A Bird’s Eye View Of The Rare Disease R&D Landscape

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The number of drugs in development for rare diseases have increased by 56%, with the number of rare diseases on the development map also increasing by 23% in just three years, demonstrating ongoing interest and seemingly increased enthusiasm for research within these areas of high unmet needs.

Rare diseases truly give meaning to the notion of unmet medical need as 95% of rare diseases do not have any drug treatments approved by the FDA. While individual rare diseases may only affect a small pool of patients, rare disease patients as a whole number an estimated 350 million people worldwide.

Perhaps most troubling is the fact that about half of these patients are children, 30% of whom will not live to see their fifth birthday according to Global Genes, a rare disease patient advocacy group. Various regulations and initiatives have been, and continue to be, implemented to both facilitate and incentivize rare disease R&D, and the pharma industry appears to be responding accordingly.

The focus of this analysis is limited to the 499 Pharmaprojects indications considered to be a rare disease, as defined by the FDA and EMA. Specifically, these are the conditions that affect 200,000 people or less in the US (FDA) or ones with a prevalence of 1 in 2,000 people, which is the equivalent of fewer than 250,000 people in the EU (EMA). Pharmaprojects last assessed the rare disease landscape in November 2013, and found that 2,907 drugs were in active development for at least one of 364 rare diseases. As of October 2016, a total of 4,549 drugs are now in development for at least one of 447 rare diseases. This is an increased drug count of 56% and 23% more rare diseases after nearly three years, demonstrating ongoing interest and seemingly increased enthusiasm for research within these areas of high unmet needs.

With regard to the breakdown by disease status, or the highest phase of development a drug has reached for a particular disease, preclinical and early-to-mid stage clinical research continues to be the most active. In addition to the large proportion of early stage development, a total of 1,387 launches have taken place. (Exhibit 1) Since drugs in development for more than one rare disease are counted for each individual indication, the same drug can be counted both across and within the same development phase. As such, this total of 1,387 launches represents 950 unique drugs that have been launched across 232 different rare diseases.

Exhibit 2 provides the development landscape across therapeutic areas (TAs) by the number of drugs as well as the number of diseases. Consistent with the 2013 analysis, Cancer and Infectious Disease (ID) continue to be the industry’s focus within active drug development and both areas are the most prolific in terms of...
As those of you in America recover from your first post-truth Thanksgiving, we hope you are at least a tiny bit thankful for Scrip and its old-fashioned adhesion to notions of objective reality.

This week we mine our databases to create a faithful portrait of the state of the industry’s R&D pipeline on page 5, as well as taking a deep, spin-free dive into the development of drugs for rare diseases (see cover story) and tuberculosis (page 20).

Elsewhere in this issue, we faithfully report the words of industry executives including those of Teva, Pfizer and Bayer as they expound upon their strategies for organic and externally sourced growth.

Turn to page 6 for a digest of the Trump/Brexit flavors sprinkled liberally over the biopharma cogitation at this year’s FT Healthcare conference in London, and to page 21 for Andy Smith’s take on pharma stock movements following the US election result. But if you are hankering after another serving cooked up in media’s post-truth kitchen, you are looking in the wrong place.

**exclusive online content**

**Video: Genmab CEO Talks About The Commercial Potential And Partnering Success Of Antibody Therapies**

Genmab’s Jan van de Winkel talks to Sukaina Virji about the excitement surrounding its multiple myeloma drug Darzalex (daratumumab), the potential of multiple sclerosis candidate ofatumumab, and how he’ll always be a scientist at heart.


**Out-Going GSK CEO Andrew Witty Tells Pharma To Evolve Or Die**

The veteran pharma executive Andrew Witty says time – if not already gone - is running out fast for those biopharma companies who have not yet begun their necessary structural transitions.

Novartis Woos Payers With Data Showing Entresto Earns Its Keep

With Entresto sales slowly climbing to $53m in third quarter, Novartis releases data supporting value of heart failure drug in preventing costly hospitalizations at the annual American Heart Association meeting.

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A s part of a package supporting its sluggish selling heart failure drug Entresto with payers, Novartis AG released additional data showing that the drug reduces the rate of heart failure hospitalizations and deaths related to the condition compared to the standard of care enalapril.

The FDA’s approval of Entresto, which combines the neprilysin inhibitor sacubitril with the angiotensin receptor blocker valsartan, in July 2015 was supported by robust outcomes data in the PARADIGM-HF study, in which it reduced the rate of death or hospitalization for heart failure — the primary endpoint — by 20% compared with the generic angiotensin converting enzyme inhibitor enalapril, in heart failure with reduced injection fraction.

Novartis said that it had designed the PARADIGM-HF trial in a way that would allow incorporation of resource utilization into labeling. This paved the way for a risk-sharing deal with Aetna Inc.

Despite positive cost-effectiveness analyses, the drug struggled to get off the ground commercially because of market access barriers by payers. At the American College of Cardiology annual meeting in March, heart failure experts complained of onerous paperwork requirements associated with getting reimbursement for Entresto.

The company presented data showing that the combination also was associated with a 20% to 24% reduction in subsequent hospitalizations compared with enalapril in a new post-hoc analysis from the pivotal trial presented on Nov. 15 at the American Heart Association annual meeting in New Orleans.

About one-third of patients hospitalized for heart failure have a repeat episode and the data are great for the patients and great for payers, said Vasant Narasimhan, global head of drug development and chief medical officer at Novartis. “In the current environment, it’s very important to generate data that is really compelling for payers,” he said in an interview.

In other data presented at the meeting, the company showed the drug was associated with lower risk for severe hyperkalemia, or high potassium, and more diuretic dose reductions.

The exec said that he hopes the data increase the confidence of physicians to use Entresto, patients to stay on therapy and payers to reimburse.

One of the biggest drivers of costs in the health system is hospitalization. By keeping patients at home and well, the data give the company a powerful argument to go to payers and say that they know patients are likely to be hospitalized multiple times over the years, he said.

Novartis is also in partnership with large insurers in the US and health systems around the world in quantifying the impact of Entresto. In addition to Aetna, the company has outcomes-based risk sharing deals in place with Cigna Corp., Humana Inc. and Harvard Pilgrim Healthcare.

In an interview from the AHA meeting, Datamonitor analyst Kevin Shannon said that sentiment toward insurance coverage at the meeting was positive and appears to have improved since the time of approval.

In addition to reimbursement problems, cardiologists have complained about the complexity of dosing (for example, the starting dose is 24 mg sacubitril/26 mg valsartan).

Narasimhan said that the PARADIGM-HF study is persuasive in terms of outcomes and that it does not think it needs to run real world outcomes trials to provide further evidence of benefit, but there is a need for real world studies on switching from other medications to Entresto and trials are ongoing in this area, he said.

“That really has been much more of our focus as well as trying to generate more data on quality of life,” he said.

THE COMMERCIAL SLOW ROAD

Novartis’ Entresto and Amgen Inc’s heart failure drug Corlanor (ivabradine), approved by FDA in April 2015, got a boost in May with recommendation for use in treatment guidelines in the US and Europe. Novartis was happy to report in the third quarter that things were improving, with $53m in sales, in line with its goal of reaching $200m in sales for 2016, though obviously far lower than what was originally expected for the drug’s first year on the market.

Entresto is one of 12 late-stage assets Novartis is counting on for good future growth, with sales of $1bn each. Amgen still has not broken out sales for Corlanor, which is a hyperpolarization-activated cyclic nucleotide-gated channel blocker approved.

Anthony Hooper, Executive-VP global commercial operations, said that a number of restrictions are in place by payers and the standard of care is in flux with respect to use of Entresto.

“So the business to date has been limited. Access is limited and a fair amount of paperwork is required by physicians and cardiologists to get patients on Corlanor,” Hooper said during the company’s Oct. 27 earnings call.

Despite inclusion in heart failure guidelines, Corlanor sales have been “modest to date as it faces payer hurdles,” the exec said, adding that the company does “not expect a dramatic change in this trend in the near future.”

Amgen and partner Cytokinetics Inc. presented additional data from the Phase II COSMIC-HF study of the new heart failure candidate omecamtiv mcebarit at the AHA meeting, demonstrating improvements in left ventricular function and volumes. Amgen has designed Phase III development, which is a cardiac myosin activator, with payers in mind. A Phase III study will begin enrolling in the first quarter of 2017.

In contrast with Amgen’s comments on Corlanor, Novartis presented a more optimistic outlook for future growth of Entresto during its Oct. 25 earnings call, noting that prior authorization requirements are easing and that the reimbursement picture will look much better in 2017.

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Teva Hits Pause On Business Development As Some Deals Stumble

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Teva CEO Erez Vigodman said the company will step away from business development for the “foreseeable future” while it digests the acquisition of Allergan’s generic drug business.

Teva Pharmaceutical Industries Ltd. CEO Erez Vigodman said the company will focus on organic growth and step away from business development for the “foreseeable future” as it digests the $40.5bn acquisition of Allergan PLC.

“A significant amount of capital has been deployed over the last 12 months to acquire assets and partner with other companies in order to enhance our existing areas of growth and create new ones,” Vigodman said during the company’s third quarter sales and earnings call Nov. 15.

“We are determined to use the [Allergan] deal as a catalyst to transform Teva even further and drive even more efficiencies throughout the entire organization,” he added.

It’s no surprise the company needs some time to execute on the enormous acquisition of Allergan’s generics. The deal, finalized in September, cemented the company’s leadership position in the segment with an 8% market share.

Even with the transformative acquisition underway, Teva continued to look outside to bolster its position in biosimilars. It announced a commercialization deal with Celltrion Inc. in October that covers biosimilars of Roche’s Herceptin (trastuzumab) and Rituxan (rituximab).

But the company also has faced some issues with smaller deals executed under Vigodman’s leadership. One is the acquisition of the Mexican pharmaceutical manufacturer Rimsa for $2.3bn in 2015, a deal intended to bolster Teva’s position in Latin America and position it for more acquisitions in the growing region.

Vigodman declared the Rimsa acquisition a “failure” during the third quarter call. Teva filed a lawsuit against Rimsa for fraud and breach of representation in the purchase agreement, he told investors, after Teva uncovered evidence of information manipulation regarding the drug development and manufacturing carried out at Rimsa over an extended period of time.

“These violations were concealed from us during the due diligence process by presenting us with false records,” he said. Teva did not disclose the situation earlier, because it was in settlement negotiations with local agencies, he said. Now Teva has put in place a full remediation plan to address the issues identified.

Teva is continuing to integrate Rimsa and the deal’s troubling result does not change the company’s plans to build a business in Mexico, Vigodman said, but it will take longer than expected. “We believe that over time we will be able to realize the opportunities that the Mexican market provides for us,” he said.

Vigodman also addressed the US Department of Justice investigation into price collusion in the generic drug industry. Reports have surfaced that charges in the case, involving several drug makers, could be filed soon.

“We disclosed, and I’m reiterating it here today, that we are not aware of any fact that would give rise to an exposure to Teva with respect to the investigation,” Vigodman said.

Teva reported third quarter revenues of $5.6bn, up 15% compared to the third quarter of 2015, primarily due to the inclusion of revenues of $887m from the Allergan generics business, following the close of the deal on Aug. 2. Gross profit was $2.8bn, up 1% compared to third quarter 2015.
INFOGRAPHIC

The R&D Year In NUMBERS

A snapshot of the industry's research and development activity in 2015/16.

**Products In Active Developement By Therapy Area**

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<thead>
<tr>
<th>Therapy Area</th>
<th>2014</th>
<th>2015</th>
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<tbody>
<tr>
<td>Alimentary/Metabolic</td>
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<tr>
<td>Blood &amp; Clotting</td>
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<td>Cardiovascular</td>
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<td>Dermatological</td>
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<td>Genitourinary</td>
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<td>Hormonal</td>
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<td>Immunological</td>
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<td>Anti-infective</td>
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<td>Anticancer</td>
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<td>Musculoskeletal</td>
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<td>Neurological</td>
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<tr>
<td>Sensory</td>
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- **14,392** products are in active development by pharma and biotech
- **11,744** of the products in development are new active substances
- **2,733** The number of products discontinued* from the pipeline so far in 2016
- **3,168** The number of products added to the pipeline in 2016

**Number of New Active Substances Launched in Their First Markets**

<table>
<thead>
<tr>
<th>Year</th>
<th>2014</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
<th>2010</th>
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<tr>
<td>2015</td>
<td>46</td>
<td>61</td>
<td>48</td>
<td>41</td>
<td>27</td>
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**R&D Spend and Pharma Sales**

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<tr>
<th></th>
<th>Pharma R&amp;D spend** ($m)</th>
<th>Pharma sales** ($m)</th>
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<tbody>
<tr>
<td><strong>All companies</strong></td>
<td></td>
<td></td>
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<tr>
<td>2014</td>
<td>143,549</td>
<td>756,670</td>
</tr>
<tr>
<td>2015</td>
<td>145,415</td>
<td>721,590</td>
</tr>
<tr>
<td><strong>Top 20 companies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>94,387</td>
<td>508,881</td>
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<tr>
<td>2015</td>
<td>94,477</td>
<td>495,214</td>
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</tbody>
</table>

**Top 10 pharma companies by 2015 R&D Spend (in $m)**

<table>
<thead>
<tr>
<th>Company</th>
<th>2014</th>
<th>2015</th>
<th>change</th>
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<tbody>
<tr>
<td>Novartis</td>
<td>8181</td>
<td>8738</td>
<td>-6.4%</td>
</tr>
<tr>
<td>Roche</td>
<td>8959</td>
<td>8694</td>
<td>3.0%</td>
</tr>
<tr>
<td>Pfizer</td>
<td>8393</td>
<td>7690</td>
<td>9.1%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>6213</td>
<td>6821</td>
<td>-8.9%</td>
</tr>
<tr>
<td>Merck &amp; Co</td>
<td>7471</td>
<td>6704</td>
<td>11.4%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>5579</td>
<td>5997</td>
<td>-7.0%</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>4534</td>
<td>5920</td>
<td>-23.4%</td>
</tr>
<tr>
<td>Sanofi</td>
<td>6203</td>
<td>5836</td>
<td>6.3%</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>5684</td>
<td>5447</td>
<td>4.4%</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>4733</td>
<td>4796</td>
<td>-1.3%</td>
</tr>
</tbody>
</table>

Footnotes:
*Either discontinued or re-classified as "No Development Reported" by Pharmaprojects during 2016 until Oct. 25
**For the Scrip 100 dataset of pharma and biotech companies with at least $1m R&D spend and/or sales of at least $10m (620 companies)
Sources: 1Pharmaprojects (Oct. 25, 2016) 2Pharmaprojects 3Scrip, Citeline 4Scrip
Seeking advice and future direction, speakers and attendees at this year’s FT biopharma conference in London were told little of substance other than to adapt to big change and that more is on the way.

A mixture of relief and apprehension was heard at this year’s FT biopharma conference with most talk centered on what Donald Trump’s shock US presidential election win and Britain’s “Brexit” vote mean for the UK Life Sciences sector amid warnings the industry must adapt further to huge challenges already facing it.

An increasingly tight, competitive landscape with aggressive resistance from governments and pushback from payers will continue to spread globally, participants were told by various speakers at the two-day FT Global Pharmaceutical and Biotechnology Conference which took place Nov. 16 – 17 just yards from the US embassy in London. Not surprisingly, the seismic shift in US politics and its likely implications for the Life Sciences sector topped the bill of topics, along with the UK’s June referendum decision to exit the European Union.

Shell Shocked Pharma Ponders Future Directions Amid Seismic Changes

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PAST
FUTURE
PRESENT

PHARMA RELIEF RALLY SEEN SHORT-LIVED

Speakers said the rally in biopharma stock prices immediately after the defeat of Democratic candidate Hillary Clinton reflected a relief rally for the sector but would no doubt be short lived. The real message is that drug prices in the US healthcare market will continue being under rising pressure, helping necessitate new business approaches if pharma companies want to be successful and grow in the future.

“It’s probably true that if Hillary Clinton had been elected that there would have been things she would have done that would have been adverse to pharma,” said David Redfern, GlaxoSmithKline PLC’s chief strategy officer, adding: “Maybe Trump will do less of that in the short term, but it’s clear the pricing trends in the US are more driven by commercial plans and Medicare and by formularies and by employers wanting to have healthcare costs to come down, putting pressure on insurers to restrict new formularies and so forth - and all of that is going to continue and probably exacerbate.”

Sanofi CEO Olivier Brandicourt agreed, saying that the post-election rally for pharma on the stock markets was welcome, “but I wouldn’t make an assumption that the future administration will not look at drug pricing and thereby add to pressure … Trump has in his administration very powerful voices who have been very vocal on drug pricing over the last few months, so altogether I would expect that market debate to continue.”

WORLDWIDE WITTY WARNING

Out-going GSK CEO Andrew Witty echoed that message more firmly in his swan song speech to the conference, warning that the heady days of pharma reaping huge profits from drugs sold in the US healthcare market at high prices are over, and that drug companies need completely new strategies - and to apply them globally - to remain viable and offset the decline in profits generated from the US.

“This industry is no longer capable of growing at the rate that it has historically grown,” Witty said. “If you believe it is capable of doing that then you have to believe one of two things: either a gigantic growth in the proportion of total US healthcare spend on drugs, or a continuation of way beyond 20% of GDP spent on US health-care. Both of those are quite challenging assumptions upon which to build your long-term strategy. Therefore, I would argue that you need to think of a very different approach.”

Witty, who took the helm at GSK in 2008 and is retiring in 2017, told a hushed audience that “the challenge for this industry is whether we’re clever enough to reinvent our commercial business models, both from a pricing view, our cost structures, and our go-to-market models, to ensure that we are able to effectively migrate from an industry which has been far too price orientated in its determinants to one that is much more volume orientated.”

Another speaker, Deloitte’s life sciences & healthcare lead Mike Standing, told the conference the dilemma facing pharma and the need to restructure is not unlike the necessary revamp that the oil drilling sector faced. “There comes a time when the business model needs a transition period to take on a different set of risks, so its move from on-shore to off-shore drilling and then from offshore to deep water drilling was a big transition for the oil industry – such transformation requires real leadership, it requires organizations to take a partnering position, but it needs to do that in the context of running its core businesses successfully at the same time,” Standing said some big pharma companies have already embarked on restructurings of comparable scale, singling out those by GSK, Roche, Novartis AG and Johnson & Johnson. “This is a long-term industry, and you might not get all the dividends in the first couple of years - but you need to do it to position yourself for the future,” he added.

Changed business models need to go hand-in-hand with more open and coordinated interactions with stakeholders if new innovative drugs are to be more readily approved and reimbursed by governments. This would benefit both sides, Brandicourt said in a speech to the conference.

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Pfizer Inc. has a goal to turn its Essential Health business unit – originally established to help the company manage the loss of exclusivity of Lipitor and other blockbuster drugs – into a growth driver. Group President John Young and other top executives outlined the strategy to get there during a media briefing at the company's headquarters in New York Nov. 10.

Essential Health has a lower profile than Pfizer's other business unit, Innovative Health, under which the company develops and markets innovative brand medicines and vaccines like Xeljanz, Ibrance and Prevnar. Nonetheless, Essential Health is a high-volume, cash-generating business responsible for marketing the company's mature drugs, including those that have lost exclusivity.

The business – which includes generic drugs, a large sterile injectables portfolio and biosimilars – is substantial. Essential Health is a roughly $24bn business, accounting for just under half of Pfizer's sales, and it generates two-thirds of the company's cash flow. It includes some 600 medicines marketed around the world.

For the last five years, Pfizer has been debating whether or not to break up its two distinct businesses into separate companies, but in September, the board of directors and executive management finally reached a decision that a split wouldn't unlock trapped value and would result in less financial flexibility.

Now that Pfizer has decided to stay as one company, management is talking about a clear strategy for transforming Essential Health into a growth driver. The proposition is challenging because of the very basis around which the unit was established in 2008, when it was called Established Products and was positioned to commercialize products after market exclusivity was lost.

"It was really pulled together by Pfizer's strategic intent to have capabilities to help us manage what five to seven years ago was the biggest wave of LOEs that any company in the industry was ever going to have to go through," Young said. Pfizer lost exclusivity for Lipitor, the best-selling drug in the history of pharma, in 2011. But by now Pfizer has largely cycled through the worst of its patent cliff, though Viagra is still set to face generic competition in December 2017.

Earlier this year, Pfizer changed the name of its Established Products unit to Essential Health, part of a strategy to expand the remit of the business beyond managing declining revenues of drugs that have lost exclusivity. The Essential Health business grew 7% in the third quarter, but the growth was because of Pfizer's acquisition of Hospira Inc. in September 2015. Excluding Hospira, Essential Health sales declined 8% year-over-year in the third quarter.

RESHAPING THE PORTFOLIO
The $16bn acquisition of Hospira gave Pfizer a substantial generic sterile injectables portfolio, vaunting the company, which sells its own branded sterile injectables, into the number one position in the space. It also gave Pfizer a leading position in biosimilars, with a portfolio of marketed biosimilars in Europe and US rights to the biosimilar Inflectra (infliximab-dyyb), which is poised to launch Nov. 21 as the first biosimilar version of Johnson & Johnson's anti-TNF Remicade (infliximab) in the US.

Pfizer also recently bolstered its Essential Health portfolio with the acquisition of AstraZeneca PLC's late-stage small molecule antibiotics portfolio for $550m upfront, plus a delayed $175m payment due in 2019. Pfizer Essential Health is the world's leading anti-infectives company, Young asserted.

The AstraZeneca deal reflects how serious Pfizer is about expanding the mandate for Essential Health to include new higher-value medicines and to use business development for growth.

Active portfolio management – including deals to expand the portfolio and to divest non-priority assets – is one of the core elements of Pfizer's growth strategy.

At the same time, Pfizer is working to identify profitable but declining areas of the portfolio that would be better in someone else's hands, Young said.

"The process is one we are still following through," he said. "In some ways we don't have a burning platform to say here's an area we absolutely have to get out of." In October, Pfizer announced it would sell Hospira Infusion Systems to ICU Medical for $1bn in cash and stock.

"That's an example of a nice business, but frankly probably has a better home outside of Pfizer," Young said.

Other elements of Pfizer's strategy include growth in emerging markets, where the company sees an opportunity for branded generics carrying Pfizer's name to stand for high quality and to make improvements on mature medicines.

"Because of the heritage of the Pfizer brand name and what it is that we stand for and the quality of the medicines we provide it is quite a unique business," Young said.

A $1BN R&D BUDGET
Pfizer is also investing in R&D in the business unit, about $1bn to $1.1bn, the unit's chief financial officer, Sanjeev Narula, said. It's only a small portion of Pfizer's broader R&D budget; the company spent $7.65bn on R&D in 2015.

Pfizer established a separate R&D organization within Essential Health about 14 months ago following the acquisition of Hospira, according to Essential Health Head of R&D Sumant Ramachandra. The unit combined the R&D work being done under the prior Established Products unit at Pfizer with some of the legacy Hospira team.

The budget is dedicated largely to maintaining regulatory standards for 600 plus brands around the world, Ramachandra said.

"What is left is quite significant, [and] will go primarily to investment in biosimilars," he said. Published online 17 November 2016
Drug count. This is true for both the total number of ‘drugs’ per TA, which includes a count for each indication when drugs are developed for more than one rare disease within the TA, and when drugs targeting multiple rare diseases within the TA are only counted once (the number of unique drugs per TA). The vast majority of anticancer drugs pursue multiple rare oncology indications, which is evident by the large difference between total and unique number of drugs. In general, most TAs do have drugs that pursue multiple indications, but not to the same dramatic extent as anticancer therapies.

ID also has the largest number of rare diseases with drugs in development, followed closely by Alimentary/Metabolic, however, both TAs also have the most designated rare diseases (represented by the total height of the columns in Exhibit 2a). Currently, drug development is active in 87% of rare infectious diseases and 92% of rare alimentary and metabolic conditions. Blood and Clotting, Genitourinary, and Hormonal all have R&D activity in each of their designated rare diseases, while the largest gap is observed in Dermatological and Cardiovascular, where 24% and 21% of their rare diseases, respectively, remain unaddressed by active drugs.

Although there appears to be some diversity given the number of diseases with active drugs, the top five rare diseases per TA by drug count indicate a skewed distribution of R&D activity. For most areas, the sum drug count for the top five indications within a TA tends to comprise the majority of the total drug count. The exceptions are Alimentary/Metabolic (106/386; 27%), ID (471/1404; 34%), and Neurological (251/599; 42%), which are also the three largest TAs with respect to number of rare diseases. Cancer is right on the edge and the sum of active drugs for the top five rare cancers represent 50% of the efforts within this area (1624/3235).

The largest rare indications by number of drugs are the top five cancers of pancreatic, ovarian, acute myelogenous leukemia, liver, and myeloma. Not only do these cancers lead the rare disease R&D overall, but the drug counts for a single cancer outnumber the total drug counts for some of the TAs. For instance, myeloma’s 255 drugs outnumber the total efforts for Sensory, Cardiovascular, Dermatological, Hormonal, and Genitourinary. The 417 drugs for the largest rare cancer, pancreatic, outpace all non-cancer TAs except for ID, Neurological, and Blood and Clotting. Outside of cancer, myelodysplastic syndrome, which can be triggered by cancer treatments, has the largest number of drugs, followed by tetanus prophylaxis.

RARE DISEASE LEADERS

Development is led by the trio of Sanofi, GlaxoSmithKline PLC (GSK), and Novartis AG, which all originated over 90 unique drugs each.

While Sanofi does top the list of key originators, it only has a small lead ahead of GSK and Novartis. After the top three, drug counts start dropping markedly. Nearly all originators are within the Top 20 Pharma peer set, based on the company’s revenue, with Eisai Inc. and the Medicines for Malaria Venture as the exceptions. The Medicines for Malaria Venture is truly an exception as it is the only non-profit foundation among the Top 15 rare disease drug originators, beating numerous pharma and biotech companies, in addition to the fact that the foundation focuses on a single rare disease.

Considering the vast majority of originators are also Big Pharma companies, the higher number of rare disease drugs could be a reflection of their large portfolios rather than their commitment toward combatting rare diseases. Besides the Medicines for Malaria Venture, whose sole focus is malaria, the non-Top 20 company Eisai is the leader by proportion of pipeline focus on rare diseases, with 43%, followed by Amgen Inc. (38%). Interestingly, Sanofi, GSK, and Novartis are still key players with a three-way tie as rare disease drugs comprise 31% of
Despite the additional challenges of developing drugs for rare diseases, it does not appear that this landscape will fade anytime soon. Sanofi, GSK, and Novartis lead the way with the largest number of drugs, as well as Eisai and Amgen who have dedicated a large percentage of their smaller portfolios to rare diseases. The pursuit of potentially life transforming treatments and preventative measures to avoid certain diseases continues, with a strong focus from the industry on ID and Cancer.

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Off-Label Communication: Pfizer Highlights Burdens Of FDA Policy

Seeking relaxation of US agency restrictions, Pfizer cites three examples where company delayed or decided against distributing medically relevant information beyond the product labeling; PhRMA survey shows almost half of all requests for information by prescribers and payers relate to off-label use.

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A t a recent US FDA hearing Pfizer Inc. highlighted three types of product-related communications that could become more prevalent if the agency revises its regulatory framework governing industry communications about off-label uses.

In two of the cases, Pfizer delayed distributing information about uses within the approved indication due to a lack of regulatory clarity. In the third case, the company did not distribute information on a pooled subgroup analysis after FDA said the proposed communication was misleading.

Although Pfizer declined to identify the drugs at issue in the three cases, the examples were aimed at showing the real-world implications of what industry says are limits to its ability to share important information not strictly within the confines of a product’s labeling due to existing FDA rules and a lack of regulatory clarity.

‘SUBSTANTIAL EVIDENCE’ STANDARD APPLIED TO COMMUNICATIONS

FDA convened the Nov. 9-10 hearing to gather input from industry, payers, consumer groups, patients and other stakeholders on issues related to communications by medical product manufacturers.

The hearing was part of the agency’s comprehensive review of regulations and policies governing firms’ communications about unapproved uses. The review was necessitated by several high-profile losses in First Amendment court cases, and the years-long requests by industry for additional guidance clarifying FDA’s regulatory approach to off-label communications.

The hearing’s first day included testimony from drug and device industry representatives who urged FDA to modernize its regulations so that companies can share truthful, non-misleading information about unapproved uses, or information on approved uses that extend beyond the product label, with health care providers and payers. Payers pushed for more access to pre-approval data.

The second day featured testimony from patient groups, academic researchers and consumer advocates, most of whom opposed any loosening of restrictions.

FDA’s next steps will be to evaluate the feedback and develop policy proposals of its own to address the changed legal landscape. Agency leadership may be skeptical of allowing more flexibility, but the incoming Trump administration is likely to be quite amenable to loosening restrictions.

In their testimony, Pfizer and the Pharmaceutical Research and Manufacturers of America (PhRMA) described the challenges companies face in determining what types of communications are acceptable from a regulatory perspective and responding to the large volume of requests for information from payers and prescribers.

Andrew Koenig, Pfizer Innovative Health’s inflammation/immunology group lead in North America medical affairs, said FDA’s current regulatory approach has negatively affected the company’s ability to share information that is “scientifically sound, medically relevant and truthfully presented — information that could and should help inform treatment decisions and patient care.”

Although the Food, Drug and Cosmetic Act requires “substantial evidence” for drug approval, “the agency, through its regulations and enforcement practices, effectively requires manufacturers to provide the same level of evidence to communicate information about a medicine’s clinical benefits – even when it is within the FDA-approved indication,” Koenig said in his written testimony. This approach constrains a manufacturer’s ability to share data and analyses that are not reflected in labeling, he said.

Furthermore, FDA’s guidance on good reprint practices “seems to pertain only to off-label uses, not on-label studies that do not fit the criteria of substantial evidence,” he said.

COMMUNICATIONS DELAYED OR REJECTED

Koenig discussed three examples where the company’s communications about uses outside of the product label were impacted by FDA’s policies. The first situation involved information on an alternative, but unlabeled, dosing regimen for an oncology drug.

“We know that many patients face tolerability issues with the labeled dosing regimen that may lead them to prematurely discontinue taking the medicine,” Koenig said. “About two years ago, several international oncology journals published results from multiple retrospective studies of our medicine in which patients who had experienced tolerability issues with the labeled dosing regimen were switched to a specific alternative dosing regimen. The publications suggested that this specific dosing regimen provided improved tolerability and was a good option for patients who could not tolerate the labeled dosing regimen.”

Koenig said that distributing reprints of the journal articles may have enabled some physicians to access the information, but “given Sunshine Act disclosure requirements, many physicians prefer not to ac-
The third scenario involved a communication based on subgroup population efficacy results from a published, pooled analysis of 10 randomized, controlled trials of one of the company’s drugs. Pfizer submitted the proposed communication to FDA for comments but 15 months later was informed by the agency that the communication was misleading.

“The agency stated that such a pooled analysis did not constitute substantial evidence or substantial clinical experience to support the claims and recommended deletion of the data,” Koenig said, adding that Pfizer never proactively shared the sub-group analysis outside of the scientific publication setting.

DEDICATED ADVISORY OPINION MECHANISM

Pfizer’s examples could lend support to an industry-backed proposal for a dedicated mechanism for FDA advisory opinions or a preclearance process for off-label communications.

The Medical Information Working Group (MIWG) is a coalition of drug and medical device companies. In 2010 as part of FDA’s transparency initiative, MIWG asked FDA to implement an advisory opinion mechanism, similar to that used by the Health and Human Services’ Office of Inspector General, so that manufacturers could obtain “timely binding advice” about proposed promotional and scientific exchange practices.

However, FDA denied the group’s request in a January 2011 report. The agency already has a process in place for companies to receive non-binding advisory comments on specific promotional pieces prior to dissemination, and the request to issue binding opinions may restrict its ability to respond to emerging issues, the report states.

At the off-label meeting, MIWG attorney Coleen Klasmeier, a partner at Sidley and Austin, renewed the group’s request for a dedicated advisory opinion mechanism.

“We continue to believe that it would encourage compliance with the law and help avoid unduly chilling beneficial speech if FDA were to accept our suggestion,” Klasmeier said in her testimony. “We ask FDA to give immediate and serious consideration to establishing a process to enable manufacturers to obtain advice from FDA on specific activities involving the dissemination of information that is not set forth in approved or cleared labeling.”

It’s possible that a dedicated advisory opinion process could be funded through a new user fee.

TAKING THE AMARIN ROUTE

PhRMA also supports the establishment of an optional preclearance process “such as the one that FDA agreed to through its litigation settlement agreement” with Amarin Corp. PLC, said Michael Labson, a partner at Covington and Burling.

Under a March 2016 settlement involving the triglyceride-lowering drug Vascepa (icosapant ethyl), Amarin may submit to FDA up to two proposed communications per year about off-label use before distributing them to doctors to determine if the agency has concerns. The settlement includes timelines for FDA review and the company’s response to any concerns flagged by the agency.

A preclearance process could be adopted as an adjunct to the existing advisory comment process or as a separate process, Labson said. “However structured, it is critical that the process provide timely feedback so that there is no undue delay in the review of proposed communications. The review would include a key focus on whether information is presented in a way that is truthful and non-misleading, including that there is appropriate contextual information and disclosures provided.”

HALF OF INFORMATION REQUESTS ARE OFF-LABEL

Like Pfizer’s Koenig, Labson also tried to highlight the current industry burden under FDA’s existing regulatory regime. For purposes of the off-label hearing, PhRMA surveyed its members to examine the extent of requests for such information by prescribers and payers.

“Based on data from 10 responding PhRMA member companies, in 2015 healthcare professionals and payers made over 340,000 total requests to the respective medical or customer service departments of these companies involving 765 total prescription drugs,” Labson said. “Of these total requests, over 180,000 requests involved having to share information from outside of the approved labeling – approximately 46% of the total requests.”

Published online 14 November 2016
Ibrance Trial Cements CDK4/6 Inhibitors As Standard Of Care In Breast Cancer

Full results for Pfizer Inc.’s cyclin-dependent kinase 4/6 inhibitor Ibrance in the confirmatory PALOMA-2 study cement the position of the class in the first-line treatment of hormone receptor-positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) breast cancer, with potential to move to the adjuvant and neoadjuvant settings. Data for Ibrance (palbociclib) in the first-line PALOMA-2 study were published in the New England Journal of Medicine on Nov. 17 by UCLA’s Richard Finn and colleagues, following up on a presentation at the American Society of Clinical Oncology meeting in June. The study examined Ibrance with letrozole in 666 postmenopausal women vs. letrozole with placebo. Ibrance/letrozole met the primary endpoint with median progression-free survival of 24.8 months versus 14.5 months for letrozole/placebo, a 42% reduction in risk of death. Overall survival is not mature yet. “CDK4 and CDK6 inhibition in combination with anti-estrogens is clearly a new standard for the treatment of advanced ER-positive breast cancer,” Johns Hopkins oncologist Antonio Wolff said in a Nov. 17 NEJM editorial accompanying the trial results. emily.hayes@informa.com, 17 Nov 2016

Intercept Seeks Long-Term Data To Build Ocaliva Market In PBC

Ocaliva (obeticholic acid) became the first new drug to market for primary biliary cholangitis (PBC) in 19 years with its June launch in the US, but its indication as second-line therapy in a chronic condition left lots of treatment questions and potential safety gaps for other PBC candidates to target. Intercept Pharmaceuticals Inc. CEO Mark Pruzanski explained in a Nov. 15 interview during the American Association for the Study of Liver Diseases meeting that his company is working toward long-term outcomes data that might mitigate some of those perceived gaps. Ocaliva is a bile acid analog that inhibits the farnesoid X receptor (FXR) and is in Phase III development for non-alcoholic steatohepatitis (NASH). The US FDA approved the drug for PBC on May 27 and formal European approval in that indication is anticipated by year’s end following a positive opinion in October from the Committee for Medicinal Products for Human Use (CHMP). joseph.haas@informa.com, 16 Nov 2016

Gilead’s Late-Stage R&D Misfire Gives Respite To Competing Myelofibrosis Therapies

The mixed top-line results from two Phase III studies of Gilead Sciences Inc.’s Janus kinase (JAK) 1/2 inhibitor, momelotinib, in myelofibrosis lifts the prospects of competitors marketing products for this difficult-to-treat disease. The results also cast yet another shadow over Gilead’s strategy to diversify its product portfolio away from HIV and hepatitis C therapies, that has been hit by several late-stage failures. Earlier this month, the US company said it would discontinue development of the LOXL2 inhibitor, simtuzumab, in non-alcoholic steatohepatitis (NASH) and all other indications, and discontinued development of the MM9 inhibitor GS-5745 in ulcerative colitis and Crohn’s disease. Development product failures are not uncommon in myelofibrosis, a rare bone marrow condition marked by disruption in blood cell production, the build-up of scar tissue in bone marrow, weakness, fatigue and an enlarged spleen. Sanofi’s JAK-2 inhibitor fedratinib failed in 2013, and CTI BioPharma Corp.’s JAK2/FLT3 inhibitor pacritinib also showed mixed Phase III results in the PERSIST-2 study this August. In Sept. 2016, Geron Corp./Janssen Inc. stopped a low-dose arm of a study in the condition involving the telomerase inhibitor imetelstat. Momelotinib did show some signs of providing a treatment benefit, including an effect on anemia-related endpoints. The JAK2 inhibitor met its primary endpoint in the SIMPLIFY-1 study of its use compared with Incyte Corp./Novartis AG’s Jakafi/Jakavi (ruxolitinib), but not in the SIMPLIFY-2 study of momelotinib compared with best alternative therapy. john.davis@informa.com, 17 Nov 2016

Amgen Plans 2017 Filings After Second Phase III CGRP Inhibitor Success

Amgen Inc.’s erenumab passed its second Phase III test in the treatment of episodic migraine headaches, keeping the company and its partner Novartis AG in the lead to bring a calcitonin gene-related peptide (CGRP) inhibitor to market. Three other CGRP-targeting biologics are in late-stage development to treat migraine headaches, but Amgen and Novartis have the only asset that’s completed Phase III clinical trials. The distinction is important, because the data reported for the four injectable CGRP inhibitors to date have been similar enough to keep analysts from declaring a clear winner based on safety and efficacy. Results from the Phase III STRIVE trial, which Amgen reported after the stock market closed on Nov. 16, also keep erenumab well ahead of oral and intranasal CGRP-targeting drugs. mandy.jackson@informausa.com, 16 Nov 2016
Bevacizumab Biosimilar Nears Market As Amgen Files First At FDA
JOHN DAVIS john.davis@informa.com

What is believed to be the first biosimilar version of Roche’s Avastin to be filed with the US FDA has come from Amgen working in collaboration with Allergan, with the two companies heading a dozen-strong group of companies racing to develop versions of the monoclonal antibody.

A biosimilar version of Roche/Genentech Inc’s Avastin (bevacizumab) has been submitted to the US FDA by Amgen Inc. and Allergan PLC, underlining their product’s leadership position among the dozen or so bevacizumab biosimilars in development, and the desire of the two US big pharma companies to broaden their oncology portfolios.

ABP 215 is the first bevacizumab biosimilar to be submitted for approval to the US FDA, Amgen believes. The product is also the first of four oncology biosimilars that Amgen and Allergan are jointly developing under an agreement signed in 2011 between Amgen and an Allergan predecessor company, Watson Pharmaceuticals Inc. Amgen is leading the collaboration in developing and initial commercialization of the four oncology products. ABP 215 is targeting a market that in the hands of Roche’s branded product saw sales of CHF5.1bn ($5.1bn) in the first nine months of this year. Amgen said it was developing ABP 215 for unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC), and metastatic carcinoma of the colon or rectum, metastatic renal cell carcinoma, and other region-specific indications.

For Amgen, developing biosimilar oncologics is an extension of its strategy to develop a series of novel oncology products, that have included bispecific antibodies and oncolytic viruses, in an effort to reinvigorate a product portfolio currently dominated by aging blockbusters like Enbrel (etanercept) and Neulasta (pegfilgrastim). These blockbusters are themselves being targeted by other companies for the development of biosimilars.

The news of the bevacizumab biosimilar filing comes at an awkward time for the development of biosimilars. The filing comes at an awkward time for the release of outcomes data, which are expected in early 2017.

GLAGOV is an intravascular ultrasound study examining the use of a monthly Repatha injection on top of background statin therapy compared with statin therapy alone in 968 patients undergoing coronary catheterization.

Positive results were reported on Nov. 15 at the American Heart Association annual meeting in New Orleans and published in the Journal of the American Medical Association by the University of Adelaide’s Stephen Nicholls and colleagues the same day. This year’s AHA meeting also featured data from The Medicines Co./Alnylam Pharmaceuticals Inc.’s subcutaneously delivered RNAi therapeutic inclisiran (ALN-POCSc), which also targets PCSK9 but is designed for much less frequent dosing.

Amgen had announced that Repatha demonstrated the ability to reduce plaque build-up in a top-line release about the GLAGOV study in late September, but the magnitude of the benefit and the strength of the data set were not clear at that time.

Participants in the study had a baseline LDL of 92.5 mg/dl.

Amgen’s Repatha Emerges Unscathed In GLAGOV PCSK9 Imaging Study

Full data from GLAGOV imaging study shows value of driving LDL below 60 mg/dl and presents no red flags for outcomes data due in first quarter of 2017.

The full dataset from Amgen Inc.’s GLAGOV imaging study shows a solid magnitude of plaque regression associated with the PCSK9 inhibitor Repatha and presents no red flags ahead of the release of outcomes data, which are expected in early 2017.

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Amgen’s Parsabiv’s Gets EU Approval While It Languishes At The FDA

Amgen Inc.’s Mimpara (cinacalcet) follow-on Parsabiv (etelcalcetide) has been waved through in the EU despite it hitting a US regulatory hurdle but analysts and Amgen believe FDA will eventually approve the drug for treating secondary hyperparathyroidism (sHPT) in adult patients with chronic kidney disease (CKD) on hemodialysis. Parsabiv had seemed set for a smooth regulatory review in the US with a data package made up of three Phase III clinical trials, including a head-to-head study comparing etelcalcetide to cinacalcet, but its road to launch hit a bump in August when the FDA issued a complete response letter for the application. Still, the European Medicines Agency a few weeks later backed the drug and on Nov. 11 the European Commission formally approved it for commercial use in the 28-nation EU. Amgen did not at the time say why it received the complete response letter for Parsabiv, since when analysts have speculated that it was related to concerns over side-effects. However, a spokesperson for the company has told Scrip the reason for the CRL was unrelated to safety issues.

sten.stovall@informa.com, 14 Nov 2016

Lilly’s Sarcoma Drug Likely To Be Used Widely Despite EU Conditional OK

The granting of conditional marketing authorization to Eli Lilly & Co.’s Lartruvo (olaratumab) by the EU Commission for the initial treatment of soft tissue sarcoma reflects the unmet need for the condition and growing flexibility shown by regulators to promising orphan drugs, forces that should combine into an acceptance of the drug by payers and regional health technology agencies in the region, analysts say. Lartruvo’s formal approval on Nov. 11 follows a recommendation for conditional marketing authorization from the European Medicines Agency in September as a new treatment for soft tissue sarcoma (STS). Having been designated as an orphan medicinal product by the EMA on Feb. 12, 2015, it is the first new therapy approved for the initial treatment of soft tissue sarcoma since doxorubicin’s approval more than 40 years ago and is the first monoclonal antibody to be granted authorization for the treatment of STS. Soft tissue sarcomas account for about 1% of all cancers. The therapy’s conditional approval is based on the results from the JGDG trial, a randomized, open label, Phase II study evaluating the safety and efficacy of Lartruvo in combination with doxorubicin. As part of Lartruvo’s EU conditional marketing authorization, Lilly will need to provide results from an ongoing Phase III confirmatory study, ANNOUNCE, a placebo-controlled, double-blind trial being conducted on 460 patients with advanced or metastatic soft tissue sarcoma. Until availability of the full data, the EMA’s drug advisory panel CHMP will review the benefits and risks of Lartruvo every year to determine whether the conditional marketing authorization can be maintained.

sten.stovall@informa.com, 14 Nov 2016

Celltrion’s Biosimilar Rituximab Edges Ahead With Korean Approval

Celltrion Inc. has received South Korean regulatory approval for its biosimilar version of Genentech Inc./Biogen Inc.’s monoclonal antibody Ma-bThera/Rituxan (rituximab), further broadening the South Korean firm’s presence as a first mover in the global biosimilar space and marking the first approval globally for the product. Sales of Rituxan, which targets CD20, totaled $7.3bn in 2015, marking the second biggest sales globally among antibody drugs after AbbVieInc.’s Humira (adalimumab). The Ministry of Food and Drug Safety approved Celltrion’s CT-P10, or Truxima, for indications including non-Hodgkin’s lymphoma, chronic lymphocytic leukemia (CLL), and rheumatoid arthritis (RA). Truxima is Celltrion’s third biosimilar antibody to receive a regulatory clearance. With the latest approval, Celltrion said it expects the ongoing regulatory process in Europe for biosimilar rituximab to progress “smoothly” following a submission to the European Medicines Agency (EMA) in October last year. After receiving the green light in Europe, it aims to begin commercialization of the product in 2017, widening the gap with its closest competitors.

jungwon.shin@informa.com, 21 Nov 2016

NICE Reverses View On Perjeta In Breast Cancer After Roche’s Price Cut

In its latest success in getting price concessions from drug makers, the National Institute for Health and Care Excellence (NICE) says it is now backing Perjeta (pertuzumab) to treat a certain form of breast cancer on the National Health Service in England and Wales after vendor Roche offered a confidential discount. The HTA’s decision endorsing the drug’s use in combination with Herceptin (trastuzumab) and the chemotherapy docetaxel as an option before surgery in patients with HER2-positive, locally advanced, inflammatory or early stage breast cancer to shrink the cancer so that it becomes operable, is a reversal of a rejection issued in May when NICE listed a number of reasons not to back Perjeta, including an inadequate data package from Roche; concerns around the use of pathological complete response as a substitute for overall survival outcomes; and the drug not being a cost-effective use of public funds.

sten.stovall@informa.com, 17 Nov 2016
Sanofi’s Franchise Defense Sees Biosimilar Insulin Lispro Under EU Review

Sanofi has filed a biosimilar version of Lilly’s antidiabetic Humalog with the EU’s CHMP, and received the all-clear for a new combination of Lantus and lixisenatide, as it tries to address difficulties in its diabetes franchise.

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The European Medicines Agency’s scientific committee, the CHMP, has begun evaluating Sanofi’s SAR342434, a biosimilar version of Eli Lilly & Co’s diabetes drug Humalog (insulin lispro). The product was accepted for review in September this year following the completion of two Phase III trials, SORELLA 1 and SORELLA 2.

The biosimilar is seen as part of Sanofi’s effort to address its difficulties in the diabetes area as sales of Lantus (insulin glargine) continue to decline in the face of competition. The company is also putting its money on sales of Toujeo, a new formulation of Lantus, as well as a combination of Lantus and the new drug lixisenatide that has just received the OK from the CHMP.

The SORELLA 1 trial involved 507 patients with Type I diabetes from the US, Europe and Japan who were also using insulin glargine, and was aimed at assessing safety and efficacy of SAR342434 and its non-inferiority versus Humalog.

Interim six-month results presented at the American Diabetes Association meeting in June this year showed the Sanofi drug to be as effective and well tolerated as Humalog. No differences were observed in the percentage of patients reporting hypoglycemia and a similar percentage of patients developed anti-insulin antibodies in both groups, according to a report in Practice Update.

SORELLA 2 was a six-month, randomized, open-label, parallel-group comparison of SAR342434 and Humalog in adults with Type 2 diabetes also using insulin glargine. The study completed in February 2016 and top-line results were expected in the third quarter of 2016.

Sanofi will be hoping the biosimilar can help it to address the problems it is experiencing with its diabetes portfolio at present. The company’s global diabetes franchise declined by 3.2% in the second quarter, followed by a further fall of 1.5% in the third quarter. In June this year, Bernstein analysts said the diabetes franchise remained “in flux,” with the company having lowered its estimates for the business twice over the past 18 months.

A key part of the problem is that sales of Lantus are falling, partly because of competition from Lilly/Boehringer Ingelheim GMBH’s biosimilar version, Abasaglar, which was launched in the EU and Japan in 2015 and is expected to reach the US market next month. Datamonitor Healthcare’s company profile of Sanofi predicts that Lantus revenues are set to fall by $5.2bn through to 2025 as a result of biosimilar competition, although it says the drug will remain a blockbuster during that period.

It remains to be seen whether SAR342434, if approved in the EU, will succeed in taking a significant market share from Lilly’s Humalog in return. Datamonitor has forecast a launch for the drug in the first quarter of 2018 in Japan, in Q4 2018 in the EU and in Q1 2019 in the US.

OTHER MEASURES TO PROTECT FRANCHISE

Sanofi has also developed Toujeo, a longer lasting formulation of insulin glargine, with the aim of positioning it as the preferred choice over both Lantus and any biosimilar competition. The product was launched in key markets including the US and the EU in 2015. In its third-quarter 2016 results presentation, the company said that Lantus and Toujeo were competitively positioned across most formularies in the US for 2017. Datamonitor says that while it expects significant revenues for Toujeo, it will probably not make up entirely for lost Lantus sales.

Meanwhile, Suliqua, Sanofi’s new combination of Lantus and the GLP-1 receptor agonist lixisenatide, is enjoying some success in Europe, having just received a positive opinion from the CHMP for patients with Type 2 diabetes. The product is expected to gain an EU-wide marketing authorization from the European Commission within two to three months.

Sales of Lantus are falling, partly because of competition from Lilly/Boehringer Ingelheim’s biosimilar

Sanofi noted in its third-quarter report that a new post-hoc analysis of data from a pivotal Phase III clinical trial with Suliqua, presented at the European Association for the Study of Diabetes (EASD), found that more patients who received the product reached their daily post-prandial glucose target than those who received only insulin glargine.

The product is also under review in the US where in August Sanofi submitted updated information on the pen delivery device as part of the NDA. “The additional information, submitted at FDA’s request, constitutes a major amendment to the NDA, resulting in an extension of the Prescription Drug User Fee Act goal date by three months, to late November 2016,” the report said.

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ACR 2016 Roundup: Remicade Copy Not So Similar; Mixed Sirukumab Results; Corbus’s Resunab Surge

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At ACR: Janssen reported data that show Celltrion’s Remicade biosimilar is not quite the same, but positive sirukumab results may not boost the Janssen and GSK biologic’s market prospects.

Drug efficacy was reported across a variety of inflammatory diseases during the American College of Rheumatology (ACR) Annual Meeting from Nov. 11 to 16 in Washington, D.C., but Johnson & Johnson’s Janssen Biotech Inc. shared data that show Celltrion Inc’s Remicade (infliximab) biosimilar may not be equivalent to the name-brand biologic in the treatment of rheumatoid arthritis (RA).

Janssen also showcased Phase III results alongside partner GlaxoSmithKline PLC for the Interleukin-6 (IL-6) inhibitor sirukumab, but the data may not improve the biologic’s competitive position versus the RA market leader, Corbus Pharmaceuticals Holdings Inc., however, saw its stock jump 51.3% to close at $8.85 on Nov. 14 after the company revealed statistically significant Phase II results for resunab in systemic sclerosis – a disease with no approved therapies.

Also, Xencor Inc. gained 11.2% to close at $25.25 based on positive interim Phase II results for XmAb5871 in IgG4-related disease, Roche’s Genentech Inc. posted significant Phase III results for the IL-6 inhibitor Actemra (tocilizumab) in giant cell arteritis, and J&J’s Janssen R&D LLC posted positive Phase II results for guselkumab in psoriatic arthritis.

REMSIMA (CT-P13) NOT SO BIOSIMILAR?

Janssen Biotech showed a mismatch between the efficacy of the anti-TNF blockbuster biologic Remicade and Celltrion’s Remsima (CT-P13) in two studies reviewing the treatment of Turkish RA patients with the two products. The data were presented during the ACR meeting less than a month after NOR-SWITCH, a Norwegian government-sponsored study, showed no statistically significant differences in treatment outcomes for patients who were prescribed Remsima in place of Remicade.

Janssen disputes the interchangeability of Remicade and Remsima in NOR-SWITCH, particularly in Crohn’s disease, and now the J&J subsidiary has its own data to support its claim that the two products do not provide similar efficacy.

A review of medical billing records from 1,044 Turkish RA patients who initiated treatment with Remicade or Remsima between July 2014 and June 2015—80% began treatment with Janssen’s product—showed a 44% discontinuation rate for Remsima versus 27% for Remicade. Also, Remsima patients were most likely to switch to Remicade while Remicade patients were switched most frequently to a different biologic.

A separate review looked at records for 3,018 Turkish RA patients who were stable on Remicade and remained on the medicine or switched to Remsima between July 2014 and June 2015. That study found that 148 patients were switched to Remsima and 70% of those individuals discontinued treatment within six months and 85% switched back to Remicade. Meanwhile, only 24% of patients who stayed on Remicade maintenance therapy discontinued treatment during similar six-month timeframes.

“Both of these studies were not randomized and, therefore, it is not known what role selection bias or the switching process itself may have played in discontinuation rates,” Janssen vice president of medical affairs Andrew Greenspan said in a statement from the company. “Nonetheless, fewer patients receiving appropriate treatment for a serious chronic condition is concerning and warrants further study.”

For its part, Celltrion commented on the NOR-SWITCH data presented during ACR, noting in a statement that “the efficacy and safety were maintained in patients switched to CT-P13 from originator infliximab and [the biosimilar] is not inferior to those who continued treatment with the originator. The results indicate that patients can be safely switched.”

SIRUKUMAB DATA VERSUS HUMIRA ARE MIXED

Janssen Biotech and GSK are developing sirukumab in a field in which it’s difficult for biologic medicines to compete given rheumatologists’ familiarity with TNF inhibitors, such as AbbVie Inc’s market-leading Humira (adalimumab) and Amgen Inc’s Enbrel (etanercept). Adding to that difficulty, the partners’ latest sirukumab data raise new doubts about the therapy’s prospects as the third IL-6 inhibitor to launch in the RA market.

Sirukumab went head-to-head with Humira in the Phase III SIRROUND-H clinical trial, which enrolled 559 biologic-naive RA patients who could not tolerate the first-line standard of care methotrexate (MTX), who were not good candidates for the oral drug due to safety concerns, or who did not see adequate efficacy on MTX monotherapy.

SIRROUND-H had two primary endpoints assessed at the end of 24 weeks of treatment: mean change from baseline in the Disease Activity Score 28 (DAS28) that’s used in Europe and the proportion of patients who achieved ACR50—a 20% improvement in DAS28 (DAS28; see table) scores. However, investigators described ACR50 responses as “similar” and not statistically significant across SIRROUND-H dose groups: 40mg of Humira every two weeks, 100mg of sirukumab every two weeks, and 50mg of sirukumab every four weeks. (See table)

Along with the mixed results, Humira may have a better safety profile than the higher sirukumab dose. At least one ad-
A Biomedtracker analysis in June of data from SIRROUND-D, which enrolled 1,670 patients with moderately to severely active RA who had an inadequate response to disease-modifying anti-rheumatic drugs (DMARDs), noted that positive results in that placebo-controlled Phase III study did not differentiate sirukumab from Roche’s Actemra or sarilumab, a new IL-6 inhibitor from Sanofi and Regeneron Pharmaceuticals Inc. that may reach the market before sirukumab.

Data versus Humira from SIRROUND-H also do not appear to substantially differentiate sirukumab from other IL-6 inhibitors or from TNF inhibitors, which are facing competition within the next few years from less costly biosimilars.

FDA approval for sarilumab was expected in October, but recently was delayed by a complete response letter related to manufacturing issues. However, Sanofi and Regeneron could move quickly to fix any manufacturing deficiencies and gain approval in the US before sirukumab, since Janssen and GSK only submitted their biologics license application (BLA) for their candidate in September.

The injectable IL-6 inhibitors also may see new competition from potentially less costly oral drugs in the near term, including the JAK1/2 inhibitor baricitinib from Eli Lilly & Co. and Incyte Corp., for which positive Phase III data versus placebo and Humira were presented during the ACR meeting.

Norwood, Massachusetts-based Corbus said that its Phase II results for resunab (JBT-101) in diffuse cutaneous systemic sclerosis exceed a “medically meaningful” threshold in the chronic, systemic autoimmune disease. Multiple doses of the drug were tested in 27 systemic sclerosis patients while 15 received a placebo. Individuals in the three resunab arms were treated with 5mg or 20mg once-daily or 20mg twice-daily for the first four weeks then transitioned to 20mg twice-daily for the next eight weeks and were monitored for four more weeks without taking the drug.

The ACR Combined Response Index in systemic sclerosis (CRISI) at the end of week 16 was the primary endpoint. The median CRISI score in the modified intent to treat population was 33% at 16 weeks versus 0% for placebo (p=0.044), but Corbus said a CRISI score of just 20% could be medically meaningful for systemic sclerosis patients.

About 90,000 people in the US and Europe – mostly women – have systemic sclerosis, a disease in which the immune system attacks healthy tissue, causing small blood vessel damage; fibrosis of the skin, internal organs, gastrointestinal tract and musculoskeletal system; and eventually cardiopulmonary disease that leads to early death. There are no treatments approved specifically for systemic sclerosis, which is treated with immunosuppressive agents, such as methotrexate and corticosteroids.

Resunab is an endocannabinoid-mimetic drug that preferentially binds to the cannabinoid-2 (CB2) receptor expressed on activated immune cells and fibroblasts to resolve inflammation and halt fibrosis. The FDA granted orphan drug and fast track designations for resunab in 2015 for systemic sclerosis, but the oral drug also is being tested in Phase II for the treatment of cystic fibrosis and skin-predominant dermatomyositis with plans for a fourth mid-stage program in lupus.

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**Pfizer Will Support Inflectra Launch With Dedicated Sales Force**

The company is on track to launch the first Remicade biosimilar in the US Nov. 21 using dedicated sales reps and resources from the innovative side of the business, though it will not be a traditional sales force.

Pfizer Inc. is on track to launch Inflectra, the first biosimilar version of Johnson & Johnson’s blockbuster anti-TNF Remicade (infliximab-dyyb) in the US on Nov. 21, Pfizer Essential Health North America Regional President Diem Nguyen said. The company plans to support the launch using a dedicated sales force while also leveraging commercial resources on the innovative side of the business.

“It will require a sales force, but not a traditional sales force,” Nguyen said, because the data packages are large and challenging to understand when it comes to comparing the similarity between products. “The field force will need to be able to have thoughtful conversations with physicians.”

Nguyen and other top executives from Pfizer’s Essential Health portfolio, including president John Young and head of R&D Sumant Ramachandra, outlined the business unit’s growth strategy during a briefing at Pfizer’s headquarters Nov. 10. Inflectra and biosimilars in general are expected to be an important driver for the business unit longer term. Pfizer has previously guided to a launch of Inflectra in late November even while patent litigation with J&J continues.

A dedicated sales force will be just one part of a three-pronged commercial strategy to support the launch, which will also include contracting and patient support services. Pfizer said it will also leverage existing hospital relationships – forged within its sterile injectable business – as it launches biosimilars. Pfizer acquired Inflectra and a substantial sterile injectables business with the $16bn acquisition of Hospira Inc. in 2015.

For more ACR Highlights click here: http://bit.ly/2eXR928

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jessica.merrill@informa.com, 14 Nov 2016
Merck KGAA Invests €260m In Production Value Chain in China

Germany’s Merck KGAA has augmented production capacity for its pharmaceutical business in China by opening a new €170m ($180m) drug plant in Nantong dedicated to the manufacture of medicines on China’s Essential Drug List (EDL). Following an initial €80m investment announced in 2013, the firm injected an additional €90m into the Nantong site, now home to the second-largest pharma manufacturing facility for Merck worldwide. Located within the greater Shanghai region, the facility sits on a 40,000 square meter site in the BioSpark cluster in Jiangsu Province, and is expected to begin commercial production in the second quarter of 2017. There is a further 20,000 square meters for future expansion and a yearly production capacity of up to 10 billion tablets is expected by 2021. In parallel with the inauguration, Merck also announced a new investment of approximately €90m to build a Nantong Life Science Center starting construction in March 2017, which will offer high purity inorganic salts, cell culture media, and rapid microbe detection reagents as a key facility within the global science products network of the company. Product offerings from the new pharma plant will include Glucophage (metformin) for diabetes, Euthyrox (levothyroxine) and Thyroisol (thiamazole) for thyroid disorders, and Concor (bisoprolol) for cardiovascular diseases, all of which are included in China’s EDL. The company said the new pharmaceutical plant will shorten the lead times required for medicine delivery when compared to importing products.

Shire Builds Confidence In $20bn Revenue Target

Shire PLC completed the acquisition of Baxalta in June this year, and as a result plans to deliver double-digit compound annual top-line growth, with more than $20bn in annual projected revenue by 2020 and about 65% of total annual revenues generated by its rare disease products. The deal increased the company’s scale in R&D and, contrary to popular thinking, “Scale does matter in rare disease,” said CEO Flemming Ornskov. Around 75-80% of the company’s programs are now in the rare disease space, added Shire’s global R&D head Phil Vickers. Combined revenues in rare diseases are projected to be $13bn by 2020, which is the most of any rare diseases company, according to Shire’s analysis. When Shire reported its third quarter earnings earlier this month, Ornskov revealed that the integration of Baxalta would involve an exit from the biosimilars space and a “streamlining” of Shire’s small but growing cancer business. While management saw the third quarter numbers as a success, analysts called the quarter a miss due to lower than expected sales of legacy Baxalta products.

Bayer, Evotec Alliances Create ‘Virtual’ Specialized Businesses WithFinite Goals

Bayer AG and Evotec AG have recently struck a second collaboration, this time in kidney disease, on the back of their successful discovery and development partnership looking at new drug candidates for women’s health indications. Bayer’s head of development for pharmaceuticals, Dr Joerg Moeller, and Evotec chief, Dr Werner Lanthaler, told Scrip more about their “modern” setup and how fixed project endings help to eradicate development bottlenecks. In Oct. 2012 Bayer and Evotec entered into a five-year multi-target strategic alliance to identify three small molecule clinical candidates for the treatment of endometriosis. Four years since signing the pact, the pair have discovered five preclinical assets and identified their first compound to take into the clinic. Following this progress in women’s health, Bayer and Evotec have now signed a second arrangement for discovery and development of drug candidates in kidney disease. In the endometriosis space, where Bayer and Evotec’s collaborative work is most advanced, there is great market opportunity as the condition is estimated to affect more than 170 million women worldwide. In parallel, available therapies for endometriosis (including off-label options regularly used) are limited. With a strong history in the areas of contraception and women’s health, Bayer is keen to be one of the first to make waves in this therapy space by producing a non-hormonal therapy option.

Onivyde Too Expensive For NICE, Despite Dearth Of Pancreatic Cancer Drugs

NICE has issued draft guidance that does not recommend Shire PLC’s Onivyde, a liposomal injectable formulation of irinotecan (Pfizer Inc.’s Campotosar and generics), The product obtained FDA approval in October 2015 as a treatment in combination with fluorouracil (5-FU) and leucovorin for patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based (Eli Lilly & Co.’s Gemzar and generics) therapy. EU approval followed this October. NICE said its appraisal committee recognized that extension to life and quality of life were important to people with this condition and understood that there have been few new treatments in this area.
Moderna and AstraZeneca entered into a collaboration to discover, co-develop and co-commercialize mRNA therapeutic candidates for the treatment of a range of cancers. The deal leverages both parties’ expertise in mRNA design and manufacturing and immuno-oncology, respectively.

Heptares Therapeutics and Allergan for muscarinic receptor agonists in CNS diseases

Allergan licensed exclusive global rights to a broad clinical and preclinical portfolio of first-in-class subtype-selective muscarinic receptor agonists in development for treating major neurological disorders from Heptares for $125m up front, plus up to $665m in development and up to $2.5bn in commercial milestones, plus royalties.

Scrip’s Best Partnership Alliance Award recognizes the importance of pharmaceutical and/or biotech companies working together to develop new medicines.

AstraZeneca and Human Longevity’s genomic partnership

This long-term partnership aims to harness the power of genomic information to propel the discovery and development of novel medicines. It will drive new drug target and biomarker identification to select patients who can respond to treatment, and could change the way clinical trials are designed.

AstraZeneca and Moderna Therapeutics for IO mRNA therapeutics

Moderna and AstraZeneca entered into a collaboration to discover, co-develop and co-commercialize mRNA therapeutic candidates for the treatment of a range of cancers. The deal leverages both parties’ expertise in mRNA design and manufacturing and immuno-oncology, respectively.

AstraZeneca and Sanofi’s Compound Collection Exchange

This highly innovative agreement facilitated the direct exchange of 210,000 compounds from AstraZeneca and Sanofi’s proprietary compound libraries. The swap represents an open innovation model between pharmaceutical companies that is unprecedented in its size and scope.

BioNTech and Sanofi’s alliance for mRNA-based IO therapies

BioNTech and Sanofi have entered into a global exclusive license agreement to leverage their respective scientific expertise and innovation in immuno-oncology. The deal covers discovery and development of up to five cancer immunotherapies, each consisting of a mixture of mRNAs.

Horizon Discovery Group and Centauri Therapeutics joint venture Avvinity Therapeutics

These two companies have formed immuno-oncology joint-venture Avvinity Therapeutics to combine Horizon’s gene editing, immunology, oncology and drug discovery capabilities with Centauri’s unique Alphamer technology and immunology capabilities to provide a powerful proprietary platform to discover and develop novel IO therapeutics.

Orion Pharma’s partnership with DZNE

Orion and DZNE (German Center for Neurodegenerative Diseases) have entered into a long-term strategic collaboration with a totally new model of public-private partnership where each side will contribute equally, sharing the risks and rewards, in developing new CNS drugs, and complement each other’s expertise and resources.

WuXi AppTec and Lilly for a novel CV candidate in China

This strategic partnership seeks to pursue parallel Chinese/global development to expedite new drug development in the most cost effective and efficient way for patients in China and around the globe. It focuses on a first-in-class therapy designed to address cardiovascular risk in patients with dyslipidemia.
EXPERT VIEW

Tuberculosis: An Old Killer Proving Difficult To Best

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With the announcement that tuberculosis surpassed HIV/AIDS in attributable deaths from infectious diseases worldwide, there has been a renewed interest in the development of new treatments and regimens for dealing with what is now the world’s number one infectious disease killer.

In 2015, the number of tuberculosis (TB) attributed deaths totalled 1.5 million, outnumbering the 1.2 million deaths due to HIV. While this represents a 47% fall in mortality from TB since 1990, the World Health Organization (WHO) estimates that the vast majority of deaths that occurred were preventable, which is problematic given the estimated 9.6 million new cases of TB in 2015 alone.

Tuberculosis is a contagious airborne disease caused by the bacterium Mycobacterium tuberculosis. It is largely a respiratory infection and up to a third of the world’s population may be latent carriers of M. tuberculosis. Latent TB is not contagious or symptomatic but carriers have a 5-10% lifetime chance of developing active TB, which is increased by a patient having a compromised immune system from HIV/another disease or immunosuppressant drugs.

Exacerbating the issue is the steady rate of drug-resistant tuberculosis (DR TB) or multidrug-resistant tuberculosis (MDR TB) (prevalence estimated to be 3-5% of TB cases worldwide). There have also been sporadic reports of extremely drug-resistant TB (XDR TB) which appears to be resistant to all the agents currently used in TB treatment.

Since TB is largely treatable with long term courses of multiple antibiotics, TB deaths are concentrated in low and middle-developed countries where access to diagnosis and treatment may be limited. Current first line treatments are not always successful, often due to DR or MDR TB, and second line treatments may take up to two years with serious side effects possible.

TUBERCULOSIS TREATMENT PIPELINE

With the rise of various drug resistant strains over the past decade and the often severe side effects of second or last line treatments, there is a pressing need for new treatments to counter the chance of a XDR TB epidemic emerging, as well as to provide greater options to both patients and treatment providers. Luckily, over the past decade the pharmaceutical industry has responded to this need and the numbers of TB treatments under development by pharmaceutical companies or public-private partnerships have increased. The vast majority of TB treatments are in preclinical development stages and are largely unproven but the greatly increased number of candidates in the past decade provides reassurance that the field is not wholly neglected.

There are three broad categories the development candidates follow. Firstly, repurposed drugs (usually antibiotics) in a higher stage of development for other indications that are also being tested for TB. The second category is vaccines against TB, which are being developed for therapeutic as well as prophylactic use, and the final and largest group is novel anti-TB drugs, primarily new antibiotic compounds. The major player in new late stage drugs for TB is TB Alliance. It is a not-for-profit organization that collaborates with pharmaceutical companies on pursuing novel compounds and focuses on the development of new combinations of drugs to treat TB with an emphasis on affordability and availability.

For the short term the primary treatment for TB is likely to remain long regimens of multiple antibiotics. However, there is promise for more diversity in potential antibiotics and therapeutic vaccines, especially those used as second/last line treatment options for drug-resistant TB variants.

The provision of effective and affordable therapeutic options is a necessity if the goals of the WHO’s End TB Strategy and Millennium development goals (reducing TB deaths by 90% and new cases by 80% by 2030) are to be achieved.

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Click here to view table showing the Clinical Stage Candidates For Tuberculosis Treatment: http://bit.ly/2f6xo40
The Post-Truth Biopharma Rally

The post-election rally in biopharmaceutical stocks was driven partly by hopes that drug pricing pressures will evaporate. However, this is a facet of post-truth culture rather than a real possibility. As Teva, Mylan and maybe Novartis have demonstrated, more is less when it comes to generic exposure.

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Ten days after the 10%jump in the NASDAQ Biotech Index (NBI) caused by the US presidential election result, the post-truth belief in what the new Republican administration will really mean for biotech has started to fade. In pharmaceuticals, the post-election rally in the NYSE Arca Pharmaceutical Index (DRG) was only about half that of the NBI and last week it lost about half that gain. Pharma’s underperformance was partly due to the last third-quarter earnings reports of the large-cap specialty pharmaceutical companies but also in anticipation of future drug pricing pressures that just won’t go away.

Teva Pharmaceutical Industries Ltd. reported its first-quarter results since the completion of the acquisition of Allergan PLC’s generics business. When I glanced at Teva’s announcement my initial thought was that a 15% increase in sales was impressive for the world’s largest generics manufacturer. However, pre-market investors were already marking down Teva’s stock price as analysts’ expectations for sales had been missed. The sales increase that was expected from a bigger generics business was offset by 7% US generic price deflation over the combined generic drug portfolio. Teva’s earnings per share (EPS) beat analysts’ consensus estimates, which I also thought might have been well received since EPS had the additional headwind of the extra share dilution issued as part of the Allergan acquisition. But any positive sentiment from the earnings beat of consensus estimates was far offset by the reduction in 2016 guidance in a set of results described as “messy” by the analysts at JP Morgan. For the first two quarters of 2016 Teva’s results had been refractory to US generic drug price deflation, probably because of growth from its branded business that is weighted towards Copaxone (glatiramer acetate) for multiple sclerosis. However, not only did branded Copaxone miss analysts’ sales forecasts in the third quarter, but after every other company with exposure to US generic drugs experienced pricing pressure, it was only a matter of time until Teva also succumbed.

In Teva’s case the decision to significantly increase its generics exposure and make its branded business a smaller part of total sales looks likely to be a strategic faux pas on a par with Pfizer Inc.’s buy-out of Sanofi’s interest in the inhaled insulin product Exubera (inhaled recombinant human insulin). As the implications for Teva’s doubling down on generic drugs at the expense of branded (or even biosimilar) drugs dawned on investors, its share price continued the pre-market mark-down and finished the week down 4.8% against the DRG’s 2.8% weekly fall. With Allergan’s biosimilar business excluded from the transaction with Teva, Allergan and partner Amgen Inc. rubbed salt into Teva’s wound last week when they filed the BLA for their biosimilar Avastin (bevacizumab). Teva meanwhile probably made a bad situation worse by announcing a pause in its business development efforts while it addressed paying down the debt it issued as a result of the Allergan and other transactions.

TRANSPARENCY CHALLENGES

At the mid-point of the year, Mylan NV’s results, like those of Teva, seemed resistant to generic drug price deflation. That resilience in Mylan’s case derived from the price inflation of its controversial branded product EpiPen (epinephrine) for the prevention of allergy anaphylaxis, rather than the complete absence of generic price deflation. Like Teva, Mylan has also been on a bigger- is-better consolidation of generic drugs drive with its most recent $9.9bn acquisition of Meda AB. When Mylan reported its third-quarter earnings on the day of the US election, the slight sales and earnings misses of analysts’ consensus estimates and the maintenance of its full-year guidance were less worrying than the level of transparency for the combined company. The analysts from Citigroup described Mylan’s results as leaving “several questions unanswered” while those from UBS were left “struggling with the limited transparency”. Mylan’s earnings commentary noted its mid-single digit US generic price erosion over last quarter but left the “organic” pricing dynamics, particularly in Europe, where EpiPen licensee Meda is based, opaque. A change in Mylan’s reporting structure seems likely to increase this opacity and with the added uncertainty of the impact of an authorized generic EpiPen in the US, Mylan’s stock price finished last week down by more than 3.8%.

Over a year since the peak in the stock prices of the constituents of the biopharmaceutical sector, companies like Teva, Lannett Co. Inc., Valeant Pharmaceuticals International Inc. and Impax Laboratories Inc. that have acquired generic assets since the peak are already either writing down the value of those acquisitions or attributing blame to them for their missed third-quarter earnings reports. As the post-truth rally in life science stocks that followed the election of Donald Trump dissipates, some of this retrenchment is because the real truth is drug pricing pressures are here to stay. As the analysts from UBS put it last week, “generic price erosion [is] getting worse on the margin”. With so many companies bulking up on their generic drug momentum only to find themselves suffering a bigger impact when they run head- long into the immovable object of price deflation, Novartis AG was left looking particularly out of touch with current events, if the rumor mill is to be believed. As reports emerged last week of its potential $8Bn acquisition of US generics company Amneal Pharmaceuticals LLC, I was relieved to find that in the words of Del Amitri, I am not always the last to know.

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Andy Smith gives an investor’s view on life science companies. He has been lead fund manager for four life science–specific funds, including 3i Bioscience, International Biotechnology and the AXA Framlington Biotech Fund, and was awarded the techMark Technology Fund Manager of the year for 2007.
Scrip's weekly Pipeline Watch tabulates the most recently reported late-stage, Phase III clinical trial developments for the more than 10,000 drug candidates under active research worldwide. To see changes to the progress of product candidates further back in the development pipeline, and a table of the week's product approvals, please visit our Pipeline Watch webpage at scrip.pharmamedtechbi.com.

### Pipeline Watch

**Selected clinical trial developments for the week 11–17 November 2016**

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<td>sofosbuvir, velpatasvir, voxilaprevir</td>
<td>hepatic C</td>
<td>POLARIS-2; Eight weeks therapy was effective.</td>
</tr>
</tbody>
</table>

*Source: Biomedtracker*
Jörg Vollmer has joined Rigontec as chief scientific officer. He brings over 17 years’ experience to the company and previously held leadership roles at Nexigen GmbH, Pfizer Inc. and Coley Pharmaceutical Group Inc. Most recently, Vollmer was CEO and managing director at Nexigen and before this, held the position of managing director and site head at Pfizer’s oligonucleotide therapeutic unit in Germany.

Gilead Sciences Inc. has promoted James R. Meyers to executive vice president, worldwide commercial operations, with responsibility for commercial operations in North America, Europe and Japan. Meyers joined Gilead in 1996 as a regional sales director and has been the senior vice president of North America commercial operations since 2007. Before joining Gilead, Meyers served in various roles of increasing responsibility in sales, training, marketing and management with Zeneca Pharmaceuticals and Astra USA.

Merck KGaA has appointed Kamal Shah head of its new global drug safety department’s innovation unit. Shah is a board certified anaesthesiologist and has held management and leadership roles in medical affairs, clinical development and drug safety at PPD, Bristol-Myers Squibb, Pfizer and Celgene.

Gamida Cell, a company focused on cancer and orphan genetic diseases, has appointed Julian Adams chair of its board of directors. Adams brings over 30 years’ experience to the company and is president of research and development at Infinity Pharmaceuticals. Before Infinity, Adams was the senior vice president of drug discovery and development at Millennium Pharmaceuticals.

C4X Discovery Holdings Plc. has appointed its chief scientific officer, Craig Fox, and chief financial officer (CFO), Bra Hoy, to its board of directors. Hoy has been appointed permanent CFO following a period as interim CFO. He carries over 20 years’ of pharmaceutical and biotechnology experience and has held various senior financial and general management positions in the UK and US. Previously, Hoy was CFO of Plethora Solutions Holdings plc; CEO of XcelLyz Limited; and senior director of Geron Corporation’s stem-cell focused UK subsidiary. Fox joined C4X Discovery in 2015 but before this he was director of respiratory research at Pulmagen Therapeutics.

The biotech Scholar Rock has named Jeffrey S. Flier to its board of directors and scientific advisory board. The company has also appointed Alan J. Buckler chief scientific officer. Flier is an endocrinologist and joins Scholar Rock after serving as the twenty-first dean of the Faculty of Medicine at Harvard University. He is the Higgins professor of physiology and medicine and Harvard University Distinguished Service Professor. Buckler brings over 25 years’ experience to Scholar Rock and has led various drug discovery programs at the Novartis Institutes of Biomedical Research. Most recently, he was vice president, cell and protein sciences at Biogen.

Terrie Curran has joined Myovant Sciences Ltd.’s board of directors as an independent director. Curran is the president of worldwide markets for the inflammation and immunology portfolio at Celgene Corporation. Previously, he was senior vice president and general manager of women’s health and endocrinology at Merck & Co. Inc.
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