoriasis, and pulmonary conditions such as asthma and chronic obstructive pulmonary disease, the company also aims to diversify into PLAG derivatives to become more of a global lipid-based drug specialist.

ONCOLOGY OUT-LICENSING STRATEGY

Based on the interim results of Phase II studies, Enzychem is now seeking to license out its three oncology programs to a global partner and is already communicating with potential companies.

"We are planning to license out the oncology indications to a single partner as it will be more favorable to jointly develop the drug," Sohn explained.

Unlike many Korean biotechs which are only developing new drugs, Enzychem is also engaged in rapidly growing API (active pharmaceutical ingredient) and contrast media businesses. These are creating synergies and generating profits that can be reinvested in new drug development, he noted.

Earlier this year, Enzychem established a US subsidiary to better handle on-site management for US clinical trials and promote strategic collaborations. It has also recently hired seasoned executives such as a new CLO (chief licensing officer) to focus on licensing and partnership deals.

The company, which is already listed on Korea's Kosdaq stock market, says it is also gearing up for a possible debut on Nasdaq in the US in the next few years.

Published online 18 September 2018
From the editors of PharmAsia News.

Novo Nordisk CEO Hopes Tresiba Can Re-Enter Germany On A Higher Price

STEN STOVALL sten.stovall@informa.com

The CEO of **Novo Nordisk AS** hopes studies of data supporting the cardiovascular and glycemic benefits of its *Tresiba* insulin product in certain sub-groups of diabetes patients will differentiate the long-acting therapy and win it a high enough price in Germany for the Danish group to start re-supplying the drug there.

The Denmark-based diabetes company launched *Tresiba* (insulin degludec) in 2015 but then withdrew it from Germany after failing to agree a price there with the national body representing health insurance funds. *(Also see "What will become of the German antidiabetics market?" - Scrip, 11 Jul, 2015.)*

Lars Fruergaard Jørgensen, Novo Nordisk CEO

> 'We're now doing analyses to break down the DEVOTE data to identify the sub-populations of patients that would benefit from that and that's what it will take to get a better – and hopefully acceptable – price for Tresiba in Germany.' – Lars Fruergaard Jørgensen

Novo Nordisk at the time said it refused to make the drug available at the price demanded by the national body, which wanted to set it at the same level as standard human insulin that has been available in Germany since the 1980s.

"We launched it there but didn't get the price we wanted so we had to pull it back," Lars Fruergaard Jørgensen said in an interview.

Tresiba is a once-daily basal insulin that provides an ultra-long duration of action beyond 42 hours. In the DEVOTE cardiovascular outcomes trial Tresiba reduced the risk of severe hypoglycemia in type 2 diabetes by 40% and the rate of nocturnal severe hypoglycemia by 53% compared to the standard of care, Sanofi's *Lantus* (insulin glargine).

"Based on the DEVOTE data we've received a request from the German authorities to see if this product can gain entry to that market. We're now doing analyses to break down the DEVOTE data to identify the sub-populations of patients that would benefit from that and that's what it will take to get a better – and hopefully acceptable – price for Tresiba in Germany," Jørgensen told *Scrip*.

But the process will take time, meaning Tresiba will not be made available in Germany anytime soon.

"In Germany there is this rule that stipulates that drugs be compared with human insulin and if you don't have that data you in principle cannot get a better price for a human insulin unless you can find in your clinical programs some populations that actually benefited from being on your product."

"The whole DEVOTE trial is showing that there is a hypo benefit from Tresiba. So, based on the rules in effect in Germany, we are doing a lot of statistical analysis, which takes a lot of time to document that you can indeed find patients that benefit from that," the Danish executive said.

He disagreed that the approach would naturally translate into a narrower patient group for Tresiba in Germany. "We don't know how it will play out. It could in fact be quite a broad population that's identified, but it's too early to say."

Published online 17 September 2018

Scrip's weekly **Pipeline Watch** tabulates the most recently reported late-stage clinical trial and regulatory developments from the more than 10,000 drug candidates currently under active research worldwide.

Click here for the entire pipeline with added commentary: http://bit.ly/2mx4jY3

Selected clinical trial developments for the week 7 September–13 September 2018

LEAD COMPANY/PARTNER	COMPOUND	INDICATION	COMMENTS
PHASE III RESULTS PUBLISHED			
Novartis	*Gilenya* (fingolimod)	multiple sclerosis, pediatric	PARADIGMS; *NEJM*, Sept. 13, 2018.
Johnson & Johnson	*Erleada* (apalutamide)	prostate cancer, castration resistant	SPARTAN; *The Lancet Oncology*, Sept. 10, 2018.
Roche	*Perjeta* (pertuzumab)	HER2-positive gastric cancer	JACOB; *The Lancet Oncology*, Sept. 11, 2018.
Array BioPharma Inc.	*Braftovi* (encorafenib) plus *Mektovi*(binimetinib)	BRAF-mutant melanoma	COLUMBUS; *The Lancet Oncology*, Sept. 2018.
PHASE III INTERIM/TOP-LINE RESULTS			
Galapagos/Gilead Sciences	filgotinib	rheumatoid arthritis	FINCH 2; met primary and all key secondary endpoints.
Merck KGaA/Pfizer Inc.	*Bavencio* (avelumab) plus Inlyta (axitinib)	renal cell carcinoma, advanced	JAVELIN Renal 101; improved PFS.
Merck & Co. Inc.	*Zerbaxa* (ceftolozane/ tazobactam)	hospital-acquired pneumonia	ASPECT-NP; met primary endpoints, non-inferior to meropenem.
Foamix Pharmaceuticals Ltd.	FMX101 (minocycline) topical	acne, moderate-to-severe	Study 22; met co-primary endpoints.
Boehringer Ingelheim GmbH	*Cyltezo* (adalimumab) biosimilar	psoriasis, moderate-to-severe	Equivalent to *Humira*.
UPDATED PHASE III RESULTS			
Johnson & Johnson/ MorphoSys	*Tremfya* (guselkumab)	psoriasis, moderate-to-severe	VOYAGE 1, 2; improved long-term patient-reported outcomes.
Leo Pharma AS	*Kyntheum* (brodalumub)	psoriasis, moderate-to-severe	AMAGINE-2, -3; rapid symptom reduction.
Sumitomo Dainippon Pharma Co. Ltd./Nitto Denko Corp.	*Lonasen* (blonanserin) transdermal patch	schizophrenia	Efficacy maintained, well tolerated.
AbbVie Inc.	risankizumab	psoriasis, moderate-to-severe	UltIMMa-1, -2, IMMvent; improved patient reported outcomes.
PHASE III INITIATED			
Roche	faricimab	diabetic macular edema	RHINE, YOSEMITE; compared with aflibercept.
Centrexion Therapeutics Inc.	CNTX-4975 (capsaicin), intra-articular injection	osteoarthritis pain	OA-303, OA-304; effect on pain of different regimens.
Apellis Pharmaceuticals Inc.	APL-2, blocks complement activation	geographic atrophy	DERBY, OAKS; multicenter studies.
Five Prime Therapeutics Inc.	bemarituzumab	gastric cancer, front-line	FIGHT; with chemotherapy.
PHASE III ANNOUNCED			
Erytech Pharma SA	eryaspase	pancreatic cancer	Trybeca-1; as second-line therapy.
PHASE II INTERIM/TOP-LINE RESULTS			
Bristol-Myers Squibb Co.	BMS-986165, oral tyrosine kinase inhibitor	psoriasis, moderate to severe	Efficacy endpoints achieved, favorable risk/benefit profile.
Verrica Pharmaceuticals Inc.	VP-102	molluscum contagiosum	Innovate; efficacy noted, well tolerated.
XBiotech Inc.	bermekimab	atopic dermatitis	Signs of efficacy, well tolerated.

Source: Biomedtracker | Informa, 2018

Executive All-Change: Bayer And Sanofi Switch

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Two of Europe's leading pharma companies, **Sanofi** and **Bayer AG**, have refreshed their executive line-up with personnel from the other company, in moves which will see a new head of pharmaceuticals at Germany's Bayer, and changes to the global business units (GBUs) of France's Sanofi that will produce a large primary care GBU and a new GBU focused on China and emerging markets.

The changes follow disappointing starts to 2018 for both companies; uninspiring financials and manufacturing issues have affected Bayer and further declines in sales in its diabetes business have held back Sanofi.

Both companies face uncertainty in their pharma business strategy. Bayer's relatively weak R&D pipeline and its likely focus on its **Monsanto Co.** acquisition may make pharma less of a priority at the company, while Sanofi has to alleviate the effects of price reductions and competitive pressures on its business.

That said, personal factors may have played their part in what's in effect a swap of executives – Bayer noted that its head of the pharmaceuticals division, Dieter Weinand, was leaving the company for family reasons. It's not particularly unusual for top executives from the two companies to move between them; Sanofi's current CEO, Olivier Brandicourt, was formerly Bayer's HealthCare chairman. In the round of executive moves announced Sept. 13, Weinand, a US citizen, is joining the executive committee of Sanofi and will be based in the US, leading a new Primary Care GBU. This enlarged GBU will combine the company's existing diabetes and cardiovascular GBU with the established products business which is currently part of Sanofi's General Medicines and Emerging Markets GBU.

The primary care GBU will focus exclusively on mature markets and Weinand, whose appointment is effective Nov. 1, 2018, will become an executive vice-president and will report directly to Brandicourt.

Although Weinand was born in Germany, he studied in New York and for more than 30 years held positions of increasing responsibilities at various companies including at **Pfizer Inc.** and **Bristol-Myers Squibb Co.**, with the last position before joining Bayer being president of global commercialization and portfolio management at **Otsuka Holdings Co. Ltd.** in Princeton, New Jersey.

NEW HEAD OF BAYER PHARMA

Stefan Oelrich, currently head of Sanofi's diabetes and cardiovascular GBU, has been appointed head of Bayer's pharmaceutical division as of Nov. 1, 2018, succeeding Weinand. Oelrich has also been appointed to Bayer's board of management.

For Oelrich, a German citizen, it's a return to a company he knows well, having joined Bayer as a commercial trainee in 1989. Over the next 20 years he held positions of increasing responsibility in Latin America, Europe and the US. His last position at Bayer before moving to Sanofi was as senior vice-president and general manager of women's healthcare in the US. Bayer AG's chairman, Werner Wenning, noted that Oelrich was a "proven expert with international experience, who is very familiar with Bayer's pharmaceutical business."

A new GBU, China and Emerging Markets, will be set up at Sanofi, and will be led by Olivier Charmeil, who is currently head of the company's general medicines and emerging markets GBU. The two refocused GBUs will be launched by the beginning of 2019, Sanofi said.

Published online 13 Sept 2018

APPOINTMENTS

Executive	To Company	New Role	From Company	Previous Role	Effective Date
Paul Firuta	Achillion Pharmaceuticals Inc	Chief Operating Officer and Executive Vice President	uniQure N.V.	Chief Commercial Officer	10-Sep-18
Andrew Cheng	Akero Therapeutics	Chief Executive Officer and President	Gilead Sciences Inc	Chief Medical Officer	11-Sep-18
Pavel Pisa	Crescendo Biologics Ltd	Chief Medical Officer	Roche	Head, Translational Medicine	11-Sep-18
Rene Hoet	Imcheck Therapeutics SAS	Chief Scientific Officer	Bayer AG	Vice President, Biologics Research	12-Sep-18
Scott Evangelista	Ironshore Pharmaceuticals & Development Inc	Chief Operating Officer and President	Quintiles	President, Integrated Engagement Services	6-Sep-18
Linda Basse	Medivir AB	Chief Medical Officer	Zealand Pharma	Medical Director	1-Oct-18
David Goren	Vaxil Bio Ltd	Chief Executive Officer and Director	AstraZeneca plc	President, Israel	6-Sep-18

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

Source: Medtrack | Informa, 2018

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