GSK’s New CEO Designate Walmsley Fortifies Volume Growth Strategy

SUKAINA VIRJI sukaina.virji@informa.com

Emma Walmsley will succeed Andrew Witty as GSK CEO when he retires on March 31st 2017. Prior to her current role as CEO of GSK’s Consumer Healthcare division, she was president of GSK Consumer Healthcare and has been a member of GSK’s corporate executive team since 2011.

Emma Walmsley will succeed Andrew Witty as GSK CEO when he retires on March 31st 2017. Prior to her current role as CEO of GSK’s Consumer Healthcare division, she was president of GSK Consumer Healthcare and has been a member of GSK’s corporate executive team since 2011.

Walmsley joined GSK in 2010 from L’Oréal where, over the course of her 17-year career, she held a variety of marketing and general management roles in the UK, Europe and USA. From 2007 she was based in Shanghai as general manager, consumer products, for L’Oréal China.

GSK says Walmsley’s remuneration package will be announced at the start of 2017.

Citi analysts claim the move was “no surprise” but acknowledge that many investors had been hoping for an external candidate, likely why the company’s share price dipped in the immediate aftermath of the announcement. However, the lost ground was reclaimed by the end of the day.

“If Ms. Walmsley is willing to critically assess GSK’s R&D productivity and make the necessary changes, the outlook for investors remains favorable in our view,” according to the analysts from Citi.

In her current role, Walmsley has overseen the creation of the consumer joint venture with Novartis and ongoing margin improvement in the consumer business. “Andrew Witty has been a strong supporter of Ms. Walmsley,” note Citi. “A lack of an R&D background or a post graduate science background does not preclude Ms. Walmsley’s ability to materially improve R&D returns so long as she has the appetite/intent to critically assess GSK’s R&D outcomes and add senior external pharmaceutical and R&D hires.”

Citi analysts “continue to doubt” that GSK’s board has any near-term appetite to spin off the consumer business until the company derives more value from ongoing improvements in its pharmaceutical division. “Given our views on Novartis’s appetite to bolster their pharmaceutical business, we anticipate that GSK is likely to acquire the outstanding 36.5% Novartis stage for around £7bn potentially prior to the official exercise data of Novartis’s put option,” they add.

‘INSIDE-OUTSIDER’

“This is an inside-outsider appointment,” Brian McGee, a pharma sector strategy specialist at consultancy Novasecta, tells Scrip. “It’s a very clear commitment by GSK’s board to the volume-first growth strategy launched by GSK in 2015.” That plan was borne out of a belief that the current sky-high pricing model in pharmaceuticals is...
The appointment of Emma Walmsley, head of GlaxoSmithKline PLC’s consumer division, as company CEO will raise eyebrows.

Sir Andrew Witty decided to retire in 2017 after much shareholder lobbying for a new head and for the break-up of the company. Witty has embraced a strategy of maintaining diversified businesses under one umbrella while peers have doubled down on core areas. And while others focused on innovation in areas supporting high prices, most notably immuno-oncology, GSK privileged lower-margin areas like consumer health, vaccines and emerging markets – or volume over price.

The company may have bowed to pressure from vocal investors to seek a new CEO, but it is notable that it didn’t bow to their preference for a “fresh pair of eyes” from outside the group. The big uncertainty now is what Walmsley’s strong grounding in consumer products signals for GSK’s already rather lackluster pharmaceuticals business. Her lack of pharma credentials could leave those who didn’t like the current CEO’s approach worrying whether Walmsley will prove to be “like Witty but worse” for GSK as a pharma company.
Duchenne Surprise: Sarepta Prices Exondys 51 Below Expectations

It sparked at least one analyst to question how Sarepta came up with a price for FDA’s first approved Duchenne muscular dystrophy treatment.

DERRICK GINGERY derrick.gingery@informa.com

Sarepta Therapeutics Inc. may have given payers a break when it priced its newly approved Duchenne muscular dystrophy treatment Exondys 51 (eteplirsen).

The announced $300,000 annual price was not as high as some had estimated and prompted Sarepta’s interim CEO and chief medical officer Edward Kaye to explain the company’s reasoning behind it.

FDA announced Sept. 19 that it had granted accelerated approval for Exondys 51 for treatment of Duchenne in patients amenable to exon 51 skipping, which is about 13% of the Duchenne population. The product is available through a once-weekly intravenous infusion of 30mg/kg.

Sarepta also received a rare pediatric disease priority review voucher, which could allow a priority review for any future application it chooses or be sold to another sponsor.

Center for Drug Evaluation and Research Director Janet Woodcock decided to overrule the review division’s recommendation to deny approval. It prompted an extraordinary appeal process that reached FDA Commissioner Robert Califf, who sided with Woodcock.

Some of Woodcock’s reasoning for her decision also raised concerns among others at FDA.

The commercial launch of Exondys 51 will begin immediately, Sarepta said in a statement.

Sarepta said the quoted price takes into account weight-based dosing over time, as well as compliance rates and mandatory government discounts.

The number seemed to surprise one analyst from Leerink Partners, who during a conference call on the approval asked about the assumptions used to determine the price, including whether the company considered a similar price for future indications. He said other analysts had expected a higher figure.

Kaye responded that the price was reasonable and took into account research and development spending, as well as post-marketing requirements and production costs.

“What we’re trying to do is be as thoughtful as possible,” he said. “Given the sensitivity to pricing, we’ve tried to be very what we think is reasonable given all of the costs for this and even the innovation that goes into manufacturing. The focus is really to try to make sure that all the patients can gain access to it.”

The price may still be expensive, but couching it as lower than expected may not draw much criticism or scrutiny, although orphan products usually do not warrant intense pricing complaints.

Because orphan treatments are difficult to develop and target small populations, there seems to be an understanding that they will be expensive, especially when they are the first for a debilitating disease.

Advocates also want to balance affordability with encouraging drug development in the sector.

POST-MARKETING TRIALS REQUIRED

Some of the revenue from sales likely will help pay for the Exondys 51 confirmatory study, which will determine whether the evidence used to grant accelerated approval leads to a clinical benefit. If not, FDA could pull the drug from the market.

FDA directed Sarepta to conduct a two-year randomized, double-blind, controlled trial in Duchenne patients amenable to exon 51 skipping that compares the approved 30mg/kg per week dose to one “that provides significantly higher exposure,” such as the same dose daily, according to the approval letter.

Trial completion is expected in November 2020 and a final report in May 2021, according to FDA’s approval letter.

Protocols have yet to be discussed with FDA, including the comparison dose for the confirmatory study, and won’t be finalized by 2017, Kaye said during the conference call.

Another trial studying patients with exons 45 or 53 looking at two “well-separated doses” also is part of the post-marketing commitments.

The accelerated approval is expected to open doors for eventual expansion of the indication, such as the other exon groups.

Kaye said in Sarepta’s statement that the company “will continue to leverage what we have learned from Exondys 51 to facilitate future development of potential new treatments targeting additional exons with the goal of one day treating all DMD patients amenable to exon skipping.”

After FDA made its concerns about the drug’s efficacy known, the Peripheral and Central Nervous Systems Drugs Advisory Committee voted against recommending that the evidence was sufficient for an accelerated or full approval.

Then, FDA asked for more data and missed its review goal.

VOUCHER TO BE SOLD SOON

The priority review voucher is another benefit of the approval, and could generate a significant cash infusion that Sarepta could use for additional research or other expenses, should it be sold.

Sarepta said during the conference call that it intends to sell it and already has reached out to several potential buyers.

Leerink analysts said in a note they expect $350m capital inflow from sale of the voucher.

Vouchers have been commanding hundreds of millions recently, but their price may have peaked.

Most recently, Gilead Sciences Inc. paid less than $338m for a voucher, a drop from the $350m AbbVie Inc. paid in 2015.

It is likely that the increased number of available vouchers is driving their price down. The pediatric rare disease voucher program has been very popular with sponsors.

The program will expire on Oct. 1 if Congress does not renew it. Orphan drug advocates are pushing for an extension, but FDA does not want the program to continue.

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More than 13 global pharma companies, including GlaxoSmithKline, Pfizer and Merck & Co., have agreed a “Roadmap” aimed at relieving the growing antimicrobial resistance crisis worldwide – as well as principles to explore alternative business models and incentives for antibiotic R&D and reimbursement.

This month the UN General Assembly confirmed, in the form of a High-Level Declaration, national, regional and international political commitment to solving the global concern of antibiotic resistance. Following suit, 13 global pharma companies, including GlaxoSmithKline PLC, Pfizer Inc., Merck & Co. Inc. and Sanofi, have agreed a Roadmap for actions they will take to help alleviate the issue.

One key concern for most pharma companies highlighted in the agreement is how to establish new business models that allow companies to see adequate return on their investment. The companies will work with government partners and payers to explore the introduction of “market entry rewards” and other incentives for new antibiotic products. The 13 companies said they are “willing to explore all options to achieve this and believe that receipt of an adequate Market Entry Reward will greatly facilitate global access and stewardship for that product.”

The firms also noted that open partnerships with public researchers would be considered to help speed up discovery and development of new antibiotics, vaccines and diagnostics. However, the companies want to explore “progress incentives, such as lump-sum payments, insurance models and novel IP mechanisms that reflect the societal value of new antibiotics and vaccines and will attract further investment in R&D.”

**WHAT INCENTIVES ARE NEEDED?**

Pfizer, one of the signatory companies, said in its soon to be published policy position on AMR that the speed and the scope of antibiotic R&D could be incentivized through a mix of economic “push and pull” incentives, as well as regulatory reforms.

It wants “push incentives” to focus on removing barriers to the developer by decreasing the costs for investments in R&D. “These incentives tend to impact the earlier stages of the development process, and include R&D tax credits and grants,” Pfizer said. While “pull incentives” would focus on the commitment of financial reward after a technology has been developed. Pfizer wants to see these include intellectual property extensions, advanced marketing commitments, monetary prizes, and market entry rewards.

Pfizer highlighted the US Generating Antibiotic Incentives Now (GAIN) Act as a successful attempt to provide incentives to drug developers in this field. Under GAIN, which offers an extra five years of IP exclusivity to recognized antibiotics, 58 antibacterial drug candidates – representing 13 different antibacterial drug classes including nine new compounds not currently used in humans – have been granted QIDP (qualified infectious disease products) status and are currently in development, with six new antibacterials approved as of January 2016. The big pharma wants to see a similar Act introduced in Europe for extra exclusivity periods for new antibiotic products.

Furthermore, Pfizer wants to see tax credits for antibiotic R&D introduced in the US. “Tax credits have appeal as they can help to significantly decrease the financial burden of R&D. They have been successfully used as part of the Orphan Drug Act, so are already proven incentives,” the company said.

Merck & Co. told **Scrip** it doesn’t believe there is a “one size fits all” solution to incentivizing antibiotic innovation. “Depending on the local context, health systems, priorities and challenges, different models can be applied to stimulate innovation and promote appropriate use. Market-based models, which build on existing systems and systems, can be fine-tuned to incentivize and reinforce antibiotic stewardship and appropriate use,” a spokesperson for Merck said.

**‘ONGOING INVESTMENT IS A CHALLENGE’**

Despite being fairly active in antibiotic development for more than 70 years, Merck said ongoing investment in this research space is challenged because “antibiotics are not valued in accordance with the benefits they bring to society.”

The company is also concerned that near-term solutions are still needed to address the reimbursement challenges of recently developed antibiotics while novel incentive mechanisms are being explored. Merck wants to see “mechanisms for antibiotics that reduce the proportion of manufacturer revenue derived from sales volume.” But to be impactful, these models must provide a return on investment that is “competitive with other therapeutic areas in order to incent the investment of limited R&D resources,” the US firm said.

GSK added that it is keen to “pilot new models with our antibiotics.” The UK pharma giant also wants to see a de-linked business model tested for antibiotic development.

GSK highlighted that its new system for sales reps could be part of the solution, too: “We have changed how we incentivize our sales representatives globally, so they no longer have individual sales targets for any medicines, including antibiotics. Our new approach helps further ensure the focus is upon appropriate prescribing.”

Beyond the economic challenges highlighted, Merck also wants to see the harmonization of clinical trial guidance across international regulatory agencies to expedite registration. “We support legislation and regulation to enable regulatory authorities to streamline, accelerate and defray the cost of clinical trials required for regulatory review and approval of antibiotics, and for new indications for existing antibiotics to address serious infections.”

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HEART FAILURE: A Growing Market

Heart failure is currently one of the most common reasons for hospitalization amongst people over 65 years of age. Causes of heart failure include atrial fibrillation, an erratic rhythm of the heart, and high blood pressure.

$14.3bn
The cost of heart failure to Americans in 2015

$30bn
The cost of heart failure to Americans by 2030

18.6m
Cases of chronic heart failure in the US, Japan, and five major EU markets in 2014

24.8m
Cases of chronic heart failure that will occur by the year 2034

23
Ongoing Phase III industry-sponsored clinical trials for Congestive Heart Failure

$776m
2015 Congestive Heart Failure (CHF) market prior to Entresto

$9.5bn
Projected CHF market with Entresto by 2024

10
Months it took Amgen and Cytokinetics to design the Phase III trial for candidate omecamtiv mecarbil after consulting payers and clinicians

One in five Americans will develop heart failure in their lifetime

Sources: American Heart Association, Datamonitor Healthcare, Citeline’s Trialtrove, Scrip
UnitedHealthcare’s decision to exclude Lantus in favor of Basaglar begs the question of how low biosimilar pricing will go, amid soaring diabetes costs.

UnitedHealthcare said that the ability to secure “very competitive pricing” led to giving Eli Lilly & Co’s Basaglar copycat insulin preferred status on its commercial formulary, while cutting Sanofi’s Lantus out and downgrading Novo Nordisk’s Levemir.

UnitedHealthcare’s commercial formulary for 2017 gives Lilly/Boehringer Ingelheim GBMH’s long-acting insulin Basaglar, an unofficial biosimilar of Lantus (insulin glargine) tier 1 preferred status on its formulary.

Lantus will no longer be covered — it had been on tier 3 — and Novo Nordisk’s Levemir (insulin detemir) will move from tier 1 to tier 2 coverage, the company said in an advisory to brokers about the changes. Explaining the change, United Healthcare noted that some $245bn is spent every year in the US on diabetes.

Lantus will also be replaced by Basaglar on the company’s Medicaid formulary. The change, however, does not apply to Medicare plans.

Following approval in December 2015, Basaglar is expected to launch at the end of this year.

United Healthcare’s changes take effect April 1, 2017, in order to give members enough time to adapt to the changes. In a webcast, company explained that it had been able to secure “very competitive pricing” for the biosimilar.

The company is the second major payer following approval in December 2015 and Novo Nordisk’s Levemir (insulin glargine) in September of that year.

UnitedHealthcare noted that Sanofi’s Lantus enjoyed a market-leading position after its US launch in 2000. Levemir launched later and had a difficult time “overcoming the market powerhouse that Lantus had become,” the firm pointed out.

“Given very little competition, Sanofi, the maker of Lantus, was able to raise their price unchecked and soon what was once a very high value medication was now showing up as a driver of pharmacy trend and overall spend,” UnitedHealthcare said.

The firm recalled how it had worked with Novo Nordisk on a deal to give Levemir preferred tier 1 status and a lower copay, a “move that was an overall winner,” in that it led to better access and lower cost.

Levermir will now have a slightly higher copay on tier 2, reflecting UnitedHealthcare’s intent to balance member access and cost savings.

The company said that it contemplated even more aggressive strategies, given the large price differential between Levermir, Lantus and Basaglar.

UnitedHealthcare also noted that it is not covering either Toujeo or Tresiba, having concluded that “unfortunately, neither one was clinically differentiated enough or at a competitive enough price to justify benefit coverage.”

TAKING THE TOLL ON LANTUS
Biosimilars have been expected to shake up the industry, with impact in direct relation to the level of discounting. Analysts had expected that Basaglar would be priced at a 15% to 20% discount, and that biosimilars later to launch would be offered at more substantial discounts, with rising competition.

The deal with UnitedHealthcare suggests that the discount was larger than 20% and “definitely more aggressive” than expected, Bernstein Research’s Ronny Gal commented to Scrip.

For Lantus, the decision means lower sales than analysts expected. Lantus had sales of $6.39bn ($7.13bn) in 2015, down 10.8% from the prior year.

Leerink Swann analyst Seamus Fernandez said in a Sept. 22 note that he expects Lantus will lose reimbursement for about 18% to 19% of the 180m US commercial covered lives in 2017, between United Healthcare and CVS Health’s decisions.

Leerink Swann had already been estimating a 15% drop in US sales for 2016 over 2015, followed by a 25% sales decline in 2017 and 2018. “While this is incrementally negative for SNY’s overall diabetes franchise, we believe the impact is already largely reflected in the stock, but likely not yet in Lantus consensus sales for 2017,” the analyst said. “The more aggressive changes in the formularies to replace Lantus with Basaglar, while negative in the short term, should remove the biggest overhang on the stock,” he added.

Morningstar analyst Damien Conover commented to Scrip that he had expected heavy competition for formulary status, but that the “bigger unknown at this point is how many employers will utilize the restrictive formularies.”

Morningstar is expecting Lantus sales to be down by 20% in the US and 35% overall in 2017.

Novo Nordisk’s Levemir could get a boost from negative decisions on Lantus, Jefferies analyst Jeffrey Holford said in a Sept. 22 note.

Whereas Basaglar will be available only in a pen device, he noted, Levemir is available as both a pen device and in vials, and therefore could gain market share from Lantus users who wish to remain on vials — about one-third of patients.
unsustainable in the long run, he explains. “But appointing Emma is also an acknowledge-ment that they need a fresh leader to drive that change. It’s kind of business as usual, but that business will be delivered very differently moving forward.”

McGee also believes GSK will undergo a cultural transformation in certain areas. “The level of accountability in those areas where she is currently not involved will change. I suspect that we’ll see a lot of measurement and leadership by KPIs. (GSK will be) a more ruthlessly focused commercial organization, probably with stronger marketing investment.”

‘The level of accountability in those areas where she is currently not involved will change’

McGee notes the parallels between Walmsley’s career and that of Novartis CEO Joe Jimenez. “He was an executive at Heinz and joined Novartis to run its con-sumers business and ended up as CEO of the whole company. So there is something about consumer marketeers bringing value to pharma companies.”

A source close to the company, who asked to remain anonymous, told Scrip that Walms-ley’s management style was “very focused and direct; she skips straight to the point.”

OTHER CANDIDATES
Other internal prospects for the top job were Abbas Hussain and Simon Dingemans. Hussain is president of global phar-maceuticals and Dingemans is CFO.

GSK won’t want a repeat of the 2007/2008 fiasco, when the two of the three unsuccessful internal candidates for the CEO role that eventually went to Witty – David Stout and Christopher Viehbacher – left within months of him being appointed.

GSK’s vaccines chief and former head of R&D Moncef Slaoui took himself out of the running for the top job in June when he announced he would be retiring from the company after Witty’s departure.)

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**GLAGOV Imaging Study Of Amgen’s Repatha Bodes Well For PCSK9 Class**

Positive results in GLAGOV lift PCSK9 inhibitor Repatha, but most likely are still not enough to get rid of reimbursement restrictions for the class, analysts say.

**EMILY HAYES** emily.hayes@informa.com

Amgen Inc’s PCSK9 inhibitor Repatha (evolocumab) demonstrated ability to reduce plaque build-up in the GLAGOV imaging study, which could pave the way for an additional indication, but it’s unclear whether this latest success will help the cholesterol drug where it needs it most – with payers.

Repatha and Sanofi/Regeneron Pharmace-uicals Inc’s competing Praluent (alirocumab) have struggled to break into the market as payers have restricted access; Repatha had sales of only $27m and Praluent $24m in the second quarter.

Payers and practitioners have signaled that they want to see data from cardiovascular outcomes trials for the PCSK9 class. Amgen’s FOURIER study of Repatha is expected to report in the first quarter of 2017, and data from Sanofi/Regeneron’s ODYSSEY Outcomes trial could come later this year. But the positive top-line results from GLAGO-V, released Sept. 20, are encouraging for a positive result in FOURIER. Full data will be presented at the American Heart Association annual meeting in November.

The GLAGOV study used intravascular ultrasound to assess effects on atheroscle-rotic plaque build-up in the coronary arter-ies of 968 patients on statins and undergo-ing coronary catheterization. The drug met the primary endpoint related to change in percent atheroma volume (PAV) after 78 weeks and had similar safety data as placebo, Amgen announced.

The positive results from GLAGOV “help bolster confidence that CV outcomes studies will be positive,” commented Biomed-track analyst Peter Chang. The study assumed a change in PAV of 0.706, based on expectations for LDL reduction associated with PCSK9 inhibitors, and participants in the study had baseline LDL of 92.6 mg/dl. It will be interesting to see the details from the study to understand whether the treatment effect was smaller or larger than expected, Chang said.
Shire Looks To Build Around Xiidra, Sanofi Faces Toujeo Challenge, Amgen Downplays Romosozumab Data

Shire, Sanofi and Amgen were among the companies presenting at the Bank of America Merrill Lynch Global Healthcare Conference Sept. 14-16 in London. Here are some key takeaways from those presentations.

JOSEPH HAAS joseph.haas@informa.com

Shire PLC talked about the rapid progress of integrating Baxalta Inc., including an increased projection of cost savings, and how it wants to build an ophthalmology franchise around recently approved Xiidra at the Bank of America Merrill Lynch Global Healthcare Conference 2016, Sept. 14-16 in London. Meanwhile, Sanofi discussed the challenges of Toujeo formulary placement in the US and what it’s looking for in M&A after missing out on Medivation Inc., while Amgen Inc. highlighted its expectations for osteoporosis candidate romosozumab.

PROGRESSING THROUGH BAXALTA INTEGRATION, SHIRE HOPES TO BUILD IN OPHTHALMOLOGY

These are heady times for Shire with the late June closing of its Baxalta acquisition, followed by the approval in July of Xiidra (lifitegrast) for dry eye syndrome, the first of what the Irish specialty firm hopes will be several approvals in the eye care space. As the integration of Baxalta progresses quickly, Shire chief financial officer Jeff Poulton said Sept. 16 that as the company gets its debt ratio in order, it will look to bring in additional assets to build out an ophthalmology franchise.

Shire has prioritized rare diseases in its deal-making in recent years, while also looking for companies that could offer both marketed products and pipeline assets, the CFO said. A deal offering all three of those characteristics has become sort of a sweet spot for Shire in business development, he added.

“I think that would be the starting place … that we use to look at deals,” Poulton said. “Now, I understand rare diseases … cut across a lot of therapeutic areas, but I would say any of the therapeutic areas that we’re in today would be places that we would be interested in potentially adding products and opportunities. Perhaps one that may get a bit more attention for a while is the ophthalmology franchise.”

FDA on July 11 approved Xiidra with a broad label for the dry eye indication, positioning the drug well to compete with Allergan PLC’s established but minimally effective Restasis (cyclosporine ophthalmic emulsion). It becomes Shire’s first approved ophthalmology drug, but the pipeline also includes other candidates that marry eye care with the company’s broader rare disease emphasis.

This includes the Phase II candidates SHP640 for viral/bacterial conjunctivitis and SHP607 for retinopathy of prematurity, as well as preclinical candidates for autosomal dominant retinitis pigmentosa (SHP630) and glaucoma (SHP639).

“Our intent is not to be a ‘one-trick pony’ in ophthalmology, but we really want to establish a sustainable leadership position,” Poulton said. “We think Xiidra is a great start in terms of a beachhead, but we want to do more. … I think that there will be opportunities for additional innovation and opportunities to bring in some additional programs there and again I think that will be a focus as we move ahead.”

“In terms of size, I don’t think we prioritize deals by size in terms of how we look at things,” he continued. “We really prioritize other things in terms of traditional valuation metrics … so size is not a sort of driving criteria. I think if you look historically at what Shire’s done, we’ve done a number of bolt-on deals certainly over the last two or three years; ViroPharma Inc., NPS Pharmaceuticals Inc. and Dyax Corp. But we’ve also done a number of pipeline deals where we brought in [assets in] Phase II in development and that seems to be a nice kind of sweet spot for Shire in terms of progression of the pipeline.”

First, however, Shire needs to reduce its debt to about two-to-three times its annual net earnings, the exec said, a benchmark it expects to reach toward the end of 2017. Perhaps helping that effort along is that Shire recently raised the estimate for cost savings expected from the Baxalta transaction by about 40%, to $700m total by the third year of integration, Poulton noted. The company also recently decided to continue Baxalta’s pipeline efforts in oncology because such assets could make a nice fit with Shire’s rare diseases portfolio.

“I would talk about this really as sort of an option for the future,” Poulton said. “There are 7,000 rare diseases that we know of today, and 50% are in specialty oncology conditions. So, our view is that long-term this may be a place that we want to be as a leader in rare...
diseases. … Over the next couple of years as we pay down debt and improve our balance sheet, this is a place that we could consider for future investment.”

**DESPITE FORMULARY ISSUES, TOUJEEO HELPING SANOFI OFFSET LANTUS DOWNTURN**

Toujeo, Sanofi’s recently launched long-acting insulin glargine product, faces some formulary challenges in the US as CVS Health Corp. decided not to list it or Sanofi’s diabetes predecessor Lantus on its preferred formulary, but the drug is one of several new launches helping the French pharma endure some multi-year headwinds causing Lantus revenues to fall, CEO Olivier Brandicourt told the conference Sept. 16.

The exec said Toujeo now accounts for about 6.4% of the insulin glargine market share in the US. It, along with the dengue fever vaccine Dengvaxia, the PCSK9 inhibitor Praluent (alirocumab) and the multiple sclerosis drugs Aubagio (teriflunomide) and Lemtrada (alemtuzumab), is more than offsetting the impact of pricing pressure and external competition faced by Lantus, which went off-patent in the US in 2015.

Toujeo now accounts for 6.4% of the insulin glargine market share in the US and along with other products is more than offsetting the impact of pricing pressure and external competition faced by Lantus

Overall, Sanofi sales are growing 2.5% year-over-year, Brandicourt said, despite Lantus’ issues and extreme pricing pressure in Venezuela. The pharma’s overall diabetes franchise revenue was down 3.8% – about what was expected – during the first half of 2016, and the CEO reiterated guidance that the franchise would post between 4% and 8% revenue decline from 2015 to 2018.

Brandicourt said CVS’ decision in August to exclude Sanofi’s two long-lasting insulin glargine products from formulary in 2017 would end access to about 15m covered lives in the US. CVS covers about 34m patients with not quite half of that number covered under its national formulary, he said.

“Nineteen million are part of the custom plans which decide whether or not to follow pieces of the national formularies or not,” Brandicourt explained. “There, you can have some leverage. If you have a good account management team there, you can negotiate plan by plan … usually regional and not national, some deal with where Lantus would stay on their formulary. So that piece of 19 million people we may have access to. The future will tell us whether or not we’ve been successful there.”

Though sales have been disappointing, the exec said anti-cholesterol Praluent is faring well despite facing formulary and other access challenges in the US. It has captured roughly 50% of the US PCSK9 market, basically level with Amgen’s Repatha (evolocumab). A less stringent application of utilization management by payers and data from the ODYSSEY cardiovascular outcomes study could both help Praluent’s cause, Brandicourt said.

As to when that outcomes data could come: “We expect the second interim data analysis for overwhelming efficacy to take place during the last quarter of this year, and if the study is indeed positive, you can expect us to move very quickly in sharing the data with payers, regulators and, of course, investors,” he said.

Meanwhile, Sanofi’s public comment on losing acquisition target Medivation to a higher bid by Pfizer Inc. remains unchanged – the price paid was too high and Sanofi was not going to budge off the parameters it had set for a deal, Brandicourt maintained. Going forward, the pharma’s business development strategy will focus on three therapeutic areas – cancer, immunology and MS, he said.

**AMGEN BULLISH ON ROMOSOZUMAB DESPITE NON-VERTEBRAL FRACTURE DISAPPOINTMENT**

The appearance by Amgen execs at BoA Merrill Lynch came just days before the big biotech was to present data from the Phase III FRAME study of its osteoporosis candidate romosozumab, partnered with UCB Group, and the company tried to get out ahead of disappointment with the miss in the endpoint for reducing non-vertebral fractures.

Chief financial officer David Meline called the drug’s market potential still “very significant.” “We already have a very strong presence in bone with Prolia (denosumab), which continues to grow very nicely,” he told the audience. “We see Prolia has been growing at a 30% annual clip. And if you look at the second quarter, the volume grew 23%. So, we see this as being complementary and synergistic to Prolia.”

At the American Society for Bone and Mineral Research meeting Sept. 18, Amgen presented data from FRAME that added to the prior top-line data that were outlined showing the antibody did not meet statistical significance for reduction of non-vertebral fractures, such as hip fractures. However, the drug has met a co-primary endpoint for reduction in new vertebral fractures, as well as a secondary end-point of reduction in clinical fractures.

Arvind Sood, Amgen’s vice president of investor relations, said that secondary endpoint is one that physicians will be greatly interested in learning more about. “These are symptomatic fractures that physicians in particular are very concerned about,” he said. “Clinical fractures is a composite endpoint of both vertebral and non-vertebral fractures and we did demonstrate an improvement, which was statistically significant.”

Sood added that Amgen believes it can position romosozumab as a once-monthly subcutaneous injection that can be utilized as add-on or subsequent to Prolia therapy, with a superior safety profile to Eli Lilly & Co’s blockbuster Forteo (teriparatide), a daily injectable that has a black box warning for osteosarcoma. “Given the very clean side-effect profile that we’ve seen so far for romosozumab, our view is that we can build a very effective value proposition around this product,” he said.

In a Sept. 19 note, Leerink Partners’ analyst Geoffrey Porges said that romosozumab has an 80% likelihood to be approved at least for vertebral fracture reduction risk and likely will compete head-to-head with Radius Health Inc’s abaloparatide.

Romosozumab is already under review at FDA, with an approval decision expected in July 2017. Amgen is waiting on the ARCH study, in a more severe population, to report in 2017 before filing in Europe.

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Positive results from the Phase III EXPAND study of oral sipo nimod in secondary progressive multiple sclerosis, presented at ECTRIMS, lift Novartis ahead of Gil enya patent expiry and may be enough to support early approval.

In addition to scoring on efficacy in a multiple sclerosis population with high unmet need, Novartis AG’s sipo nimod demonstrated an attractive safety profile in the EXPAND study, data that position the drug to succeed the company’s ageing Gil enya and possibly support early approval.

Sipo nimod (BAF312) is an oral, spingo sine-1-phosphate (S1P) receptor modula tor and a follow-on to Gil enya (fingolimod), which goes off patent in the US in 2019.

Novartis released full results for sipo nimod in the trial in secondary progressive multiple sclerosis (SPMS), a type of MS with few treatment options, at the European Committee for Research and Treatment of Multiple Sclerosis (ECTRIMS) in London on Sept. 17. The drug demonstrated a significant 21% reduction in risk of disability progression after three months, the primary endpoint, and had an even greater benefit at the six-month time point in the 1,651-patient study.

“IT was encouraging to see that the risk reduction was actually higher at the six-month mark (26%) – which was one of the study’s secondary endpoints,” Datamonitor analyst Ines Guerra said in an interview from the meeting.

Safety was in line with other drugs in the same class, investigators reported.

The company had announced positive top-line results from the study in August but analysts were keen to see the details of the safety data to see if the drug is better tolerated than Gil enya.

Importantly, the overall rate of infection was similar to placebo – 49% vs. 49.1% – and there was no signal for malignancy (see table).

“The incidence of cardiac disorders was also low, which is quite encouraging as one of Gil enya’s main drawbacks is its increased risk of cardiac complications,” Guerra said.

In addition to a warning for infection, Gil enya’s labeling includes a warning for increased blood pressure and a requirement for monitoring during treatment. At the start of treatment, all patients must be observed for bradycardia for six hours, including monitoring of pulse and blood pressure hourly.

The rates of serious cardiovascular events and serious infections for sipo nimod vs. placebo were 0.8% vs. 0.5% and 3.5% vs. 2.9%, respectively.

Compared to Gil enya, sipo nimod was designed to target a different set of receptors and has a much higher blood-brain barrier penetration, allowing more drug to get into the central nervous system, which is particularly important in treating secondary progressive MS, Vasant Narasimhan, chief medical officer and global head of drug development at Novartis, said in an interview.

The drug has a short half-life and the company hasn’t seen the cardiac adverse events that it has seen with Gil enya, he said.

TRIAL MAY SUPPORT ACCELERATED FILING

SPMS is a more advanced type of MS and is a challenging disease target. Previously, Biogen Inc. tested Tecfidera (dimethyl fumarate) and Tysabri (natalizumab) in this population but wound up discontinuing research.

In a Sept. 19 note, Jefferies analyst Jeffrey Holford said that about one-fourth of MS patients will go from having relapsing remitting MS to SPMS within 10 years and over 75% will have SPMS within 10 years. “IT is estimated that at any one time around 30% of MS patients have SPMS but currently, there are very limited options for treating this stage of the disease,” he noted.

Novartis has guided for a filing in 2019, but Holford believes that the single placebo-controlled EXPAND study may support a filing for accelerated approval, considering the trial’s large size.

Though there have been failures for drugs tested specifically in SPMS, Bryan Garnier analyst Eric Le Berrigaud noted that several drugs have benefited from a wide label including SPMS as a subgroup of RRMS patients.

“The issue is that in real life, patients developing SPMS are unlikely to remain untreated, although it is difficult to determine a standard-of-care to ask BAF312 to be compared to,” Le Berrigaud said in a Sept. 19 note.

“Given the limited treatment options for SPMS and impressive data for BAF312, we believe it is possible that regulators will view the full data from the EXPAND study as being sufficient for accelerated approval,” Holford concluded.

Novartis Narasimhan said that the company will be in discussions with regulatory authorities as to whether a single study is enough for approval, in light of large unmet need, or whether an additional study will be needed.

Expanded Select Safety Data

<table>
<thead>
<tr>
<th>ADVERSE EVENTS (≥5%)</th>
<th>SIPONIMOD (N=1,099)</th>
<th>PLACEBO (N=546)</th>
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</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>49%</td>
<td>49.1%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>37.9%</td>
<td>32.1%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>24.5%</td>
<td>20.1%</td>
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<tr>
<td>General disorders and administration site conditions</td>
<td>24.4%</td>
<td>20.1%</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>17.1%</td>
<td>17%</td>
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<tr>
<td>Cardiac disorders</td>
<td>11.9%</td>
<td>10.1%</td>
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<tr>
<td>Neoplasms, benign and malignant</td>
<td>10.3%</td>
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<tr>
<td>Metabolism and nutrition disorders</td>
<td>7.7%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>7.6%</td>
<td>6.8%</td>
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</table>

Source: Lugwig Kappos (University Hospital, Basel, Switzerland), ECTRIMS, 2016

Published online 19 September 2016
Allergan PLC took its time observing the non-alcoholic steatohepatitis (NASH) drug pipeline, but moved quickly and aggressively when the company found what it was looking for. Allergan revealed in separate announcements on Sept. 20 that it could spend more than $1.7bn to buy Tobira Therapeutics Inc. and its two-drug NASH cocktail plus a preclinical chaser from Akarna Therapeutics Inc.

Allergan’s chief research and development officer David Nicholson told Scrip that the company has been looking at the NASH space for a while, so it acted fast – and spared no expense – to buy Tobira after the San Francisco-based firm reported Phase II data in July for lead drug candidate cenicriviroc (CVC). The CCR2 and CCR5 inhibitor, Tobira’s Phase I DPP-4 inhibitor and Akarna’s FXR agonist give Allergan three different approaches to NASH with multiple combination therapy options to treat the large and growing form of non-alcoholic fatty liver disease (NAFLD).

The eye-popping total value of Allergan’s bid for Tobira is just $5m shy of $1.7bn. The acquisitive big pharma will pay $28.35 per share up front – six times Tobira’s Sept. 19 stock price of $4.74. Nearly two-thirds of the deal’s value, however, comes from the $49.84 per share in contingent value rights (CVRs) that Allergan may pay Tobira shareholders during the next several years if the company’s assets achieve certain development, regulatory and commercial milestones.

Altogether, the deal terms give investors a potential return of 19 times Tobira’s share price before Allergan announced the companies’ agreement. That’s why Tobira’s stock soared 720.9% – or more than eight times its prior value – to close at $38.91 on Sept. 20.

The value of Allergan’s second NASH deal is harder to determine, however. The company will pay $50m up front for privately held Akarna plus undisclosed fees related to clinical, regulatory and commercial milestones for AKN-083. Akarna’s lead NASH drug candidate is one of several compounds the firm has under development in a preclinical pipeline of farnesoid X receptor (FXR) agonists.

Nicholson indicated in an interview about the Tobira deal, but prior to the Akarna announcement, that Allergan was on the hunt for more NASH drug candidates.

“We strongly believe that combination therapy attacking different points in [the disease] continuum is going to be important,” he said. “We really are just unraveling the different causes of [NASH], so we’ll continue to look at different ways of treating the disease.”

**EXPANDING THE GI FRANCHISE BEYOND IBS AND COLITIS**

Allergan thinks the NASH drugs fit well into the company’s gastrointestinal (GI) franchise, which includes older therapies for Crohn’s disease and ulcerative colitis, like now-generic Azicol (mesalamine), and newer treatments for irritable bowel syndrome (IBS).

Allergan previously extended the reach of its GI franchise through its predecessor Actavis’s acquisition of Forest Laboratories Inc. in 2014. Forest and Ironwood Pharmaceuticals Inc. had an agreement to market Linzess (linaclotide) for IBS with constipation, while Forest acquired the more recently approved Viberzi (eluxadoline) for IBS with diarrhea when it bought Furiex Pharmaceuticals Inc. in 2014.

The Tobira and Akarna deals further extend Allergan’s reach beyond marketed drugs for IBS and ulcerative colitis, and pipeline programs in diabetic gastroparesis, into a liver disease with a large market estimated at 5% of the US population.

NASH numbers are driven by growing rates of obesity and diabetes, since the disease is characterized by excess fat and inflammation in the liver. The inflammation leads to fibrosis that can progress to cirrhosis, portal hypertension, liver cancer and liver failure.

There are no approved therapies for NASH, but the most advanced NASH drug in development is Intercept Pharmaceuticals Inc’s Ocaliva (obeticholic acid), which was approved in June to treat primary biliary cholangitis.

Tobira’s Phase II data for CVC were viewed skeptically by investors, because the drug missed the primary endpoint of improvement in the NAFLD activity score (NAS), but met the secondary endpoint of reducing liver fibrosis after a year on therapy. More patients treated with CVC achieved a one-point or greater reduction in liver fibrosis scores, which range from F0 to F4, than patients treated with a placebo.

Tobira’s Phase II fibrosis data were important to Allergan, because the FDA has said that fibrosis reduction of one point with no change in NALFD activity scores would be an approvable endpoint, Nicholson said.

Evercore ISI analyst Umer Raffat said in his analysis of Allergan’s Tobira buy that CVC’s effect on fibrosis must be confirmed at two years in the ongoing Phase II study and in a Phase III trial to justify the deal’s value. Both the two-year Phase II results and initiation of a Phase III study are expected in 2017.

**THE NEXT NASH FRONTIER: COMBINATION THERAPIES**

CVC was the main driver of the deal, but Tobira’s DPP-4 inhibitor evogliptin was intriguing in its own right, since NASH is a multifactorial disorder.

“NASH won’t be treated with one drug,” Tobira Chief Financial Officer Christopher Peetz told Scrip in June. “With our safety data so far and our once-daily dosing, CVC can be a backbone in combination therapies.”

Peetz noted that evogliptin’s effect on metabolic factors associated with NASH gave Tobira “a more complete approach” to the disease. He anticipated that development of the CVC-evogliptin combination would be one to two years behind CVC monotherapy.

Published online 21 September 2016
The outcome of the June 23, 2016 referendum on the UK’s membership of the EU stunned not only the nation, whether you voted to leave or remain, it sent shockwaves through Europe and beyond. The UK’s pharmaceutical industry made no secret of its stance: it was all about remain – but it got a Brexit. Scrip’s Sukaina Virji gathered a group of pharma industry experts who spent their summer working on making the best of the situation. Here’s an edited recount of their insightful discussion.

Sukaina Virji: What do we actually know about the upcoming Brexit?

Ian Schofield, principal analyst, Scrip: We know that we’ll have to trigger Article 50 to start the negotiation process for disentangling ourselves from the EU. We don’t know what kind of relationship we will have with the EU eventually. Once the Brexit negotiations are finished we’ll have to start negotiating trade agreements with the EU. Until then it’s very difficult to say what the implications will be for the life sciences as it depends very much on whether we end up with a Norway style agreement, a Swiss type agreement, or a complete withdrawal.

Certain things are likely to happen. The European Medicines Agency will probably move from London to another EU country, although there are suggestions that there might be some way of working around that by having some operations in the UK and some in another EU country.

It will be very important to try and avoid regulatory divergence between the UK and EU because companies rely to a huge extent on the same regulations across the EU single market. Other considerations to take into account are the UK’s participation in the future EU patent system: we could well lose the branch of the new unified patent board that’s supposed to be setting up in London.

The one front where there probably won’t be much change is pricing and reimbursement, health technology assessments, as they tend to be a member state responsibility.

SV: What key concerns did the Brexit result throw up?

Steve Bates, chief executive, BIA: My main worry was that this was a big degree of uncertainty put into a long scale business that’s global in its perspective. From a UK trade association point of view, if you look at big revolutionary moments such as the American declaration of independence or perhaps the French revolution, many things changed but also many things didn’t. If you look at the diet of the French peasant between 1750 and 1850, despite the French revolution, it didn’t fundamentally change. If you look at the strengths of the UK ecosystem in bioscience, the fantastic science from the more experienced universities, the talent and the opportunities, the money that comes from London and beyond into this sector; these aren’t likely to be significantly affected by a Brexit.

Harren Jhoti, CEO, Astex Pharmaceutical: My biggest concern was access to talent, to people, because at the end of the day our industry is based on a foundation of being able to access the best scientists, best clinicians, best regulatory folk, from around the world. If that is at risk, then we could see a gradual erosion of the science base in the UK.

Jo Pisani, partner leading the UK pharma and life sciences consulting practice, PwC: On June 24 we were overwhelmed with queries from different parts of the world and a lot of it was about uncertainty. The government has underwritten Horizon 2020 commitments but, nonetheless, we have seen some collaborations fall away. [Horizon 2020 is the EU’s €80bn research and innovation program, running from 2014-2020 – Ed.] The regulatory framework concerned a lot of our global clients and the view was that if you’ve got one system for 27 countries and another system for the UK, what does that say about the UK in terms of priorities around market access and launch capabilities? With multinational companies that haven’t got a strong presence in the UK, there are different levels of knowledge about what’s going on and this can lead to kneejerk reactions. Unfortunately, we have seen some foreign direct investment decisions being reversed at the last minute, collaboration agreements being dismantled, clinical trials locations [changed]. The critical
thing at the moment is to convey confidence about the UK biosciences ecosystem.

SV: What are the key elements of the Brexit strategy from a pharma perspective?
SB: The BIA and the ABPI, with support from PwC, have worked hard to produce information for the new UK government telling them about the needs and priorities of the sector from a global and local perspective in terms of what they need to focus on in the negotiations. We engaged with over 150 companies in 50 hours of workshops; it's been a busy summer, but we are now in a position to be able to help the government with their thinking.

Lindsey Barras, director in global immigration, PwC: The [new] government sees the value of the skilled people that this industry brings in, at the same time - remember these are people in new roles - they're struggling to create something that gives enough flexibility and makes the EU happy, yet gives the British public the feeling that they've been heard, because within the vote it was very clear that immigration was a key area of concern - people felt that our borders were too open.

HJ: We need in the shorter term to have a position on the EU citizens already here. We have significant numbers of EU staff across the industry; in my company we have around 20% and there is an understandable level of uncertainty in those people's minds as to what's going to happen.

Virginia Acha, executive director, ABPI: We have been bringing ministers up to speed on how comprehensive regulatory policy works within the life sciences. It shapes the way we do our clinical research, it shapes the way we develop and produce our medicines, the manufacturing process, the way we authorize and provide them to patients, and critically how we follow up with the use of that medicine in practice. A lot of those European laws that shape our sector were British ideas. As I tried to explain to ministers, they are like standards of any sort. The more you diverge from a global standard, the more you need a good reason why somebody would want to do that niche approach. And really the globalization and standards we have were driven there, not because of some sort of trade requirement, but because that's where the science is taking us. We need to follow the science, and then is it really such a big surprise that this convergence is possible?

SV: What happens next on the Brexit front?
SB: Much of this discussion is predicated at a political level, so it's important to have an understanding of some of the upcoming events in the European political calendar. In the UK, an important moment will be in early October, when the Prime Minister [Theresa May] gives a speech to the Conservative Party Conference, a bit like the State of Nation, where she'll be likely to flesh out some of the thinking. There's likely to be further discussions with the EU towards the end of the year, and the triggering of Article 50 could happen early in the New Year. It's also important to look at the context of domestic politics in other European nations. We will see some of this Brexit discussion through the prism of those political contexts because if those political contexts change, it could change the nature of the debate.

SV: What opportunities does Brexit throw out?
JP: We shouldn't lose sight of the fact that UK life sciences is tremendously vibrant, so there are three areas of opportunities that I would mention. Innovation, particularly around advanced therapies. Monoclonal antibodies are an example of a technology that we didn't throw our weight behind and we saw a lot of that move beyond the UK's borders. Financing is another one. We have a mature end-to-end system but we need more scale, longer investment cycles and also diversification beyond different therapeutic areas. The third area is the NHS. Looking at the NHS as a single system, effectively looking like a single patient to the outside world, can we encourage rapid uptake in innovation within the NHS? I'd be very positive about the future for UK life sciences but we just need that back and momentum.

SB: I look at this from the perspective of the things that have perhaps not gone well for the UK as a member of the EU that could have the opportunity to go well going forwards. One example is the area of cell therapy. There's a case in the EU Courts called the Bruestle Judgement, well-known to people developing cell therapies, which I think within a UK court might have been decided differently. So perhaps where you have European case law around emerging technologies and how they are patented, there is the potential for there to be a divergence. The second example is what I would describe as the non-scientific approach to GM foods which has been taken by the EU in the last few years. If you look at BIO in the US, the sister organization to the BIA, they have a vibrant and active agricultural biotechnology segment. We don't have that in Europe; there aren't any companies, in a sense the development of that industry has been stifled by EU rules.

HJ: What I'd probably think about is trying to establish stronger links with the largest pharmaceutical market in the world, North America, as well as some of the emerging markets. The old Commonwealth links, perhaps there's opportunities there. Certainly there's a lot of talent there. India produces thousands of PhD candidates every year and certainly that skill set would be very useful. Also, training our own people; [Brexit] gives us an opportunity to energize that - persuading the government to think more about science and technology in the UK education system since we are going to be restricted in getting EU talent, we'll have to grow our own.

LB: That's one positive from an immigration perspective. Probably one of the biggest challenges over the last five or six years has been a focus on this arbitrary net migration number. Potentially we won't have as many EU people coming, so we can be more flexible with non-EU migration which will be useful when we talk about the trade agreements, if we want people from the US or elsewhere, there is opportunity to have a system that works better than it currently does. Even before Brexit there was talk about doing an overhaul of the process.

SV: Do we have a timeframe?
JP: The clock starts when Article 50 is triggered and then we've got two years. It can be extended but you need the other 27 countries to agree unanimously, which will take two years in itself. So we're advising companies around scenario planning. What are the different scenarios both in terms of velocity and impact? How does it impact your business and how do you mitigate the risks?

The other important thing to mention is that other sectors are going through similar challenges. It is important for the sectors to remain aligned because there are interdependencies.

HJ: We also need to remind ourselves that we are working in a fiercely competitive sector. So while the executives running the companies are distracted by this huge issue, they're not building the company. All our competitors around the world are building their companies. There's no answer to that, but we know the EU doesn't move very fast.

SB: So for those planning for 2017, the UK will still be in the EU, the regulatory processes will be as they are now, and people should get on with their work.
Cancer focused and charging forwards, AbbVie makes 2017 the year its pipeline will expand a little more. Scrip looks at the company’s growing oncology portfolio and what is yet to come and speaks to medical affairs head Bianca Wittig about challenges intertwined with oncology R&D.

Having spent the majority of this year investing heavily in its oncology pipeline, including an acquisition focused on cell therapy assets, AbbVie Inc. is confident it will make clinical progress in cancer in 2017 – boasting a growing pipeline which includes around 16 compounds in more than 200 active trials.

Following a recent event at the Oslo Cancer Cluster in Norway, of which AbbVie is a pharma partner, Bianca Wittig, medical affairs, oncology, spoke to Scrip about why AbbVie is pushing its oncology portfolio and what we should expect from the unit in the near future.

“We are striving to outsmart cancer by exploring and investing in understanding new pathways, such as the BCL-2 pathway and new technologies such as CRISPR/Cas9, to tackle some of the most widespread and difficult-to-treat cancers like chronic lymphocytic leukemia and its associated genetic mutations,” Wittig said.

Of its Phase I to Phase III compounds targeting oncological indications Wittig said, “It is our hope that all of these compounds will bring value in advancing our understanding of this devastating diseases and improving outcomes for patients.”

According to Biomedtracker, AbbVie has compounds in development targeting 46 various cancer indications, including hematological conditions and solid tumors. This is the largest number of assets for any of the disease spaces AbbVie is active in, which also include respiratory, endocrine, infectious disease, neurology and others (see chart below).

The company’s interest in oncology was sparked 20 years ago when scientists from Abbott Laboratories, now AbbVie, began research on the process of apoptosis. “As our journey continues, oncology remains a significant growth platform for AbbVie and we continue to build a portfolio that allows us to discover and develop innovative cancer therapies that aim to disrupt the natural progression of cancer cells,” said Wittig.

DEAL SPREE
In 2016, AbbVie picked up early-stage assets for its oncology pipeline via deals with Argenx and CytomX Therapeutics, and expanded its cell therapy research for cancer indications through the acquisition of Stemcentrx Inc. AbbVie also launched a three-year collaboration with The University of Texas MD Anderson Cancer Center, a world renowned oncology research center, to carry out studies for new approaches in immuno-oncology. “AbbVie has invested significantly in oncology, both in terms of the time and resources,” Wittig said.

One of the most promising assets from its 2016 deal spree is rovalpituzumab tesirine, known as Rova-T, a Stemcentrx compound, currently in registration trials as a third-line therapy for small cell lung cancer (SCLC). Rova-T has previously shown promising single-agent activity in terms of overall response rate, clinical benefit rate and progression-free survival in third-line small cell lung cancer. As such, AbbVie said it is “rapidly advancing” studies to evaluate Rova-T in earlier lines of therapy for SCLC, including combination studies with both chemotherapy and immuno-oncology agents.”

However, Rova-T has yet to impress analysts in larger patient populations, leaving some wondering if AbbVie overspent on Stemcentrx. The big pharma forked out $5.8bn upfront and agreed to another $4bn in milestone payments tied to this drug and four others from Stemcentrx. This pricey deal was surprising as AbbVie had not long before spent $21bn on Pharmacyclics Inc.

AbbVie has previously said it believed Rova-T could earn approval as first-line therapy in SCLC.

Published online 23 September 2016
**Artios Launches With £25m To Study ‘PARP-esque’ DNA Damage Response Inhibitors**

Artios Pharma Ltd., a new company focused on developing novel cancer treatments targeting DNA damage response, has been launched with a £25 million series A financing led by SV Life Sciences. DNA damage response is a mechanism through which cells repair damaged DNA. However, research suggests tumors manipulate this ability, which allows them to mutate and evolve. Compounds such as the PARP inhibitor Lynparza (olaparib; AstraZeneca PLC) target a tumor’s remaining DNA repair mechanisms to cause its selective death, a concept known as ‘synthetic lethality.’ Artios is being led by CEO Niall Martin, previously director of drug discovery at KuDOS Pharmaceuticals which was sold to AstraZeneca in January 2006 for $210m. Martin was project leader on KuDOS’ PARP inhibitor program and played a key role in identifying Lynparza. Prior to joining Artios, Martin co-founded and served as COO at Mission Therapeutics, a company focused on ubiquitin pathways. Artios will use the proceeds of its series A round to build a pipeline of first-in-class DNA damage response therapies.

sukaina.virji@informa.com, 21 September 2016

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**EPIC Fail For Mast Therapeutics’ Lead Drug Sends Shares Into Freefall**

San Diego, California-based Mast Therapeutics Inc. is pinning its hopes on its vasodilating AIR001 program for heart failure following the second Phase III failure for its sickle cell disease candidate vepoloxamer. Mast’s share price on the NYSE plummeted by more than 80% to $0.11 on the morning of Sept. 21 following the announcement made late on Sept. 20. The Phase III EPIC study missed its primary endpoint of a significant reduction in the mean duration of vaso-occlusive crisis (VOC) compared with placebo in sickle cell disease patients. Neither were there any significant differences between the treatment groups in the intent-to-treat population for the two secondary efficacy endpoints: rate of re-hospitalization for VOC and the occurrence of acute chest syndrome. The top-line data spell the end for the product, and a switch in focus to the company’s other clinical-stage candidate AIR001, CEO Brian M. Culley said. The company will review the full data set from EPIC. “In addition, we plan to perform an interim analysis of the ongoing heart failure trial of vepoloxamer,” he said. “However, based on the data we’ve seen to date, we expect we will terminate all clinical development of vepoloxamer.” “Consequently, while we evaluate our options, we intend to significantly and immediately reduce our operating expenses and continue our efforts with AIR001, our lead asset in heart failure with preserved ejection fraction.” AIR001 is in a 100-patient Phase II study expected to complete enrollment by the end of 2017.

alex.shimmings@informa.com, 21 September 2016

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**Genentech, BioNTech Pact Aims To Make Targeted Cancer Vaccines**

Genentech will tap expertise of privately-held BioNTech in a collaboration aimed at developing individually tailored vaccines for use against a broad range of cancers, which the duo says offers “a new treatment paradigm” for oncology. Genentech Inc. and Germany’s BioNTech AG believe that together they can leverage the US-based Roche division’s portfolio of approved and investigational cancer immunotherapies and the privately-held biotech’s proprietary mRNA cancer vaccine technology platform to develop bespoke cancer vaccines for individual patients. Most approaches to cancer vaccines have been unsuccessful due to difficulties identifying the correct cancer targets, or antigens, to vaccinate against. But the duo says that with advanced sequencing and analysis, it is now possible to identify the unique “neoantigens” specific to each person’s cancer, and use them to tailor a cancer vaccine. Therapeutic cancer vaccines have a checkered history, with limited success like Dendreon’s Provenge, but there’s a new wave of interest for use in conjunction with cancer immunotherapy; a cancer vaccine could prime the immune system to seek specific molecular targets. Ugur Sahin, BioNTech’s CEO, noted the mutations in cancer patients’ tumors can act as excellent targets for developing vaccines.

sten.stovall@informa.com, 22 September 2016

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**Glenmark Primes Complex Generics Play With Abraxane Copy Deal**

Glenmark Pharmaceuticals Inc. US has entered into a development, license and commercialization agreement with Particle Sciences Inc for a generic version of Celgene Corp.’s Abraxane (paclitaxel protein-bound particles for injectable suspension). The deal will see Particle develop the product exclusively for Glenmark in return for milestone payments at various stages of the product’s development from the Indian group, including royalties on sales. Glenmark has global exclusive marketing and distribution rights of the product upon commercialization. Asked about the firm’s preference to source the product from Particle rather than pursuing in-house development, Glenmark’s chair and managing director, Glenn Saldanha, told Scrip that Particle Sciences has “very strong” technical capabilities and understanding of particulate injection products and this can be leveraged to develop the generic version of Abraxane.

anju.ghanurde@informa.com, 21 September 2016
Lundbeck’s STARSHINE Fades As Idalopirdine Fails First Phase III Alzheimer’s Test

Lundbeck’s 5-HT6 antagonist idalopirdine failed its first Phase III test, but as Axovant awaits data from its Phase III study for a competing Alzheimer’s therapy, it’s still unclear whether the entire drug class is doomed to the same fate.

MANDY JACKSON mandy.jackson@informa.com

30 September 2016

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AZ Hopes Coupling GLP-1 Bydureon and SGLT-2 Forxiga Is Paradigm Shift

Results of AstraZeneca PLC’s late-stage study dubbed DURATION-8 is the first trial to evaluate the combination of the two diabetes treatments Bydureon (GLP-1) and Forxiga (SGLT-2) and confirmed what many experts had presumed - that they work better together than separately at reducing blood sugar in patients whose diabetes couldn’t be controlled with first-line therapy metformin, potentially opening a new treatment approach. The study, released at this year’s annual meeting of the European Association for the Study of Diabetes (EASD) in Munich, Germany and simultaneously published in The Lancet Diabetes & Endocrinology, hit all primary endpoints, reducing blood sugar, weight and systolic blood pressure in patients with type 2 diabetes, versus each medicine on their own, and showed cardiovascular risk benefit. It showed that at 28 weeks a 2 milligram weekly injection of Bydureon (exenatide extended-release formulation) along with a daily 10 milligram tablet of Forxiga (dapagliflozin) reduced HbA1c from baseline to 1.95%, bettering the 1.58% decline with exenatide and 1.37% fall with dapagliflozin alone, respectively. AstraZeneca hopes the study’s results will spur the use by doctors of the combo and thereby delay moving type 2 diabetes patients on to insulin.

ECTRIMS 2016: Biogen Makes Headway in MS Remyelination Studies

Biogen has received a clutch of useful data from the initially disappointing SYNERGY trial, and is now evaluating the design of further possible Phase II clinical studies of opincumab, a potential myelin repair agent for the treatment of multiple sclerosis. “What was important about the study was that we were trying to identify, for the first time, patients who might benefit from a remyelination strategy,” said Biogen researcher Diego Cadavid during the ECTRIMS, held in London on Sept. 14 to Sept. 18. Younger patients, and those who had MS for a shorter duration, appeared to be better responders to opincumab, as did those with less severe damage to the brain, as measured by volume loss, Cadavid said. The study is one of the first to evaluate the “neuroreparative” activity of a potential therapeutic agent in the clinic, and a drug that blocks and reverses one of the key characteristics, demyelination, of MS would be a key therapeutic strategy. SYNERGY is certainly the largest clinical study investigating remyelination to be conducted to date, with just over 400 evaluable patients. Opincumab is a fully human monoclonal antibody that blocks LINGO-1, a CNS-specific negative regulator of myelination and axonal regeneration that in an earlier Biogen Phase IIa study, RENEW, showed signs of beneficial effects in some patients with the pre-MS condition acute optic neuritis. So it was quite a disappointment earlier this year when Biogen reported top-line data from the 72-week SYNERGY study showing opincumab did not meet the primary endpoint, a multicomponent measure including improvement in physical and cognitive function, and disability.

ECTRIMS 2016: Alextrema Is Paradigm Shift About the Study was that we were trying to identify, for the first time, patients who might benefit from a remyelination strategy,” said Biogen researcher Diego Cadavid during the ECTRIMS, held in London on Sept. 14 to Sept. 18. Younger patients, and those who had MS for a shorter duration, appeared to be better responders to opincumab, as did those with less severe damage to the brain, as measured by volume loss, Cadavid said. The study is one of the first to evaluate the “neuroreparative” activity of a potential therapeutic agent in the clinic, and a drug that blocks and reverses one of the key characteristics, demyelination, of MS would be a key therapeutic strategy. SYNERGY is certainly the largest clinical study investigating remyelination to be conducted to date, with just over 400 evaluable patients. Opincumab is a fully human monoclonal antibody that blocks LINGO-1, a CNS-specific negative regulator of myelination and axonal regeneration that in an earlier Biogen Phase IIa study, RENEW, showed signs of beneficial effects in some patients with the pre-MS condition acute optic neuritis. So it was quite a disappointment earlier this year when Biogen reported top-line data from the 72-week SYNERGY study showing opincumab did not meet the primary endpoint, a multicomponent measure including improvement in physical and cognitive function, and disability.

ECTRIMS 2016: Alemtuzumab Benefits Continue Six Years

Clinical follow-up for up to six years after the start of treatment with Sanofi’s multiple sclerosis therapy, Lemtrada (alemtuzumab), confirm that it produces a durable response, with improvements in disability and declining adverse event severity, backing the idea that it could be used more widely in patients with early disease. In a number of countries, alemtuzumab is indicated for second or later lines of therapy, mainly because of concerns about adverse events and resource-hungry monitoring requirements. Nonetheless, sales of Lemtrada and another of Sanofi’s MS drugs, Aubagio (teriflunomide), are increasing, suggesting clinicians are increasingly reassured about their use.

Amgen’s Amjevita Approved As First Biosimilar To AbbVie’s Humira

With the approval of Amgen Inc.’s Amjevita (adalimumab-atto), the big biotech is about to begin its move from a strictly brand-name sponsor to commercializing biosimilars as well. Marketing biosimilars will be more akin to brand drugs than small molecule generics, and the high cost of production and development are expected to result in smaller price differentials. Amgen decided years ago to go all-in on biosimilars, taking advantage of its biologics manufacturing expertise. Beyond Amjetiva, Amgen has eight other programs in its biosimilar pipeline. “Approval of Amjevita is an exciting accomplishment as it marks a new chapter in Amgen’s story of being a leader in biotechnology,” Sean Harper, Amgen executive VP-R&D, said in a release. “In addition, Amjevita holds the potential to offer patients with chronic inflammatory diseases an additional treatment option.” FDA approved Amjevita, a biosimilar to AbbVie Inc.’s Humira (adalimumab), on Sept. 23, marking the fourth US biosimilar approval and the first one referencing the blockbuster tumor necrosis factor inhibitor. Humira is the top-selling drug product in the world and brought in over $4bn in the second quarter, 17% growth despite the anticipation of biosimilars. Approval followed a unanimous advisory committee recommendation in July supporting licensure as a biosimilar in arthritic, dermatologic and inflammatory bowel disease indications.

R&D BITES
How Many Pricing Hearings Add Up To Action On Pricing Transparency?

CATHY KELLY cathy.kelly@informa.com

Mylan’s discussion of how the drug supply chain absorbs pricing for EpiPen raised more questions than it answered during a House Oversight Committee hearing

Mylan Pharmaceuticals Inc. may be regretting its tactic of trying to deflect criticism over big EpiPen price increases by arguing that more than half of the drug’s $608 list price is being absorbed by the drug supply chain, which is leading to calls for more transparency, particularly around pharmacy benefit managers.

The argument raised many more questions than Mylan CEO Heather Bresch was prepared to answer at a House Oversight and Government Reform Committee hearing Sept. 21. And it led to confusion, frustration and repeated requests for additional information from committee members, indicating the ordeal is not over for Mylan.

“You can make this thing go away by being open and candid with us and we don’t think you are,” committee chair Jason Chaffetz, R-UT, told Bresch as the nearly four-hour session was winding down. “That’s why we’re in the I-don’t-know-what-hour here [of the hearing] and we’re asking you to provide more information.”

In response to the public outcry over its repeated price increases for the emergency treatment for anaphylaxis, Mylan has offered a flow chart showing that the $608 list price is actually reduced to $274 after fees, rebates, discounts and allowances are paid to middlemen such as wholesalers, pharmacy benefit managers, insurers and pharmacies.

Bresch stated many times at the hearing that after cost of goods and marketing expenses are deducted from EpiPen revenue, Mylan is realizing only about $50 in profit per pen. She also said Mylan would be receiving “much less” in profits from an upcoming authorized generic of EpiPen. The company has announced it would make the authorized generic available with a list price of $300 as a way to effectively to lower the cost of the treatment.

However, she declined to provide a specific estimate on profits on the authorized generic or on how current profits for EpiPen compare with previous years, when the product was less expensive. She promised to get more company documents to members over the next 10 days to respond to their questions.

Ranking member Elijah Cummings, D-MD, accused her of obscuring information to an extent on par with the behavior of Turing Pharmaceuticals AG’s former CEO Martin Shkreli, who invoked his fifth amendment rights when summoned by the committee in to address steep price hikes for Turing’s Daraprim (pyrimethamine).

Rep. Blake Farenthold, R-TX, expressed the kind of confusion over how the supply chain affects pricing that many members seemed to feel. Referring to an earlier exchange about Bresch’s salary, he said: “I think I now understand why you make $18m. Trying to figure out the complexities of drug pricing has me really flummoxed. … It’s so incredibly complicated it makes airline pricing look reasonable.”

“I want to fix this because it’s not just your product that’s the problem,” Farenthold stated. “How do we fix this where you can make a reasonable profit and the drug can be available at a price that people understand?”

Bresch agreed that the drug supply channel is overly complicated and emphasized the need for greater transparency by all members of the chain.

“The system has been around for decades and it certainly hasn’t kept pace with the evolving health care crisis our nation faces,” she said. “I believe that first there needs to be more transparency in the system and I certainly welcome the opportunity to sit down in a more holistic way and have the conversation. But the whole supply chain has to be involved in that.”

Mylan’s effort to shine a light on how much of a drug’s price is consumed by the supply chain did elicit some comments from members about the need for more transparency around what PBMs are making.

Rep. Buddy Carter, D-GA, asked Bresch to describe the amount of rebates given to PBMs for EpiPen. And when she said she didn’t have a “breakdown” on what the various middlemen receive, he said: “Nor do I and I’m a pharmacist. In fact nobody knows, that’s the problem. Nobody knows how much of [the price] is going to PBMs because there’s no transparency.”

However, Carter continued, “what we do know is this: prescription drug prices have soared and so have the profits of PBMs. They are in the billions of dollars. Until we have more transparency in the PBM market, we’re going to continue to see these kinds of cost increases.”

GROWING MOMENTUM FOR CHANGE?

Some members also expressed frustration with the number of companies whose drug pricing tactics are being called into question, suggesting there is growing momentum in Congress for action that would rein in increases.

“Unfortunately, this is not our first hearing on such matters,” said Rep. Michelle Lujan-Grisham, D-NM. “We are talking and dealing with Turing and Valeant and Mylan and Gilead and seeing a really disturbing pattern where Congress provides a variety of mechanisms to invest in innovation … and what we get in return is a monopoly using your generic … in a way we did not intend, and having a hearing where we’re not going to get any relief.”

She added “I don’t think we’ve gotten many of our questions answered because in fact, Mr. Chairman, it is true it is very complicated. We have created an environment where they don’t have to be transparent – so they aren’t.”

“I think we ought to do transparency legislation,” Lujan-Grisham said. “I think there’s a whole host of ideas where we could lead instead of being dragged down this path, where we are upset for our constituents but none of these prices will shift on their own at these companies’ hands.”

In the Senate a recently-introduced bipartisan bill that would require pharmaceutical manufacturers to justify any price increase over 10% is one worth watching.

Published online 22 September 2016
Natco Doubles Down On US With Ambitious ANDA Plan

Natco Pharma Ltd. made global headlines four years ago when India’s patent authority gave the mid-sized firm a compulsory license to produce a generic version of Bayer AG’s cancer drug Nexavar (sorafenib) at a price 97% below the patent-protected original. Huge controversy ensued with pharma multinationals accusing India of flouting patent rights and predicting a wave of such licenses, which hasn’t materialized. In the meantime, things have been going well for Natco, which launched a reverse-engineered version of Nexavar for $171 month (still unaffordable for most Indians living on less than $2 a day), compared to the $5,000 a month for Bayer’s branded version. Between fiscal 2012-16, Natco’s revenues have grown at a compound annual growth rate (CAGR) of 20%, and the 25-year-old firm, based in the southern city of Hyderabad, has been reporting a lot of good news lately. This has included first quarter net profit that soared 70% to INR390.2bn ($7.1m) from a year earlier, on sales which jumped 38% to INR2.977bn, considerably overshooting brokerage forecasts. The company, which tags itself as “resisting the usual” in finding affordable answers to complex medical problems, is now basking in buy recommendations for its shares, which closed flat on Sept. 22 at INR632.20 but well above their 52-week low of INR2.977bn, considerably overshooting brokerage forecasts. The company, which tags itself as “resisting the usual” in finding affordable answers to complex medical problems, is now basking in buy recommendations for its shares, which closed flat on Sept. 22 at INR632.20 but well above their 52-week low of INR2.977bn, considerably overshooting brokerage forecasts.

Jim O’Neill Is ‘Free For Global AMR Role’ After Leaving UK Government

Having suddenly resigned from the UK Government Jim O’Neill says he’s now available to take on a global role, if asked, to promote concrete action on tackling antimicrobial resistance within promised timeframes. Lord O’Neill of Gatley – ex-chair of Goldman Sachs Asset Management and the man appointed by former UK Prime Minister David Cameron to launch and chair a review into the crisis of antibiotic resistance, has suddenly resigned as Treasury minister and immediately tells Scrip he would now like an unencumbered role – perhaps with the UN – in which to work with countries and drug makers to ensure they make good on recent pledges to effectively combat antibiotic resistance. O’Neill’s resignation, announced Sept 23, came two days after a high-level UN meeting saw all 193 member countries sign a declaration in which they pledged to take concrete action on tackling antimicrobial resistance. That followed from the G20 communiqué earlier in September in which the world’s richest countries promised to promote prudent use of antibiotics and called for options to tackle AMR. Following suit, 13 global pharma companies issued a Roadmap for actions that they will take to help alleviate the issue. Much of the momentum which culminated in those declarations resulted from O’Neill’s AMR reviews, the last of which was issued in May. The former Goldman Sachs executive, also a key advocate of the UK forging strong links with China, was commercial secretary for 18 months. His network helped get the G20 this summer under China’s leadership to include the issue of antimicrobials on the global agenda. Asked what he’ll do now that he has left government, O’Neill said “I’m a free, able and willing agent now,” adding that he’s be open to a role at supranational level, if offered one, to keep the AMR momentum going.

Teva Preps For SD-809 Tardive Dyskinesia Filing By The End Of 2016

Teva Pharmaceutical Industries Ltd. is on track to file a high-profile drug in its specialty portfolio, deutetrabenazine (also known as SD-809), for the treatment of tardive dyskinesia by the end of 2016, after a second Phase III trial read out positively, the company announced Sept. 22. The timeline positions Teva competitively in a race with Neurocrine Biosciences Inc., which filed its vesicular monamine 2 transporter (VMAT2) inhibitor valbenazine with FDA in August for the treatment of tardive dyskinesia, the repetitive and uncontrolled movements that can affect patients across a range of conditions. The first treatment to address the disorder could represent a significant commercial opportunity, since around 500,000 people in the US are thought to have it, often as a result of treatment with medications for psychiatric conditions like schizophrenia and bipolar disorder. Teva already has an application pending for deutetrabenazine at FDA for a different, smaller indication, chorea associated with Huntington disease. The application received a complete response letter from FDA in May, though Teva assured investors it would be able to quickly resubmit the application by the end of September, positioning it for a potential approval in April 2017. Teva’s second Phase III trial for deutetrabenazine in tardive dyskinesia, AIMS-TD, measured change in Abnormal Involuntary Movement Scale (AIMS) score from baseline to week 12 for three fixed-doses of the drug versus placebo, versus a titrated regimen to optimal dose used in the first Phase III study, ARM-TD, which reported out in June 2015.

penelope.macrae@informa.com, 22 September 2016

sten.stovall@informa.com, 23 September 2016

jessica.merrill@informa.com, 22 September 2016
Glass Ceiling Cracked; Pharma Forges Path To Gender Equality By 2040?

One woman CEO is an improvement, but at this rate gender equality won’t arrive before immuno-oncology goes generic.

JOHN HODGSON john.hodgson@informa.com

The announcement on Sept. 20 that Emma Walmsley would be GlaxoSmithKline PLC’s next CEO means that the proportion of female CEOs among the pharmaceutical industry’s top 10 biggest companies will increase infinitely in March 2017; it was 0% in 2015 and in 2016 and will be a massive 10%.

But the proportion of women among within the senior executive teams of those top 10 companies remains below 20%, despite a slight uptick from the level in 2015. Clearly that is well below the proportion of women employed in pharma as a whole, around 45-50%.

Table 1 shows the current inequalities among senior management teams in pharma.

AstraZeneca leads the way, followed by AbbVie, both companies hovering around the 30% female mark.

Sanofi is second last with only one female in its executive team of 13. Sanofi’s team lost a woman and gained two men in shuffling its management team between 2015 and 2016.

Novartis is plumb bottom: no women featured in its 2015 executive team and its 2016 team is equally gender-exclusive.

However, Novartis has done something to address the dearth of women in pharmaceutical upper management. It cut the size of its management team down from 15 to 11, thereby reducing the number of non-women executives counted in the overall statistics. Johnson & Johnson contributed in a similar way, although its executive team does contain two women.

Across the top 10 companies in 2016, women represented 22 out of 115 executive team members in total (19.1%) compared with 22 out of 123 (17.9%) in 2015. The executive team reductions at Novartis and J&J in effect contribute all of that increase. The increased female headcount at AbbVie (+1) was countered by the reduction at Sanofi.

Perhaps big pharma’s big strategy for gender balance is to cut out the men rather than increasing women.

However it is achieved, a linear increase of 1.2 percentage points per annum would mean that top pharma could be on the cusp of executive gender equality by 2040, several years after the wave of immune-oncology therapies currently in development will have lost market exclusivity.

The picture is slightly brighter at board level (at least for those who think that equality of numbers is a less contrived state of affairs). Women represent 31 out of 116 (26.7%) of the board members among the top 10 companies, virtually the same as in 2015 (26.8%).

As head of the Consumer Division at GSK, Emma Walmsley was relatively well-placed to assume the CEO’s mantle. History shows that the CEO job frequently goes to divisional heads, major regional heads, chief operating officers and occasionally to chief counsel.

On that basis, perhaps the most likely internal candidate as the second female CEO among the top 10 companies would be Laura Schumacher, general counsel at AbbVie. She is in the right sort of job in a company with a CEO that has probably done enough to feel he can move on.

Sanofi’s general counsel Karen Linehan, or Bahija Jallal, president of AstraZeneca’s MedImmune subsidiary, are in the right jobs, too, but their way is blocked by relatively new incumbents.

Table 1. The top 10 global pharmaceutical companies ordered by the proportion of women in their executive management teams

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>WOMEN/TOTAL EXECUTIVES 2015</th>
<th>WOMEN/TOTAL EXECUTIVES 2016*</th>
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</thead>
<tbody>
<tr>
<td>AstraZeneca PLC</td>
<td>4/13</td>
<td>4/12</td>
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<tr>
<td>AbbVie Inc.</td>
<td>2/8</td>
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<td>3/13</td>
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<td>Gilead Sciences Inc.</td>
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<td>3/13</td>
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<td>Merck &amp; Co. Inc.</td>
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<td>Johnson &amp; Johnson</td>
<td>2/16</td>
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<td>Roche</td>
<td>2/11</td>
<td>2/11</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>2/13</td>
<td>2/12</td>
</tr>
<tr>
<td>Sanofi</td>
<td>2/12</td>
<td>1/13</td>
</tr>
<tr>
<td>Novartis AG</td>
<td>0/15</td>
<td>0/11</td>
</tr>
<tr>
<td>Total</td>
<td>22/123</td>
<td>22/115</td>
</tr>
</tbody>
</table>

Scrip Intelligence research; *As of 21 September 2016
Stockwatch: Fanning The Embers Of M&A

ANDY SMITH owner@indysmith.com

A drug approval at Sarepta, two acquisitions by Allergan and $15bn worth of dry powder at Takeda has prompted “biotech off to the races” commentary by analysts and the press. This froth will probably dissipate.

The unexpected and controversial approval of Sarepta Therapeutics Inc’s Exondys 51 (eteplirsen) for Duchenne muscular dystrophy (DMD) paved the way for analyst and social media commentators to peg Sarepta as an imminent take-out candidate. The analysts from Piper Jaffray were quick to upgrade their rating and price target to $64, those from Oppenheimer plucked $76 out of the air while the astrologers from Baird took the biscuit and raised their share price target from $23 to $102. Sarepta closed the week at $57.83 – a 102% jump over five trading days that lifted the NASDAQ Biotech Index (NBI) by 2%.

A conditional approval for an orphan drug, albeit without a convincing demonstration of efficacy, certainly makes Sarepta more valuable to someone of the risk- and price-insensitive controversial asset acquirer persuasion, although the two most likely candidates – Valeant Pharmaceuticals International Inc. and Endo International PLC – have had their acquiring wings clipped by profit warnings and debt burdens. Throughout the week the analysts at Piper Jaffray continued to add fuel to the Sarepta fire by downplaying its $300,000 net price for Exondys 51 and preferring to headline their research with a $665,000 average annual gross price. The analysts at Jefferies were more circumspect in their coverage, upgrading their rating to hold and their share price to $50 but pointing out that the FDA’s action was ‘in contrast to our thesis’. The analysts at Cowen were less introspective when they wrote that they were ‘not surprised by this approval’, omitting to mention to their research at the end of February when they determined that ‘a near-term eteplirsen approval is unlikely’.

All this fawning and tune-changing probably had less to do with the fundamental changes at Sarepta brought on by Exondys 51’s accelerated approval and more to do with the attractions to an investment bank of an imminent secondary share offering. This duly arrived towards the end of last week but was underwritten by two investment banks that had not (yet) covered Sarepta.

Allergan PLC’s acquisition of two companies last week built on the rising tide of analyst commentary around a gold rush of acquisitions of US biotechnology companies. Press reports of Takeda Pharmaceutical Co. Ltd’s interest in deploying $15bn for M&A the previous week generated three research notes from the analysts from Citigroup, highlighting their clients Synergy Pharmaceuticals Inc. and The Medicines Company amongst others as likely targets. This was just after The Medicines Company had reported negative news on the interim analysis for one of its products. Allergan’s acquisitions of Tobira Therapeutics Inc. and Akarna Therapeutics Inc. appeared on no sell-side imminent M&A list that I had read but were enough to light the blue touch paper on the stock prices of any other company developing drugs for non-alcoholic steatohepatitis (NASH), even that most unlikely target, Gilead Sciences Inc.

PTC, unlike Sarepta, conducted two large placebo-controlled Phase III studies in order to demonstrate Translarna’s lack of efficacy in DMD patients. The analysts from Jefferies were right to point out the ‘limited impact’ of Sarepta’s aberrant approval of Exondys 51 on PTC Therapeutics Inc.’s refusal to file letter from the FDA for Translarna (ataluren) in the treatment of DMD. This is because PTC, unlike Sarepta, conducted two large placebo-controlled Phase III studies in order to demonstrate Translarna’s lack of efficacy in DMD patients. This did not stop investors buying up shares of PTC and fellow BioMarin Pharmaceutical Inc. whose stock prices finished last week up 28% and 1%, respectively. BioMarin’s subdued share price performance in response to the FDA’s open-door policy on previously failed DMD drugs probably had more to do with it being rumored as a possible acquirer for Sarepta.

Thankfully, cooler heads started to prevail towards the end of last week when the analysts from Cowen published their 2,966-page Biotechnology Quarterly report in which the NBI was reported to be 27% below July 2015’s high and ‘there is not much enthusiasm for biotech among [generalist] investors’. In recent weeks the acquisitions of GW Pharmaceuticals PLC and Biogen Inc. have been rumored, bathed in the supporting glow of sell-side validation, and then disapproved again. Whilst there is indeed a dire need at big pharmaceutical and biotechnology companies like Johnson & Johnson and Gilead to buy commercial-stage products, as Pfizer Inc. demonstrated with its acquisition of Medivation Inc., perhaps one reason for their reticence is that the NBI is only 27% below its all-time peak.

This continuing crying wolf will continue to grate on investors’ view of the sector. In their quarterly review, the analysts from Cowen cited the political environment, the move away from risky assets and the perceived lack of new product launches as being responsible for the lacklustre opinion of the prospects for biotech stocks. I would venture that it is also the sell-side’s promotion of their corporate clients as imminent acquisition targets despite the significant differences from those companies recently acquired that will continue to keep a lid on the sector. The title of the Hall & Oats 1984 track offers some good advice. Some things are better left unsaid.

The Magna Biopharma Income fund holdings include Allergan, Gilead and Pfizer.

Andy Smith is chief investment officer of Mann Bioinvest. Mann Bioinvest is the investment adviser for the Magna BioPharma Income fund which has no position in the stocks mentioned, unless stated above. Dr Smith gives an investment fund manager’s view on life science companies. He has been lead fund manager for four life science–specific funds, including International Biotechnology Trust and the AXA Framlington Biotech Fund, and was awarded the Technology Fund Manager of the year for 2007.
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.

Late-stage clinical developments for the week 16 September - 22 September 2016

<table>
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<tr>
<th>LEAD COMPANY</th>
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<td>Allergan PLC</td>
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<td>AstraZeneca PLC</td>
<td>-</td>
<td>cediranib</td>
<td>ovarian cancer</td>
<td>EU</td>
</tr>
<tr>
<td>AbbVie Inc.</td>
<td>-</td>
<td>Cokiera (dasabuvir, ombitasvir, paritaprevir, ritonavir)</td>
<td>hepatitis C</td>
<td>EU</td>
</tr>
<tr>
<td>Bayer AG</td>
<td>-</td>
<td>Adempas (riociguat)</td>
<td>pulmonary arterial hypertension associated with congenital heart disease</td>
<td>EU</td>
</tr>
<tr>
<td>Advanced Accelerator Applications SA</td>
<td>-</td>
<td>Lutathera (lutetium labeled somatostatin analog)</td>
<td>carcinoid tumor</td>
<td>EU</td>
</tr>
<tr>
<td>Teva Pharmaceutical Industries Ltd.</td>
<td>Active Biotech AB</td>
<td>Iaquiminod</td>
<td>multiple sclerosis</td>
<td>US</td>
</tr>
<tr>
<td>Sarepta Therapeutics Inc.</td>
<td>-</td>
<td>Exondys 51 (etiplirsen)</td>
<td>Duchenne muscular dystrophy</td>
<td>US</td>
</tr>
<tr>
<td>Allergan plc</td>
<td>Adamas Pharmaeuticals Inc.</td>
<td>Nanzaric (memantine and donepezil) extended release tablets</td>
<td>Alzheimer's disease</td>
<td>US</td>
</tr>
<tr>
<td>Recordati Industria Chimica &amp; Farmaceutica SPA</td>
<td>Apricus Biosciences Inc.</td>
<td>Vitaros (alprostadil)</td>
<td>erectile dysfunction</td>
<td>Czech Republic, Slovakia</td>
</tr>
</tbody>
</table>

Source: Biomedtracker
OncoLogic company, Nouscom, has appointed Marina Udier Blagovic to the newly created position of chief operating officer. Jean-Paul Prieels will also be joining the company as non-executive director along with Vincent Brichard and Gianni Gromo, who have been appointed board observers. Blagovic joins the company from Versant Ventures where she was an operating principal, prior to this she was the global head of neurodegeneration at Novartis. Before Novartis, Blagovic worked in the healthcare sector of McKinsey & Company in Chicago. Prieels was senior vice president of research and development at GSK Biologicals (now GSK Vaccines). He currently serves as director of Vaximm AG and is on the independent advisory board of Curevac. He has also been member of the scientific advisory board of the Singapore Bioprocessing Technology Institute. With over 25 years’ experience, Brichard spent 15 of those at GSK, where he was senior vice-president in R&D and on the board of directors. He is currently on various scientific councils and boards of directors.

Chad Bateman has been appointed Inotec AMD Limited’s CEO – effective Oct. 1, 2016. Most recently, Bateman was vice president and general manager, Europe and a member of the extended global leadership team of Acelity. He also carries 20 years of experience in sales and marketing and worked in organizations like Olympus and CR Bard Inc.

Swedish Orphan Biovitrum AB (Sobi) has appointed Milan Zdravkovic senior vice president, head of research and development – effective Nov. 1, 2016. Zdravkovic joins Sobi from Novo Nordisk where he spent 18 years in the research and development organization, with his most recent role being corporate vice president, obesity.

Cambridge based Dragonfly Therapeutics Inc. has added medical doctor and Stanford University’s scientist Ronald Levy, to its scientific advisory board. He specializes in lymphoma including Non-Hodgkin’s Lymphoma, Burkitt’s Lymphoma and Hodgkin’s Disease. Currently he is a member of the National Academy of Sciences and of the Institute of Medicine.

Nina Henderson has been appointed to Hikma Pharmaceuticals Plc’s board as an independent non-executive director. She will become a member of the audit, remuneration and nomination committees. Previously Henderson was corporate vice president of Bestfoods where she held various international general management and executive marketing positions for global consumer branded and food service businesses. Currently she is director of Regus Plc. where she is chair of the Remuneration Committee and CNO Financial Group Inc. and she is also director of the Visiting Nurse Service of New York Inc., including VNSNY Choice Health Insurance and VNSNY Home Health Care. Hikma has also announced that independent directors, Michael Ashton and Ron Goode, are both retiring from the board. Ashton who joined the board in 2005 will step down in 2017 and Goode, who joined in 2006, will step down in 2018.

Hugh O’Dowd has been appointed Neon Therapeutics’ CEO, succeeding interim CEO Cary Pfeffer, a partner at Third Rock Ventures, who is assuming the position of chair of the company’s board of directors. O’Dowd joins Neon from Novartis where he held various leadership roles, including chief commercial officer and health of global strategy of Novartis Oncology. He started his career in the pharma industry in 1992 at Glaxo in sales and later moved to Novartis.

Cancer focused Jounce Therapeutics has appointed Stephen Farrand chief technical officer. He was previously vice president, bioprocess development at Merck where he was part of the development and first approval of Keytruda.
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