Immediate industry reactions to Britain’s decision to leave Europe, the result of a public referendum held last month, were modest and even UK headquartered biotechs appeared nonchalant about the potential disruption.

Anne Hyland, chief financial officer for UK-based biotech Kymab Ltd., told Scrip in a recent interview that she was disappointed in the UK’s decision to leave the EU – but not overly concerned. “The markets are overreacting and things will calm down,” Hyland said. "Biotech by its nature is an international business so I don’t see any immediate impact on Kymab or the wider UK biotech industry. We are a strong industry.”

Hyland said the UK still has all the initiatives biotech companies need to carry out their research and it is still a ‘great place to do business’. However, she highlighted tasks ahead for the UK biotech industry: “We will have to work through the ramifications of this decision. We have a European Patent Office, European legislation around drug development, etc. – but we have great leaders in the industry across the UK and Europe that will be able to manage these changes. The UK is pragmatic; it will get on and solve the problems that arise.”

While the UK scrambles to explain itself – terms like “Regrexit” were trending on Twitter almost immediately after the referendum result was announced on June 24 – and to reform its collapsing government, industry should be taking a rational approach to prepare for the worse and hopefully experience fewer effects in the years of disruption that will follow Britain’s exit from the EU.

Initial concerns for businesses and scientists in the fallout of Brexit have centered on a few key points: funding, regulations and access.

Scrip, with data from Informa pharma intelligence products, has taken a closer look at how Brexit might disrupt funding in the UK and how the region might become less attractive for areas of drug development, such as clinical trials and regulatory applications.

EU FUNDING FOR UK PROJECTS
It might be surprising – particularly to some Leave Campaigners – that the UK receives more funding from and has more individual projects funded by the European Research Council than any other EU member state. Brexit could threaten £8.5bn of EU funding for the UK life sciences sector over the next four years (see Figure 1).

COMPANY HEADQUARTERS
The UK also has more pharma and biotech companies headquartered in the region
Before the UK’s EU referendum, our industry was quite vehement that pharma would be better off with the UK in the EU. But since the British public voted to withdraw from the European bloc, sending global stocks and currencies into turmoil, what happened? Stock market investors decided it was a good thing for UK pharma.

GSK’s share price shot up immediately on the day the result was announced, went on rising healthily for nearly two weeks and has since hovered around the £16.50 mark, some 15% above its level immediately before the referendum closed and 20% above where it finished last year. Similarly, AstraZeneca bolted upwards on the day after the referendum and is coasting along on a plateau around 15% higher than its pre-Brexit vote level. It has almost recovered the 18% of its value it had lost since the turn of the year. It’s a similar picture with Shire, GW Pharma and Hikma.

Brexit might not be a good thing for UK patient access to innovative medicines, UK access to EU funds and R&D projects (and vice versa) or regulatory simplification – but what do markets care about those things?
Enbrel Biosimilar Market In Sandoz’s Grasp; Will Cost, Litigation Derail It?

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With the FDA giving an overwhelmingly positive review of Sandoz Inc’s application for its biosimilar version of Enbrel (etanercept), which is sold in the US by Amgen Inc., the product appears to be headed to the US market – pending a likely blessing from the agency’s advisory panel, which is meeting on July 13. But Sandoz must still get past litigation and convince prescribers and patients its etanercept biosimilar provides value over Enbrel.

The FDA has given another warm embrace to a biosimilar application – this time for Novartis AG unit Sandoz Inc’s version of Amgen Inc’s Enbrel (etanercept), a tumor necrosis factor blocker that first entered the US market in 1998. In briefing documents released ahead of a July 13 meeting of the FDA’s Arthritis Advisory Committee, regulators declared that Sandoz’s data demonstrated its biosimilar, which currently goes under the moniker GP2015 while it’s awaiting a trade name, was “highly similar” to Amgen’s US-licensed Enbrel, notwithstanding minor differences in clinically inactive components.

They also said they found no clinically meaningful differences in the safety, purity and potency between GP2015 and Enbrel in the studied indication of plaque psoriasis and said Sandoz had provided scientific justification for extrapolating its clinical data to the other indications for which the innovator is licensed in the US: rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis.

While there’s frequently some surprises at FDA advisory committee meetings, the panel is expected to give its blessing after hearing from regulators and Sandoz officials during the morning session of the meeting and spending the afternoon mulling over whether there’s any reason to hold up GP2015’s approval – ultimately voting on whether the evidence supports the biosimilar’s licensure.

A QUICKER LITIGATION PATH

Even if GP2015 wins a swift approval from the FDA, Sandoz still must face a lawsuit brought by Amgen and Roche, which have accused their rival of trying to “reap the commercial benefits” provided to biosimilar manufacturers under the Biologics Price Competition and Innovation Act (BPCIA), while seeking to avoid the obligations Congress established under the 2010 law “to protect innovators.”

In their lawsuit filed in the US District Court for the District of New Jersey, the companies asserted Sandoz has been “piggybacking on the fruits” of the innovators’ “trailblazing efforts” and had infringed five Enbrel patents – two owned by Roche and three by Amgen’s subsidiary Immunex Corp, which it acquired in 2002.

If the district judge orders a preliminary injunction, “that’s going to govern whether Sandoz can launch before the court’s final decision on the merits of the patent infringement claims against the company, regardless of when the FDA approves the product,” said New York lawyer Robert Cerwinski, a partner in the intellectual property litigation group at Goodwin Procter. “That’s what’s going to control it.”

If Amgen believes it has a strong case for a motion for preliminary injunction, “then getting that issue resolved early and getting that injunction in place early is going to be a benefit,” Cerwinski said.

Cerwinski said he didn’t see anything in the recent Federal Circuit decision that would bar Amgen from arguing that it should still get its six months of keeping GP2015 off the US market, even if the district court doesn’t grant the preliminary injunction.

“One of the policy reasons for having the 180 days is to give the parties enough time to file and have a preliminary injunction motion decided,” he said. “If a preliminary injunction is denied before the 180 days, however, that reason won’t exist.”

SWAYED ON COST?

Even though the FDA is not supposed to consider pricing when it comes to its application evaluations, panelists are likely to raise the issue of whether GP2015 will provide value to patients over Enbrel.

After all, the matter of cost savings has come up at both previously held advisory committee meetings for biosimilar drugs: Sandoz’s Zarxio (filgrastim-sndz) and Celltrion Inc’s and Pfizer Inc’s Inflectra (infliximab-dyyb).

Normally the “cost” topic is shunned by the FDA, but even Center for Drug Evaluation and Research Director Janet Woodcock has raised the issue at advisory committee hearings and other venues.

Sandoz currently is the only company with a biosimilar on the US market – Zarxio – and it was priced at only a 15% discount to the innovator, Amgen’s granulocyte-stimulating factor Neupogen.

Sandoz spokesperson Leslie Pott told Scrip the company has not yet disclosed how much it plans to discount its etanercept biosimilar.

“While it’s too early to speculate about the price of the proposed Sandoz etanercept biosimilar, our pricing approach will balance our commitment to increasing patient access and helping healthcare systems generate savings while building a sustainable biosimilars business model that can continue to offer high-quality biologics to patients in the US,” she said in an email response to questions.

Some have argued that over time, the prices of biosimilars will eventually come down, although the products overall aren’t expected to provide the same types of savings as generic drugs.

It’s also too early to tell whether biosimilars will gain the same type of acceptance from prescribers and patients as the small-molecule copycat products have done – an outcome that may take several more products beyond Sandoz’s to know for sure.

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Half of 2016 Biotech IPOs Positive At Mid-Year; 2015 Success Rate Sours

It hasn’t been easy for biopharmaceutical firms to go public in the US during 2016, but as of the end of June the scrutiny seems to be paying off – at least for investors in half of this year’s first-half initial public offerings.

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Eighteen therapeutics developers launched IPO in 2016, raising $1.2bn in total net proceeds and generating an average return of 10.8% as of June 30. Nine of the companies produced a positive return at mid-year and nine had a negative return versus their IPO stock price. But with only 18 IPOs so far in 2016 versus 34 biopharma first-time offerings at the mid-point of 2015, which raised a total of $2.9bn in net proceeds, investors clearly are responding to the now poor performance of companies that went public last year.

Comparing like with like, therapeutics firms that launched IPOs between January and June of 2015 had an average return of 15.9% versus their offering price as of June 30 last year. At that point, 18 of the 34 generated a positive return – slightly more than half. However, those same companies, minus one that’s since been acquired, had an average return versus their IPO prices of -28.9% as of mid-2016. Only seven of the 33 that went public during the first half of 2015 were generating a positive return.

The Nasdaq Biotechnology Index (NBI) has fallen only 15.9% from the beginning of 2015 through June 30 of this year, which means that biotech stocks in general are performing better than biotech companies that went public during the past year and a half. But the broader Nasdaq stock index has gained 2.5% in the same time frame, so biotech overall is doing much worse than public companies in other technology and science-based industries.

Despite their relatively poor performance, biotech companies continued to launch more US IPOs in 2016 than any other industry. The National Venture Capital Association (NVCA) reported recently that 12 venture-backed companies went public and raised $893.9m during the second quarter of this year – a 50% increase in the number of VC-backed IPOs versus the first quarter – with biotech leading the way.

“Biotech IPO activity continues to be the bright spot to an otherwise sleepy IPO market for venture-backed companies,” NVCA President and CEO Bobby Franklin said in the organization’s second quarter report on VC exits via IPOs and mergers and acquisitions.

Following a June IPO by the web-based phone and text message service provider Twilio, Franklin said, “We will be watching closely to see if this finally opens the doors for other venture-backed technology companies to float on the public markets. However, in the first half of 2016 we’re well behind the pace of where we were at this time [in] the prior two years, and if we continue to see more private capital flow into later-stage companies in the entrepreneurial ecosystem, it’s likely that the IPO slumber may continue in the second half of the year.”

VENTURE VERSUS PUBLIC FINANCING: VC DEALS DOMINATE

Indeed, even biopharma venture capital funding continues to remain at a high level despite a drop in IPO exits for VC firms. Big venture funding rounds are driving the quarterly biotech VC totals to record levels, but large investments are being made in both early-stage and clinical-stage therapeutics companies.

However, smaller venture financings are picking up as well. In a recent roundup of five biopharma VC financings, after Morphic Therapeutics’s $51.5m Series A round, the next largest deal was a £12m Series A round for Storm Therapeutics.

Not that VC fundraising is a walk in the park, but it may be easier and less frustrating than raising capital in the public markets. Nine of the 18 biopharma companies that went public during the first half of 2016 took their offerings to market within an earlier proposed price range and the other nine priced their IPOs well below the preliminary range.

Perhaps that’s why no biopharma firms have filed documents with the US Securities and Exchange Commission (SEC) to support a new IPO so far in July. Only two therapeutics developers filed S-1 registration statements with the SEC in June to begin the process of going public: Kadmon Corp. LLC and Syros Pharmaceuticals Inc., which priced its IPO on June 30 – just in time for inclusion in Scrip’s roundup of first half 2016 IPO activity. The table above outlines individual stock performance for this year’s 18 companies that were brave enough to enter the tough market for public biopharma firms. One theme for 2016’s IPO market has held true all year: gene therapy, gene editing and immuno-oncology specialists are the best performing newly public therapeutics companies this year.

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Could Pfizer Choose To Consciously Stay Coupled?

The end of the Pfizer/Allergan merger dream brought the Pfizer break up decision timeline back to the fourth quarter of 2016. Since Ian Read first floated the idea back in 2011 it has been regarded as question of when, not if, but this has now been challenged by one intrepid analyst.

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“We are increasingly of the view that [Pfizer Inc.] management is NOT going to pursue a split up, at least at the current point in time,” writes Bernstein’s Tim Anderson. “This is a new perspective for us.”

He has based his changed outlook on three main factors:

1. A conversation with the CEO where “he alluded to the possibility that splitting up the company could be disruptive to cash flows and balance sheet strength relative to [Pfizer] as a single company.”

2. On a sum-of-the parts basis, “it is not clear that splitting up unlocks substantial additional value” which “begs the question…why split.”

3. When the split idea first emerged, Pfizer’s growth prospects seemed challenging. “Fast forward to today, however, and [Pfizer’s] growth looks better.”

The alternative viewpoint has sparked discussion among investors.

“I was quite worried when I first read it as we hold it in the fund and I believe there’s a separation premium included in Pfizer’s valuation, and has been for a while,” said Andy Smith, chief investment officer of Mann Bioinvest, which is the investment adviser for the Magna BioPharma Income fund. “The [NYSE] Arca Pharmaceutical Index is slightly up today [July 18] and the Pfizer share price slightly down so that could be the start of that premium dissipating if the split is not enacted.”

Dr Smith has mixed views on whether he is for or against a break up. “I think that the split would have been a no brainer had Pfizer been able to merge with AstraZeneca or Allergan and if they don’t announce any change to their plans, it might imply some other M&A has to happen before the split to get critical mass. In that respect, and long-term, I like the businesses together as last quarter’s financial proved, but I like to think of them doing M&A for the benefit of the whole sector that would then enable the split.”

“Datamonitor Healthcare expects Pfizer’s Q2 results to shed more light on its decision to separate its innovative and established business by the end of 2016 and the pursuit of attractive M&A to facilitate the split,” lead analyst Ali Al-Bazergan told Scrip. “The potential for a break-up is supported by autonomous decision making, clearer growth prospects, operational benefits, and shareholder value creation.” However, the lack of clarity around trapped-value could mean that a split may be dilutive, “leaving the current structure to be a more compelling route.” At the moment Datamonitor Healthcare believes a split looks more likely, “but we await more information from Pfizer as the company is further expected to leverage its financial capacity after Hospira and Anacor by targeting companies that will support the growth trajectory of its innovative pharmaceuticals business.”

“Pfizer remains a company in flux,” notes Bernstein’s Anderson. “In 2011 it articulated a future where, because of past M&A, the company would likely split itself up.” Yet Pfizer continued down the M&A path, securing acquisitions and attempting others. But it could be argued “that the imperative to split up is much weaker than it was in early 2011,” he says. “At current prices, the stock remains inexpensive relative to peers, but it needs to be appreciated that this has often been the case over the last decade.”

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than any other EU country – a total of 436 businesses. More than Germany, which has 414 companies headquartered in the country; France, which has 304; Sweden, 220; and rounding out the top five countries is Spain, with 203. It’s possible the UK’s separation from the single EU market could dissuade pharma and biotech companies from claiming UK domicile. It might also lead to UK headquartered businesses seeming less attractive to potential acquirers or partners.

**CLINICAL TRIALS IN UK**

Finally, Scrip and TrialTrove found that the UK currently has the second highest number of ongoing global clinical trials among EU member states, being beaten only by Germany. This figure could fall in the wake of Brexit as study sponsors would be required to file a Clinical Trial Authorization (CTA) in the UK, separately from the single common application companies currently do for the batch of EU countries (see Figure 2).

It’s possible that the UK will begin to be excluded by pharma and biotech firms filing new drug applications too, with novel products getting delayed entry to the country because companies might choose to focus on the 500 million potential patients in Europe versus the 60 million patients in the UK.

The UK’s current regulator, the MHRA, will need to prove it is fit for purpose if the bulk of drug approval applications are switched from the European Medicines Agency to the local agency.

Even trade organization BioPartner UK is predicting a downturn for the UK life science sector. In a recent advertising email for its upcoming conferences the group leads on the devaluation of the pound to boast its discounted entry fees for delegates.

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FDA To Join The ‘Real World’ Under PDUFA VI

Under round six of the user fee agreement with industry, the FDA is pledging to explore the use of real-world evidence, strengthen the patient’s voice in the drug review process and boost the agency’s postmarketing surveillance abilities.

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The FDA has decided to join the real world next year – or at least, explore it, in terms of what type of data it will consider from innovator drug makers. Under negotiations with the biopharmaceutical community for the sixth round of the reauthorization of the Prescription Drug User Fee Act (PDUFA), which will run from fiscal years (FYS) 2018 through 2022, the FDA has agreed to take a look at using real-world evidence in its decision-making processes, according to the agency’s proposed commitment letter, which was posted online on July 15.

PDUFA, initially passed by Congress in 1992, gives the FDA the authority to collect user fees from manufacturers to help speed the reviews of drug applications. The funds are intended to be used by the agency to hire more staff, improve the FDA’s systems and help it establish a better managed review process, in exchange for meeting certain performance goals.

PDUFA V will come to a close on Sept. 30, 2017, so lawmakers must renew the user fee program before FY 2018 begins.

The agency launched its PDUFA VI process last summer by holding a public hearing on July 15, 2015, and regulators and industry spent much of the past year wrangling over the details.

The FDA plans to hold another hearing on Aug. 15 to give the public an opportunity to weigh in on the commitments the agency has agreed to with industry.

The FDA must send its final proposed PDUFA VI performance goals letter by Jan. 15, 2017 to Congress, which must then craft legislation to reauthorize the program – a bill that generally ends up being packed with numerous rider provisions, often unfunded mandates, by the time it’s adopted by House and Senate lawmakers and has crossed the president’s desk.

Nonetheless, the negotiation process has helped smooth the PDUFA reauthorization path to ensure the FDA and industry each get what they want.

PDUFA, said Stephen Ubl, president and CEO of the Pharmaceutical Research and Manufacturers of America (PhRMA), is “vital” to ensuring the FDA fulfills its mission of protecting public health.

Jim Greenwood, head of the Biotechnology Innovation Organization (BIO), insisted the goals and commitments in the PDUFA VI letter were “thoughtful and carefully negotiated.”

JOINING THE DATA REVOLUTION

In the letter, the FDA said it recognized that as it participates in the current “data revolution,” it’s important the agency considers the possibilities of using real-world data as a key tool in evaluating the safety and effectiveness of new medicines.

But regulators said before they can engage in such an effort, they must first know what questions to ask, including how such data can be generated and used appropriately in product evaluation, what the challenges are to appropriate generation and use of these data and how to address those challenges.

The FDA has committed to holding at least one public workshop by no later than the end of FY 2018 with patients, industry, academia and other stakeholders to discuss issues related to the use of real-world evidence in the regulatory decision-making process.

The forum would be used to examine the benefits to patients, regulators and drug manufacturers of using real-world evidence in the FDA’s decision-making processes; the challenges faced in obtaining that information and ensuring its quality and how to mitigate those obstacles; the methods for collecting, analyzing and communicating those data; and the appropriate context for use in ensuring a product’s effectiveness.

The FDA vowed that by no later than the end of FY 2019, it would conduct – or fund a contractor to do it – pilot studies, methodology development projects or other appropriate activities aimed at addressing key outstanding concerns and considerations in the use of real-world evidence for regulatory decision making.

Regulators said they also would consider available input and publish draft guidance on how real-world evidence may contribute to the assessment of safety and effectiveness in regulatory submissions, like the approval of new supplemental indications and for the fulfillment of postmarketing commitments and requirements. The FDA said it would work toward publishing a revised draft or final guidance within 18 months after the close of the public comment period.

INTEGRATING THE PATIENT’S VOICE

Several groups, including PhRMA, BIO and the National Health Council, particularly praised the FDA for including provisions in its goals letter for strengthening the patient’s role in the drug review and approval processes – going well beyond the agency’s current Patient Focused Drug Development (PFDD) program piloted under PDUFA V.

The FDA said it would strengthen its staff capacity by integrating clinical, statistical,
psychometric and health outcomes research experts into review teams to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions.

The agency said it would hold public workshops, and from the input it gleans, develop a series of guidance documents to focus on approaches and methods to bridge from the initial PFDD meetings to “fit-for-purpose” tools to collect “meaningful” patient and caregiver input for ultimate use in regulatory decision making.

Regulators laid out a timeline in their PDUF VI commitment letter for those draft guidances.

**BOOSTING BIOMARKER CAPACITY**
The FDA also plans to beef up its staff capacity to enhance its biomarker qualification reviews and said it would pilot processes to engage external experts.

The agency pledged to convene a public meeting to discuss the taxonomy for biomarkers used in drug development and a framework with appropriate standards and scientific approaches to support them, including scientific criteria to determine acceptability for a qualification submission and essential elements of a formal biomarker qualification plan. The FDA agreed to also publish biomarker-related draft guidances by the end of FY 2018.

**POSTMARKETING EFFORTS**
Also among its commitments, the FDA said it would use its PDUF VI user fee funds to conduct a series of activities to systematically implement and integrate its Sentinel System – a collaborative project between government agencies and the private sector aimed at using existing and planned databases to track, collect and analyze adverse event reports about drugs, vaccines and medical devices – into its pharmacovigilance practices.

Those activities, regulators explained, would involve augmenting the quality and quantity of data available through Sentinel, improving methods for determining when and how that information is used and comprehensive training of review staff on the use of the system.

“Continued development and integration of the Sentinel system is needed to realize the system’s full value to the postmarketing safety review process,” the FDA said in a July 19 Federal Register notice, which posted early online on July 15.

The FDA said it would evaluate additional ways to facilitate public and sponsor access to Sentinel’s distributed data network to conduct safety surveillance.

The agency pledged that by the end of FY 2019, it would hold or support a public meeting aimed at discussing current and emerging Sentinel projects and would seek stakeholder feedback and input about gaps in the current system.

Among its targeted activities involving Sentinel, the FDA said it would facilitate integration of the system into the agency’s drug review program in a “systematic, efficient and consistent way” by the end of FY 2020.

The agency said it plans to analyze and report on the impact of the Sentinel expansion and integration on the FDA’s use of the system for regulatory purposes by the end of FY 2022.

**FINANCIAL TRANSPARENCY**
As part of its efforts to be more transparent and accountable, the FDA said it would conduct activities to evaluate the financial administration of the PDUF program to help identify areas to enhance efficiency.

The FDA said it plans to contract with an independent third party to conduct an evaluation of the PDUF program resource management during FY 2018 to ensure user fee resources are administered, allocated and reported in an efficient and transparent manner.

The agency said the contractor would be charged with recommending options to enhance the efficiency of user fee administration and suggesting options on the most effective governance model to support the FDA’s drug review program.

The contractor also would be tasked with recommending options to enhance the accuracy of the FDA’s user fee estimation methods. The FDA said it would publish a PDUF five-year financial plan no later than the second quarter of FY 2018, with updates to follow on that timeline each subsequent fiscal year.

The agency plans to hold a public meeting no later than the third quarter of each fiscal year starting in FY 2019 to discuss the PDUF VI financial plan, along with the FDA’s progress in implementing modernized time reporting, resource capacity planning and the updated user fee structure.

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**Top Institutions Join Forces To Create Cell Culture Models To Speed Research**

Four top cancer research centers are to pool their expertise to forge a new initiative to develop cancer cell models that, it is hoped, will accelerate research into the disease.

The National Cancer Institute (NCI), Cancer Research UK, the Wellcome Trust Sanger Institute and the foundation Hubrecht Organoid Technology are joining forces to develop the Human Cancer Models Initiative (HCMI) with the aim of bringing together expertise from around the world to make around 1,000 cancer cell models.

The HCMI collaborators aim to speed up development of new models and to make research more efficient by avoiding unnecessary duplication of scientific efforts. They say the HCMI could transform research and will allow scientists to study many aspects of cellular biology and cancer, including how the disease progresses, drug resistance, and the development of precision medicine treatments.

The scientists will use new techniques to grow cell models that will resemble more closely the tissue architecture and complexity of human tumors than the cell lines that are currently employed. This means they should reflect the biology of tumors more accurately and better represent the patient population, the scientists say.

The tumors and the derived models will also be genetically sequenced, and researchers will have access to this information, as well as the anonymized clinical data about the patients and their tumor.

Furthermore, the models will be made using tissue from patients with a variety of cancers, and they may include rare and pediatric cancers which are underserved by the existing cell lines.

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Lilly Teams Up With Boehringer Ingelheim To Boost Abemaciclib

The two big pharmas are working together in oncology in an effort to advance combination therapies in both their growing, but young oncology pipelines.

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In its most recent tie-up with Boehringer Ingelheim GMBH, Eli Lilly & Co. has inked a research collaboration to test its late-stage cancer asset with an early-stage compound from its partner. The tie-up has the potential to advance both companies in the oncology space.

Lilly and BI announced July 13 that they will test Lilly’s cyclin-dependent kinase (CDK) 4/6 inhibitor abemaciclib with BI’s insulin-like growth factor (IGF)-1/IGF-2 ligand neutralizing antibody BI 836845 in a Phase Ib trial that looks at safety and tolerability in patients with HR+/HER2- metastatic breast cancer.

‘The rationale for the collaboration is based upon the hypothesis that these two agents, in combination, could offer a more complete pathway interference and could potentially prolong cell cycle arrest’

Should the result be positive, the combination will move on to Phase II testing and will expand to other solid tumors. BI will sponsor the study, which is set to begin enrollment in late 2016. The companies could not elucidate on further timing for data from the study.

“The rationale for the collaboration is based upon the hypothesis that these two agents, in combination, could offer a more complete pathway interference and could potentially prolong cell cycle arrest. For HR+ HER2- mBC patients, this could translate to a reversal of resistance to hormone therapy,” said the companies in a statement.

While this is the first collaboration between the two companies in oncology, BI and Lilly have long been partnered in the diabetes space with compounds across several classes, including the SGLT-2 inhibitor Jardiance (sitagliptin). Lilly said recently at an investor day that it intends to have a portfolio in oncology that is just as prominent as its diabetes offerings.

Lilly, which promised investors another 14 compounds will make it to market by 2023, has pitted abemaciclib as the most prominent piece of its oncology portfolio. The potential blockbuster is currently competing against Novartis AG’s ribociclib to chase Pfizer Inc’s Ibrance (palbociclib) to market. Ibrance, the first-in-class CDK 4/6 inhibitor, is already poised for blockbuster status a little more than a year after gaining approval and recently released abstracts from the American Society of Clinical Oncology (ASCO) meeting have people buzzing about the drug’s potential.

Analysts are now debating whether ribociclib or abemaciclib can compete with Ibrance and which is poised to take a larger share of the market – Lilly insists abemaciclib is best-in-class.

Lilly’s oncology strategy is built on three pillars – cell signaling, tumor microenvironment and immuno-oncology – and is based on the idea that it can create combination therapies across these three areas. Beyond the collaboration announced with BI, abemaciclib is also being tested with Merck & Co. Inc’s Keytruda (pembrolizumab) and AstraZeneca PLC’s estrogen receptor antagonist Faslodex (fulvestrant). No other abemaciclib combinations have been publicly disclosed, said the company.

As for BI, the company has recently changed strategic directions and is trying to build its own pipeline in oncology. Currently, its pipeline is largely early stage, with concentrations in lung, colorectal, breast, ovarian, head and neck, liver, kidney and blood cancers. The company says it has over 400 employees around the world focusing on oncology.
Flagship Ventures Tempts Former Merck CMO With ‘Creative’ Mentoring Role

When Merck & Co. Inc.’s former chief medical officer Michael Rosenblatt retired earlier this year, he had no shortage of opportunities to go back to work, which is what he’ll do in September as the CMO at Flagship Ventures – a newly created position in which Rosenblatt will mentor the venture capital firm’s portfolio companies. “Flagship proposed something creative and compelling,” Rosenblatt said in an interview, noting that this may be the first time a VC firm has hired a CMO. But now that Flagship’s investment portfolio includes about 40 therapeutics companies with more than 40 clinical trials under way, it makes sense to have an in-house mentor to guide biopharma entrepreneurs through the research and development process. And Flagship’s stable of startups will only keep growing, since the VC firm is in the middle of investing capital from a $537m fund it closed in 2015. “It used to be that you got a drug approved and that got you to the goal line. Now, you have to prove to insurers and payers around the world the value of the drug,” Rosenblatt said. The patient perspective has become vital in drug development, he noted, that it wants industry to listen to patients. With experience working in both pharma and academia, Rosenblatt also hopes to help Flagship build new bridges between academic researchers and biotechnology entrepreneurs who may able to translate basic science into new medicines.

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FTC Review Ongoing As Teva/Allergan Await Final Approval

“We have been working very closely with the FTC since we announced the acquisition last July and have made significant progress since that time,” a Teva Pharmaceutical Industries Ltd. spokesperson told Scrip. “The status … is that Teva has filed all of the documents with the FTC, including all contracts related to the divestitures/remedies, necessary to complete the final review. We are awaiting their final approval.” However, Teva revealed in an SEC filing on July 11 that the deadline to complete the transaction had been extended from July 26, 2016 to October 26, 2016. Teva agreed to buy Allergan PLC’s generics business – formerly the company known as Actavis – one year ago for $40.5bn. Since then the two companies have been working on a series of divestments in a bid to secure antitrust approval. The most recent divestment agreement was announced on June 27 by Mayne Pharma Group Ltd. of Australia, which said it would buy a portfolio of US generic products from Teva and Allergan for $652m. The portfolio consists of 37 approved products and 5 FDA-filed products in a range of territories and indications. Speaking at the Goldman Sachs Global Healthcare Conference on June 8, Teva’s global generic medicines group’s head Sigurdur Olafsson attempted to address potential concerns that some investors might have with regard to the deal falling apart at the last minute. Published online 07-11-2016

Japan Rebound For Amgen With Daiichi Biosimilars Deal

Daiichi Sankyo Co. Ltd. is to commercialize in Japan a portfolio of nine biosimilars sourced from Amgen Inc., in a move that will significantly expand the Japanese firm’s presence in the growing sector as it faces the upcoming expiry of its top conventional drug. The deal is also a plus for Amgen after it was recently hit by Takeda Pharmaceutical Co. Ltd.’s decision to scale back a long-standing Japanese R&D alliance, and added to the good news from a US FDA advisory committee that voted unanimously to back the approval of Amgen’s biosimilar adalimumab. Under the new Daiichi tie-up, the US firm will develop and manufacture the nine products and its partner will file and hold the marketing authorizations and commercialize and distribute the products. Amgen retains limited co-promotion rights in Japan as part of the deal. The nine assets are at various stages of development but the firms did confirm the pact includes three Amgen molecules that are currently in Phase III programs. These are the anti-TNF alpha product adalimumab (ABP 501), a biosimilar of AbbVie Inc.’s Humira for rheumatoid arthritis and other inflammatory conditions; the VEGF A-targeting cancer product bevacizumab (ABP 215), a biosimilar of Roche’s Avastin; and trastuzumab (ABP 980), which targets HER2 in breast and gastric cancer and is a version of Roche’s Herceptin. The other biosimilars that Amgen has already disclosed that it is developing (but not confirmed to be a part or not of the Daiichi deal) are rituximab and cetuximab in oncology, and another anti-TNF antibody, infliximab. No details of the financial aspects of the transaction were released by either side, and Daiichi Sankyo in Japan declined to release to Scrip details of the other products that might be included in the alliance. It was also tight-lipped on when the first launches might be.

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Shire To Launch Potential Dry Eye Blockbuster After FDA Backs Xiidra

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Securing FDA approval for its novel dry eye treatment Xiidra (lifitegrast) gives Shire PLC a potential blockbuster and key future growth driver whose indication and label are more comprehensive than that of its closest approved rival.

FDA approval of Shire PLC’s Xiidra (lifitegrast ophthalmic solution) for treating dry eye came 10 days earlier than expected and paves the way for the product’s launch in the third quarter of 2016 as the only prescription eye drop approved in the US specifically to treat both the signs and symptoms of the condition.

Xiidra’s indication for both signs and symptoms of dry eye is more comprehensive than that of the key approved competitor, Allergan PLC’s Restasis (cyclosporine), which is only marketed to increase the eyes’ natural ability to produce tears. Restasis has become a major ophthalmic brand despite modest efficacy. Analysts believe Shire’s twice-daily eye drop solution will expand the value of the overall ophthalmic market.

“The label is as strong as we could have hoped for covering both the signs, ie, what the doctor can see on corneal staining, and symptoms being what the patient feels. This is notably stronger than competitor Allergan Restasis which is only approved for tear production, a weaker label, yet sells c$1bn a year,” Bank of America Merrill Lynch said in a reaction note.

“We expect the Xiidra approval to expand the dry eye category from around$1.4bn currently to $3bn, analysts at Leerink said in their note to investors. Leerink foresees lifitegrast sales of $900m and $1.3bn by 2021 and 2026 respectively and noted the therapy’s staying power given Xiidra’s composition of matter patent expires around May 2026 while its method of use patent expires in 2029. In announcing its decision to back the eye drug, the FDA said the safety and efficacy of Xiidra was assessed in over a thousand patients, in four separate, randomized, controlled studies using patients ranging 19 to 97 years of age, of which most were female (76%). “The studies found that groups treated with Xiidra demonstrated more improvement in both the signs and the symptoms of eye dryness than the groups treated with placebo,” the agency said.

Shire, which reports second quarter annual results on Aug. 2, has been busy building an ophthalmic business and between 2013-2014 bought three ophthalmic companies: Premacure, which has a protein therapeutic for retinopathy of prematurity, an orphan condition; Bikam Pharmaceuticals (autosomal-dominant retinitis pigmentosa, also a rare disease); and SARcode Bioscience, which it bought in 2013 and brought with it the dry eye treatment lifitegrast, which was filed for approval in March 2015.

“As Shire’s first FDA-approved medicine in ophthalmics, this significant milestone advances our goal of becoming the global leader in this category, where there are unmet patient needs. We have a robust ophthalmics pipeline, and we look forward to leveraging Xiidra as our entrée into the space as we continue to develop additional innovative eye care treatment options.” An estimated 16m adults in the US are diagnosed with dry eye disease, which is associated with inflammation that could lead to damage to the surface of the eye.

“Shire says lifitegrast is a natural complement with Foresight’s FST100 (povidone iodine 0.6% and dexamethasone 0.1%), a Phase III candidate for infectious (bacterial or viral) conjunctivitis (pink eye) which would also provide an alternative to antibiotics commonly used to treat conjunctivitis.

Shire on June 3 completed the company’s combination with Baxalta Inc., giving the Dublin, Ireland-based group strength in hematology and immunology and boosts its leading position in angioedema, enzyme replacement therapy, endocrinology and gastrointestinal diseases. Ophthalmics is now clearly being added to that list. Published online 07-12-2016
Teva’s Rosy View For A Happy Union With Allergan Generics

The company provided updated mid-term guidance for the combined company, net revenues of $26.7bn to $27.8bn in 2019. The deal is expected to close any day, management assured investors.

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Teva Pharmaceutical Industries Ltd. provided updated financial guidance for the company, accounting for the acquisition of Allergan PLC’s generic drug business, out to 2019 during a conference call July 13. The on-the-fly call seemed engineered in part to assure investors that the merger is on track to close soon, despite the fact that the deadline Teva originally gave for closing the deal has come and gone – twice.

Management used the platform to update investors on some of the financial technicalities of the $40.5bn acquisition, which they said is on track to close any day regardless of a recent extension. In a filing with the US Securities & Exchange Commission July 13, Teva disclosed that the deadline for closing the deal was extended to Oct. 26, three months beyond the previous deadline of July 26, making some investors nervous.

CEO Erez Vigodman insisted the deal remains on track and is expected to close at any time. “We are not aware of anything that would be expected to prevent the closing of this transaction,” he said. The company originally expected the deal, announced in July 2015, to close in the first quarter of 2016. In February, the company warned the timeline could move into the second quarter, which has now also passed.

Instead of dwelling on the hold-up by the US Federal Trade Commission (FTC), Vigodman said the deal is so close to being finalized the time seemed right to provide an updated outlook for the combined business. A more comprehensive overview will occur following the completion of the deal, he said, when Teva will have full insight into the pipeline it is acquiring.

The combined company will generate $26.7bn to $27.8bn in revenues in 2019, up from the $19.7bn Teva generated as a standalone business in 2015, the firm forecast. EBITDA will be between $10.7bn to $11.5bn in 2019, the company said, representing mid-point compound annual growth rate of about 14% from 2015 to 2019. Net income will grow from Teva’s $4.7bn in 2015 to between $7.5bn and $8.1bn in 2019, the firm predicted.

When the deal was announced in July 2015, Teva said the company would have pro forma revenues of $26bn and combined EBITDA of approximately $9.5bn expected in 2016.

The latest forecast to 2019 does not include generic competition to the newer 40mg version of Copaxone (glatiramer), dosed three times a week. The franchise is a cornerstone of Teva’s branded specialty business, and the company has had success switching patients from the once-daily formula to the new version, despite the launch of the first generic version, Novartis AG’s Glatopa, in June 2015.

Nonetheless, maintaining exclusivity for the 40mg version beyond 2017 is not a guarantee; rival Mylan NV announced that the US Patent and Trademark Office (PTO) instituted an inter partes review (IPR) proceeding against three of four patents protecting the 40mg version. For now, Teva’s current guidance anticipates $200m to $300m in sales erosion for the product each year.

There are some changes to the financial outlook, Vigodman said. For example, compared to the company’s original estimate that it would have to divest products that generated $500m in revenues and $300m in EBITDA in 2015, the actual amount of product divestitures is about double, currently around $1.1bn in revenues and $600m in EBITDA.

Nonetheless, he said the company still expects to achieve the previously outlined $1.4bn in synergies, though because of the delay in closing and larger than expected amount of the divestitures, it will take one year longer to achieve those savings, now forecast to be by the end of 2019.

Teva has announced several deals to divest products required by the FTC to complete the Allergan generics merger. In June, the company unveiled a deal to offload 15 generic drugs and a host of pipeline products to Impax Laboratories Inc. for $586m, another to divest eight ANDAs to Dr. Reddy’s Laboratories Ltd. for $350m in cash and a smaller deal with Sagent Pharmaceuticals Inc. covering several ANDAs for $40m.

The proceeds generated from the sale of products will be significantly greater than Teva originally forecast, the chief executive added, about $2.9bn versus $400m. The company also expects to generate about $1bn from working capital adjustments and proceeds of the sale of certain products back to Allergan. In one instance, the company outlined in the SEC filing that authorized generic versions of Actonel and Carafate would no longer be included in the buyout and that the cash consideration would be reduced by $221m.

As a result of the changes, the total net cost of the deal to Teva is reduced, now $35.1bn versus $40.1bn when the deal was announced, reducing Teva’s debt financing needs, Vigodman said.

When pressed by analysts during the July 13 conference call if the level of divestments were enough to get FTC’s blessing, Vigodman responded, “The answer is yes.” Now investors will just have to wait...

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A recent report from IMS Institute of Healthcare Informatics shows that diabetes patient adherence to medication regimens is costing patients and the country more than good health.

Even though the diabetes market is saturated with a multitude of drug options for patients with the chronic disease, there are still a variety of issues that complicate treatment and create undue burden on the healthcare system. One of the biggest challenges to the treatment of diabetes is not a lack of medications, but adherence to those drugs by patients.

Approximately 46% of Medicare patients with diabetes have suboptimal levels of therapy adherence and persistence, according to a July 12 report released by the IMS Institute for Healthcare Informatics. The report notes that these patients have trouble taking the proper dosage at the correct times and often don’t stay on the drugs long enough to make a significant impact.

The lack of adherence and persistence in diabetes patients leads to a whole host of issues, including elevated blood glucose levels, health complications for patients and ultimately avoidable costs to the healthcare system.

Diabetes is one of the most widely-treated diseases, with more than 55 marketed drugs available from just the top 10 companies in the space, according to Biomedtracker. These marketed products include multiple offerings across categories, including insulin, oral DPP-4s, injectable GLP-1s and oral SGLT-2s.

The pipeline is just as impressive. Market leaders Novo Nordisk AS and Eli Lilly & Co. each have strong pipelines with 14 and eight compounds, respectively, across drug classes. Meanwhile, Sanofi’s Lantus is currently struggling to hold its share of the insulin market, even as a biosimilar of the product is expected to hit the US market before the end of the year.

ADHERENCE ISSUES ADD UP
Despite the abundance of effective drugs, they don’t work unless patients take them. Those patients that don’t take their medications as prescribed tend to have HbA1c levels that are 17% higher and are more likely to experience complications like nephropathy, visual impairment, kidney failure, leg amputations and heart attacks.

Ultimately, all of these issues lead to further strain on the healthcare system. In 2012, diabetes cost the US healthcare system $176bn annually, with almost 60% of costs coming from patients in the Medicare system and almost the same percentage of costs coming from complications of diabetes.

IMS’ CORE Diabetes model – a system used to estimate costs – expects type 2 diabetes-related complications will cost US Medicare $100bn annually. Approximately 3.9%, or $4bn, of those costs are avoidable, according to the report, which notes those costs are due to poor patient adherence.

It’s not just the US that is having this problem, the IMS report concludes. “The underlying patterns that we saw in all countries included patient engagement, patient attitudes towards disease and medication. Overall, it’s similar across all countries,” Murray Aitkin, executive director of IMS Institute for Healthcare Informatics, told a July 11 briefing. “You’ll see the same attitudes in patients across the world, whether that be a lack of health literacy, skepticism of treatments and a belief in the likelihood of complications, financial concerns and so on.”

Yet, Aitkin pointed out that the levels of non-adherence are very different across countries. For example, the US had the lowest level of non-adherence with about 46% and highest in Brazil at 77%. The reports looked at six countries: the US, UK, Brazil, Germany, Mexico and Saudi Arabia. IMS Institute for Healthcare Informatics conducted the report along with Lilly Diabetes.

The report suggests better identifying patients that are likely not to adhere to medication regimens, improving access to medications and disease education, expanding care teams and financial assistance, and using digital technology to help patients with drug management.

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Horama Joins Race To Develop Gene Therapies For Eye Diseases

The French company, Horama, which is working with specific serotypes of adeno-associated virus (AAV) that may have potential benefits as vectors for novel gene therapy approaches to retinopathies, has just appointed an experienced CEO Christine Placet and completed a smallish Series A to move two promising gene therapies into clinical studies, and to build up its drug development team. Previously Placet was CEO of the neurodegeneration-focused Trophos SA, that was acquired by Roche for €470m ($521m) in 2015, and she appears to have the knack of working in hot research areas. The development of gene therapies for retinal diseases is one such swelling sector, that is buoyed by pilot studies that have suggested benefits, companies like US-based Spark Therapeutics Inc. that are nearing the market with a gene therapy, and the hope that injecting such therapies into the eye will be a relatively straightforward procedure and have only local activity, with little exposure of the rest of the body to administered genes. There are potential breakthroughs happening in the development of small molecules too for retinal diseases, promising a diversity of potential approaches for so-far untreatable conditions that often lead to blindness. Horama’s vectors include recombinant AAV serotypes four and five that are engineered to contain specific genes and gene promoters and are injected subretinally between the retinal pigment epithelium and the layer of photoreceptors in the eye. The vectors are taken up into the nuclei of photoreceptor cells where they start to synthesize healthy proteins, replacing the output of mutated genes. The introduced genes are not integrated into the cellular genome and, because photoreceptor cells don’t undergo cell division, it is hoped that one dose may produce therapeutic proteins over the long term. Published online 07-12-2016

CytRx Will Need ‘Stunning’ OS Data To Get Chemo Agent Back On Track

CytRx Corp. saw its stock drop as low as $0.75 per share this week on the back of poor Phase III data for its lead drug – modified chemotherapy agent aldoxorubicin – which have left analysts questioning whether the company’s plan for further examination can save this study. The Los Angeles-based firm reported top-line Phase III data for aldoxorubicin, a modified version of the chemotherapy agent doxorubicin, on July 11, in which CytRx’s agent did not show a significant difference on progression-free survival compared to investigator’s choice therapy. In the trial, patients treated with aldoxorubicin showed medium PFS of 4.17 months versus 4.04 months for alternative chemotherapy treatment. However, the most immediate indications of therapeutic activity, objective response rate (ORR) and disease control rate (ORR + stable disease ≥ 4 months), – the study’s secondary endpoint – showed a near doubling in the aldoxorubicin arm compared with investigator’s choice, including in patients who previously received treatment with doxorubicin. The product binds doxorubicin to albumin via a linker to help target its delivery to the protein-hungry tumor and is designed to reduce the side-effects of the older chemotherapy, particularly on the heart. Analysts at Biomedtracker said the poor Phase III results were a “devastating hit” to CytRx. “Previously, the drug had posted generally promising results in a front-line setting where an OS benefit had not been shown, but the statistically significant PFS hazard ratio was at least encouraging,” Biomedtracker said in an analysis of the top-line Phase III data. “Those results did not translate into the larger Phase III study (which also enrolled patients differently in the second-line treatment setting rather than first-line).” Published online 07-14-2016

Sage Drug Could Help Take Stigma Out Of Postpartum Depression

SAGE Therapeutics Inc. could offer the one in eight new mothers suffering from postpartum depression (PPD) freedom from the overwhelming condition with the first-ever drug to specifically treat PPD if the rapid and durable response to SAGE-547 in a small Phase II clinical trial holds up in future studies. “I’m incredibly optimistic,” said University of North Carolina (UNC) associate professor Samantha Meltzer-Brody, who runs the first specialized hospital unit in the US for the treatment of PPD – a perfect partner for a company with the only drug in clinical development for the condition. SAGE-547 is in Phase III for super-refractory status epilepticus (SRSE) with data expected before the end of 2016. But given the 70% remission rate seen in women with severe PPD and the high unmet need, Sage may pursue an expedited path to approval for the maternal condition. “These are the most dramatic data anyone has seen in this patient population, based both on efficacy and rapidity of response,” Sage CEO Jeff Jonas told Scrip. That’s why the company will talk to the US FDA about whether it must run a Phase III clinical trial to support approval or if the planned expansion of its Phase II trial would be sufficient for accelerated approval in the PPD population. Jonas said SAGE-547, if approved, would lay the medical and commercial groundwork for SAGE-217, Sage’s oral follow-on product candidate. Published online 07-14-2016
Allergy vaccine sector is poised to globalize

The failure of Circassia’s cat allergy vaccine product in a Phase III study, and other recent setbacks including a one-year delay to Allergy Therapeutics’ US ambitions, have not stymied the excitement in a sector that promises new approaches to grass, tree, peanut and other food allergies, and much more convenient treatment regimens.

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The allergy vaccine sector is in good shape, with companies investing in and testing new approaches, some consolidation among allergy-focused firms, and a desire among companies to “go global” and to break out of their European strongholds, says Manuel Llobet, CEO of Allergy Therapeutics PLC, a rapidly growing UK-based allergy company.

The sector may have been stunned by the recent failure of Circassia Pharmaceuticals PLC’s investigational cat allergy product, Cat-SPIRE, in top-line results from a Phase III study, with the failure blamed on an extremely high response by patients to placebo.

And the gloom was compounded a week later by Allergy Therapeutics reporting a Phase II dose-ranging study for its grass allergy vaccine, GrassMATAMPL (known as Pollinex Quattro Grass in Europe) in its US development program that did not come up with useful data.

But such doom was overdone, according to Allergy’s Llobet, who noted his company’s clinical results came when the atmosphere was charged with the approaching Brexit vote in the UK, where both Circassia and Allergy Therapeutics are headquartered and listed. The inconclusive nature of the dose-response study was “surprising but part of the process. Many clinical research programs have studies that are inconclusive,” he commented.

When cooler heads prevail, the allergy vaccine sector is likely be seen in a brighter light. “The allergy market is rapidly expanding and the sector is going global, with companies signing licensing deals for Russia, Southeast Asia and other parts of the world,” Llobet said. Analysts at Informa Pharma Intelligence’s Biomedtracker have put the likelihood of US approval of Pollinex Quattro Grass at 62%, the average for products at its stage of development.

Currently, Europe accounts for more than 90% of the allergy vaccine market, but work is underway to change that concentration. “Since 2012, allergy companies have raised €1.3-1.4bn ($1.4-1.5bn) to conduct research, and several novel approaches are being evaluated, including three companies working on peanut allergy,” Llobet noted in a recent interview with Scrip.

Two new allergy products have also been approved for marketing in the US since 2014 – Merck & Co. Inc.’s sublingual tablets against grass pollen (Grastek) and ragweed (Ragwitek) – and more are on the way, including Allergy Therapeutics’ GrassMATAMPL. Indeed, Allergy Therapeutics is continuing to grow its own allergy business.

In a trading update released July 13, the Worthing, UK-based company said it expected revenues in the 12 months to June 30, 2016 to be around £48.5m ($64.86m), up 12% as-reported or up 19% in constant currency terms – the weakening euro during most of the 12 months has had a negative impact on financial results, the company said.

Its market share has increased from 10% to 12% across European markets, principally Germany, Austria, Spain and the UK, in a market that in overall terms has been flat. Full preliminary results for the 12 months will be reported in September.

THE ROLE OF EXPOSURE CHAMBERS

The Phase IIb dose-ranging study results reported by Allergy Therapeutics on June 27 with GrassMATAMPL were from one of a number of studies in its US development program, Llobet said. In that study, G204, a mobile environmental exposure chamber was being used for the first time in a US study, and was exploring higher doses of the allergy vaccine, but failed to give a conclusive answer to what is the most suitable dose. Such chambers are being used in an effort to prevent confounding factors such as exposure to other environmental allergens from influencing the results.

“We are still investigating why the chamber study did not allow us to pick a dose to go into Phase III studies in the US, but in the meantime we have decided to conduct a dose-ranging study using the Conjunctival Provocation Test (CPT), that has previously outlined a dose-response relationship for another of the company’s investigational products, Pollinex Quattro Birch,” Llobet said.

This is expected to start in 2017, and the amended process will delay the US Phase III study by a year, but Allergy Therapeutics expects to use the time usefully to prepare for what could be the first introduction of an ultra-short-course subcutaneous allergen specific immunotherapy (SCIT) in the US. “It’s disappointing but has to be looked at in context. In a few years we will have global companies exploiting a global market,” Llobet commented.

RECOMBINANT PEPTIDES VERSUS MODIFIED ALLERGENS

Allergy Therapeutics is curious about the potential use of the well-defined allergenic peptide approach used by Circassia and several other companies for desensitization, compared with its own modified complete allergen approach, and is going to test both approaches in animal studies with its potential peanut vaccine.

The future competition for Allergy Therapeutics’ products is likely to be fierce. The Switzerland-based company Anergis SA that is developing “contiguous overlapping peptides” for allergies, recently reported its potential birch pollen product, AllerT, has shown safety and efficacy in a Phase IIb study. And the French company DBV Technologies SA has a transdermal peanut allergy product, Viaskin Peanut, in a pivotal Phase III study, with topline results expected in the second half of 2017. 

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A tense advisory committee meeting, where many of the panelists admitted they lacked a complete understanding about biosimilars and patient advocates expressed anxiety over the products, could signal difficulties with adoption and success in the marketplace.

Even though the FDA’s 26-member Arthritis Advisory Committee on July 12 voted unanimously to back licensure of Amgen Inc’s biosimilar version of AbbVie Inc’s Humira (adalimumab), getting there was a chore – potentially signaling the difficulty of what’s ahead for companies in educating prescribers and the public, which will be needed to achieve market success.

Indeed, it was apparent early on that several of the panelists had trouble even grasping the idea of what it means to be a biosimilar, versus an interchangeable product.

“You have people who are clinicians and you are asking us to make a judgment that is out of our comfort zone,” declared panelist Therese Wolpaw, vice dean for educational affairs at The Pennsylvania State University College of Medicine.

Nikolay Nikolov, clinical team leader in the FDA’s Division of Pulmonary, Allergy, and Rheumatology Products, said the agency made every effort to compile an advisory committee that would have the right expertise.

“I can confess that this was extremely difficult, but we did what we could,” Nikolov said.

He acknowledged that even though the panel was “somewhat a very diverse committee,” many of the clinicians were not familiar with the concepts that were discussed – admitting it was “a lot to ask” of the advisers.

But with the difficulty the committee had in coming to “grasp with understanding the purpose and the pathway for biosimilarity,” panelist Mara Becker, an associate professor of pediatrics at the University of Missouri-Kansas City, questioned how information about biosimilars will be disseminated to prescribers and patients “so they understand it, too?”

“I think it’s going to be really important as we move forward as we address these new agents, not only for acceptability and for safety, but for the public to understand the rationale and how they were approved,” Becker said.

“We certainly acknowledge the community’s nervousness and need for additional reassurance or confidence that these products would work in different indications,” Nikolov said.

Many on the committee said they were concerned about the anxiety expressed by most of the nearly 20 public speakers at the July 12 meeting over whether biosimilars will be similar enough to the innovator biologics, particularly in the non-studied indications, for which the FDA has allowed the data to be extrapolated.

Numerous speakers said they were worried about “non-medical switching,” in which they said insurers and pharmacy benefit managers could force patients stable on certain biologics to use biosimilars or interchangeable – insisting they could be subjected to adverse immune responses.

Steven Kozlowski, director of the FDA’s Office of Biotechnology Products, pointed out the “reality is” that each lot of an innovator biologic slightly differs from one to another, so “without knowing it, there have been subtle differences” in the drugs patients already have been getting.

Nonetheless, he acknowledged there “really is an education issue” with biosimilars.

While panelist Steve Solga, a gastroenterologist in Bethlehem, PA, said his vote on Amgen’s biosimilar was “easy” because the advisers were asked a narrow question, “I’ve not seen such a disconnect between the charge to the committee and the concerns of the public.”

“The disconnect is really quite remarkable,” Solga declared. He insisted there needed to be some sort of a public forum where prescribers’ and patients’ concerns could be “fully and completely” aired.

Solga also urged the public speakers to try to sit down with Sen. Lamar Alexander (R-TN), chair of the Senate Health, Education, Labor and Pensions Committee, to try to get congressional action to alleviate some of their concerns, “because we didn’t get done what we needed to get done today for them.”

“I know we are not being charged to talk about things like cost and other areas, but that’s the silo mentality, which a patient never exists in, since they are constantly having to deal with all of these different things,” said the committee’s consumer representative, Jennifer Horonjeff, a research fellow and patient advocate at the Center for Immune Disease with Onset in Childhood at Columbia University. “We need a way to figure out a way to bridge that gap so that they can better understand.”

“We really need to think about the consumer,” Horonjeff said, pointing out that biosimilar makers won’t succeed until they get patients on board.

WHAT’S INDUSTRY DOING?

Amgen officials have long acknowledged that for the US biosimilars market to be successful, there needs to be trust in the products by prescribers and patients, meaning companies will need to be transparent and accountable. Amgen said it has created a website to help educate doctors and consumers about biosimilars.

It also is a member of various organizations whose mission it is to provide education about the products, including the Biosimilars Forum, which consists of a mixed bag of traditionally brand-name and generic firms. Other members include Allergan PLC, Boehringer Ingelheim GMBH, Coherus BioSciences Inc., EMD Serono Inc., Epirus Biopharmaceuticals Inc., Merck & Co. Inc., Pfizer Inc., Samsung Bioepis Co. Ltd., Sandoz Inc. and Teva Pharmaceutical Industries Ltd.

Washington lawyer Michael Werner, a partner at Holland & Knight and the policy adviser for the Biosimilars Forum, said the organization has created the Partnership for Biosimilars Education and Access, which is focused on improving the understanding of biosimilars in the US and addressing barriers to access and awareness of biosimilars.
**Juno ROCKeTs On Fast Clinical Hold Resolution**

The FDA lifted a clinical hold on the Phase II ROCKeT clinical trial for Juno’s lead CAR-T therapy candidate JCAR015 less than a week after it was instituted, allowing the company to proceed without using fludarabine in a pre-conditioning chemotherapy regimen. Juno Therapeutics Inc. soared in after-hours trading on July 12 following the company’s late-day announcement that a clinical hold on its Phase II ROCKeT clinical trial for the chimeric antigen receptor T-cell (CAR-T) therapy JCAR015 has been lifted just a few business days after the US FDA instituted the hold in response to three deaths in the study. Seattle, Washington-based Juno fell more than 27% after the stock market closed on July 7 when the company first revealed the clinical hold, despite assurances that the FDA was likely to expedite its review of the ROCKeT enrollees’ deaths. The trial, which is testing JCAR015 in the treatment of certain acute lymphoblastic lymphoma (ALL) patients, will continue without the use of fludarabine in a pre-conditioning chemotherapy regimen. Juno speculated that the three cases of lethal cerebral edema observed in ROCKeT were caused by fludarabine, which was added to cyclophosphamide to prime the immune systems’ of adults with relapsed or refractory B-cell ALL. The FDA responded quickly to the company’s request to resume enrolling patients in ROCKeT as long as the trial’s protocol required pre-conditioning with a cyclophosphamide-only chemotherapy regimen. Juno rose 25% to $34.75 after the stock market closed on July 12 in response to the news. The announcement carries a mix of good and bad news for the company, however, since pre-treating patients with fludarabine plus cyclophosphamide improved response rates, progression-free survival and overall survival in earlier studies for JCAR015, other Juno CAR-T therapies and competing product candidates. Removing fludarabine from the ROCKeT trial could impact the reengineered T-cells’ efficacy in advanced ALL patients.

**UK Cancer Drugs Fund Reforms Get Cautious Welcome, But More Needed**

NHS England has finalized and published new arrangements for commissioning cancer medicines - including the use of the Cancer Drugs Fund - addressing some of the concerns voiced during the run-up consultation period by charities, patient groups and the pharma industry. The new Cancer Drugs Fund will now have clear entry and exit criteria allowing medicines to move in and out over time, whereas the old fund only had entry points. There is also a much needed system for getting some promising new cancer medicines to National Health Service patients more rapidly, while gathering evidence about their effectiveness. But the pharmaceuticals industry is not pleased with changes compelling companies that have therapies in the reformed CDF to pay for any future CDF over-spend. “That effectively means companies getting squeezed twice – once individually when getting drugs into the CDF and then collectively if the fund exceeds its budget,” said Paul Catchpole, value and access director at the Association of the British Pharmaceutical Industry (ABPI). Under new guidance from NHS England, the previous Cancer Drugs Fund - first established in April 2011 as a temporary solution to support clinicians and their patients gain access to cancer drugs not routinely available on the NHS - will switch to a ‘managed access’ fund, with a fixed annual budget of £340m. Publishing of the reforms, unveiled late on July 8, followed a 12-week consultation that ended in February. The previous Cancer Drugs Fund was originally due to end in 2014, having acted as a bridge to a new system of value-based pricing. But proposals for value-based pricing were not pursued, so the CDF was extended further to the end of March 2016, having first closed in May 2015 to new drugs pending the start of the new scheme that now starts at the end of July. Under the incoming system, effective July 29, all new cancer drugs will be referred to the National Institute For Health and Care Excellence (NICE) for appraisal, a process which will start much earlier than previously with the aim of publishing draft guidance prior to a drug receiving its marketing authorization and then final guidance within 90 days of marketing authorization wherever possible. Any drugs receiving either a draft recommendation for routine commissioning or, where uncertainty exists, a recommendation for use within the CDF will receive interim funding from the CDF from the point of marketing authorization. NICE will then normally issue final guidance within 90 days of marketing authorization. If drugs are recommended for routine commissioning at this point, they will go into the normal commissioning stream. If medicines are recommended for substantive entry into the CDF, a joint NHS England and NICE CDF investment group will meet to agree the terms of any commercial access agreement, including evaluation criteria and a timescale for evaluation to complete. At the end of the CDF evaluation period, NICE will re-appraise the drug with the aim of making a final positive or negative assessment as to whether the drug should be routinely commissioned. **Published online 07-11-2016**
The UK Competition and Markets Authority is looking into claims that some generic prices have been raised excessively, while a proposal by health secretary Jeremy Hunt that such price hikes could be systematically monitored could well go ahead after he retained his post in the new prime minister’s cabinet.

As the UK Competition and Markets Authority continues its inquiry into allegations of steep price rises on some off-patent drugs, the news that Jeremy Hunt is to stay on as secretary of state for health in the cabinet of newly appointed prime minister Theresa May means that he may now pursue his suggestion for a system of routine and systematic monitoring of price increases on generics.

Hunt, who managed to retain his job amid the political earthquake caused by the prime minister’s cabinet changes on June 13 and 14, announced at the beginning of June that he had asked the CMA to look into allegations by The Times newspaper that some pharmaceutical companies in the UK had raised the prices of certain patent-expired drugs excessively by dropping the brand names and marketing them as generics, thereby putting them outside government price controls. The inquiry is part of the CMA’s ongoing investigations into excessive price increases.

In a June 13 letter to Hunt, Dr Sarah Wollaston MP, who chairs the House of Commons Health Committee, said that the actions “of one pharmaceutical company” had cost the NHS “in excess of ten million pounds last year simply due to the recategorization of medications.”

She said that while she was aware that Hunt had asked the CMA to look urgently at the issue as part of its ongoing investigations, it was nonetheless “worrying that such apparent abuses have been going undetected and that the scale of the issue and the full cost to the NHS is unknown.” She asked what steps he could take to ensure that the allegations were appropriately investigated, and how such “extraordinary rises in medication prices” would be tackled in future.

“Given the responsibility of the NHS to spend its resources wisely, what measures will be put in place to ensure that the NHS always obtains value for money when purchasing medicines, and that any abuses such as those alleged in the Times article are identified early and stopped?” Wollaston asked.

In a reply published on July 11, Hunt said the government had voluntary and statutory schemes in place to “consider the prices of branded and generic medicines rather than consider each product individually,” and that legislative provisions allowed it to intervene with regard to drug prices. “However, any investigation would require a high-level and detailed knowledge of the company’s business to be able to make a judgement as to whether a particular price increase was justified,” he told Wollaston.

Furthermore, he continued, the cost of any medicine has to be balanced against “the importance of meeting the individual treatment needs of patients and potential additional costs to the NHS is supply is interrupted, for example, adverse outcomes owing to the stopping of treatment.”

CONSULTATION RESPONSES BEING EXAMINED

Hunt said that while the current pricing arrangements worked well for most products, there were “anomalies, and we do keep the system under review and pursue improvements as appropriate.” He noted that a consultation began in September 2015 asking for views on whether the secretary of state should be able to limit the prices of generics where there was no competitive market to secure value for money.

“The consultation closed on 4 December 2015 and we are continuing to consider carefully all the consultation responses,” Hunt said.

‘Solutions need to be found which include no allowing monopoly provision & possibly the NHS developing a plant to manufacture drugs’

He added that he was “considering putting measures in place to routinely and systematically monitor significant prices increases of generic medicines,” and that he would be “keeping an eye on developments in this area very carefully.”

Whether he still intends to pursue such measures remains to be seen. Shortly after his position as health secretary was confirmed on July 14, he tweeted: “Reports of my death have been greatly exaggerated... Thrilled to be back in the best job in government.”

MORE CONCERNS OVER PRICING

In a separate June 28 letter to John Wass, professor of endocrinology at Oxford University, Parliamentary Undersecretary for Life Sciences George Freeman had also noted the government’s examination of the consultation responses on generic prices, saying that “we want to look in particular at the impact on small and medium-sized businesses, while securing the medicines patients need at a cost that the NHS can afford.”

Wass had written to Hunt on June 10 to express concern about “major price hikes in generic drugs about which I have been alerting the Department of Health for well over a year.” He said it was “frankly scandalous that huge sums of money have been expended on these drugs” and that the DH “seems to have done nothing or very little to ameliorate the problem.”

The price increases were “up to 1,000%,” Wass said, adding that “solutions need to be found which include no allowing monopoly provision and possibly the NHS developing a plant to manufacture some of these drugs.”

Published online 07-14-2016
Deal Watch: Flagship Ventures Doubles Down On Microbiome

Two of the VC’s biotechs merged to create an immuno-microbiome company, while Seres is working with Emulate on better tech for microbiome research. UK specialty pharma Martindale acquired small hospital products-focused UK firm Viridian, and Bayer and X-Chem expanded their drug discovery alliance.

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Scrip regularly covers business development and deal-making in the biopharmaceutical industry. Below is a roundup of some of the most noteworthy transactions that occurred between July 8-13. Deal Watch is supported by deal intelligence from Strategic Transactions.

EVELO/EPIVA
A pair of microbiome-related deals with ties to venture capital outfit Flagship Ventures were announced July 12, with Flagship-backed biotechs Evelo Therapeutics and Epiva Biosciences merging to create an immuno-microbiome company that will develop next-generation therapies for cancer, autoimmune disease and inflammatory disease. The new company will operate under the name Evelo Biosciences, led by CEO Simba Gill and chair Noubar Afeyan, also the CEO of Flagship Ventures.

The VC firm launched both companies out of its Flagship VentureLabs Innovation foundry in 2014, following up on previous forays into microbiome therapies such as Seres Therapeutics Inc., launched in 2012.

Evelo says its platform combines expertise in microbiology, immunology, pharmacology and computational biology and that it has identified specific bacteria that offer the ability to “modulate the immune system in defined ways.” The new company will create therapeutics that activate the immune system against tumors or down-regulate the immune system to address inflammatory or autoimmune disorders. Although the Cambridge, Mass.-based biotech’s website does not include any pipeline information, it says the firm has identified several candidates for oral delivery “with the potential for many more.”

The company resulting from the merger will have 42 employees and combine each firm’s research and intellectual property to date, encompassing more than 50 patents and applications. Flagship has provided more than $40m in financing to the firms so far, with plans for additional investment “to support its rapid growth.”

“As the microbiome field begins to turn its attention to diseases beyond gut infections, we see the combination of these two first-mover companies as an important strategic development aimed at creating sufficient mass to lead the field,” Afeyan said.

SERES/EMULATE
Also on July 12, Flagship-backed Seres announced a collaboration with “organs-on-chips” biotech Emulate Inc. to advance the latter’s Intestine-Chip platform, a micro-engineered, living-tissue based system that models the human intestine. Earlier this year, Emulate raised a $28m Series B round with involvement from its Series A investors.

Via its involvement in this collaboration, Cambridge, Mass.-based Seres plans to use the Emulate technology to identify novel bacteria compositions that may offer therapeutic potential. David Cook, the biotech’s executive vice president of R&D, said Emulate’s platform consists of multiple human cell types that may provide greater accuracy in recreating human gastrointestinal tissue and replicating interaction with the microbiome than previous conventional cell culture approaches have allowed.

Flagship was among the primary investors in Seres’ initial public offering in January 2015, which netted the firm $143m. Over four venture rounds, Flagship and its syndicate have raised $134m for Seres.

MARTINDALE/VIRIDIAN
UK specialty pharma Martindale Pharma announced the acquisition of Viridian Pharma July 11 at undisclosed terms, but said the deal bringing in a set of niche pharmaceutical products would be immediately accretive.

Martindale said the deal fits into its larger strategy to expand its product portfolio and support growth of its range of hospital-initiated medicines on offer. Viridian, established in 2002, has developed five drugs with regulatory approval in the UK, all of which represent first-to-market specialty drugs for the hospital setting.

Martindale has worked with Viridian to manufacture and market two of those products, a caffeine citrate injection and a caffeine citrate oral solution, both for apnea of prematurity in preterm babies. The other products include a sodium chloride oral solution to correct hyponatraemia in infants, a sodium citrate solution to prevent respiratory complications in pregnant women undergoing caesarean section, and peppermint water for symptomatic relief of minor upper digestive irritation.

BAYER/X-CHEM
Bayer AG has expanded a drug discovery collaboration with X-Chem Inc. first signed in 2012, to use the Waltham, Mass., biotech’s DEX platform to discover novel small molecules across a broad range of therapeutic areas and target classes. The firms signed a multi-target deal in 2012, but it was not disclosed until 2014: Bayer has licensed two compounds under the partnership to date, including a cardiovascular disease candidate in December 2014.

Under the initial agreement, Bayer paid upfront cash and provided research funding, with option exercise fees for each licensed program as well as preclinical, clinical, and sales milestones and potential sales royalties. The renewal and expansion focusing on innovative lead structures for complex drug targets in areas of high unmet medical need, announced July 12, provides X-Chem additional upfront and R&D funding, as well as the possibility of up to $528m in development and regulatory milestone payments, plus sales royalties and sales milestones. Bayer gets an exclusive option to license any candidates discovered over the course of the collaboration.
Is The Pharma Industry Blind To Talent From Other Sectors?

Restrictive hiring and executive board appointments from within just the immediate biopharma industry will be detrimental to growth for the UK life science industry, according to a new white paper of employment practices.

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While it’s not the first time the spotlight has fallen on pharma companies for only employing staff from the same limited pool of candidates, DHR International has highlighted in a new report that a downwards trend has emerged concerning the number of executive board members with experience outside of the pharma, biotech or banking industries.

Data from the executive search firm’s recent white paper, The Pharmaceutical Industry Increasingly Looking Inwards For Leadership Roles Despite Significant Challenges On Horizon, show that only a quarter (26%) of executive board members in UK-listed pharma companies is recruited from outside of the industry – this is down from 40% in 2010. This number drops to 15% when you look for executive board members from non-pharma, biotech or banking backgrounds.

However, the trend in the UK is reversed in other sectors amongst CEO appointments: DHR found that between 2012 and 2015 almost a quarter (22%) of all CEOs brought in via a planned succession had experience from outside the sector – an increase from 14% in 2004 to 2007.

Meanwhile, European pharma and biotech companies appear better at recruiting board members with non-pharma backgrounds, with around 34% of executive board members possessing experience outside the pharma, biotech and banking sectors in 2015.

The white paper authors said: “Whilst nobody would deny the importance of technical and scientific understanding at board level in healthcare companies, the side effect can be a perceived lack of diversity.” They noted that this is particularly relevant in 2016 when companies are facing a sticky climate with significant challenges, including declining R&D productivity, increased threat from generics and pressure on margins from key customers. “Such major problems may require innovative thinking both at a strategic and at an operational level. Bringing in fresh thinking from outside the sector could deliver that,” the authors said.

The report analyzed board compositions for 24 of the UK’s largest pharma companies and boards of the top five European pharmaceutical companies.

Report author Alin Popescu, a partner at DHR International and a member of the European Life Sciences Practice, highlighted that restrictive hiring within pharma companies could result in the industry becoming resistant to change. The report authors highlighted R&D productivity as an upcoming challenge, noting that while the models and strategies in this area have remained unchanged for decades, there is disruption building in the form of new computer technologies. “As R&D involves the analysis of huge volumes of data, the pharmaceutical sector is being encouraged to look at how other sectors have embraced ‘big data’ to stimulate innovation,” Popescu said.

The authors concluded that for many pharmaceutical companies it may be the case that leaning towards proven performers in their own sector is attractive in slightly uncertain times. However, the report suggests companies should instead be seeking expertise from industry veterans in sectors that have already weathered vast market disruptions – such as the FMCG (fast-moving consumer goods) sector. “A lot of leaders from the FMCG sector have experience of achieving substantial cost reductions in recent years by completely overhauling their supply chain models,” DHR said.

WHAT PHARMA HAS TO SAY

A spokesperson for UK pharma giant GlaxoSmithKline PLC told Scrip, “As a company we are very open to bringing in talent from other sectors.”

The big pharma said it “welcomes different insights from other sectors” and highlighted as an example its head of consumer business, Emma Walmsley, who joined GSK from L’Oreal. GSK’s spokesperson also noted that its president of the pharma business, Patrick Vallance, came to the company from academia. GSK added that for its early talent programs, which focus on graduates, it specifies that applicants should have unrelated degrees; for example, for an IT placement it does not seek computer science graduates.

Meanwhile, Roche – which was highlighted by DHR as a “best practice” company because of the non-pharma background of CEO Peter Grant – said diversity plays a crucial role in its recruitment processes. “Different backgrounds, views and thinking styles are needed in order to be able to discover the best ideas and bring truly innovative solutions to patients around the world,” a spokesperson for the company told Scrip.

For its board members, Roche said: “The board of directors needs to be able to carry out its control function as well as talk at eye level and work together with the group management. Expertise, experience and diversity, among others, play a vital role in the composition of the board.”

Published online 07-12-2016

Pharmaceutical Board Experience – UK

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<td>All board members with no pharmaceutical, biotech or banking experience</td>
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Source: DHR International
Get Ready For Pharma’s Predictable Half-year Surprises

JOHN HODGSON john.hodgson@informa.com

It is coming up to half-year results season and two things are entirely predictable: there will be many surprises and hardly any of them will be good.

Starting this week with Novartis AG, Johnson & Johnson and Roche followed next week by Eli Lilly & Co., GlaxoSmithKline PLC, Bayer AG, AstraZeneca PLC, Sanofi and Merck & Co. Inc., the pharmaceutical majors will roll out their big wheels to tell investors how things have been going in the first half of the year and how forecasts of just six months ago need to be tweaked in the light of reality.

Results seasons traditionally are turbulent: it is not a coincidence that when CEOs open their mouths to express naked financial truth, more investors than usual change their minds about the wisdom of holding shares in drugs companies. On the day Alex Gorsky announced J&J’s 2015 full year results back in January, for instance, 19 million J&J shares changed hands, over three times as many as on an average day. Kenneth Frazier spoke in February: twice as many Merck shares changed hands then as normal. Pascal Soriot started a week of high-volume (3-4 times average) down-trading in AstraZeneca the same way.

And the pattern persists across a spectrum of biopharmaceutical companies: trading volumes rise before results announcements and the upsurge extends several days afterwards. Investors apparently hear, or expect to hear, something that changes their view of a company. And they often don’t like what they hear.

But even if the news is good and a stock rises, significant increases in trading volumes still reflect badly on company management. Jumps or falls in stock prices and volumes represent communications gaps or, at least, an imbalance in understanding between a company’s executives and its owners.

To get a handle on this gap, I compared the magnitude of the investor surprise response (trading volume) for routine annual reporting with the response to more unexpected events.

One tumultuous industry-shaking event in 2015 enabled ready calibration of this scale of investor uncertainty.

On “Black Monday,” Aug. 24, 2015, trillions of dollars of value was wiped off company valuations globally following concerns about the stability of the Chinese economy. It wasn’t just the pharma sector but drugs firms, especially large ones, were badly hit. Prices of the top 50 European and US companies’ stocks fell 4-10%. Trading volumes in the week of Black Monday were 2-4 times larger than in the previous week.

For big pharma, the release of Novartis’ 2015 full-year results had a BMR of 0.84, while Merck & Co’s was 0.79 and Pfizer’s was 0.92. Gilead Sciences Inc’s number was 0.92, Amgen Inc’s 0.82, J&J’s 0.75 and AbbVie Inc’s 0.73. Apparently, investors find the release of pharma company financials 70-90% as traumatic as they found Black Monday.

Sometimes it’s more traumatic. The 2015 results from Novo Nordisk AS, Bristol-Myers Squibb Co., GSK, Eli Lilly and Regeneron Pharmaceuticals Inc. all elicited a bigger investor response than Black Monday did (BMR=1.1-1.4). And over three times as much AstraZeneca stock was traded around its results than on one of the worst days global stock exchanges have witnessed.

That near-universal stock shock gives an indication of the effect on pharma stocks of an event that clearly lies outside the control of any pharma management. But the question is, how does the impact of Black Monday compare with that of events that are part of the management remit?

To get a crude answer to that, I have used relative trading volume to assign a Black Monday Rating (BMR) to stock shifting events on a company-specific basis. The BMR for any event is the ratio of the amount of stock shifting on the day of the event divided by the amount that shifted on Black Monday. Black Monday itself rates at 1.0: events that are less disturbing to the market have a rating less than 1.0; anything that perturbs a stock more will rate higher than 1.0.

Surprisingly, and somewhat disturbingly, markets appear to be as surprised by routine pharma financials as they do about Chinese economic downturns.

For big pharma, the release of Novartis’ 2015 full-year results had a BMR of 0.84, while bigger investor response than Black Monday did (BMR=1.1-1.4). And over three times as much AstraZeneca stock was traded around its results than on one of the worst days global stock exchanges have witnessed.

The issuance of financial results is not usually the biggest trauma for pharma investors even though it often comes close. The US Treasury ruling that blocked the Pfizer-Allergan merger in April caused upward trading in Pfizer at five times its Black Monday level, while trading rose seven-fold for Allergan PLC (down). And Gilead’s Jan. 29 announcement that John Martin would move aside as CEO had a BMR of 1.4, bigger than the 0.92 for its results a few days later.

Half-year results don’t usually have quite the same stock-moving power as full year results, perhaps because fewer people are paying attention. But sometime they do and often, they are not far behind. All of which means that the brokers are going to be getting busy over the next few weeks.

Published online 07-18-2016
Scrip’s weekly **Pipeline Watch** tabulates the most recently reported late-stage clinical trial and regulatory developments from the more than 10,000 drug candidates currently under active research worldwide.

**Late-stage clinical developments for the week 8–14 July 2016**

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<td>–</td>
<td>Tagrisso (osimertinib)</td>
<td>non-small cell lung cancer</td>
<td>Canada</td>
</tr>
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</table>

**SUPPLEMENTAL REGULATORY APPROVAL**

| Amgen Inc.               | –               | Repatha (evolocumab) Pushtronex system | hypercholesterolemia                           | US     |
| Pfizer Inc.              | –               | Prevnar 13 vaccine                     | pneumonia prevention                           | US     |
| Galderma SA (Nestle SA)  | –               | Differin (adapalene) 0.1% gel          | acne                                            | US     |
| Takeda Pharmaceuticals USA Inc. | –           | Dexilant (dexlansoprazole) capsules and tablets | gastroesophageal reflux disease | US     |

**REGULATORY FILING ACCEPTED**

| Swedish Orphan Biovitrum AB | –               | Orfadin (nitisinone)                  | hereditary tyrosinemia type-1                  | Canada |
| Cipher Pharmaceuticals Inc. | Ferrer International | ozenoxacin                           | impetigo                                       | Canada |

**ORPHAN DRUG DESIGNATION**

| Akari Therapeutics PLC   | –               | Coversin (tick-derived small protein) | paroxysmal nocturnal hemoglobinuria            | EU     |

**BREAKTHROUGH THERAPY DESIGNATION**

| Loxo Oncology Inc.       | Array BioPharma Inc. | LOXO-101                            | solid tumors                                   | US     |

**PRIORITY REVIEW**

| Janssen Pharmaceuticals Inc. | –               | Vérmox (mebendazole) 500 mg chewable tablet | soil-transmitted helminthiasis                  | US     |

**PHASE III TRIAL INITIATION**

| Novartis AG              | –               | Cosentyx (ustekinumab)                | psoriasis                                      | –      |

*Source: Sagient Research’s BioMedTracker*
Cancer Research UK has appointed Peter Chambré trustee. He is currently chair of various life sciences and healthcare companies including Immatics Biotechnologies and OneMed and chairs Cancer Research’s commercialization arm, Cancer Research Technology Ltd. (CRT). Chambré is also director of Spectris PLC and Imperial Innovations PLC and was previously CEO of Cambridge Antibody Technology PLC until its acquisition by AstraZeneca in 2006.

Andreas Rummelt, former CEO of Sandoz, has joined LEUKOCARE’s supervisory board making him the second former executive from big pharma on the company’s board, on which Jean-Paul Prieels, who held executive positions at GlaxoSmithKline, also serves. Rummelt joined Sandoz Pharma Ltd. in 1985 and was CEO of Sandoz, the generics division of Novartis up until 2008. Currently he is running a consulting business based in Switzerland and is on the board for various companies including Alexion Pharmaceuticals, Alvogen and Xellia Pharmaceuticals.

Astellas has appointed Joseph Devaney vice president, government affairs and policy, Americas. Devaney joins Astellas from Sanofi where he spent 20 years in various roles, most recently being vice president of federal and state relations. Prior to Sanofi, Devaney was director of state government affairs for Sandoz, which became a part of Novartis in 1996.

Hearing company, Decibel Therapeutics has appointed Steven H. Holtzman president and CEO, he will be succeeding interim CEO Kevin Starr, who will remain chair of the company’s board of directors. With 30 years’ experience, Holtzman joins the company from Biogen Inc. where he was executive vice president, corporate development before which he was founder, CEO and chair of Infinity Pharmaceuticals Inc.

Women’s health company, Juniper Pharmaceuticals Inc. has appointed Alicia Secor president and CEO – effective Aug. 1, 2016. With more than 25 years’ leadership experience, Secor joins Juniper from Zafgen Inc. where she was chief commercial officer. Previously, Secor was at Genzyme Corporation for 15 years and served in various leadership roles, the most recent being global general manager for the metabolic disease business.

Stephen Hoffman has been appointed chair of Bicycle Therapeutics’ board of directors. Currently Hoffman is president of 10X Capital Inc. and senior advisor to PDL BioPharma Inc., he is also on the board ofDicerna Pharmaceuticals Inc., AcelRx Pharmaceuticals Inc. and Genocea Biosciences Inc. Previously he was managing director at Skyline Ventures and general partner at TVM Capital before which he served as chair, president, CEO and director of Allos Therapeutics Inc.

Asterias Biotherapeutics, a company focused on regenerative medicine, has appointed Ryan Chavez executive vice president of finance and general counsel. Most recently Chavez was vice president and general counsel of Mallinckrodt’s auto-immune and rare disease division, prior to which he was associate general counsel at Questcor. Before Questcor, he was at the law firms of Stradling, Yocca, Carlson & Rauth and Rutan & Tucker.

Novo A/S has announced that Kasim Kutay will become the company’s new CEO – effective Sep. 1, 2016. Kutay began his career at Morgan Stanley where he spent 18 years advising healthcare companies and later joined investment bank, Moelis & Company, where currently he co-head of Europe and serves on its management committee.
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