Scrip
Informa Pharma Intelligence
No. 3989
January 31, 2020

Biopharma Leaders Join Trump And Thunberg In Davos

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

After focusing on the year ahead in biopharma business at the J.P. Morgan conference in San Francisco last week, the sector's attention has switched to the World Economic Forum in Davos, Switzerland from 21-24 January.

The annual "big picture" summit brings together politicians, economists, academics and business leaders, and this year has been kicked off with a typically provocative address by US President Donald Trump, who contradicted growing concern about climate change, decrying what he called the "prophets of doom" on global warming.

Trump is withdrawing the US from the Kyoto climate agreement, but nevertheless did pledge to join a new global initiative to plant 1 trillion trees, an effort aimed at soaking up rising levels of carbon dioxide in the atmosphere.

17-year-old environmental campaigner Greta Thunberg made her own address to the meeting shortly afterwards, and berated world leaders for a lack of action, and said planting trees was not enough.

She called on corporations, banks and governments to halt fossil fuel investment and extraction. "Planting trees is good, of course, but it's nowhere near enough," Thunberg said. "We don't need to lower emissions….Emissions need to stop."

BIOPHARMA'S BIG THINKERS

The future of healthcare, and the role of business and new technologies are once again a key theme at Davos, and many biopharma executives are joining the conversation this year.

These include Werner Baumann, CEO of Bayer, who spoke on a panel on 21 January about 'When Humankind Overrides Evolution,' focusing on gene-editing technologies for use in agriculture, food and medicine. Meanwhile Takeda CEO Christophe Weber joins a discussion on shaping the future of health and healthcare systems on 22 January.

Speaking on the gene-editing panel, Baumann said there was "less and less trust in society for the advances of technology," adding that "the only way to get beyond it is that we do a better job in terms of explaining what we are doing."

Bayer is working with CRISPR Therapeutics on CRISPR/Cas9 gene-editing in hemophilia, ophthalmology and autoimmune diseases, but also has a major stake in genetically modified seeds via its Monsanto division.

He called for absolute transparency from corporations and governments on gene-editing technology, but also decried the previous "insane dominance" that anti-GM crop campaigners have been allowed to wield.

Others taking part include Stéphane Bancel, Moderna Therapeutics' chief executive, and Julie Gerberding, EVP and chief patient officer for MSD, who will be on a panel looking at breakthroughs in cancer care on 24 January, while Lars Rebien Sørensen, chairman of the Novo Nordisk Foundation, chaired a debate on one of the biggest risks to future healthcare, antimicrobial resistance (AMR), on 21 January. *(Also see "Novo Executive Calls For 'Real AMR Action' In Davos " - Scrip, 20 Jan, 2020.)*

Novartis's chief executive Vas Narasimhan will join a panel hosted by Fast

CONTINUED ON PAGE 4

from the editor

eleanor.malone@informa.com

Last week, Johnson & Johnson fulfilled its time-honored duty of kicking off the annual financial results reporting season, as we report on p8. The company has managed to shore up its all-important immunology franchise against biosimilar erosion: while sales of its one-time mainstay blockbuster Remicade slipped 17% in the third full year since the US launch of a biosimilar, it succeeded in growing its overall immune drug portfolio. Partly this was down to impressive growth outside the US, but even US sales grew, thanks to J&J's success in launching and expanding the indications for newer products in a highly competitive field. Oncology, which is driving much of the biopharma industry, also served the group well.

But there was little detail on the launch performance of the esketamine nasal spray for treatment-resistant depression, Spravato, which was approved in the US in March then the EU in December. Hailed as an important new product, its cost and complexity of administration may be hampering its uptake.

The US Institute for Clinical and Economic Review (ICER) questioned its long-term benefits and risks and calculated that its $32,400 US list price offered "low value for money" and should be discounted by 25-52%. It also warned that even with the called-for price reduction, treating more than 20-30% of eligible patients would have budgetary impacts that could displace other needed services or push up insurance costs. Over in Europe, Spravato has just been knocked back for reimbursement in England in draft guidance from NICE. For more on this, check out online coverage in Scrip and sister publication Pink Sheet.

Scrip
Informa Pharma Intelligence

LEADERSHIP
Phil Jarvis, Mike Ward, Karen Coleman

SUBSCRIPTIONS
Dan Simmons, Shinbo Hidenaga

ADVERTISING
Christopher Keeling

HEAD OF PUBLICATION DESIGN
Gayle Rembold Furbert

DESIGN
Paul Wilkinson

EDITORIAL OFFICE
Blue Fin Building
3rd Floor, 110 Southwark St
London, SE1 0TA

CUSTOMER SERVICES
US Toll-Free: +1 888 670 8900
US Toll: +1 908 547 2200
UK & Europe: +44 (20) 337 73737
Australia: +61 2 8705 6907
Japan: +81 3 6273 4260
Email: clientservices@pharma.informa.com

TO SUBSCRIBE, VISIT
scrip.pharmaintelligence.informa.com

TO ADVERTISE, CONTACT
christopher.keeling@informa.com

All stock images in this publication courtesy of www.shutterstock.com unless otherwise stated

exclusive online content

Market Snapshot: Migraine Prevention Therapies' Slow Road To Blockbuster Status

MANDY JACKSON mandy.jackson@informausa.com

The launches in 2018 of three closely watched calcitonin gene-related peptide (CGRP) inhibitors as preventive therapies and the anticipated launches of three more products against the same target have brought new attention to migraine decades after the launch of triptans – the last big class of drugs to treat the disease's debilitating headaches and other symptoms. But while the migraine market is large, the first round of CGRP inhibitors have yet to achieve blockbuster status.

Amgen Inc./Novartis AG's Aimovig (erenumab) targets the CGRP receptor while Eli Lilly & Co.'s Emgality (galcanezumab) and Teva Pharmaceutical Industries Ltd.'s Ajovy (fremanezumab) both target the CGRP ligand; all three are approved to prevent headaches in patients diagnosed with chronic migraines (15 or more headaches per month) and episodic migraines (14 or less). The drug makers estimated that 6 million people in the US alone are eligible for preventive treatment with one of these new biologics.

Aimovig, Emgality and Ajovy have shown similar efficacy in clinical trials, cutting the number of headache days that many migraine patients experienced by half or more. And since doctors have seen many people respond well to these treatments in the real world, it would seem that growth is guaranteed given the need for new medicines in this space.

Published online 23 January 2020

To read the rest of this story go to: https://bit.ly/3aN0UcT

inside:

CONTINUED FROM PAGE 1

Company to explore the role of CEO as "disruptor in chief," something he has been pursuing with the "Unbossed" cultural shift in the company.

The conference is not simply focused on political and corporate leaders making well-intentioned statements on trade and global co-operation, however.

Two years ago President Trump met Bayer's Baumann and Novartis's Narasimhan and other corporate leaders at a private dinner.

Bayer CEO Werner Baumann

This time around, the US presidential election on 3 November is drawing closer, and despite impeachment proceedings against Trump, many predict he could be returned to office for a second term.

Biopharma leaders are sure to want to impress upon the president their views on US healthcare reform, including Trump's own suggestion of international reference pricing. This is something the sector fears almost as much as Democrat candidate proposals for "Medicare for All" and US government price negotiations with the industry.

China's vice-premier Han Zheng also gave a speech in Davos on 21 January, and defended globalisation while making veiled criticism of Trump-led US market protectionism.

China is now firmly established as the biopharma's second biggest market – but is less open to discussions with industry on political policy-making than the US. The sector has just agreed to slash prices of scores of medicines in China by more than 60% in order to secure inclusion on the state-run insurance scheme.

Published online 22 January 2020

Novo Executive Calls For 'Real AMR Action' In Davos

STEN STOVALL sten.stovall@informa.com

Time is fast slipping away for finding workable solutions to address antimicrobial resistance, and the World Economic Forum's annual meeting this week offers a rare opportunity to spur action, says Lars Rebien Sørensen, chairman of the Novo Nordisk Foundation. The foundation is sponsoring a panel debate on AMR on the first day of the elite gathering in Davos, Switzerland, in hopes of spurring real action on the issue.

The annual World Economic Forum from 21-24 January will be attended by heads of state, global business leaders and others who have great influence on setting policy, both nationally in their own countries, and potentially worldwide.

"Hopefully with this discussion on AMR we can promote understanding and discussion about finding solutions in Davos and hopefully take this effort further," Sørensen told *Scrip* in advance of the Tuesday panel.

The backdrop is well known - with estimates suggesting 700,000 people a year die as a result of AMR, big pharma having largely exited the space, and no viable reward system in place for supporting novel antibiotics, there is a void where potential pandemics could thrive, said Sørensen, a former CEO of Danish diabetes specialist Novo Nordisk AS.

"The market for new antibiotics is broken. We need action on AMR from the responsible players in national health systems, from pharmaceuticals manufacturers, research-based organizations, generics makers. We need to get them together to come up with solutions, otherwise we will soon have a major problem on our hands," the executive said.

Novo Holdings has tried to make a difference by establishing an alternative funding entity called REPAIR (Replenishing and Enabling the Pipeline for Anti-Infective Resistance) Impact Fund which invests in start-ups, early-stage companies and corporate spin-outs across Europe and North America involved in discovering and early-stage development of therapies to combat AMR. "We decided 18 months ago to set up REPAIR with the aim to try to kick start a movement that would put AMR higher on the agenda because this is an underappreciated risk that society is facing," Sørensen explained.

"The whole infrastructure of continuing the development of these new product ideas has deteriorated. The whole pipeline of developing new antibiotics has been deteriorating. Meanwhile many former pharma producers have left the antibiotics space, and many of the research-based entities have collapsed. The situation is therefore actually worse than it was a year and a half ago, in terms of bringing antibiotics forward," he added.

Speakers headlining the Davos AMR panel on Tuesday will be Novo Holding's Sørensen, Jayasree Iyer who heads the Access to Medicine Foundation, the director general of pharma manufacturing trade body IFPMA Thomas Cueni, and Wellcome Trust CEO Jeremy Farrar. The panel's chairman will be Kevin Outterson, who heads the Boston-based CARB-X non-profit partnership for accelerating antibacterial research.

The discussion will have as a starting point the view that government intervention and policy change is essential and demand both long-term and short-term solutions to battle AMR, including market entry rewards, perhaps designed as prescription models along the lines of pilots underway in the UK and Sweden.

"By conducting their own pilots, Sweden and the UK are acknowledging that this is a huge problem. But it is not nearly enough to just have two countries engaged in this effort to find a workable reward model for antibiotics," Sørensen said.

"Pharmaceuticals is a global business. It calls for a much larger market and much more investment. The pharmaceutical companies have the capabilities; they have the manufacturing sites, some of them are research-based and they therefore have the research capabilities. Some are generics manufacturers and have the manufacturing capabilities."

Published online 21 Jan 2020

AstraZeneca Pledges To Become Carbon-Negative By 2030: **https://bit.ly/203ay1l**

UK Biotech Financing Holds Up Despite Woodford and Brexit

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

New figures show that 2019 was another strong year for the UK biotech sector, with a total of £1.3bn ($1.71bn) raised by companies, underlining its status as the leading cluster in Europe.

This was a strong showing despite global economic uncertainty, plus the more local problems of the implosion of Neil Woodford's investment funds, and the UK's long-running political paralysis caused by Brexit.

Much of this Brexit uncertainty is now over, as the UK's exit is set to be confirmed within days, but Boris Johnson's policy of 'non-alignment' with the European Union could undermine UK biotech's long-term growth trajectory.

Despite these problems, 2019 was the fifth year in a row that the sector had raised over £1bn across all financing routes. The year's total of £1.33bn was, however, a sharp decline compared to the previous year's tally of £2.20bn, though this may prove to be an outlier fuelled by 2018's exceptional number of IPOs, such as those from Autolus Ltd. and Orchard Therapeutics Ltd.

Data published by the UK BioIndustry Association (BIA) and Informa Pharma Intelligence (the publisher of *Scrip*) in the report show that venture capital was responsible for the lion's share of the total in 2019 (£679m) with a much smaller amount (£64m) raised via IPOs – most of this from the sector's single US NASDAQ launch, from Bicycle Therapeutics.

The remaining sum of £596m came from all other public financings. The year's single biggest fundraising in the sector was a series B round, the £100m raised by T-cell therapy focused Achilles Therapeutics in September.

Overall, the figures confirmed once again the UK's lead in Europe in terms of venture capital raised, accounting for a quarter (26%) of the continent's total.

The BIA has reiterated that the UK is the third global life sciences cluster behind the twin US hubs of Cambridge, MA and the San Francisco bay area.

The biotech association's chief executive Steve Bates has just returned from the J.P. Morgan investor conference in San Francisco, where the BIA worked alongside the government to promote the UK as a destination for biotech investment.

This included an eye-catching investment by Novartis in a large-scale clinical

TURN TO PAGE 6

CONTINUED FROM PAGE 5

trial and market access deal with NHS England for its late-stage cardiovascular drug inclisiran.

Bates said: "The UK biotech sector continues to chart an ambitious global path. With five consecutive years of raising over £1bn and a 400% increase in investments since 2012, the sector is in a very strong position heading into a new decade.

"It's clear that UK biotech companies remain an attractive investment opportunity for global investors, meaning there's a greater diversity of capital than we saw five years ago."

However the sector has a big Brexit cloud over it. After nearly four years of uncertainty the UK is set to confirm its exit from the EU at the end of January, but life science leaders have been alarmed by signals from the UK government that it does not intend to align with EU regulations.

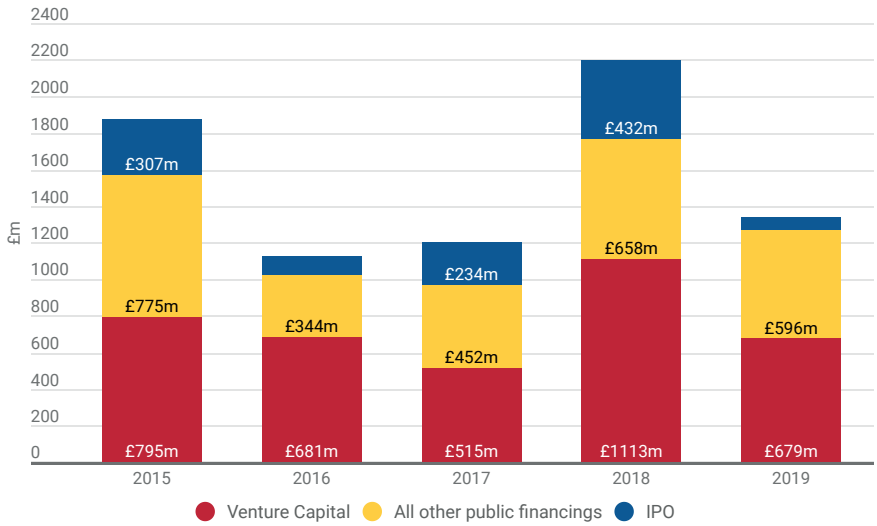
The sector has long warned that such a move would severely disadvantage the UK, forcing it to set up its own regulatory arrangements separate from the European Medicines Agency (EMA), and making it a less attractive market in the process.

The BIA is working hard with UK government agencies such as the Office For Life Sciences (OLS) to introduce new incentives and streamlined regulatory processes to mitigate any such impact, but still hopes to persuade the government to remain aligned as closely as possible with the EU.

Beyond Brexit, Bates is calling for extra measures from the UK government to stimulate investment in the UK.

UK biotech finance raising 2015–2019

After a record-breaking 2018, totals raised by UK biotechs fell back to £1.33bn ($1.74bn) in 2019



Source: BIA: *Global and growing: UK biotech financing in 2019*

"While we welcome overseas investment, diversifying the domestic life sciences investor base is critical to capturing the full benefits of this key sector of the UK economy," he said.

He called on the government to leverage new scale-up capital through the British Business Bank and the UK pension funds industry, with more grant funding for early-stage companies through the existing Biomedical Catalyst fund.

Dan Mahony, partner, Polar Capital, commented in the report that it was always going to be hard to follow the great success of 2018, but said VC funding remained "reasonably robust" in 2019. Nevertheless he noted that Brexit had been the chief cause for a drying up of funding for small companies. "In the UK public markets, it has been a much more difficult year with few IPOs and a handful of follow-on offerings. Barring a couple of exceptions, stock performance has in general been disappointing for life sciences companies."

Companies such as Autolus, AdaptImmune and Bicycle Therapeutics saw their share prices decline in 2019, either due to underwhelming clinical development news, links to the Woodford debacle, or market adjustments during the year. The long term success of the sector will be heavily dependent on how well the companies can convert their promising science into commercial products, though access to continued funding will also be a crucial factor. *Published online 23 Jan 2020*

Amgen To Buy Out Japan JV With Astellas

IAN HAYDOCK ian.haydock@informa.com

Amgen Inc. has confirmed it will purchase the 49% of shares in its Japanese joint venture Amgen Astellas BioPharma KK currently held by Astellas Pharma Inc., effective 1 April, converting the Tokyo-based operation into a wholly owned affiliate.

The move is as envisioned in the original strategic alliance contract signed between Amgen and Astellas in 2013, under which the JV started operations that year to bring a portfolio of five novel Amgen products to the Japanese market. Astellas initially used its development and marketing capabilities to get the products to market, while participating financially, while Amgen benefited from a strengthening commercial presence.

Since being set up, Amgen Astellas BioPharma has now grown into an organization with over 600 employees and fully integrated operations that have enabled it to become a marketing authorization holder for its products in Japan.

The venture has already launched Repatha (evolocumab) for familial hypercholesterolemia or hypercholesterolemia in patients with high cardiovascular event risk who do not adequately respond to statins, Blincyto (blinatumomab) for patients with relapsed or refractory B-cell acute lymphoblastic leukemia, and Evenity (romosozumab) for osteoporosis patients at high risk of fracture.

The new post-buyout renamed Amgen KK Japanese subsidiary, which will remain in Tokyo but at a different site, will continue to co-promote these three products with Astellas, which will remain responsible for distribution and sales beyond 2020.

The Otezla (apremilast) business acquired from Celgene for $13.4bn last November has already been incorporated into Amgen KK's structure with the establishment of a new Inflammation and Immunology Business Unit. The drug is approved globally in various indications including psoriasis. Japan is seen as one of the key growth markets for the PDE4 inhibitor. *(Also see "Amgen's $13.4bn Otezla Buy Helps Bristol/Celgene Merger Close By Year-End" - Scrip, 26 Aug, 2019.)*

No financial details of the joint venture buyout transaction were provided. No upfront or milestone payments were involved in the original agreement, as part of which the JV's sales were booked by Astellas, with Amgen to receive royalties and costs and profits to be split equally.

Amgen Astellas head Steve Sugino will continue to serve as president of Amgen KK.

Published online 23 January 2020

Piramal Profits As It Sheds DRG To Clarivate For $950m

VIBHA RAVI vibha.ravi@informa.com

Just over a decade after the sale of the Piramal group's formulations business to Abbott Laboratories Inc., chairman Ajay Piramal has stitched up another profitable deal. Piramal Enterprises Ltd. (PEL) is selling its stake in fully owned Decision Resources Group (DRG), a healthcare research and consulting company, to Clarivate Analytics Plc for $950m.

The divestment gives PEL $900m in cash and an undefined stake in Clarivate worth $50m post a year of the deal closure. PEL realized 2.3 times its initial equity investment on Indian rupee terms after acquiring DRG from private equity firm Providence Equity Partners in 2012 for $650m, of which $260m was infused as equity.

"We are pleased to have grown DRG's market leadership over the last few years and believe that to further accelerate DRG's growth trajectory, it requires scale and size. Clarivate Analytics is well positioned to provide the required platform for the next phase of growth," said Ajay Piramal.

"This is a milestone acquisition which doubles the size of our life sciences business...(and) is accretive to our 2020 earnings," said Jerre Stead, Clarivate Analytics executive chairman and CEO. Clarivate said it expects to achieve cost synergies of approximately $30m within the first 18 months of the transaction closing.

While the PEL board has approved the stake sale, it needs shareholders' nod at a meeting to be held on 13 February. The deal is expected to be completed by 28 February.

DRG, referred to as PEL's healthcare insights and analytics business, contributed INR13.30bn ($187.2m) or 10% to PEL's revenues for the financial year 2019 but reported a net loss of INR2.18bn. During the first half of fiscal year 2020, it had revenues of INR6.52bn, a 14% increase over the same period in the previous fiscal year.

PEL's pharmaceutical business, which brought in 36% of its FY2019 revenues, has also been growing steadily and the company is expected to introduce several products in 2020 as a non-compete clause with Abbott has ended.

In 2010, PEL, then known as Piramal Healthcare Ltd, had sold its formulation business to Abbott for $3.7bn, making a sizeable profit in the process.

DEAL STRENGTHENS FINANCES

PEL had invested the sales proceeds in setting up a financial services business and acquiring a diverse set of companies and assets. The returns have been mixed.

While the investment in Vodafone paid off handsomely in 2014, with PEL making a reported 52% return on its 11% stake sale in Vodafone India Ltd to a subsidiary of Vodafone Group Plc, the bet in financial services hasn't worked to plan.

This business, which accounts for over half of PEL's revenues, ran into trouble due to exposure of its loan book to the real estate sector and small and medium-sized manufacturing companies, which were hit by a business slowdown. While borrowers found it difficult to pay back their loans, a large proportion of short-term borrowings meant PEL faced an imbalance in its funds flow.

To improve liquidity and its debt-equity ratio, PEL has been raising equity funds, apart from reducing short-term borrowings and diversifying its loan book. As part of a plan to bring in around INR100bn in PEL via equity, a INR17.5bn preferential allotment of compulsory convertible debentures was made to Canadian institutional investor, Caisse de dépôt et placement du Québec (CDPQ), and a rights issue of INR36.5bn to existing shareholders is currently underway, set to close 21 January.

"Company is also subsidiarizing its pharma business and working towards raising additional around 20% equity capital in the pharma business to tap organic and inorganic growth opportunities. Along with the ongoing equity capital raise in PEL, this transaction not only further strengthens the company's balance sheet but also marks another step towards significantly unlocking value in future," said Ajay Piramal. *(Also see "Piramal Eyes 20% Pharma Stake Sale" - Generics Bulletin, 8 Jan, 2020.)*

PEL is looking at monetizing more of its investments in the Shriram group of companies too. In June 2019, Piramal Enterprises sold its stake in Chennai-based Shriram Group's Shriram Transport Finance for INR23bn. It is also looking to exit Shriram Capital Ltd, in which it holds a 20% stake. Once the stake sales are through, Piramal Enterprises can increase its focus on building the pharmaceutical business into the formidable entity it used to be.

Published online 20 January 2020

J&J's Gorsky Hails Strong Performance By Immunology Therapies Tremfya, Stelara

JOSEPH HAAS joseph.haas@informa.com

Johnson & Johnson has made a major push with its immunology portfolio even as its mature Remicade (infliximab) franchise began to wane and faced biosimilar competition. CEO Alex Gorsky cited the immunology sales performance as a particular factor in the company's fourth quarter and full year 2019 success.

Gorsky told the 22 January earnings call he was "extremely proud" particularly of the immunology group's sales performance. "The way that they were able to manage the biosimilar impact with Remicade while simultaneously launching multiple new indications for compounds like Stelara, launching Tremfya," he said. The interleukin-23 inhibitor Tremfya (guselkumab) moved into blockbuster territory during the third quarter, which the company attributed in part to head-to-head data against Novartis AG's IL-17 blocker Cosentyx (secukinumab). *(Also see "J&J's Tremfya Gets Its Blockbuster Wings " - Scrip, 15 Oct, 2019.)*

Remicade brought in $1.04bn globally during the fourth quarter, down 16% from $1.24bn one year earlier, due to biosimilar competition and increased discounts. In the US, quarterly sales of $755m meant a 10.4% decline. For the full year, Remicade sales of $4.38bn decreased 16.8% from $5.33bn in 2018, with US sales down 16% to $3.08bn. Remicade sales have been dropping for years, as Pfizer Inc. and Celltrion Inc. launched Inflectra (infliximab-dyyb) in November 2016. But J&J has held it off to a large degree due in part to J&J signing exclusive contracts with payers to cover Remicade. *(Also see "Exclusive Remicade Contracts Are Slowing Biosimilar Uptake" - Scrip, 1 Aug, 2017.)*

J&J reported 4.4% global sales growth for its pharmaceuticals division in the fourth quarter, with full-year sales growth for the entire company of 2.8%, not counting the impact of foreign exchange rates. Gorsky noted this was J&J's 36th consecutive year posting overall revenue growth.

Immunology tallied $3.52bn worldwide on the quarter, up 5.4% year-over-year, with US sales of $2.52bn up 6.8% and ex-US revenue just over $1bn up 1.9%. For the year, immunology revenue of $13.95bn was up 6.3%, mirroring a 6.3% uptick in US sales to $9.64bn and a 65% increase ex-US to $4.31bn.

Gorsky pointed out that for the full year, J&J pharmaceuticals posted 5.8% sales growth not including foreign exchange, which outpaced the company's peers. This performance "more than offset the loss of exclusivity due to biosimilar competition and generic erosion as well as new competitive entrants and other market pressures," he said. "Now, it's important to note that our robust growth can be attributed to volume, not price, and our sales growth is a reflection of the increased number of patients we're reaching with our transformational medicines for unmet needs."

TREMFYA, STELARA POST DOUBLE-DIGIT GROWTH

Indicated for psoriasis, Tremfya global sales tallied $270m during the fourth quarter, with the US total of $199m a 39.7% year-over-year increase. Outside the US, where Tremfya has been available for less than a year, sales reached $71m. The overall increase for the quarter compared to Q4 2018 was 55.1% For the full year, the product realized worldwide sales of $1.01bn, with US sales of $764m up 68.5%.

The traction is notable given the crowded competitive field for Tremfya, where it contends with the IL-17 blockers including Cosentyx and Eli Lilly & Co.'s Taltz (ixekizumab), as well as the second-to-market IL-23 blocker, AbbVie Inc.'s Skyrizi (risankizumab), which was approved last April. *(Also see "AbbVie's Humira Succession Plan Begins Taking Shape With Skyrizi US Approval" - Scrip, 24 Apr, 2019.)*

J&J hopes to grow Tremfya's sales further this year with supplemental approval applications for psoriatic arthritis pending in the US and Europe backed by the Phase III DISCOVER-1 and DISCOVER-2 trials. *(Also see "J&J Targets Tremfya Growth In PsA" - Scrip, 13 Nov, 2019.)*

Now J&J's top-selling pharmaceutical product, Stelara (ustekinumab) posted 18.6% worldwide growth during the quarter to $1.7bn. The US figure of $1.19bn was up 18.4%, while international sales of $506m were up 19.1%. For the full year, Stelara totaled $6.36bn, a 25.2% increase, with US sales of $4.34bn up 25.3%. At the J.P. Morgan Healthcare Conference on 17 January, J&J's worldwide chairman of pharmaceuticals Jennifer Taubert predicted that J&J's sales momentum would continue with 10 launches – including label expansions for already approved drugs – expected between 2019 and 2023. *(Also see "J&J To Power Ahead With 10 Launches In Four Years " - Scrip, 17 Jan, 2020.)*

The oncology franchise also produced a strong quarter with worldwide sales of $2.72bn up 10.6%. Darzalex (daratumumab) and Imbruvica (ibrutinib) were the top sellers, with the former yielding $830m globally, up 44.5% year-over-year, and the latter, partnered with AbbVie, bringing in $875m, up 26.6%. Overall, cancer therapy brought in $10.69bn in 2019 for J&J, an 11.9% uptick over 2018.

J&J still is not breaking out individual sales numbers for major depressive disorder drug Spravato (esketamine), launched last March. In September, the firm filed a supplemental new drug application (sNDA) to add treatment of MDD with suicidal ideation to the product's US label. *(Also see "J&J Looks To Expand Spravato Label To Suicidal Ideation" - Scrip, 10 Sep, 2019.)* Vice president of investor relations Christopher DelOrifice told the call that "patient demand continues to build [for Spravato], and the unmet need remains very high. New patient starts continue to steadily increase each month with over 3,500 patients being treated to date."

In a same-day note, Morningstar analyst Damien Conover pointed out that pharmaceuticals continues to be J&J's strongest-performing unit, compared to consumer health and medical devices,

despite the impact of generic and biosimilar competition. "Generics to cancer drugs Zytiga (abiraterone) and Velcade (bortezomib) as well as biosimilar pressure to immunology drug Remicade weighed on the overall drug sales," he wrote. "However, newer drugs launched in those indications offset the generic competition. We expect continued strong growth from newer drugs, including cancer drugs Darzalex and Erleada (apalutamide) as well as immunology drug Tremfya."

Erleada, which is approved to treat non-metastatic, castration-resistant prostate cancer, brought in $116m during the fourth quarter and $332m for full-year 2019. *(Also see "J&J's Erleada Approved By FDA In New Prostate Cancer Indication " - Scrip, 19 Sep, 2019.)* Zytiga worldwide revenue of $677m during the fourth quarter was a 12.9% decrease, while Velcade's $115.2m meant a 55.2% decline.

AWAITING OPIOID SETTLEMENT FINALIZATION; STAYING THE COURSE IN M&A

J&J really had nothing new to report about its expected settlement in the ongoing opioid lawsuits – the company has reserved $4bn for damages in the pending cases. *(Also see "J&J Oklahoma Judgement May Set Benchmark For Massive Opioid Resolution" - Pink Sheet, 26 Aug, 2019.)*

"With respect to the opioid settlement and agreement in principle that was announced shortly after our Q3 earnings, where we set aside $4bn, we continue to work with the negotiating committee of the state attorney generals to finalize the agreement in principle," chief financial officer Joseph Wolk said. "We remain, I would say, cautiously optimistic that that's progressing very well. We're highly engaged to the extent we can be to finalize that agreement in principle, and we hope to hear more over the coming months from the lead negotiators representing not just the states, but as you know, the counties and municipalities."

The company added that it expects its cash flows to decrease by about 10% in 2020 due to the opioid settlement. Bernstein analyst Ronny Gal estimated this could mean a cash flow decline of as much as $2bn for J&J, but added in a 22 January note that the company's cautious optimism that a settlement is near was a good sign for all of the companies affected by the settlement process.

Gorsky indicated that J&J's approach to business development would continue to focus on bolt-on type acquisitions rather than larger deals, noting that across all three of its business areas, the company paid more than $7bn in 2019 for 11 acquisitions and six licensing agreements. "We have continued, I think, our pattern of tuck-in acquisitions where we get new technologies, as you saw that we did with both XBiotech Inc. and other opportunities in our pharmaceutical business," the exec said, adding that J&J will continue looking at opportunities "across all three of our segments."

In December, J&J paid $750m up front to license worldwide rights to XBiotech's interleukin-1 alpha antagonist bermekimab in Phase II for atopic dermatitis and hidradenitis suppurativa.

Published online 23 January 2020

AstraZeneca's Dobber On Ramping In Renal, Expanding In CV And Business Development

JESSICA MERRILL jessica.merrill@informa.com

This year AstraZeneca PLC Biopharmaceuticals President Ruud Dobber is focused on executing on the company's expansion into kidney disease with the launch of Lokelma (sodium zirconium cyclosilicate) underway for hyperkalemia and a second potential approval, roxadustat, anticipated later in 2020.

Dobber, who oversees AstraZeneca's global drug portfolio outside of oncology, talked with *Scrip* at the J.P. Morgan Healthcare conference in San Francisco on 14 January. He has been leading the biopharmaceuticals business for a year, having previously run AstraZeneca's North American commercial operations. He discussed the ongoing expansion in renal disease, the company's commitment to cardiovascular disease, including the move into heart failure, and business development.

The commercial oncology business is overseen by David Fredrickson, who separately talked to *Scrip* about the launch of Enhertu (trastuzumab deruxtecan) in HER2-positive breast cancer. *(Also see "J.P. Morgan Notebook Day 2: Bourla Feels Pfizer's Underappreciated, GSK Prepares For Myeloma First And More" - Scrip, 15 Jan, 2020.)*

Among the launches on the biopharmaceutical side of the business are two in renal disease: Lokelma, which was approved by the US Food and Drug Administration (FDA) for hyperkalemia in 2018 but didn't launch until mid-2019, and roxadustat for the treatment of patients with anemia from chronic kidney disease.

Dobber confirmed that AstraZeneca filed an application for roxadustat with the FDA before the end of the year. The drug, developed with partner FibroGen Inc., is a first-in-class HIF-PH inhibitor that has shown improved safety and efficacy in clinical trials over the standard of care, erythropoiesis-stimulating agents, and which AstraZeneca hopes will be approved for both CKD patients on dialysis and those not on dialysis. *(Also see "Clear Path For AstraZeneca's Roxadustat After Reassuring Safety Data" - Scrip, 11 Nov, 2019.)(Editor's note: this story has been updated to reflect that AstraZeneca expects FDA approval, but not necessarily the launch, of roxadustat in 2020).*

"From a market access perspective this is a tough area."
– Ruud Dobber

BUILDING MARKET ACCESS IN "A TOUGH AREA"

Both launches are core elements of AstraZeneca's strategy to expand in kidney disease beyond diabetes, where it has long had a presence. In 2018, AstraZeneca renamed its CVMD (cardiovascular/metabolic disease) therapy area to CVRM (cardiovascular/renal medicine) to reflect the growing emphasis on renal disease outside of diabetes. *(Also see "Next Up For AstraZeneca: Building Out In Renal Disease " - Scrip, 24 Oct, 2018.)*

Both launches will be challenging as AstraZeneca ramps up in a new space that presents specific market access challenges, both around commercial payer dynamics and Medicare restrictions for drugs administered in dialysis centers under the end-stage renal disease bundled payment system.

"From a market access perspective this is a tough area," Dobber acknowledged.

The company has established a renal commercial sales force for the launch of Lokelma, which will likely be expanded to support the launch of roxadustat, Dobber said.

With the launch of Lokelma, AstraZeneca is competing against Vifor Pharma Group's Veltassa (patiromer), which was approved by the FDA in 2015, but carries warnings about constipation and can interact with other oral drugs.

"We are extremely pleased because within the six months after the commercial launch we are equivalent or even higher in what is called new-to-brand prescriptions, which is an incredible achievement of the medical and commercial team so quickly," Dobber said.

There is significant underdiagnosis in the space because of lack of awareness on the part of general practitioners and cardiologists and to a smaller extent nephrologists, the exec explained.

Hyperkalemia is high serum potassium concentration in the blood that can be asymptomatic but can cause long-term damage. It is often caused by CKD or other metabolic deficiencies. The standard of care has been a restrictive diet or an old generic medicine, sodium polystyrene sulfonate, that carries a lot of side effects. There are roughly 3 million patients in the US with hyperkalemia, according to AstraZeneca.

"Hyperkalemia is not always seen by payers as an area of high unmet medical need, so we need to do a lot of education," Dobber said. "Our access is getting better every day and the expectation clearly is that we will exceed Veltassa for 2020 from

a prescription standpoint." Senior VP for market access Rick Suarez also talked to *Scrip* about the launch. "We are very pleased with payers' willingness to add it to formulary and preferred positions at that," Suarez said. "Some of the largest Medicare payers in the country have done so, and we are also seeing very good uptake in hospitals."

As for the anticipated launch of roxadustat, Dobber said it is a complex product with two separate segments of the market to target, dialysis and non-dialysis.

"We will have specific people detailing in the dialysis centers versus [to] nephrologists working in hospitals and clinics," he said. "We have a very strong field force already but probably it is reasonable to say that we will expand it a little bit more."

As for the challenging reimbursement environment for bundled payments in dialysis centers under Medicare, Suarez said the company is prepared.

"The bundles create their own challenges because the legislative environment can change at any time, but we feel we have a good grasp of how it is currently reimbursed and how our product will be treated in the bundle," Suarez said. "Time will tell."

MOVING BEYOND DIABETES WITH FARXIGA

In addition to the two new launches, AstraZeneca also has a potential large commercial opportunity coming in the first half of the year from the approval of the diabetes pill Farxiga (dapagliflozin) for the treatment of heart failure. The FDA granted a priority review for Farxiga for the reduction of cardiovascular death or worsening of heart failure in adults with reduced ejection fraction (HFrEF) both with and without type 2 diabetes, with action expected in the second quarter. *(Also see "AZ's Farxiga Gets FDA Priority Review For Heart Failure" - Scrip, 6 Jan, 2020.)*

The filing represents a significant opportunity for AstraZeneca to expand the SGLT2 inhibitor outside of diabetics. Farxiga was already approved to reduce the risk of hospitalizations for heart failure in type 2 diabetics with cardiovascular risk factors in October, the first SGLT2 to win the indication.

"It will open up a completely new patient population," Dobber said. "We have high expectations of course for this opportunity." The expanded filing was based on the Phase III DAPA-HF trial that showed the drug reduced the composite endpoint of cardiovascular death or worsening heart failure by 26% when given on top of standard of care, with benefits seen in both diabetics and non-diabetics. *(Also see "Farxiga Data Change Heart Failure Treatment Outlook" - Scrip, 2 Sep, 2019.)*

He said AstraZeneca will remain committed to the diabetes space, but that within diabetes, the focus will move more toward cardiovascular disease and comorbidities of diabetic patients. That comes after another major diabetes player, Sanofi, announced in December that it will end diabetes research altogether. *(Also see "Sanofi, Long-Time Leader In Diabetes, Is Exiting Diabetes Research" - Scrip, 10 Dec, 2019.)*

A HIGH BAR FOR CARDIOVASCULAR DISEASE

At a time when there is some renewed interest in the cardiovascular disease therapy among some big pharma players, Dobber reiterated AstraZeneca's commitment to the space.

"There is a lot of attention of oncology and the breakthroughs in oncology, but we need to understand the number one killer in the world is still cardiovascular disease by far," he said. AstraZeneca is looking increasingly at inflammation as a trigger for atherosclerotic plaques and heart attacks, with work ongoing in R&D.

But it is a challenging space. He pointed to AstraZeneca's experience with Epanova (omega-3-carboxylic acids) as an example of just how tough the cardiovascular space can be. The company announced on 13 January the discontinuation of the cardiovascular outcomes trial testing Epanova in patients with high triglycerides who are at increased risk of cardiovascular disease due to a low likelihood of success. *(Also see "AZ Halts Epanova Study As High Placebo Effect Kills Acasti's Omega-3 TRILOGY-1 Trial " - Scrip, 14 Jan, 2020.)*

The drug was first approved by the FDA in 2014 for the treatment of high triglycerides, but a positive cardiovascular outcomes trial would have opened the drug up to a potentially broader cardiovascular risk reduction claim. A rival drug, Amarin Corp. PLC's Vascepa (icosapent ethyl), has succeeded where Epanova failed, resulting in mega-blockbuster sales expectations from some analysts. *(Also see "Sales Already Growing As Vascepa Secures Cardio Approval" - Scrip, 16 Dec, 2019.)*

"This is a very hard place because the bar is very high," Dobber said of the cardiovascular therapeutic area. "But that makes it also very attractive if you find a molecule that can further reduce [the risks]."

As for building in cardiovascular disease through business development, Dobber said it is challenging to find a breakthrough asset. "As a large company, we are scanning every day potential opportunities," he stated. He said CEO Pascal Soriot and chief financial officer Marc Donoyer would take a critical view of any assets he might bring to their attention because of the high valuations. But, he added, "if it makes sense, there is a clear willingness to in-license or buy those new assets, but there are not too many," he said.

Two areas AstraZeneca has identified as new areas for expansion are gene therapy and cell therapy, he added. "It is fair to say we are not one of the frontrunners at the moment, but clearly there is a huge commitment from our R&D colleagues in order to have a close look," Dobber noted.

Published online 23 January 2020

Roche Gears Up For Potential Neuroscience Breakthroughs

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

One of the most eye-catching remarks made at last week's J.P. Morgan conference in San Francisco was a bold prediction by Roche's pharma division head Bill Anderson.

He told investors: "We think that neuroscience has the potential to be in the '20s what oncology has been in the last decade…and we have a very strong scientific and development effort there."

This is a bold statement – as oncology looks unlikely to be knocked off the number one spot in terms of biopharma revenues – but neuroscience could nevertheless prove to be one of the decade's big growth drivers.

In terms of sheer numbers of patients, within neuroscience it is of course Alzheimer's disease where the greatest unmet need is, and 2020 may see an historic (and most likely controversial) approval of Biogen's aducanumab by the US Food and Drug Administration.

Roche is one of the many other companies with a stake in Alzheimer's research (its gantenerumab is in Phase III), but the field is littered with failures, and real clinical progress against this disease may still be some years away.

However it is the runaway success of Roche's multiple sclerosis drug Ocrevus (ocrelizumab) which has convinced the Swiss pharma company it can build an industry-leading neuroscience portfolio.

The company has a number of key clinical trial readouts and milestones in neuroscience to watch out for in 2020 and 2021, reflecting a broader increase in activity across the broad therapy area.

A FIRST IN HUNTINGTON'S DISEASE?

The first significant milestone of the year for Roche in neuroscience is the anticipated FDA approval of its spinal muscular atrophy (SMA) candidate risdiplam.

This is the first oral treatment for the condition (being developed for types 1,2, and 3 of the disease), and will challenge Biogen's Spinraza (nusinersen) and Novartis's gene therapy Zolgensma (onasemnogene abeparvovec).

Anderson hinted last week that the company intends to undercut its rivals on price, with the aim of maximising its share of the market, as it looks unlikely to show clinical superiority against its competitors.

Meanwhile, Roche and Ionis Pharmaceuticals Inc.'s first-in-class Huntington's disease therapy HTT-ASO (RG6042) could be filed and approved by the end of 2020.

The drug entered a pivotal Phase III trial, GENERATION-HD1 last year, with a primary completion date of March 2022, but the urgency of unmet need for patients means regulators are likely to accept earlier data for filing.

Roche is expected to seek approval based on open-label extension study which is due this year, as well as on interim biomarker data from Generation-HD1 and results from a natural history study.

All of which means HTT-ASO could be approved by the end of 2020.

Speaking to *Scrip* at the J.P. Morgan conference, Roche's head of global product strategy, Teresa Graham, said the company was gearing up for significant expansion in its commercial operations for neuroscience therapies.

The company is already undergoing a major reorganisation of its commercial operations, with its US arm Genentech leading a shift away from a product-focused marketing structure to a geographical approach aimed at reflecting the priorities of local healthcare systems, including market access and reimbursement issues.

Graham said this same approach was now being taken in the neuroscience therapy areas it is preparing to enter.

"We're spending a lot of time getting to know the [physician] community to really figure out what they need, and what their patients need. We're trying to take a very customer-centric approach in all of our sales and marketing activities going forward."

She noted that many of the patient needs in these disease area differed greatly from cancer – they are more chronic conditions, and physicians can be more safety adverse, with fears of disability a leading concern.

"That does require you to have a different approach. I think we have cut our teeth in MS with Ocrevus, and there are a lot of lesson learned that we are able to apply."

SAREPTA GENE THERAPY PARTNERSHIP

Perhaps Roche's most remarkable progress in the field last year came with the unveiling of a deal with Sarepta, in which the big pharma company would commercialise the specialist company's gene therapy for Duchenne muscular dystrophy. It signed a deal worth $1.15bn which would see it take charge of marketing the drug in all global markets outside the US. Read the full article here

The gene therapy candidate, SRP-9001, is expected to produce pivotal data in

Roche's neuroscience pipeline

DRUG	INDICATION	CATALYST	DATE
Risdiplam	Spinal muscular atrophy types 1,2,3	US FDA approval (expected)	24 May 2020
HTT-ASO (RG 6942)	Huntington's Disease	Follow up from Phase I/II and potential filing	H1 2020
Satrolizumab	Neuromyelitis optica spectrum disorder (NMOSD)	US FDA approval (expected)	Q3 2020 (estimated)
Balovaptan	Pediatric autism	Phase II data	H2 2020
SRP-9001*	Duchenne Muscular Dystrophy	Phase I/II	Early 2021

* Ex-US commercial deal with Sarepta

early 2021. Phase I data suggest it could be the first true breakthrough in halting or reversing the disease, raising microdystrophin expression levels to 74-96% of normal levels three months after treatment in four patients.

"There's still definitely a lot of work to do, I'm really excited about that data," said Graham.

"It is very rare for us to do an ex-US deal like that, but the overlap with SMA is perfectly synergistic with the portfolio that we already have. This is the first drug that's really shown any kind of benefit [in Duchenne] so I think it could be transformational for those kids."

Sarepta and Roche will face competition from Pfizer and Solid Biosciences rival Duchenne gene therapy, SGT-001. This product was placed on clinical hold by the FDA in November after a patient experienced a serious adverse event, however this is an increasingly common precaution taken in gene therapy.

Neuroscience differs considerably to oncology and other therapy areas better known to Roche, so the company is already laying the groundwork on clinical infrastructure (e.g. readiness for intrathecal injections for Huntington's disease) and market access (including novel payment methods) in these therapy areas.

Published online 21 January 2020

New CEO Brett Monia Takes The Lead As Ionis Prioritizes Non-Partnered Programs

MANDY JACKSON mandy.jackson@informausa.com

Ionis Pharmaceuticals Inc. has monetized its expertise in antisense drug discovery by linking up with bigger biopharmaceutical companies to lead late-stage development and commercialization. But going forward, new CEO Brett Monia said, the company will be more selective about entering into new collaborations and prioritize Ionis-owned drug candidates.

Scrip spoke with Monia about Ionis's future in an interview at the J.P. Morgan Healthcare Conference earlier this month in San Francisco. Monia, a founding scientist of Ionis who most recently served as chief operating officer, took the helm from longtime CEO Stanley Crooke in a planned leadership transition at the start of 2020. The change comes as the company's pipeline is set to deliver regulatory filings for 10 or more partnered and wholly-owned drugs over the next three to five years.

Brett Monia was a founding scientist at Ionis

Source: Ionis Pharmaceuticals Inc.

Some things at Ionis will stay the same as the company enters a new leadership era, including its commitments to advance the science of RNA-targeting medicines and to its existing partners. However, Monia said, "the company is in a different place today than before. We're in a very strong financial position. That gives us leverage to invest … in technologies to expand the scope of antisense."

"In addition, we will begin to prioritize the Ionis-owned pipeline," he continued. "We've done a lot of partnerships over the years very successfully, and although we're much more careful and much more selective in the partnerships we do today … we'll continue those, but we'll also build out the Ionis-owned pipeline and build commercial capabilities internally to maximize the commercial value of drugs that we develop and bring to approval ourselves. That's a significant change."

The company's three marketed drugs include Tegsedi (inotersen), approved in the US and Europe for polyneuropathy associated with hereditary transthyretin-mediated (TTR) amyloidosis, and Waylivra (volanesorsen), approved in the EU for familial chylomicronemia syndrome (FCS); both are commercialized by Akcea Therapeutics Inc., an Ionis affiliate majority owned by the parent company. *(Also see "Akcea C-Suite Upheaval's Reasons Unclear, Firm Set To Take In More Ionis Programs" - Scrip, 23 Sep, 2019.)*

Its third commercial product is the first-to-market spinal muscular atrophy (SMA) drug Spinraza (nusinersen), which is approved in the US and EU, and marketed by Biogen – Ionis's most frequent collaborator. Biogen paid $1bn up front in 2018 to enter into its sixth agreement with the company; the 10-year partnership is focused on drugs for neurological and ophthalmic indications. *(Also see "Biogen Re-Ups With Ionis In Search Of A Neuroscience 'Innovation Engine'" - Scrip, 20 Apr, 2018.)*

Ionis had $2.2bn in cash at the end of the third quarter of 2019, but expected a significant increase by the end of the year from product sales, royalty revenue and partnership fees announced early in the fourth quarter. Pfizer Inc. agreed in October to pay Akcea $250m up front – half of which will go to Ionis – to collaborate on the development of AKCEA-ANGPTL2-LRx, which is designed

to reduce the production of angiopoietin-like3 (ANGPTL3) protein for the treatment cardiovascular diseases. *(Also see "Pfizer Reaffirms CV Disease Commitment With Deal For Akcea's ANGPTL3 Drug" - Scrip, 7 Oct, 2019.)*

Also, Bayer AG was required to pay Ionis a $10m milestone fee based on the German big pharma's decision in October to take IONIS-FXI-LRx into Phase II; the antithrombotic antisense drug candidate that reduces production of factor XI. *(Also see "Bayer/Ionis Advance Next-Generation Antithrombotic After Positive Clinical Results" - Scrip, 10 Oct, 2019.)*

Ionis's commitment to bringing in outside technology will be another big change for the company, which traditionally has been a seller, not a buyer, of novel science.

"Now, with our financial position and where the technology is – it's validated, it's delivering medicines, we expect 10 or more new potential filing applications for approval over the next three to five years – we're really running with a lot of momentum these days," Monia said. "It gives us the opportunity to invest in new technologies that do things that antisense maybe doesn't do so well today, like reaching new organ systems and new cell types, and genomics investments that allow us to select new targets so that we continue to populate our pipeline for years to come."

NEUROLOGY PIPELINE CONTINUES TO EXPAND

"Our two largest and most productive franchises are cardio-metabolic and neurodegenerative diseases," Monia noted.

In the ongoing commercialization of Spinraza, the drug gained a new competitor last year with US Food and Drug Administration approval of the Novartis AG gene therapy Zolgensma (onasemnogene abeparvovec) and could have a second competitor with US FDA approval of Roche's risdiplam, which is expected in May. *(Also see "Genentech's SMA Type 1 Data Strengthen Case Backing Risdiplam Approval" - Scrip, 23 Jan, 2020.)*

Zolgensma generated $160m in sales during the third quarter – its first full quarter on the market – while Biogen reported $547m in third quarter Spinraza sales, which was up 12% from the second quarter and generated $82m in royalty revenue for Ionis in the July-to-September period. *(Also see "Novartis's Zolgensma Finds Commercial Legs In A First For Gene Therapy" - Scrip, 22 Oct, 2019.)*

Other progress in the company's neurology pipeline in 2019 and early 2020 includes enrollment of the first patient by Roche in a pivotal trial for IONIS-HTT-Rx (RG6042) in Huntington's disease, Biogen's initiation of a Phase III trial for tofersen in the reduction of superoxide dismutase 1 (SOD1) in patients with amyotrophic lateral sclerosis (ALS), and initiation of Phase III trials in TTR amyloidosis patients who experience polyneuropathy and in patients who have cardiomyopathy with AKCEA-TTR-LRx.

AKCEA-TTR-LRx was developed using Ionis's Ligand Conjugated Antisense (LICA) technology platform, which is designed for selective delivery to the targeted cell type, allowing for greater potency, less frequent dosing, new routes of delivery for antisense drugs and delivery to new organ systems.

The company has six drugs in clinical development for neurological indications with more coming, since it plans to move six Ionis-owned programs into the clinic in 2020, including a treatment for Angelman syndrome. Also, Biogen selected four additional neurological disease targets in 2019 to move into drug discovery.

"So many other companies have exited neuro or tried to slow down or tried to acquire from other companies, largely because they have failed, whereas we believe we've cracked the code in neurodegenerative diseases," Monia said. "That was based on 10 years of investing in research to deliver our drugs to the central nervous system … I think we've only scratched the surface in CNS and there's a lot more coming."

MORE ALSO COMING IN CARDIO-METABOLIC, RARE DISEASES

The CEO said Ionis's cardio-metabolic pipeline also has a lot more programs coming, including drug candidates that may take the company's antisense technology into large population diseases.

"This now gets us into very large populations of patients – tens of millions of patients – with cardiovascular disease due to risk factors that haven't been treatable or addressable with other platforms," Monia said. "A drug like our [lipoprotein(a), or Lp(a)] program where Lp(a) is a risk factor that can be thought of like cholesterol is a risk factor. If you have really high Lp(a) levels – it's genetically determined – you're at high risk of cardiovascular disease."

This program, AKCEA-APO(a)-LRx, is being tested in patients with cardiovascular disease in a Phase III trial initiated by Novartis. Akcea and Ionis split a $150m license fee for the asset in early 2019 when Novartis opted in to the development program. *(Also see "Deal Watch: Novartis Opts In On Lipoprotein A Candidate From Akcea" - Scrip, 25 Feb, 2019.)*

More recently, Ionis and Akcea announced positive top-line Phase II results on 22 January for AKCEA-APOCIII-LRx, which is designed with the LICA technology to inhibit production of apolipoprotein-CIII in patients who are at risk of cardiovascular disease due to high triglyceride levels. The drug lowered triglyceride levels in a dose-dependent manner with the highest monthly dose of 50mg cutting fasting triglycerides to 150mg/dL or less

Ionis By The Numbers

- Three approved drugs: Spinraza, Tegsedi, Waylivra
- Five Phase III programs: IONIS-HTT-Rx (RG6042) in Huntington's disease with Roche, tofersen in SOD1 ALS with Biogen, AKCEA-APO(a)-LRx in cardiovascular disease with Akcea and Novartis, AKCEA-TTR-LRx in hATTR polyneuropathy with Akcea and AKCEA-TTR-LRx in hATTR in cardiomyopathy
- Ten or more new Phase II trial starts in 2020
- Five or more new Phase III starts in 2020-2021
- Ten or more new drug application submissions by 2025

in more than 90% of patients versus less than 5% of patients in the placebo group.

"We believe monthly dosing is a critical advantage that may ultimately allow these drugs to treat larger populations, particularly ones with asymptomatic conditions," Needham analyst Chad Messer said in a same-day note suggesting that the AKCEA-APOCIII-LRx data validate Ionis's LICA technology.

The companies plan to move AKCEA-APOCIII-LRx into a Phase III trial in patients with FCS – a disease in which patients are unable to break down fats, leading to pancreatitis – and they intend to explore further development of the drug for other rare and common diseases associated with high triglycerides.

William Blair analyst Myles Minter pointed out in a 22 January note on the AKCEA-APOCIII-LRx top-line data that the candidate is a follow-on to Waylivra for which the FDA issued a complete response letter in 2018. *(Also see "Keeping Track: Busy August Ends With Approval For Doravirine, CRLs For Dasotraline And Waylivra" - Pink Sheet, 3 Sep, 2018.)* Ionis and Akcea still intend to pursue approval of Waylivra in the US while advancing AKCEA-APOCIII-LRx for FCS.

INFECTIOUS DISEASES, ONCOLOGY AND BEYOND

"Where are we going beyond this in the future? We, of course, have other areas that we're working in – in infectious diseases and an HBV program; oncology is a growing area for us and other disease areas as well," Monia said.

GlaxoSmithKline PLC opted in to develop a pair of drug candidates for the hepatitis B virus (HBV) in August.

"One area that we're moving into, where I think we've optimized the technology enough to deliver, is in pulmonary diseases, where we're actually delivering our drugs by aerosol delivery to the lung and we're moving into cystic fibrosis, idiopathic pulmonary fibrosis, COPD, chronic bronchitis, severe asthma," Monia said. "We haven't proven it yet, but I'm hopeful toward the end of this year we'll have enough clinical data to conclude that we've validated the approach."

He noted that most of Ionis's drugs are administered subcutaneously with a self-administered pen or locally, but the company believes it has figured out how to deliver its drugs orally as well and will have data in 2020 on its first oral therapy.

"It may sound a bit audacious, but I really believe Ionis has the potential to be the best company in the biotech industry, because of the size of our pipeline, the performance of our technology and where I see it going," Monia said. "There's a reason why so many companies want to partner with us – they want access to this technology, because they see what it's delivering."

Published online 24 January 2020

Horizon Sees Blockbuster Future For Tepezza After US Approval

ANDREW MCCONAGHIE andrew.mcconaghie@informa.com

Horizon Therapeutics PLC has gained approval for its thyroid eye disease treatment Tepezza (teprotumumab-trbw) from the US Food and Drug Administration, six weeks ahead of schedule.

The Dublin, Ireland-domiciled company has gained notoriety in recent years, thanks to its practice of buying up established drugs and hiking its prices, and was among 22 companies ejected from US industry association PhRMA in 2017 for not investing enough in innovative medicines.

But since then, chairman, president and CEO Timothy Walbert has steered the company towards more novel medicines development, and the approval of Tepezza, which had secured FDA breakthrough therapy designation, is seen as a turning point by the company's leadership.

Tepezza is the first FDA-approved treatment for thyroid eye disease (TED), an autoimmune disease associated with proptosis (eye bulging), diplopia (double vision), blurred vision, pain, inflammation and facial disfigurement.

The company has announced that Tepezza will be priced at around $14,900 per vial, or approximately $200,000 per patient per year. This combined with a US market of 15,000 to 20,000 patients means the company expects to hit peak sales in excess of $1bn a year.

The drug is a targeted inhibitor of insulin-like growth factor-1 receptor (IGF-1R), administered to patients once every three weeks for a total of eight infusions.

Analysts at Jefferies note that the FDA has granted Tepezza a broad label of "treatment of thyroid eye disease" without any limitations or mention of active or inactive disease, and therefore conclude that this should help it achieve rapid uptake. The analysts also believe the company has prepared the market well for launch, establishing relations with leading ophthalmologists and endocrinologists.

"Today is a great day for people living with thyroid eye disease, a rare, vision-threatening disease that previously had no FDA-approved treatment options," said Timothy Walbert.

Walbert also noted that the approval was the company's first biologic. Acknowledging its former notoriety and efforts to change, he called the approval a "key step in our evolution to an innovation-focused biopharma company, developing new medicines for debilitating diseases with few or no treatment options."

The FDA approval was based on results from a Phase II study and a Phase III confirmatory OPTIC study. The OPTIC study found that significantly more patients treated with Tepezza (82.9%) had a meaningful improvement in proptosis (≥2mm) as compared with placebo patients without deterioration in the fellow eye at week 24.

Additional secondary endpoints were also met, including a change from baseline of at least one grade in diplopia in 67.9% of patients receiving Tepezza compared with 28.6% of patients receiving placebo at week 24.

Horizon must conduct a post-marketing safety study in a larger patient population as was agreed at the Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) FDA Advisory Committee meeting on 13 December. The study will also evaluate retreatment rates relative to how long patients receive the medicine.

Published online 22 January 2020

AZ's Lynparza Gets Prostate Cancer Priority Review

KEVIN GROGAN kevin.grogan@informa.com

AstraZeneca PLC's hopes of having a fourth tumor type approved for Lynparza have received a big boost with US regulators agreeing to a quicker evaluation of the firm's PARP inhibitor for prostate cancer.

AZ and Clovis neck and neck in prostate cancer

The UK major and partner Merck & Co. Inc. have announced that a supplemental new drug application for Lynparza (olaparib) has been granted a priority review by the US Food and Drug Administration for patients with metastatic castration-resistant prostate cancer (mCRPC). This will speed up the review period from the standard 10 months to six months and AstraZeneca noted that the Prescription Drug User Fee Act (PDUFA) date is set for the second quarter of 2020.

The FDA's decision is based on results from the Phase III PROfound trial, which were presented during the European Society of Medical Oncology congress in Barcelona last year. They showed that Lynparza significantly reduced the risk of disease progression or death by 66% (7.4 months vs. 3.6 months) compared with

Johnson & Johnson's Zytiga (abiraterone) or Pfizer Inc./Astellas Pharma Inc.'s Xtandi (enzalutamide) in patients with BRCA1/2 or ATM-mutated mCRPC, the primary endpoint of the trial.

The trial also showed that Lynparza reduced the risk of disease progression or death by 51% (5.8 months vs 3.5 months) compared with Zytiga and Xtandi – which are androgen deprivation therapies – in the overall trial population of patients with homologous recombination repair (HRR)-mutated mCRPC. AstraZeneca noted that PROfound was the first positive Phase III trial testing a targeted treatment in biomarker-selected prostate cancer patients.

If all goes smoothly at the FDA, AstraZeneca and Merck will be entering a large market. Prostate is the second most common cancer in men, with an estimated 1.3 million new cases diagnosed worldwide in 2018. AstraZeneca stated that approximately 10-20% of men with advanced prostate cancer will develop CRPC within five years, and at least 84% of these will have metastases at the time of diagnosis.

Lynparza has quickly become a key drug for AstraZeneca, with sales in the first nine months of 2019 hitting $847m, up 93% on the like, year-earlier period. It is marketed for ovarian cancer and BRCA-mutated metastatic breast cancer, and at the end of 2019, the FDA approved the drug for use in a third tumor type, pancreatic cancer, less than two weeks after its advisory panel gave a narrow nod to the new indication. *(Also see "Lynparza Gets US OK For Pancreatic Cancer " - Scrip, 30 Dec, 2019.) (Also see "US FDA Approval Of Lynparza For Pancreatic Cancer Opens Door For PFS Endpoint In Disease" - Pink Sheet, 7 Jan, 2020.)*

PRIORITY REVIEW FOR RUBRACA TOO

The news will have been closely noted by Clovis Oncology Inc. especially since its PARP inhibitor Rubraca (rucaparib) was granted a priority review for mCRPC just last week (15 January). The PDUFA date for the US firm's drug is 15 May, so the race to be the first approved targeted therapy for prostate cancer is set to be a close one.

Clovis's filing is based on the results from the TRITON trials program, in particular the TRITON2 study which showed a 44% response rate with Rubraca in BRCA-mutated CRPC, and a 52% prostate-specific antigen (PSA) response.

Beating AstraZeneca and Merck to a first approval in CRPC would help Clovis start to catch up on its big pharma rivals and could lead to preferential use as clinicians gain familiarity with PARP in this patient population. Rubraca is currently approved for ovarian cancer but sales have been underwhelming in comparison to Lynparza.

At last week's J.P. Morgan Healthcare conference in San Francisco, Clovis discussed its unaudited revenues for 2019 which revealed full-year Rubraca sales of $142-$143m. The company was positive about its performance in Europe, following successful launches in the UK and Italy (with launches in France and Spain coming next month) but SVB Leerink analyst Andrew Berens issued a note on 14 January claiming that management's comments on Europe "suggest that US sales may be flat to down."

Lynparza and Rubraca are both ahead of the other PARPs in prostate cancer. In October last year, the FDA granted breakthrough therapy designation to J&J's Zejula (niraparib) in BRCA-mutated mCRPC cancer patients after androgen receptor therapy and taxane chemotherapy on the back of positive Phase II data. GlaxoSmithKline PLC acquired Zejula in its $5.2bn purchase of Tesaro Inc. last year; the drug is approved for ovarian cancer but J&J holds the prostate cancer rights to the PARP.

ORPHAN DRUG STATUS FOR IMFINZI

The Lynparza announcement was not the only piece of good news for AstraZeneca's oncology franchise on 20 January. The company noted that its PD-L1 inhibitor Imfinzi (durvalumab) and the anti-CTLA4 antibody tremelimumab have been granted orphan drug designations by the FDA for liver cancer.

The agency has granted orphan drug status on the basis of the ongoing Phase III HIMALAYA trial, testing Imfinzi as a monotherapy and in combination with tremelimumab in patients with unresectable, advanced hepatocellular carcinoma. Results from the study are scheduled for later this year.

Published online 21 January 2020

Genentech's SMA Type 1 Data Strengthen Case Backing Risdiplam Approval

JOSEPH HAAS joseph.haas@informa.com

With top-line, pivotal data showing efficacy in infants with type 1 spinal muscular atrophy (SMA), Genentech Inc. has bolstered the case for approval of risdiplam, a survival motor neuron-2 (SMN-2) splicing modifier under review at the US Food and Drug Administration with a 24 May action date.

On 22 January, the Roche affiliate reported that risdiplam demonstrated statistical significance in infant patients with type 1 SMA aged one to seven months for the ability to sit up without support for at least five seconds, which the company called a medically meaningful motor milestone improvement. The top-line data were from part two of the pivotal FIREFISH study; part one of that study investigating risdiplam's safety and optimal dosing were included in the new drug application at the FDA, along with safety and efficacy data from the SUNFISH study in patients with type 2 or type 3 SMA. *(Also see "Keeping Track Of Thanksgiving Leftovers: Risdiplam, Artesunate Highlight Glut Of Submissions/Filings" - Pink Sheet, 5 Dec, 2019.)*

THE FOUR TYPES OF SMA

- Type 1 onsets from birth to six months of age with a lifespan of two years; mortality usually associated with pulmonary complications
- Type 2 occurs between the ages of six and 18 months, with life expectancy around 30 years and respiratory impairment
- Type 3 occurs between ages two and 17, lifespan near-normal or normal but roughly 50% end up wheelchair-bound

TURN TO PAGE 18

CONTINUED FROM PAGE 17

- Type 4 is adult onset after age 20, normal life expectancy but progressive muscle weakening

Roche/Genentech are seeking a broad label in SMA, which is characterized by four types of the disease with type 1 being the earliest to onset and having the most severe mortality. *(Also see "The SMA Market: Assessing The Unknowns" - In Vivo, 26 Nov, 2019.)* Although the data included in the NDA do not include efficacy data for type 1 SMA, it is possible that given the unmet medical need in SMA, the FDA may approve a broad label including type 1 patients while awaiting confirmatory data. Roche previously has said it anticipates two-year efficacy data from FIREFISH in late 2023. *(Also see "Roche Makes Case For Its Oral SMA Drug Risdiplam As Filings Beckon" - Scrip, 6 Feb, 2019.)*

In an email exchange with *Scrip*, the company indicated it continues to hope for a fairly broad indication. "Th[e] body of data submitted in the NDA includes results from risdiplam treatment in people living with SMA Types 1, 2 and 3," it said. "We are in ongoing discussions with the FDA, and sharing new data on risdiplam as it becomes available, including FIREFISH Part 2. … Our current focus is to closely work with the FDA to explore broad access to risdiplam for all individuals in the community who might benefit."

Risdiplam would be the third drug to reach market for SMA, following Biogen Inc.'s blockbuster Spinraza (nusinersen), approved by the FDA in 2016, and Novartis AG's gene therapy Zolgensma (onasemnogene abeparvovec-xioi), approved in May 2019. However, as an orally administered liquid risdiplam would be the first at-home administered option, which would be given daily. *(Also see "Rapid US FDA Review For Roche's SMA Contender" - Scrip, 25 Nov, 2019.)*

Spinraza is administered three times annually as an injection into the patient's spinal cord, while Zolgensma, which currently is approved only for patients two-years-old and younger (type 1), is an intravenous therapy approved for one-time use. The company is working to expand use into the larger type 2 and 3 populations with an intrathecal formulation of Zolgensma, but the FDA placed the program on a partial clinical hold in October due to preclinical findings of dorsal root ganglia (DRG) mononuclear cell inflammation. *(Also see "US FDA Puts IT Zolgensma Studies On Partial Clinical Hold" - Scrip, 30 Oct, 2019.)*

At the J.P. Morgan Healthcare Conference on 13 January, David Lennon, CEO of Novartis's AveXis Inc. subsidiary, which developed the gene therapy, said the company is working to reply to the FDA's safety concerns this quarter in hopes of getting the Phase II STRONG study underway again.

"The important thing is to recognize that was an important safety finding reported to the FDA. They wanted to understand better what that safety finding was," Lennon said. "What we saw was a minimal to marked inflammation and degeneration of some dorsal root ganglia," which are sensory neurons that affect tactical function, usually to painful or hot/cold stimuli.

"Now, we haven't seen any impact of that in the clinical trials overall," he continued, "and when you actually look at the preclinical data that we had, while the individual cellular impact can be described as we said, it's not every DRG that gets impacted. It's not every cell in the DRG that are impacted that show that degeneration and there were no neurological findings in the non-human primates that were studied."

STILL ROOM FOR RISDIPLAM

While the market is gaining more options, Genentech noted that a majority of SMA patients are untreated.

The company thinks, however, that the systemic impact of an oral therapy may offer a broader benefit than the targeted therapies from Biogen and Novartis. "Increasing evidence suggests that the loss of SMN protein may affect many tissues and cells throughout the body and that SMA is a multisystem disorder," Genentech told *Scrip*. "Risdiplam distributes systemically and preclinical data show that it increases SMN protein in multiple tissues. This ability to increase SMN protein in the CNS and peripheral tissues in the body is the key advantage of daily oral administration. Risdiplam may therefore have potential benefits beyond motor neurons which could be important for achieving optimal clinical outcomes."

In a 23 January note, Deutsche Bank analyst Richard Parkes said the FIREFISH part two data, including no reported treatment-related safety findings, offers further de-risking of risdiplam behind the confirmatory data from SUNFISH. "We continue to see sales of CHF2bn-3bn [about $2.06bn-$3.1bn] as realistic given its oral administration and likely approval in a broad age range of patients, making it a major contributor to Roche's growth through near-term pressures," he said.

Because the SUNFISH and FIREFISH studies have enrolled patients up to 25 years of age, approval of risdiplam likely would mean a much larger addressable patient base than applies to Zolgensma, the analyst added. "If, as we suspect, detailed data confirm that risdiplam's efficacy is competitive with Biogen's intrathecally administered Spinraza and Novartis' Zolgensma, we believe its advantageous oral administration and broad label could open up a very large opportunity," Parkes said.

Datamonitor Healthcare analyst Sophie Ng offered *Scrip* a similar assessment, saying "we believe that risdiplam will have a large opportunity to shift the market share in Roche's favor once it has gained approval, especially with the completion of FIREFISH study reinforcing the positive safety profile of risdiplam," as well as the demonstration of efficacy in type 1-3 patients.

Considering the data from Biogen's perspective, Credit Suisse analyst Evan Seigerman speculated that Roche might price risdiplam lower than Spinraza to encourage use, especially in type 2 and type 3 SMA patients. He wrote on 23 January that the FIREFISH part two data "further highlight the threat" to Spinraza from risdiplam. Spinraza has a first-to-market advantage and had been dosed in more than 9,300 patients as of the end of September, he added.

Price does offer another avenue of differentiation in SMA. Novartis grabbed headlines last May when Zolgensma became the world's highest-price drug therapy, with a price tag above $2m. *(Also see "It's Official: Novartis SMA Gene Therapy Zolgensma Is World's Most Expensive Drug" - Scrip, 24*

TURN TO PAGE 20

Citeline Awards

Informa Pharma Intelligence

(Previously known as the CARE Awards)

Book your table

Citeline Awards 2020

Thursday, April 30, 2020
Hyatt Regency Boston, Boston, MA

www.clinicalresearchexcellence.com

SPONSORSHIP AND TABLE BOOKING ENQUIRIES:
Christopher Keeling
T: +44 (0) 20 3377 3183
E: christopher.keeling@informa.com

GENERAL ENQUIRIES:
Jo Kirkpatrick
T: +44 (0) 20 7017 7180
E: jo.kirkpatrick@informa.com

Sponsored by

medidata

CONTINUED FROM PAGE 18

May, 2019.) The pharma hoped to gain payer acceptance with an annuity-type payment model in which the drug would cost $425,000 annually over five years, and CEO Vas Narasimhan noted that chronic therapy with Spinraza would have approximately double the cost at about $4.1m over 10 years of therapy. Zolgensma brought in $160m in the third quarter of 2019, its first full quarter on the market – outpacing analyst expectations of about $100m. That's not much compared to Spinraza's $547m for the same time period – year-over-year growth of 17% – but Novartis signaled it expected continued growth in Q4. *(Also see "Novartis's Zolgensma Finds Commercial Legs In A First For Gene Therapy" - Scrip, 22 Oct, 2019.)*

"While the impact of Novartis' Zolgensma has been relatively muted, we think that the likely approval and launch of risdiplam could impact Biogen's Spinraza franchise," Seigerman said. He projects $2.21bn in global sales of Spinraza in 2020, declining to $1.79bn by 2022.

Published online 23 January 2020

Health Sector On High Alert As Wuhan Coronavirus Spreads

BRIAN YANG brian.yang@informa.com

January is usually a busy shopping month for people in China as they get ready for the week-long Spring Festival and lunar new year celebrations. In the central city of Wuhan, a set of symptoms quietly went around one of the crowded wet markets in the city of 11 million.

First, one patron at the Southern China Seafood Market fell ill. Then quickly others started coughing and developing flu-like symptoms and were sent to local hospitals for care.

Since the first reported case on 31 December, the virus - now identified as a novel coronavirus (2019-nCoV) - has since spread from central Wuhan to the megacities of Beijing, Shanghai and Shenzhen and other Chinese cities, and isolated cases have recently made their way to other Asian countries including Japan, South Korea and Thailand.

The cases are quickly piling up. Local Wuhan health authorities initially reported roughly 40 confirmed patients and no fatalities, but by 12 January, more than 100 cases and one death had been confirmed. As of 21 January, the figure had nearly tripled to 291 cases, as reported by the China National Health Commission, with three deaths. A separate report showed that as many as 14 medical workers had also been affected, and person-to-person transmission has now been confirmed.

On 20 January, the Chinese government officially designated 2019-nCov as a Category 2 infectious disease and started taking measures to prevent and control it as a Category 1 infectious condition, meaning that a mandatory quarantine may be required by the government.

The World Health Organization says that that China is sharing the genetic sequence of the new virus, which will be used by other countries to develop specific diagnostic kits.

The spread of the virus has once again put China in the forefront of a battle against a novel and deadly outbreak, following on from the SARS (severe acute respiratory syndrome) outbreak in 2002.

Antivirals were already becoming a hot area for local researchers and US returnees to set up bioventures to develop treatments for infections ranging from influenza to respiratory syncytial virus. *(Also see "Ark Bio Of China Bets On Untapped Pediatric Antiviral Market Where Few Have Succeeded" - Scrip, 20 May, 2019.)*

HARD TO TREAT

"Coronavirus is an RNA virus that has no therapeutic agent available. RNA viruses are very challenging to develop a drug against compared with DNA viruses [such as HIV, hepatitis B and some herpes viruses]," Jim Wu, CEO and founder of Shanghai-based antiviral developer Ark Biosciences Inc. told *Scrip*.

Fear is evident. First the timing - the end of January is the busiest travel season in China, when 300 million people are estimated to hit the road to join families in the Chinese New Year celebrations, the biggest festival of the whole year.

The worries are also particularly pronounced in a country where memories of the SARS outbreak are still vivid. In early 2003, the outbreak killed 800 people and thousands of cases were reported worldwide.

Compared to 17 years ago, China has also grown by leaps and bounds, from a economy worth less than $2tn to become the second largest in the world. But doubt persists over whether the country and its health sector can effectively control the outbreak.

So far, the responses from health companies to the emerging outbreak have largely focused on diagnosis and there is no treatment so far. Several companies including genome sequencing firm BGI Genomics Co. Ltd. have rushed to develop test kits for medical facilities to detect the viral infection.

As many companies introduce new products to the market, a launch strategy combined with strong execution have been important to a company's growth in a Chinese market increasingly embracing novel drugs instead of generics.

DIAGNOSTICS, TCM MAKERS SEE GAINS

Meanwhile, Chinese medical experts are suggesting that early detection, diagnosis and quarantine will be key. Zhong Nanshan, a physician from Guangzhou Hospital and well-known for his expertise in respiratory diseases, said the new Wuhan and Guangdong cases show increasing person-to-person transmission. The massive movement of travelers during the holiday period adds another layer of complexity and people should

take precautions and avoid large crowds, he added.

As many as 24 publicly traded health companies have seen their shares rise by up to 9% on expectations they may benefit from the outbreak. The pharma beneficiaries include makers of ingredients for antivirals and antibiotics such as Dongbei Pharma, Lukang Pharma, New China Pharma and Lianhuan Pharma.

Traditional Chinese medicines firms have also seen some large share gains of up to 10%. One of these, Xiangxue Pharma, manufactures oral liquids for flu and another, Yilin Pharma, markets such medicines for avian flu.

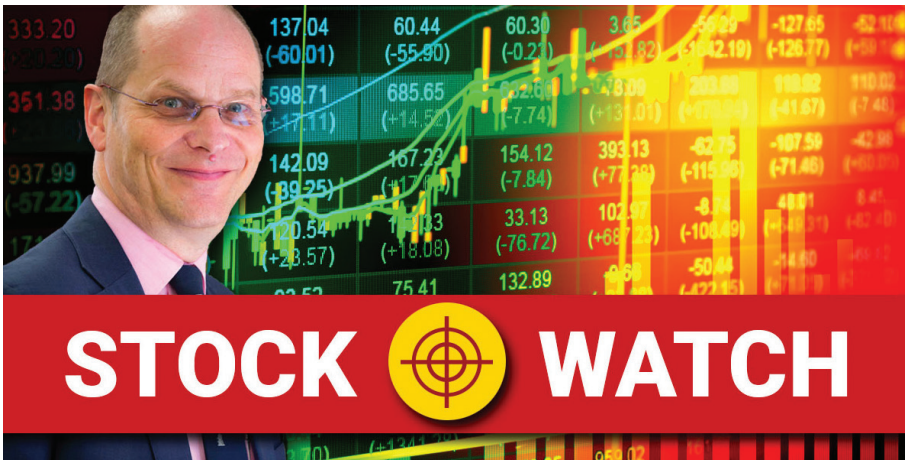
Among diagnostics companies, large players such as BGI and Chinese firm Dian Diagnostics are rushing to have their testing kits ready for hospital lab use, although none seem to have been granted formal approvals from the National Medical Products Administration.

Large companies aside, smaller players are also emerging to seize the opportunity. Shenxiang Bio for one announced a rapid diagnostic kit that can detect the 2019-nCoV virus in as little as 30 minutes.

Published online 22 January 2020

Stockwatch: Earnings Season Catches An Early Cold As Coronavirus Sweeps In

ANDY SMITH owner@ndysmith.com



It is traditional for the largest healthcare company in the world to be the first to report in earnings season. Often, and because of Johnson & Johnson's conglomerate status with its pharmaceutical, medical device and consumer divisions, J&J sets the early mood for life science earnings. For the fourth quarter and full year 2019, this mood initially looked chilly for J&J as it modestly missed analysts' consensus estimates of revenues.

Revenue rose by 2.8% to $20.7bn for the fourth quarter (and by 1% for the full year) and was driven by the 4.4% rise in fourth-quarter pharmaceutical sales. This pharmaceutical performance continues to put its consumer and medical device divisions into the shade even in the face of biosimilar and generic competition to its former blockbusters Remicade (infliximab) and Zytiga (abiraterone) respectively, and foreign currency headwinds. *(Also see "J&J's Gorsky Hails Strong Performance By Immunology Therapies Tremfya, Stelara" - Scrip, 22 Jan, 2020.)* J&J's annual earnings of $15.1bn – which were down 1% year-on-year but modestly beat analysts' estimates – could not lift the stock price, which finished down just over 1% on the day of the announcement and 0.3% for the shortened trading week. This was probably due to its lackluster 2020 guidance that included 4-5% revenue growth.

CORONAVIRUS R&D

While J&J was reporting on the tangible sales of its products, other companies that don't have product sales were jumping on the coronavirus bandwagon. As fears rose for a global respiratory viral epidemic driven by the 2019-nCoV virus that started in Wuhan China and looked likely to depress the Chinese economy further, companies like Inovio Pharmaceuticals Inc., Moderna Inc. and Novavax Inc. among others were making the best of a bad situation.

Inovio announced that it had won a grant of up to $9m from a non-profit organization to develop a vaccine against the 2019-nCoV virus and its stock price responded with a nearly 20% jump on the week (against the NASDAQ Biotech Index's 3.5% decline). Nearly two decades ago, Inovio was a DNA electroporation company targeting head and neck cancer. After that platform failed to generate a commercially viable product, it morphed into a DNA vaccine company. In nearly 20 years of failing to bring a product to the market, what is the likelihood that Inovio can generate a commercially viable DNA vaccine for 2019-nCoV in a few months?

As a fund manager through the tragic events of 11 September 2001, my fund's performance was cushioned to some extent by its holdings in Human Genome Sciences Inc. and Acambis PLC. Although not as quick off the mark as Inovio, Human Genome Sciences announced both the development of its post-exposure anti-anthrax toxin monoclonal antibody ABthrax (raxibacumab) and its FDA fast track designation in 2003. This was followed in 2005 by the US government purchasing tens of thousands of doses of the investigational treatment to stockpile as part of Project BioShield. But it was not until after its acquisition by GlaxoSmithKline PLC, and following a complete response letter in 2009, that ABthrax was finally approved by the FDA in 2012. Monoclonal antibodies in 2003, like DNA vaccines today, were seen as a quicker way to bring products to

TURN TO PAGE 23

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

PIPELINE WATCH, 17–23 JANUARY 2020

Event Type	Lead Company	Drug Name	Indication	Comments	Change To LOA (%)	LOA (%)
Phase III Published Results	Horizon Therapeutics PLC	Tepezza (teprotumumab)	Thyroid Eye Disease	OPTIC, NEJM, 23 Jan 2020	-	-
Phase III Published Results	AbbVie/Neurocrine	Orlissa (elagolix)	Uterine Fibroids	ELARIS UF-I,II; NEJM, 23 Jan 2020	-	-
Phase II/III Updated Results	Roche/PTC Therapeutics	risdiplam	Spinal Muscular Atrophy, Type 1	FIREFISH Part 2; Met Primary Endpoint	-	-
Phase III Top-Line Results	Hutchison China MediTech	surufatinib	Pancreatic Neuroendocrine Cancer	SANET-p; Achieved Primary Endpoint	0	10
Phase III Top-Line Results	BeiGene, Ltd.	tislelizumab	Non-Small Cell Lung Cancer, First-Line	w/paclitaxel + carboplatin; Met Primary PFS Endpoint	0	35
Phase III Clinical Hold	PledPharma AB	PledOx (calmangafodipir)	Chemotherapy Induced Peripheral Neuropathy	POLAR-M; Recruitment, Dosing Halted	0	53
Phase III Trial Initiation	Aldeyra Therapeutics, Inc.	reproxalap	Allergic Conjunctivitis	INVIGORATE; A RASP Inhibitor	0	58
Phase III Trial Announcement	UCB SA	rozanolixizumab	Immune Thrombocytopenic Purpura	myOpportunITy1,2; In Adults	0	20

Source: Biomedtracker | Informa, 2020

CONTINUED FROM PAGE 21

market, although at the time, monoclonal antibodies had significantly more clinical validation than DNA vaccines have to date. It therefore seems unlikely that Inovio will break its product development duck any time soon.

Moderna announced a similar collaboration to Inovio's but with an NIH facility with unspecified financial terms to develop an mRNA vaccine against 2019-nCov. Moderna was founded in 2010 and after a decade of work recently announced Phase I results from its mRNA vaccine against the herpesvirus cytomegalovirus (CMV) – a double-stranded DNA virus. *(Also see "Moderna Edges Closer To Becoming A Mid-Stage Drug Development Company" - Scrip, 12 Sep, 2019.)* Moderna's stock price rocketed up on this announcement and finished the week up by around 1%. Apart from the technical difficulties of applying its early development of a CMV mRNA vaccine to a rapidly mutating single-stranded RNA virus, the bullishness of Moderna's announcement was probably misplaced. After the events of 11 September 2001, Acambis already had a smallpox vaccine in late-stage development with a stockpile supply agreement that included the potential for investigational use. But the product – ACAM2000 – did not gain FDA approval until 2007, a year before Acambis's acquisition by Sanofi.

MEETING THE MARKET NEED

The last commercial evaluation I did before I left a pharmaceutical company for investment management was on a systemically administered interleukin-2 receptor agonist (IL2-RA) for viral respiratory infections. The product was easily a bust when I compared the available clinical data to our OTC orally administered paracetamol/acetaminophen products whose time to symptom resolution was virtually the same as the IL2-RA. Sometimes nuts don't need sledgehammers. How, therefore, are these bandwagon-jumping announcements on novel therapies from last week likely to be viewed in a few years? Well, one of the characteristics of a market bubble is that low quality stocks outperform high quality stocks.

For anthrax and smallpox, the individual and public health outcomes of an infection are dire and the unmet need obvious. For 2019-nCov, the mortality seems to be lower than recent non-Ebola viral outbreaks and irrespective of the time and difficulty to produce a stockpile of even an investigational-use product, the need for either a new DNA or mRNA vaccine seems debatable. For a viral respiratory disease normally resulting in the common cold with low mortality, the need may instead be for medicines that are widely available now, with almost no side effects and proven activity in treating viral respiratory infections. Step forward J&J's McNeil Consumer Healthcare division, which – like other consumer healthcare companies – produces drugs that are cheap and effective at lowering temperatures, decongesting and reducing the time to recovery. Unlike full-year 2019, perhaps J&J's first-quarter 2020 results will be buoyed by the demand for such treatments.

Andy Smith gives an analyst and former investor's view on life science companies. He joined the research house Equity Development in October 2019 having previously been an analyst at Edison group and a Senior Principal in ICON PLC's Commercialization, Pricing and Market Access consulting practice. Andy has been the lead fund manager for four life science–specific funds, including 3i Bioscience, International Biotechnology and the AXA Framlington Biotech Fund, was awarded the techMark Technology Fund Manager of the year for 2007 and was a global product manager at SmithKline Beecham Pharmaceuticals.

Published online 28 January 2020

APPOINTMENTS

Executive	To Company	New Role	From Company	Previous Role	Effective Date
Ivor Macleod	Athersys Inc	Chief Financial Officer	Eisai Inc	Chief Financial Officer and Chief Compliance Officer	31-Jan-20
Nicola Heffron	bluebird bio	Senior Vice President, Europe	Celgene	Head, Global Marketing, Myeloid Portfolio	16-Jan-20
Scott Holmes	Disarm Therapeutics	Chief Financial Officer	Kiadis Pharma	Chief Financial Officer	13-Jan-20
Onaiza Cadoret-Manier	Ionis Pharmaceuticals Inc	Chief Corporate Development and Commercial Officer	Grail Biosciences	Chief Commercial Officer	9-Jan-20
Jennifer Chien	Krystal Biotech Inc	Chief Commercial Officer	Sanofi Genzyme	Vice President and Head, Genetic Diseases, US Rare Disease	20-Jan-20

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

Source: Medtrack | Informa, 2020

DAMAGED?

Emirates SkyCargo

Never with us.

Concerned about the safety and integrity of your pharmaceutical cargo? Don't be. Emirates Pharma have you covered. We understand the importance of life-changing medicines, which is why we've developed an advanced transportation system specifically for temperature-sensitive pharmaceuticals. With state-of-the-art transit processes, cool chain facilities, quick transfers and a network of over 155 destinations across 6 continents, why would you risk shipping your precious cargo with anyone else?

Emirates Pharma

FLY BETTER

skycargo.com/emiratespharma