Sanofi Goes Public With Hostile Medivation Bid

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ollowing weeks of speculation, Sanofi has gone public with its hostile offer for Medivation. Analysts are all in agreement that the deal would make “strategic sense” for Sanofi, but it’s likely other suitors will throw their hats into the ring. Meanwhile, Medivation fails to see how its investors would benefit from the acquisition. The offer for Medivation follows CEO Olivier Brandicourt’s reorganization of Sanofi in which oncology is one of the businesses where he plans to build a competitive position.

Sanofi says it made a non-binding proposal to acquire San Francisco-based Medivation Inc. for $52.50 per share, an all-cash transaction valued at $9.3bn, almost two weeks ago. It proposes that Medivation would sit within its successful Sanofi Genzyme specialty unit.

In a public follow-up letter dated April 28 and addressed to Medivation’s CEO David Hung, Brandicourt says he first called Hung about a potential combination of the companies on March 25 but “you said you were unwilling to meet.” The offer was then sent on April 15. “We have not heard anything from you in almost two weeks… We do not understand the delay in responding,” complained Brandicourt. The $52.50 per share proposed purchase price represents a premium of over 50% to Medivation’s two-month volume weighted average price (VWAP) prior to there being takeover rumors – but just 1% to the closing price on April 27.

Medivation failed to see how its investors would benefit from an acquisition at $52.50 in cash per share, so it announced its rejection of Sanofi’s unsolicited buyout offer while the French pharma firm was conducting its earnings conference call on April 29.

Medivation felt that the deal was not in its or its shareholders best interests, however, noting that Sanofi’s offer “substantially undervalues” the company. Hung accused Sanofi of taking advantage of the recent decline in biotech stock values to acquire Medivation at a price well below its 2015 peak of $67.78 per share.

“Sanofi’s opportunistically-timed proposal, which comes during a period of significant market dislocation, and prior to several important near-term events for the company, is designed to seize for Sanofi value that rightly belongs to our stockholders. We believe the continued successful execution of our well-defined strategic plan will deliver greater value to Medivation’s stockholders than Sanofi’s substantially inadequate proposal,” Hung said.

Medivation has one marketed drug, the prostate cancer therapy, Xtandi (enzalutamide), and two additional oncology assets in clinical development.

Goldman Sachs analysts have forecast Medivation sales of $1.15bn in 2017, rising to $1.71bn in 2020. They believe the deal makes “strategic sense” as it strengthens Sanofi’s position in the key US oncology market, and would immediately enhance earnings. Sanofi has experience in the prostate cancer space through marketing Jevtana (cabazitaxel; with sales of €321m in 2015). Medivation’s Xtandi is co-marketed with Astellas in the US, and Medivation gets royalties for ex-US sales. Xtandi had 2015 sales of around $2bn. Its two late stage assets are talazoparib, a PARP inhibitor in Phase III development for breast cancer (acquired from BioMarin Pharmaceutical in 2015); and pidilizumab, a humanized monoclonal antibody in Phase II development for DLBCL.

“An acquisition of this nature could, in one go, boost Sanofi’s prostate cancer presence and rejuvenate its oncology

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The news this week of an $18bn “merger of equals” between Quintiles and IMS Health was as surprising as the mating of two different species. Perhaps in the same way that our first reaction to a liger or a wholpin is one of incredulity and suspicion (did that actually work?), investors immediately recoiled from the planned coupling of the CRO giant and the behemoth of prescription data. Quintiles’ share price plummeted 8.9% before closing down 2.4% on the day of the announcement while IMS dropped 8.1% before closing down 3.5%.

For the two firms’ clients, though, the abnormality of the union could be what makes it attractive. Pharma companies know that grasping the big data bull by the horns promises great rewards both in product R&D and in the commercial sphere, and can help shape conversations with payers. But data from different domains is siloed, so hard to cross-link and fully exploit. Bringing together market leaders in pre- and post-market data could help fix that. Like the mule, the offspring of this deal could prove more useful to pharma than either of its parents.
The innovative nature of Novartis AG’s new chronic heart failure therapy Entresto counted towards NICE’s appraisal committee clearing its use in Britain’s National Health Service, despite a cost-effectiveness ratio that was close to the upper limit for gaining a positive recommendation.

Novartis’s high-profile oral chronic heart failure therapy Entresto (sacubitril plus valsartan) has been recommended for use in England and Wales’s National Health Service (NHS) by the UK HTA body, the National Institute for Health and Care Excellence (NICE), giving a boost to a product that has so far found it difficult to live up to its potential blockbuster status.

Final NICE guidance was published on April 27 confirming a provisional positive recommendation issued Dec. 11, 2015 on the use of Entresto within the NHS in England and Wales. The guidance by the internationally well-respected organization may improve prescriber sentiment towards Entresto, and boost its sales, after having been launched in the US in the middle of last year, and in its first markets in Europe at the end of 2015. The drug only generated $17m in sales in the first quarter of 2016. Germany’s IQWiG also ruled provisionally in Entresto’s favor several weeks ago, as did the Scottish Medicines Consortium.

In the NICE guidance, Entresto is recommended as an option for treating symptomatic chronic heart failure with a reduced ejection fraction, in patients with New York Heart Association (NYHA) class II to IV symptoms, a left ventricular ejection fraction of 35% or less, and who are already taking a stable dose of ACE-inhibitors or angiotensin II receptor blockers (ARBs).

The positive recommendation came despite NICE’s appraisal committee calculating the incremental cost-effectiveness ratio (ICER) for Entresto as being between £26,000 ($38,000) and £30,000 ($43,000) per quality-adjusted life year (QALY) gained, near the upper limit of what NICE considers cost-effective for use in the NHS. What seemed to count in Entresto’s favor was its innovative nature, in a disease area that has seen little innovation over the past 25 years.

NICE’s director of valuation Carole Longson said the £3-a-day drug would be used in people with severely reduced ejection fraction who are almost constantly bedbound, helping them take part in normal daily activities and reducing their need for hospital treatment. But Longson pointed out the guidance does not recommend Entresto’s use in patients with mild symptoms, or those who have not already been treated with an ACE-inhibitor or an ARB.

The company has set a modest sales target of around $200m this year for Entresto, as cardiologists are likely to continue to take a cautious approach to prescribing, preferring not to change the medication in heart failure patients with stable disease.
Valeant Reset: Will It Cure What Ails It?

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In Valeant Pharmaceuticals International Inc’s long-awaited 10-K, which finally got filed with the Securities and Exchange Commission (SEC) on April 29, the company disclosed new investigations into its business pricing and business practices and further pulled back the veil on its relationship with Philidor Rx Services LLC – the specialty pharmacy for which the Canadian drug maker had a shady distribution partnership, which has since ended.

Valeant also confirmed reports it was bringing on new members to its board – nominating Argeris Karabelas, a partner at Care Capital and the founder and former chairman at Novartis BioVenture Fund; Rursel Robertson, executive vice president and head of anti-money laundering at BMO Financial Group; and Amy Wechsler, a New York dermatologist.

“The three new directors seem to have the right background,” said BMO Nesbitt Burns Inc, analyst Alex Arfaei.

Michael Pearson, who has been replaced as CEO by Joseph Papa, who also is taking on the role of chair at Valeant, and former chief financial officer Howard Schiller are standing down for re-election.

The board had tried in March to oust Schiller, who was accused of “improper conduct” but he denied those charges and refused to resign.

Five other current board members also will not be standing for re-election at the June 14 annual meeting. Billionaire activist shareholder Bill Ackman, along with four others, have been nominated for re-election to the board.

Valeant also said that, going forward, one or more independent board members would periodically attend the company’s planning and forecasting telephone conferences and its periodic business reviews “to monitor, and, if necessary, address any tone at the top, management override, corporate governance, internal control and accounting and financial reporting issues.”

“Only time will tell if this amounts to meaningful, substantive change – or if it’s simply rearranging deck chairs on the Titanic in a desperate attempt to fool the business community into believing the company is headed in a different direction,” charged Sen. Claire McCaskill (D-MO), who a few days earlier had convened a hearing with her Republican counterpart on the Senate Aging Committee, Sen. Susan Collins (R-ME), who chairs the panel, focused on Valeant’s pricing practices. “But at this point, we all have reasons to be skeptical. The cultural and structural problems at Valeant run bone-deep and if there’s going to be any future for the company they’re going to have to stop exploiting patients, hospitals and the government in an attempt to enrich themselves and their shareholders.”

McCaskill also criticized Valeant’s plan to pay its new CEO Joseph Papa about $67m – a compensation package that could end up being worth $500m.

INVESTIGATIONS
Collins and McCaskill, as well as the Republican and Democratic leaders of the House Oversight and Government Reform Committee, have been digging into significant price hikes by Valeant and other companies.

But the Senate and House investigations into Valeant are among many ongoing probes of the firm’s business and pricing practices.

Along with investigations by the SEC, prosecutors in New York and Massachusetts and the Texas Medicaid program, Valeant disclosed in its 10-K filing that North Carolina and New Jersey have recently opened new probes.

In March, Valeant received an investigative demand from North Carolina’s Department of Justice seeking materials related to the production, marketing, distribution, sale and pricing and patient assistance programs related to three of the company’s drugs – Nitropress (sodium nitropusside), Isuprel (isoprenaline) and Cuprimine (penicillamine).

On April 20, Valeant received a subpoena from the New Jersey State Bureau of Securities requesting documents concerning the company’s former relationship with Philidor, its accounting treatment for sales to the specialty pharmacy, the drug company’s financial reporting and public disclosures and other matters. The company said it was cooperating with both new investigations. Valeant said it may be making changes in the way it conducts its business and to its business strategy.

“Some of these changes may be significant,” it said.

The firm said it was assessing its practices related to pricing and “considering certain changes thereto.” At the April 27 Senate hearing, Ackman said it wanted to see a 30% across-the-board reduction in the prices of Nitropress and Isuprel charged to hospitals.

FINANCIAL WOES
Valeant said its filing of the 10-K has “cured in all respects” the default under the company’s senior note indentures triggered by the failure to timely file the form. The firm said it remains in full compliance with its credit agreement. Valeant had delayed the 10-K due to an internal investigation into its dealings with Philidor.

The company had previously disclosed it had identified misstatements related to Philidor that reduced its fiscal year 2014 revenue by about $58m and net income by about $33m. Valeant also identified misstatements in the first quarter of 2015, consisting primarily of the reversing effect on earnings of the 2014 misstatements, which reduced revenue by about $21m, but increased net income by $24m.
ONE SIZE DOES NOT FIT ALL.

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Bayer Thins R&D Pipeline, Backs Finerenone In Kidney But Not Heart Disease

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Germany’s leading pharmaceutical company Bayer has taken future competition into account when stopping the Phase III development of finerenone for congestive heart failure, and targeting specific CHF patients for treatment with another potential cardiovascular, vericiguat.

The German multinational Bayer AG has bowed to the likely highly competitive nature of the congestive heart failure (CHF) market in future years by not starting a Phase III study of the mineralocorticoid receptor antagonist finerenone in the condition, saying the decision was made for “commercial reasons.”

Still, finerenone will continue to be evaluated for use in the treatment of diabetic kidney disease in an ongoing Phase III study, reported Bayer’s outgoing CEO Marijn Dekkers during a first-quarter analysts’ briefing held Apr. 26.

The company said it would also only continue to evaluate in late-stage studies the guanylate cyclase (sGC) stimulator vericiguat in CHF patients with a reduced ejection fraction, and not those with a preserved ejection fraction. A Phase II study in patients with heart failure with a preserved ejection fraction did not meet its endpoint, Dekkers noted. Vericiguat is being developed in a partnership with Merck & Co. Inc.

And because of the highly competitive nature of drugs being developed for renal anemia, Dekkers said Bayer was also evaluating whether to proceed with Phase III studies of the hypoxia-inducible factor-prolyl hydroxylase (HIF-PH) inhibitor molidustat, or whether to find a development partner or license it out. Top-line results of Phase II studies with molidustat showed a positive outcome, but a Phase III program would require larger outcome studies, the Bayer executive said.

Analysts questioned why the competitive landscape in heart failure was different for finerenone and vericiguat, with Bayer’s pharma division head Dieter Weinand responding by saying the decisions depended on the expected commercial environments for the two products. The diabetic kidney disease indication was always the main driver of finerenone’s development, while it has already been decided that vericiguat would go into Phase III later this year, in CHF patients with reduced ejection fractions, Weinand said.

The answers didn’t completely satisfy analysts, who pointed out Novartis AG’s Entresto (sacubitril plus valsartan) has been considered to be a new gold standard in CHF for more than a year, and Bayer’s decision doesn’t appear to have been triggered by more data.

CANCER DRUGS DISCONTINUED

Other mid-stage pipeline products could be discontinued by the company. A decision to continue with the development of the PI3K inhibitor copanlisib for non-Hodgkin’s lymphoma will depend on the results of Phase II studies that are running in parallel with Phase III studies, Dekkers said. The Phase II data are expected in the third quarter of this year.

During the first quarter of 2016, Bayer has already decided not to pursue the development of the investigation product refametinib in cancer, and has returned the project to Ardea Biosciences Inc. The company has also ended the development of BAY 1007626 and roniciclib. But one piece of good news was that Bayer intends to move the oral progesterone receptor modulator vilprasin into Phase III for uterine fibroids, after a first Phase II trial in the condition indicated it had a “very competitive” profile.

PIPELINE STILL STRONG

Is Bayer’s mid-term pipeline strong enough to eventually replace its current high-growth marketed products? Weinand told analysts the company has 17 new products in Phase III and 18 in Phase II, including finerenone, vericiguat, vilprasin and the partial adenosine A1 agonist BAY 1067 197.

The company also has ODM-201 in Phase III studies for non-metastatic castrate-resistant prostate cancer, another anticancer anetumab in Phase II, and is evaluating its radiotherapeutics platform. And although Bayer has not participated in the first wave of immune-oncology products, it expects to be present during the next wave of such products, Weinand said.

Analysts at Deutsche Bank noted the pipeline rationalization announced will likely keep commentators focused on Bayer’s plans for pipeline renewal that is likely to include a combination of in-licensing, acquisition and in-house projects. Credit Suisse analysts were more concerned, saying the pipeline update was a significant fall-out from an already thin pipeline.

In the 2016 first quarter, Bayer’s pharmaceutical sales increased by 12% to €3.9bn ($4.4bn), driven by five recently launched products, Xarelto (rivaroxaban), Eylea (aflibercept), Shire’s (regorafenib), Xofigo (radium-223 dichloride) and Adempas (rioniciguat), whose sales in total amounted to €1.2bn, up 35% on the previous first quarter and representing nearly a third of the company’s pharmaceutical sales. Xarelto gained market share and is the leading anticoagulant worldwide, Eylea sales were up 49% on the previous first quarter, and Xofigo sales increased by 37%. During the quarter, group sales increased by 3% at constant currencies to €11.9bn, led by its life sciences businesses.
Panel: Pricing Dilemma Divides Industry Stakeholders

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Drug pricing has become the most contentious issue in the pharma world over the last two years as politics has dragged the subject into the mainstream conversation. Yet, even those within the industry have different ideas on how the problem can be fixed.

Panelists from pharma, biotech, pharmacy benefit managers and hospitals all expressed their views on the hot button issue during the first day of the World Medical Innovation Forum on April 25 in Boston – each viewing pricing from a drastically different perspective and pushing their own agenda as the right way forward.

“The demand for breakthrough therapies has never been greater. The demand for medicines for smaller and smaller patient populations has never been greater. Yet, the environment to deliver, the price of value, has never been more constrained,” said Paul Hudson, Executive Vice President of AstraZeneca PLC North America.

While Hudson expressed his frustration with the inverse relationship between demand for better products and the price the market will bear, he did note that countries outside of the US have not yet figured out how to best handle the issue either. “You should be careful what you wish for with QALYs (Quality-Adjusted Life Years) and the UK healthcare system. I think access to new and innovative treatments is more difficult and more challenging in the universal healthcare system, because you don’t really pay for your healthcare. I think here, because of the premiums and what families invest in their healthcare, they demand greater access to more innovative medicine. You have to have a way of assessing against the current US standard and not just the bits you cherry-pick from other healthcare systems,” added Hudson, a Brit himself.

Others at the conference emphasized the need for fixing the pricing dilemma as well. Betsy Nabel, President of Brigham and Women’s Hospital as well as a professor of medicine at Harvard Medical School, told the audience that she believes the problem needs to be handled by the stakeholders in the private sector – swiftly.

“As we think about pricing and how best to deliver for our patients, one solution is to ask the private sector to solve this. And why the private sector? Because you can make an argument that the market can come to a far better decision than the government and government regulation,” she said. “The private sector – commercial payers, academic medical centers, pharmaceutical companies, biotech, venture, pharmacy – has to have a roundtable and fix this. It might be a difficult task, but we either sit down and sort this out together or (the Centers for Medicare & Medicaid Services (CMS)) is going to sort this out for us and we know the kind of record that CMS has.”

Not all the panelists had such a shrewd view of government regulation, but they did see eye-to-eye on some things. “Everything we do, we look at through the lens of the cancer patient. For patients, survival is the key, but also quality of life, side effects. I totally agree with Betsy that this needs to be a multi-stakeholder approach, but we need to make sure that the voice of the patient takes front and center,” added Gary Reedy, CEO of the American Cancer Society.

‘An acquisition of this nature could, in one go, boost Sanofi’s prostate cancer presence and rejuvenate its oncology pipeline’

“Sanofi are likely to need to pay a higher premium if they wish to acquire this company,” suggested the Exane analysts. “We believe other suitors may now step in. Medivation’s partner on lead drug Xtandi, Astellas Pharma Inc. would be an obvious candidate.”

Goldman Sachs analysts noted that Astellas had a ‘standstill’ agreement restricting it from acquiring Medivation, “but according to Astellas this can be broken if there is an unsolicited bid” which now seems to have occurred. Pfizer Inc, AstraZeneca PLC and AbbVie Inc. are also thought to be in the running as potential bidders.

Sanofi clearly would benefit from its proposed $9.3bn purchase of Medivation based on the French company’s first quarter earnings, which show a pharmaceuticals business that’s suffering from competition, US drug pricing pressures and foreign currency exchange issues.

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pipeline,” said Deutsche Bank analysts optimistically.

Exane BNP Paribas analysts also concluded a Medivation acquisition could be a “sensible strategic deal” for Sanofi. “It would fill an earnings gap for Sanofi but not significantly improve the pipeline outlook, in our view,” they added.

The Exane analysts also claimed the acquisition “could proceed independently of the proposed Consumer/Animal Health asset swap with Boehringer Ingelheim” (expected to close by end 2016), which will provide a €4.7bn cash influx to Sanofi.

Continue reading ‘An acquisition of this nature could, in one go, boost Sanofi’s prostate cancer presence and rejuvenate its oncology pipeline’ at scripintelligence.com
Lilly Executes Growth Strategy As New Products Drive Sales Gains

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Despite late-stage clinical trial failures and questions surrounding the company’s most closely-watched Phase III program, Eli Lilly & Co. is reaping the rewards of recent pipeline successes with new products making up the largest share of first quarter 2016 sales growth.

Lilly’s $4.87bn in first quarter revenue was essentially in line with analyst consensus of $4.88bn and non-GAAP earnings per share (EPS) of $0.83 missed expectations by two cents, but a positive showing for relatively new products offered some hope for the future and contributed to the company’s decision to raise its revenue and earnings guidance for the year. However, after the Phase III failure of the cholesterol-lowering drug evacetrapib last year, all eyes are on the Phase III clinical trial for the Alzheimer’s therapy solanezumab – Lilly’s next potential mega-blockbuster product.

New therapies will contribute to Lilly’s $20.6bn to $21.1bn in expected 2016 revenue and $3.50 to $3.60 in non-GAAP EPS for the year versus the company’s prior guidance of $20.2bn to $20.7bn in revenue and $3.45 to $3.55 in EPS. However, Lilly said most of its greater expectations for 2016 are based on reduced foreign exchange impacts and an improved tax rate.

NEW PRODUCTS CONTRIBUTE TO GROWTH

But with new products making up 5% of Lilly’s 7% year-over-year increase in first quarter revenue, it appears that the company is making efforts to meet the four big goals that executives first outlined in January 2015.

“We continue to make steady progress against each of our strategic objectives: driving revenue growth, expanding margins, sustaining the flow of innovation, and deploying capital to create value,” Lilly Chief Financial Officer Derica Rice said during the company’s earnings conference call on April 26.

Product launches for the diabetes medicines Jardiance (emaglitinib), Trulicity (dulaglutide) and Basaglar (insulin glargine), and for the cancer therapies Cyramza (ramucirumab) and Portrazza (necitumumab), were credited with providing the majority of Lilly’s revenue growth in the first quarter.

The company only began to ship the newly-approved psoriasis therapy Taltz (ixekizumab) to customers in April, so it did not shed light on early sales figures, but Lilly won EU approval for the biologic on April 25 and promotional efforts are expected to begin in Europe in June.

Sales for Jardiance nearly doubled during the January-to-March period to $38.2m from $19.3m a year earlier; Trulicity brought in $143.6m versus $18.3m; Basaglar generated $10.9m in first quarter sales; Cyramza grew 94% from $67.5m to $131m; and Portrazza garnered $1.7m in first quarter sales.

Portrazza was approved in the US in November in combination with gemcitabine and cisplatin to treat metastatic squamous non-small-cell lung cancer (NSCLC) and won EU approval for the same indication in mid-February. While Cyramza won its first US FDA approval in April 2014 for gastric cancer and subsequent US indications for NSCLC in December 2014 and colorectal cancer (CRC) in April 2015, the VEGF receptor-targeting biologic was just launched in the EU during the first quarter to treat locally advanced or metastatic NSCLC and metastatic CRC.

However, Portrazza, Cyramza and Alimta (pemetrexed) are facing competition in the US from immuno-oncology therapies – the PD-1 inhibitors Opdivo (nivolumab) from Bristol-Myers Squibb Co. and Keytruda (pembrolizumab) from Merck & Co. Inc. Lilly Oncology President Susan Mahoney said during the company’s earnings call that there will always be a need for the three therapies among certain lung cancer patients, but for Cyramza, most of its growth is in gastric and colorectal cancers.

New competition is particularly bad news for Alimta, which is facing patent challenges in multiple markets. A UK court ruled in favor of Allergan PLC in February, allowing that company to move forward with a generic version of the drug in the UK, France, Italy and Spain. Another patent battle was lost in Germany in March 2015.

While Lilly continues to “actively defend” its Alimta patents, Mahoney noted that the company’s financial guidance anticipates the entry of at least one generic competitor in Europe in 2016. Alimta sales slipped 2% in the first quarter to $564.2m.

DIABETES REMAINS KEY BUSINESS SEGMENT, HIGH GROWTH AREA

Basaglar, Lilly’s version of Sanofi’s Lantus (insulin glargine), won FDA approval in December, but the company will not market the product in the US until December of this year under a patent settlement agreement with Sanofi. However, Lilly and partner Boehringer Ingelheim GMBH already are selling the insulin copycat as Abasaglar in Europe. It also is available in Canada and Japan.

Jardiance sales are rising at a brisk pace based on “game-changing” data from the EMPA-REG cardiovascular outcomes trial (CVOT), which were widely expected to boost sales of Lilly’s drug and other SGLT-2 inhibitors. In fact, Rice said the SGLT-2 class surged by 45% during the first quarter.

“We continue to see regulatory approval of EMPA-REG OUTCOME data [later in 2016] as a catalyst for growth for both the class and for Jardiance. The other catalyst for growth is inclusion of these data in treatment guidelines,” she said, noting a favorable guideline update in Canada during the first quarter.

Lilly has similar hopes for its GLP-1 receptor agonist Trulicity, which is being studied in a CVOT known as REWIND. Interim data will be reviewed later this year and the trial will conclude in late 2018.

AstraZeneca PLC is restructuring and streamlining its commercial and manufacturing operations under a new cost-cutting effort in order to save $1.1bn annually from 2017 and focus internally on just three core areas.

The operational changes will incur a one-time restructuring charge of $1.5bn and will be completed by the end of fiscal year 2017. However, in the long run, the cash saved will be redirected towards AstraZeneca’s oncology portfolio and for striking partnerships in “opportunity-led” parts of the company’s pipeline – such as infection, neuroscience and inflammatory disease outside of the respiratory field.

‘We built our pipeline with great success, in fact more than we expected to, and we now have a tremendous number of exciting projects in oncology and specialty care’

Announcing the plans during the company’s first-quarter earnings call on April 29, CEO Pascal Soriot said, “We are further sharpening our strategic focus on our main therapy areas, intensifying our efforts in oncology and accelerating collaborations in opportunistic areas. We are also driving greater efficiency across the organization to support the advancement of our strategy.”

As part of this cost-cutting action the company will concentrate on oncology, cardiovascular and diabetes programs internally and pursue other therapy areas mainly through external partnerships.

Meanwhile Soriot said AstraZeneca is at a “pivotal point” in its evolutionary shift into more of a specialty care business. “We built our pipeline with great success, in fact more than we expected to, and we now have a tremendous number of exciting projects in oncology and specialty care… We’ve seen the need for us to invest more in oncology, to invest more in preparing all those launches and to invest in specialty care,” he said.

Marc Dunoyer, executive director and chief financial officer, added that “In oncology we have one of the most exciting and balanced pipelines in the industry that we will further advance. But we plan to go faster and further.”

The annual cost savings following the restructure are expected to be reflected primarily in AstraZeneca’s core SG&A figures from 2017. SG&A costs in 1Q16 declined by 6% to $2.1bn. The UK big pharma also reiterated its FY16 guidance and 2023 revenue target of $45bn.

EIGHT PIPELINE TERMINATIONS

In the first quarter of the year AstraZeneca suspended trials for eight of its products, including two Phase III studies.

While four of the program suspensions were early stage, two Phase II and two Phase III trials have also been pulled from the company’s R&D line-up.

AstraZeneca noted that in 1Q 2016 it ended development of Brilinta (ticagrelor) in ischemic stroke after it failed to meet the primary endpoint of a Phase III outcomes study. Brilinta is already approved for the treatment of acute coronary syndrome and is in Phase III trials for atherosclerosis and peripheral arterial disease.

A Phase III study testing Tagrisso (osimertinib) in combination with durvalumab as a second-line treatment for T790M mutation-positive non-small cell lung cancer was also suspended in the first quarter due to safety concerns. Two trials had been paused in Oct. 2015 due to an increase in the incidence of interstitial lung disease-like reports. The company’s Phase III CAURAL study has now been terminated. Tagrisso is already approved as a monotherapy for advanced non-small cell lung cancer (NSCLC). Meanwhile, in the first-line setting, AstraZeneca’s FLAURA trial for mono-therapy Tagrisso in NSCLC is now fully recruited.

1Q In Numbers

- Total revenue for 1Q16: $6.1bn
- Core EPS for the quarter: $0.95
- Product sales for new oncology portfolio in 1Q16: $1.2bn
- Total sales from growth platform (including respiratory portfolio, Brilinta, diabetes portfolio, emerging markets, Japan and new oncology products): $3.4bn
- FY16 total revenue guidance: low- to mid-digit percentage decline
- FY16 EPS guidance: low- to mid-digit percentage decline

Click here to view all pipeline terminations in 1Q16: http://bit.ly/1W4AHeP
What's On CEO Andrew Witty's To-Do List Before Exiting GSK

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The company showed signs of stabilization in the first quarter, as Witty insisted his diversified strategy is beginning to pay off. But a new CEO will have to contend with the potential entry of Advair generics.

GlaxoSmithKline PLC CEO Andrew Witty has a year left on the job, time he would like to use to convince investors his diversified strategy is the right one for the company. The UK drug maker delivered 8% sales growth and an 8% increase in core earnings growth in the first quarter, driven by vaccines and consumer health care – signs that the strategy is gaining momentum.

Pharmaceuticals sales fell 1% to £3.59bn ($5.22bn), but management said the business is on track to return to growth in 2016, while vaccines grew 23% and consumer health care grew 26% off of substantially smaller bases.

The company raised its guidance for the year slightly, targeting core earnings-per-share growth of between 10% to 12% on a constant exchange rate basis.

Witty said delivering on the sales and earnings targets for the year is one of the top items on his list to complete before leaving the company in early 2017. GSK announced in March that it is looking for a successor to Witty, who will retire in 2017 after nine years at the helm and 31 years at the company.

The management transition comes as some investors have become increasingly concerned about the company's stagnant growth and Witty's emphasis on relying on businesses like vaccines and consumer health care to drive the enterprise while the pharmaceuticals business struggles.

To deliver sales and core earnings growth in his last full year at the firm, Witty said he will focus on successfully integrating the consumer and vaccines businesses acquired from Novartis AG last year.

"It's very important to me that we continue the momentum of our new products, to have 20% of our pharma business now coming from new products," Witty said. "I want to keep those new products moving forward."

His other priority will be moving the pipeline forward. In 2016/2017, Witty said there are roughly 30 Phase II clinical trials and 20 Phase III clinical trials slated to start.

"So there's an awful lot that needs to be moved forward, and I think we can really lay the foundation for that."

In terms of what might be the top priority for Witty’s successor, the chief executive responded to an analyst question that it will be left to that person to determine and likely will be driven in part by the global environment.

"The world is focused on pricing. The world is focused on more regulatory pressure and the volatility of global economics," he said.

"So I'm sure that's going to be what drives the external agenda, but it will be up to them individually to set their own priorities."

GSK's board of directors is evaluating both internal and external candidates to fill the job. "They are going to be looking for somebody who punches a lot of tickets," Witty said. Nonetheless, he said the board and management are very aligned on executing on the company’s near-term strategy.

"That's one very key dimension of this equation, because when you know what the strategy of the company is for the foreseeable future then you can essentially look for somebody to execute that strategy and to build on it," he said.

DEFENDING AGAINST ADVAIR GENERICS

One of the challenges for any incoming CEO will be navigating the potential loss of the aging asthma drug Advair Diskus (fluticasone/salmeterol) to generic competition.

Sales of Advair have been declining due to price pressure, and newer respiratory drugs like Breo Ellipta (fluticasone/vilanterol) and Anoro Ellipta (umeclidinium/vilanterol) haven't picked up the slack. Sales of Advair slipped 19% in the first quarter to £753m ($1.1bn), while sales of Breo picked up steam, up more than 100% to £111m ($161.4m) and sales of Anoro were just £33m ($48m).

DeFenDIng a gaInst aD vaIr generIcs

GSK has already absorbed some of the impact, anyhow, because of the pricing pressure Advair has experienced from payers in the US. The upside, Witty said, is that it has started to move the products into a price range where generics could be less of a threat to the brand.

"I think we have a number of defenses to be able to maintain our portfolio, which we're obviously very much focused on," Witty said.
**Shire Outlines Baxalta Integration Strategy**

Overall, the Dublin-headquartered specialty firm reported product sales of $1.627bn for the first quarter of 2016, up 14% year-over-year. As usual, the top-seller was attention-deficit/hyperactivity disorder (ADHD) stalwart Vyvanse (lisdexamfetamine), which posted 22% growth to $509m on the quarter. It also was a strong quarter for Shire’s hereditary angioedema franchise, as FirAZYR (icatibant) sales increased 39% to $128m and Cinryze (C1 esterase inhibitor) sales rose 11% to $164m. Initially launched as a hostile bid in mid-2015, Shire’s acquisition of Baxalta was agreed upon in January at a price of roughly $32bn, in a transaction that will leave Shire owning 66% of the combined company and Baxalta 34%. Shire CEO Flemming Ornskov said that if shareholder and regulatory approvals come through as expected, the merger should close on or around June 3. He said the deal will bring Shire opportunities in hematol-ogy, immunology and cancer. Shire intends to follow the model of previous acquisitions to “leverage our existing experience in the rare disease space to maximize the growth and value from these assets,” Ornskov stated.

**AbbVie Gains Platform With Stemcentrx Buyout**

As part of its strategy to offset the coming Humira patent cliff, AbbVie Inc. is looking to oncology as a “significant pillar of growth” going forward, a gambit CEO Richard Gonzalez says will benefit greatly from both the pipeline candidates and the solid tumor R&D engine his company will obtain in the $5.8bn purchase of Stemcentrx announced April 28. The transaction was unveiled in tandem with AbbVie’s first quarter earnings call, during which the company reported an 18.2% year-over-year increase in net revenues to $5.96bn, with Humira (adalimumab) up 14.9% to $3.58bn. The firm’s hematology asset Imbruvica (ibrutinib), partnered with Johnson & Johnson, posted what Gonzalez termed “strong growth” to $381m on the quarter. J&J reported first quarter sales of $281m worldwide, up from $116m in the year-ago quarter. AbbVie hopes to continue its oncology expansion with the Stemcentrx play. The firm agreed to pay $2bn in cash and $3.8bn in stock for Stemcentrx, making it one of the highest valuations ever for a venture-backed biotech takeover, along with up to $4bn in regulatory and clinical development milestones to Stemcentrx shareholders.

**Panel: Investing Beyond IO Set To Heat Up**

Panelists at the World Medical Innovation Forum discussed the new opportunities they are looking at and where the money will be going in the future. While immuno-oncology has been a hot space for investors over the last few years, some of venture capital heavyweights are looking for new areas. A panel of the who’s who in biotech venture investing at the World Medical Innovation Forum in Boston on April 26 told the audience that they are moving their money into newer areas these days. Amir Nashat, managing partner at Polaris Partners, as well as the other members of the panel, were optimistic that biotech investing is still going strong, even as the rest of the market has lagged in 2016. Nashat also noted that immuno-oncology has given both investors and the industry a new jolt of excitement that is bringing money to the table elsewhere.

**Amgen Earnings Beat Expectations**

Amgen Inc.’s first quarter revenue and earnings beat consensus estimates without a meaningful contribution from sales of the cholesterol-reducing biologic Repatha (evolocumab), but the company is pushing back against payers that are denying reimbursement to appropriate patients. Thousand Oaks, California-based Amgen reported on April 29 that it generated $5.5bn in first quarter 2016 revenue, which was 10% above the same period in 2015 and $200m above consensus. The company also posted a 17% jump in adjusted earnings per share (EPS) to $2.90, which was a $0.30 improvement over analyst expectations. But Repatha is expected to add very little to the company’s sales tally before cardiovascular outcomes data are reported later this year, since US payers have refused to cover 77% of prescriptions written for the PCSK9 inhibitor, even for patients who meet the FDA’s requirements. Repatha sales during the first quarter totaled $16m worldwide, including $14m in the US. Amgen’s competitor Sanofi was due to report its first quarter earnings on April 29, including sales for the PCSK9 inhibitor Praluent (alirocumab), which it developed with Regeneron Pharmaceuticals Inc. Amgen executive vice president of global commercial operations Anthony Hooper said during the company’s April 28 earnings conference call that US cardiologists are frustrated, because many patients who could be appropriately treated with the biologic under Repatha’s US FDA-approved label cannot get access to the medicine. Hooper noted that Amgen is talking to payers about making sure that patients who qualify for treatment are able to fill prescriptions. Repatha was specifically approved to lower low density lipoprotein cholesterol (LDL-C) in adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD) when statins alone do not lower LDL-C to recommended levels. It may also be prescribed to treat homozygous familial hypercholesterolemia (HoFH) in combination with statins and other therapeutics.
Significant updates to the ICH GCP guidelines, currently pending approval in draft form, not only harmonise the conduct of clinical trials, in light of various regulatory reforms by ICH member states, but also establish novel forward-thinking standards.

These changes have broad implications for sponsors and it is important that they are ready to adapt to the changes and embrace a shift in processes and behaviours. Most importantly, sponsors need to be aware of the requirements for a new risk management paradigm and the introduction of a revised framework that facilitates more future proof adoption of innovative technologies. CROs and Investigators will also be impacted by the guidelines and need to take notice of what will be demanded of them.

The most significant changes in draft ICH E6 (R2) are highlighted below, as they herald changes in the way sponsors, CRAs and investigators currently operate.

**1 Risk Management at the core of Quality**

Perhaps the most significant change in the upcoming ICH GCP is the requirement to adopt risk management principles in a Quality Management System and in Monitoring.

Sponsors need to fulfil the principles of a Quality Management System based on the risks and possible or detected errors in critical data and processes. The Quality Management System is to incorporate the tenets of recent risk and decision sciences, including decisions related to tolerability of risk, as well as ALCOA communication and record keeping. Anticipated risks and errors as well as observed errors need evaluation, management and control; plans need to be adapted as necessary.

In terms of monitoring, the 2013 Risk and Quality Based Monitoring principles issued by the FDA and the EMA are combined in the new draft ICH GCP (R2); encouraging a risk based, quality by design combination of central and site monitoring in order to conduct clinical trials with greater efficiency.

At the heart of the approach is the determination of critical data and processes which drive risk governance, risk assessment, risk evaluation, risk management and control, risk communication, adaptation to risk and risk reporting. This has the potential to transform how sponsors view monitoring processes in the future.
Closing the Loop of significant non-compliance

ICH GCP (R2) also includes the principle for sponsors to address detected significant non-compliance through root cause analysis, and prevention of reoccurrence.

Outside of reporting, the addendum specifies three core distinct needs: significant non-compliance identification, root cause analysis, and bespoke corrective and preventive action. The currently predominant practice of 100% source data verification (SDV) in monitoring and ‘retraining of sites’ when issues are detected does not support these core requirements of the addendum, nor do many risk-based monitoring (RBM) initiatives.

At the heart of significant non-compliance is an error that matters in critical data or process, or a combination of such errors, which lead to risks to human subject protection or reliability of study data.

Sponsors should consider the inclusion of human factor analysis and classification system (HFACS) in their Root Cause Analysis systems. HFACS is the advanced level in Root Cause Analysis and enables specific actionable outcomes; HFACS has a proven track record as the source of significant safety improvements in e.g. the aviation industry. It enforces the identification of the Human Factor which led to the error, and helps to move away from often irrelevant prevention methods such as ‘retrain the site’. For example, the solution to the human factor ‘process’ source of recurrent incorrect centrifugation of blood samples could be an improved label on the blood sample tubes rather than a retraining.

Technology with paper as golden inspiration

To encourage sponsors to adopt innovative technologies, the ICH GCP 2016 is introducing a new framework that resolves previous ambiguities in compliance requirements. This is a positive development since previous guidance sometimes stifles innovation.

The source of this inspiration is paper management: the access control, data perenniality, and overall ALCOA principles of paper are the basis for the technology requirements. In the same way that corrections such as strike through and red notations are seen in ancient scriptures such as the 1200 year old Book of Kells, it will be essential that both the original source document and edits made are still clearly auditable in the future.

The framework addresses three main concerns. First, it specifies requirements for the validity, longevity and fidelity of trial data as Sponsors transition from paper systems to digital records, update their digital systems, or change from one technology to another. Second, it encourages standard processes to avoid situations where real-time data aggregation and visualisation may inadvertently influence trial outcomes inappropriately early in the trial process. Finally, to resolve concerns that digital trial databases can obscure unauthorized changes to primary data, the framework expands on the need for control by investigator/institutions of their generated data and documents.

Oversight by investigators

Enhanced oversight requirements will apply to investigators delegating tasks and investigator institutions deploying services to third parties. Sponsors and CROs will need to consider how to enable effective and efficient support to sites in order to meet this oversight need.

The investigator and institution should also maintain quality and control at all times of data and documents provided to sponsors.

Requirement for sponsors to demonstrate oversight of tasks delegated to CROs

ICH GCP (R2) 2016 requires that sponsors maintain oversight of tasks delegated to CROs. Therefore CROs will need to provide effective systems for transparency of data and tasks to enable effective sponsor oversight, and sponsors will need to deploy oversight systems for tasks assigned to third parties.

CROs deploying subcontractors will also need to firstly seek the sponsor’s approval on delegation.
Ironwood Buys AstraZeneca’s Zurampic As Ideal Linzess Complement

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W hat was AstraZeneca’s trash is now Ironwood’s treasure, as it pays $100m up front, along with milestones and royalties, to acquire gout drug approved in December, but not yet launched.

Ironwood Pharmaceuticals Inc. has been looking to acquire an on-market or market-ready product to pair commercially with its gastrointestinal drug Linzess (linaclotide), and it thinks it hit that target at very reasonable terms in acquiring the unlaunched gout drug Zurampic (lesinurad) from AstraZeneca PLC.

In a deal announced April 26, the Cambridge, Mass.-based company said Zurampic — approved by the US FDA on Dec. 22, but not yet launched — offers the chance to target many of the same primary care physicians now being contacted for Linzess and will leverage its existing commercial operation without great additional expense. AstraZeneca had held off on launching the drug, which doesn’t fit into its core areas and doesn’t have the ideal profile, as it considered prospects for “externalization.”

Ironwood plans to launch Zurampic around the midpoint of the second half of this year, CEO Peter Hecht said during a same-day investor call, and looks forward to the anticipated late 2016 filing and 2018 approval of a fixed-dose combination of lesinurad and another gout drug, allopurinol, that will be transferred over by AstraZeneca under the agreement.

The deal divests AstraZeneca of the key asset from its 2012 $1.26bn buyout of Ardea, although the pharma retains rights to other pipeline assets it acquired in that transaction. Ironwood, however, does get an option on a follow-on gout compound discovered by Ardea, RDEA3170, in Phase II.

Ironwood will pay $100m up front for US rights to all products containing lesinurad, along with up to $165m in milestone fees, which Hecht said are largely contingent upon commercial success. AstraZeneca also will get single-digit sales royalties on product sales under the deal. The pharma will manufacture and supply Zurampic to Ironwood, provide undisclosed product support services and retain responsibility for a postmarketing study of the drug for renal and cardiovascular safety that is due by 2025.

Zurampic was approved as a once-daily, 200mg oral tablet. It is the first inhibitor of uric acid transporter URAT1 approved for gout, and the first product approved in roughly 60 years for treating insufficient excretion of uric acid. But the drug faced problems with the safety profile and was submitted at a lower dose, which had less efficacy. FDA’s Arthritis Drugs Advisory Committee supported the clinical benefit but was mixed on the safety profile.

The indication is for second-line, combination therapy with a xanthine oxidase inhibitor (generic allopurinol or Takeda Pharmaceutical Co. Ltd’s Uloric (febuxostat) in patients with hyperuricemia associated with uncontrolled gout who have not achieved target serum uric acid levels with XO1 monotherapy. The FDA label includes a black box warning that acute renal failure has occurred in Zurampic clinical trials and was more common when the drug was given alone.

FDA required the sponsor to conduct a postmarketing study of the drug’s impact, in combination with background XOI therapy, on renal function, adverse renal events and an independent assessment of cardiovascular safety based on adjudication of prospectively defined and collected CV events.

DIVESTMENT MOTIVATED BY FOCUS, NOT SAFETY, IRONWOOD CLAIMS

Asked on the call why AstraZeneca would divest a recently approved asset for which it paid a premium price just four years ago, Hecht asserted the pharma’s decision was more about strategic focus on immuno-oncology than on getting rid of a drug with a questionable safety profile.

“The development program was very strong,” he said on the call. “The regulatory package was very strong. They did a fabulous job negotiating what I think is really a quite good label that effectively captures the benefit and the risk in the product well. And ... they prepared a terrific launch package in every level, from marketing materials to medical affairs. I think at the strategic level, AstraZeneca is moving very strongly — they’ve been quite public about it — toward immuno-oncology and their three core strategic areas. And primary care isn’t one, [so] this is an outside of the core area.”

Ironwood cited market estimates that about 4m Americans are being treated for gout with XO1 agents, and that roughly half of those have uncontrolled disease. This leaves a market opportunity for Zurampic of about 2m patients who are highly motivated to alter their treatment to reduce suffering and doctors who are very open to the potential added benefits of Zurampic’s mechanism of action.

Hecht called the addition of Zurampic to Ironwood’s portfolio “a great strategic fit,” noting that uncontrolled gout is a similar opportunity to irritable bowel syndrome with constipation and chronic idiopathic constipation, which are being addressed with Linzess.

“Critically, this transaction enables us to further leverage Ironwood’s demonstrated commercial capability,” the exec said. “It provides the opportunity to maximize and strengthen our sales capability by expanding our primary care coverage, focusing on top prescribers and early adopters.”

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Data Trumps Anecdotes, Emotion At Sarepta Panel

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A t a highly charged April 25 meeting of the FDA’s Peripheral and Central Nervous System (PCNS) Advisory Committee, which concluded with angry shouting from parents and patient advocates, a majority of panelists said Sarepta Therapeutics Inc. failed to provide sufficient efficacy data for its Duchenne muscular dystrophy drug eteplirsen to win US approval – accelerated or standard, although the votes were much closer on the former than on the latter question.

Now, though, it’s up to the FDA on whether it will take that advice – with all eyes on Janet Woodcock, director of the Center for Drug Evaluation and Research, who on more than one occasion during the more than 11-hour-long meeting emphasized that even though the statutory standard for efficacy was clear, the agency has some flexibility, particularly when it comes to a rare, life-threatening disease like DMD, a progressive muscle degenerative condition that primarily affects boys, who often don’t live beyond 30 years.

Indeed, Woodcock even pointed out the FDA has been “instructed” to take the patient community’s views into account when asked by one PCNS panelist whether the committee should consider the testimony they heard at the meeting from the more than 50 people, including young boys with Duchenne who participated in Sarepta’s trial, or were not able to do so, their parents and other advocates, including a member of Congress, Rep. Mike Fitzpatrick (R-PA), who pressured regulators to approve eteplirsen, noting he carried a letter with him signed by 108 of his Capitol Hill colleagues.

Earlier in the day, Woodcock even suggested it may be worse for the FDA not to approve a drug for a “devastating” disease that’s actually effective – declaring the consequences would be “extreme” for patients – although she emphasized regulators were still grappling with eteplirsen’s efficacy benefit.

Robert Temple, deputy director of the FDA’s Office of Drug Evaluation I, noted that while regulators had raised a lot of questions about Sarepta’s single trial, known as Study 201/202, with specific concerns about whether there was “improper influence” – pointing out the difficulty of controlling bias in historical control studies – he also told panelists they “may have heard testimony from patients that they didn’t think that would alter the level of effort that people made.”

“So those kinds of factors are certainly things that are up for discussion,” Temple said. While “a lot of people don’t like historically controlled trials,” he said those types of studies “can be an adequate and well controlled.”

Ellis Unger, director of the FDA’s Office of Drug Evaluation I, told PCNS members they had to “try to reconcile what you heard from the patients” with the “actual hard data you’ve been analyzing today.”

But it was the comments from one committee member, Chiadi Onyike, an associate professor of psychiatry and behavioral sciences at Johns Hopkins University in Baltimore, that stirred outrage from the audience of patients and parents.

Onyike insisted Sarepta’s 12-patient study failed on “scientific grounds” to prove efficacy and the anecdotal testimony from patients and parents during the open public hearing “wasn’t properly measured in the study.”

So, Onyike said, “I hope you would consider as a patient community participating fully in controlled trials so you are not in this position in the future” – remarks that drew immediate fire from Duchenne advocates.

Sarepta management had explained the reason they hadn’t conducted a placebo-controlled trial for eteplirsen was because at the time they launched the 12-patient study, there wasn’t enough of the drug manufactured. And by the time there was a larger supply of the experimental medicine, patients already heard reports about its efficacy and so it became “unfeasible” since no patient wanted to risk getting the placebo.

But Sarepta leaders pointed out the firm has a confirmatory Phase III trial, known as PROMOVI, underway, which plans to enroll up to 80 patients with genetic deletions amenable to correction by exon 51 skipping in the treatment arm and 80 in the untreated group not amenable to exon 51 skipping.

Analysts, however, questioned whether that trial would satisfy the FDA.

VOTES

The PCNS voted 7-6 that Sarepta had failed to provide substantial evidence from adequate and well-controlled studies that eteplirsen induced production of dystrophin – a protein essential for normal muscular structure and function and the lack of which is at the heart of DMD – to a level that is reasonably likely to predict clinical benefit.

In other words, the committee voted against an accelerated approval of eteplirsen.

The initial vote on that question was 8-5, but one panelist, Paul Romitti, a professor of epidemiology and toxicology at the University of Iowa, said he’d “hit the wrong button,” and voted “no” when he meant to vote “yes,” so the change made it an even tighter split among the PCNS panelists – something that may give Woodcock some leeway to work with if she’s truly inclined to get eteplirsen to patients sooner rather than later, as some analysts have speculated.

The committee voted 7-5, with one abstinence, the decisions to administer the 6-minute walk test, versus conclusions that the patient could no longer walk, failed to be sufficiently objective and free of bias and subjective decision-making by patients, their caregivers or their health care professionals to allow for a valid comparison between patients in Study 201/202 and an external control group.

A majority of the panel said they believed there was no effect of North Star Ambulatory Assessment results on the persuasiveness of the findings in Study 201/202.

An even greater number of the committee said they thought there was no effect of the other tests of physical performance, like rise time or the 10-meter run or walk, on the persuasiveness of the findings in the Sarepta trial.

For the final question, the panel voted 7-3, with three abstentions, the clinical results of Sarepta’s single historically-controlled study failed to provide substantial evidence that eteplirsen was effective as a treatment for DMD.

Billy Dunn, director of the FDA’s Division of Neurology Products, noted the “emotion and passion in the room was clear” and tried to reassure the patients and parents at the PCNS meeting “we listened carefully” to their testimony and would take the information “under serious consideration.”

The panel’s rejection was just the latest blow to the DMD community.
Court: No Herceptin Biosimilar Tag For Indian Trastuzumabs

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A n Indian court appears to have delivered a frontal blow to defendants Biocon and Mylan in a hotly contested case concerning their biosimilar versions of Roche’s Herceptin (trastuzumab).

The court has, in an interim ruling, suggested that the regulatory approvals for the biosimilars may not have been aligned with Indian guidelines for such products and that both Biocon and Mylan can keep their drugs on the market but can’t call them biosimilar to Herceptin. The court even put forth an option for Biocon to reapply for its license should it wish to claim biosimilar as a description of its product or part of its promotional campaign.

It’s not clear if the interim ruling could have any ripple effects on other biosimilar trastuzumabs approved or in the approval stage

The high-decibel case in the Delhi High Court pitching plaintiff Roche against the Drugs Controller General of India (DCGI) and partners Biocon Ltd. and Mylan NV has seen a string of allegations and counter-allegations so far, including Biocon’s reference to Roche’s attempts to act as a “super regulator.”

In an interim order dated April 25, Judge Mannmohan Singh said that he was of the view that the approvals granted to [Biocon’s J CANMab and [Mylan’s] Hertraz are “not on the basis of the adherence” of the Guidelines of 2012 [on Similar Biologics] and rules framed under the [Indian] Drug Act. The final finding in this respect, he though maintained, is yet to be arrived after the present suit is heard on completion of the trial.

The court also specified that Biocon and Mylan may continue to manufacture, market and advertise their product under their respective brand names based on the approvals already granted but without calling their product as “bio similar and/or biosimilar to Herceptin, Hercion, Biceltis” or in any way ascribing any bio-similarity with that of Roche’s products in any press releases, public announcements, promotional or other in printed form and from relying upon or referring the plaintiffs’ names.

The Delhi High Court, in an interim order dated Feb. 5, 2014, restrained both Biocon and Mylan from “relying upon or otherwise referring to” Roche’s Herceptin and its second brands Hercion or Biceltis, or any data relating to trastuzumab marketed as the three brands cited.

Judge Singh said that Biocon and Mylan may manufacture and market the drug by qualifying the INN name trastuzumab but not use the name stand alone on the carton or package insert as a brand name.

“The defendants can use the INN name as Biocon’s trastuzumab or Mylan’s trastuzumab wherever applicable to describe the composition of molecule on the product as well as in its insert and not in a prominent manner. The said expression shall be used at the bottom part of the carton and should be in small size letters than their respective brand names,” details in the 227-page order added.

Judge Singh also restrained Biocon and Mylan from using the data relating to manufacturing process, safety, efficacy and tests conducted for the safety of the drugs as complained of by Roche till the time the final decision on the issue of the biosimilarity is made in the suit. This is in view of “prima facie findings” that the use of the data by the defendants in the product insert without undergoing the entire process of the trials is “misleading.”

Roche said that the ruling sends a “strong, positive” signal that the development, manufacture and approval of biosimilars in India must be subject to “rigorous” clinical and regulatory standards as per the applicable law.

It noted that the court had made clear that the approvals granted to the companies “are not in accordance with the existing protocol” for biosimilars and, therefore, their drugs cannot be considered biosimilars. “We took this action because as the holder of the Herceptin trademark and innovator of trastuzumab, we have a duty to ensure that if a company claims its product is a biosimilar of, or similar to our innovator product, then it actually satisfies the criteria for a biosimilar.”

Biocon, though, underscored that the court judgment does not restrict the sale and manufacture of its trastuzumab, “which is in the interest of patients.”

“However, we understand it has some observations with respect to packaging and labelling, which we will address appropriately. CANMab has undergone all applicable comparability studies,” the Indian firm said.

It also added that it had just received the copy of the interim order which it was studying and will examine all options.

“The current judgment will not affect our product portfolio,” Biocon said.

It’s not immediately clear if the interim ruling could have any ripple effects on other biosimilar trastuzumabs approved or in the approval stage.

RE-APPLY
Interestingly, Judge Singh also put forth an option for Biocon suggesting that if it intends to claim biosimilar as a description of its product or part of its promotional campaign or otherwise in any other form, it can, if so advised, “re-apply the license” before the relevant authorities including the DCGI.

In such an event, the court said that the DCGI and the authorities and committees framed therein should decide the approval application in accordance with the Rules and Guidelines of 2012 and also the observations made by the court in the present order. Alternatively, Biocon could await the outcome of the present suit and can continue with the present arrangement as an interim measure, it added.

CLICK Read full story at: http://bit.ly/21iZw6o
The FDA on April 29 approved Acadia Pharmaceuticals Inc’s Nuplazid (pimavanserin) as the first product in the US treat hallucinations and delusions associated with Parkinson’s disease psychosis. The medicine has the potential to be the company’s first billion dollar product.

With the FDA’s approval in hand for Nuplazid (pimavanserin), Acadia Pharmaceuticals Inc now will put its efforts into marketing the drug, which has the potential to be the company’s first billion dollar product.

The medicine, which Acadia plans to put on the US market in June, is the first product approved in the US to treat hallucinations and delusions associated with Parkinson’s disease psychosis (PDP).

Before the FDA’s gave its blessing to Nuplazid, analysts at Sagient Research’s BioMedTracker, an affiliate of Scrip, put the chances of approval at 94%.

Acadia has not yet disclosed the pricing for Nuplazid, but the company plans to hold a conference call with investors and analysts on May 2, where more details may become available. But Acadia said it plans to launch a financial and patient access assistance program, known as Nuplazid Connect.

Nuplazid will only be available through a specialty pharmacy network, Acadia said. Nuplazid is the first selective inverse agonist of the 5-hydroxytryptamine 2A (5-HT2A) receptor approved in the US for Parkinson’s and as such has established a new class of medicines: selective serotonin inverse agonists.

The drug not only preferentially targets 5-HT2A receptors, which are thought to play an important role in PDP, but it also avoids activity at dopamine and other receptors commonly targeted by antipsychotics.

Typical therapies for Parkinson’s, which affects about 1 million Americans and up to 6 million people worldwide – with about 40% having PDP – consists of drugs that stimulate dopamine to treat patients’ motor symptoms such as tremor, muscle rigidity and difficulty with walking. But, explained Michael Okun, medical director of The National Parkinson Foundation, Nuplazid works in a “whole new way” – treating hallucinations and delusions without blocking dopamine receptors, therefore, not impairing motor function in patients with PDP.

Nuplazid’s application was based on data from the pivotal Phase III trial, known as Study -020, and other supportive studies, which Acadia said represented the largest research and development program in the PDP space. Nuplazid significantly reduced the frequency and severity of psychotic symptoms, versus placebo, on the scale for assessment of positive symptoms of Parkinson’s disease, or SAPS-PD. That benefit was achieved without impairing motor function, Acadia reported.

The most common adverse reactions of 5% or greater and twice the rate of placebo in the study were peripheral edema and confusional state.

As an atypical antipsychotic drug, Nuplazid’s labeling must carry a black-box warning alerting prescribers and patients about an increased risk of death associated with the use of those types of drugs to treat older people with dementia-related psychosis. The boxed warning also emphasizes that no drug in the atypical antipsychotic class is approved to treat patients with dementia-related psychosis.

Other sections of the labeling warn that Nuplazid should be avoided in patients with known QT prolongation or in combination with other drugs known to prolong QT interval, including Class 1A antiarrhythmics or Class 3 antiarrhythmics, certain antipsychotic medications, and certain antibiotics.

Nuplazid also should be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of Torsade de pointes or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and presence of congenital prolongation of the QT interval. But analysts don’t think the black box or other warnings will get in the way of Nuplazid’s sales, given the unmet need for the medicine, which in 2014 was dubbed a breakthrough therapy by the FDA – a designation intended to help speed products for life-threatening conditions to the market.

Nuplazid was overwhelmingly backed by an FDA advisory committee.

At a March 29 meeting, the FDA’s Psychopharmacologic Drugs Advisory Committee (PDAC) voted 12-2 Nuplazid’s benefits of about a 23% improvement in PDP symptoms, which the FDA called “minimal,” outweighed its risks of serious adverse events, like cardio-respiratory arrest, heart attacks, respiratory distress, sepsis and septic shock, or death.

“I was persuaded by the really terrible quality of life that these patients have,” said PDAC chair David Brent, academic chief in the Division of Child Adolescent Psychiatry at the University of Pittsburgh School of Medicine in Pennsylvania. “I think as long as they can be given an informed choice about the risks, I think they ought to have the option.”

Brent said he also was convinced “by the fact there really is nothing else.”

“Even if the effects are modest, you have to compare it to what’s available right now, which with what we’ve been presented is nothing,” he said.

In two earlier questions, the committee voted 12-2 that Acadia provided substantial evidence of the effectiveness for Nuplazid as a treatment for PDP and 11-3 the company had adequately characterized the safety profile of the medicine.
Erbitux Being TAILOR-Made For Chinese First-Line mCRC Market, But Brand Recognition Is Merck’s Real Goal

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Merck’s plans to penetrate the Chinese market further with its anti-EGFR cancer therapy Erbitux (cetuximab) have received a boost with a Phase III TAILOR trial showing significant benefits when used first-line in metastatic colorectal cancer in this population.

The German company says it will work to make the product available for patients in China as a first-line treatment as soon as possible. But it seems that the real benefit for the German company of any label expansion will be in helping it build its brand presence in China rather than in absolute sales.

Erbitux was first approved in China for use in combination with irinotecan or as a single agent for metastatic colorectal cancer refractory to irinotecan in 2006, but the standard first- and second-line regimens for colorectal cancer there are FOLFOX and FOLFIRI.

An expanded approval in China would bring it into line with other major markets. First-line treatment of RAS wild-type metastatic colorectal cancer with Erbitux plus FOLFOX or FOLFIRI is already recommended in clinical guidelines by both the US National Comprehensive Cancer Network and the European Society for Medical Oncology clinical guidelines.

But such a label expansion to first-line use is unlikely to do much for the product’s global sales, says Datamonitor Healthcare analyst Dr Dustin Phan. “Not only are both regimens effective and widely used for colorectal cancer globally, but Erbitux recently failed to receive a recommendation from NICE for first-line use due to its lack of cost-effectiveness. It’s hard to imagine that a cost-competitive national healthcare system like China’s would not make a similar assessment. This would then limit the drug’s first-line use in China to RAS wild-type mCRC patients with private insurance or self-funding. Merck has charity assistance schemes in place to promote the use of the Erbitux. Under these programs, patients will have a self-pay period of three months as opposed to six months. However, the relative high-cost of treatment for the majority of the Chinese population will still limit the drug’s peak patient share.”

Another problem for Merck is that Erbitux is also expected to experience loss of patent exclusivity in China in the second quarter of 2017, which will result in biosimilar competition and erosion of branded sales, with the first cetuximab biosimilars expected to reach the market in 2020. “In addition, many branded drugs are extensively copied by domestic generics companies before their patents expire, and counterfeit drugs continue to be a significant problem in the Chinese market,” said Phan.

“Ultimately, I really see the results of this study (and the likely resulting label expansion) as an opportunity for Merck to establish a presence in the Chinese market. Roche is currently the biggest presence in the Chinese CRC market with Avastin, and Merck is likely trying to break into the Chinese market where brand recognition is an important factor,” he added.

The top-line data from the 397-patient TAILOR study show that it met its primary endpoint of significantly increasing progression-free survival (PFS) in patients with RAS wild-type metastatic colorectal cancer (mCRC) treated with Erbitux (cetuximab) plus FOLFOX chemotherapy, compared with FOLFOX alone.

Secondary endpoint results also support the superiority shown for PFS, Merck said, and the safety profile was similar to that seen in other pivotal trials. Secondary endpoints include overall survival, best overall response rate, time to treatment failure and rate of curative surgery for liver metastases.

The full study results will be submitted to upcoming international scientific meetings.

“This marks a significant step in the execution of our strategy in oncology, notably the expansion in growth markets like China,” said Luciano Rossetti, head of global research and development of Merck’s biopharma business. They “reinforce the value and imperative of RAS biomarker testing in clinical practice, so as to provide patients with the right targeted therapy,” he added.

Merck has a keen interest in China. As well as tapping into local innovation by nurturing Chinese start-ups, it has been strengthening its own presence in recent years in China. China has the world’s second-largest single pharmaceutical market with an estimated annual growth rate of about 9% through to 2018.
AbbVie Partnership On CD71 Gives CytomX Big Upfront

Antibody-drug conjugates have taken a back seat to cancer immunotherapy as the hot modality in oncology of late, but AbbVie Inc. and CytomX Therapeutics Inc. unveiled a partnership on April 20 to develop an ADC in a deal that CytomX cites as further validation of its Probody technology platform. AbbVie is paying $30m up front to co-develop and potentially co-commercialize a Probody-drug conjugate against CD71, also known as transferrin receptor 1 and highly expressed in a number of solid and hematologic cancers. Unlike prior deals around the Probody platform with Pfizer Inc. and Bristol-Myers Squibb Co., CytomX will have greater involvement in this partnership, with responsibility for development through the end of Phase I and a right to either co-commercialize in the US or share US profits. The deal was the third cancer-focused tie-up AbbVie announced during the week of April 18.

AZ’s Zavicefta Gains EU Positive Opinion

The CHMP followed recent EMA guidance to take a flexible approach to drugs against multi-resistant pathogens when recommending approval for AstraZeneca’s latest antibacterial Zavicefta. AstraZeneca PLC’s new antibacterial, Zavicefta (ceftazidime plus avibactam), has been recommended for approval in the EU by the top advisory panel, the Committee for Medicinal Products for Human Use (CHMP), for use in the treatment of patients infected with multi-drug resistant bacteria, so-called “superbugs,” as well as several other severe bacterial infections. The committee recommended approval for infections caused by multi-drug resistant pathogens on the basis of a limited set of data, but this was in line with guidance from the European Medicines Agency (EMA) issued in 2013, the agency noted. That guidance allows a flexible approach to be taken to the development of new antibiotics for human use, targeting multi-drug resistant pathogens in areas where treatments are needed.

Gilead Gets CHMP Nod for New HIV Combo

Gilead has received the green light in the EU for marketing its newest fixed-dose HIV treatment Odefsey but its cannibalization of predecessor product Complera will not reach levels expected in the US as generic versions of older HIV combos are set to arrive earlier in the EU. The EU’s CHMP has given Gilead Sciences Inc. the go-ahead for the marketing of its new fixed-dose combination HIV treatment Odefsey (emtricitabine 200 mg/rilpivirine 25 mg/tenofovir alafenamide 25 mg; R/F/TAF). The product is fixed-dose combination of 200 mg of Gilead’s emtricitabine, 25 mg of its tenofovir alafenamide with 25 mg of Janssen-Cilag Ltd.’s (Johnson & Johnson) rilpivirine, and is the latest product in the two companies’ development and commercialization agreement, which produced the predecessor product Evipera/Complera (rilpivirine/emtricitabine/tenofovir disoproxil fumarate). The tenofovir alafenamide (TAF) component is a new tenofovir produg that has similar efficacy to tenofovir disoproxil fumarate (Gilead’s Viread or TDF) at one tenth of the dose. Gilead also notes that TAF has also shown improvement in surrogate laboratory markers of renal and bone safety compared with TDF in clinical trials in combination with other antiretroviral agents.

Biogen’s Zinbryta Gets EU Nod

Biogen and AbbVie Inc.’s multiple sclerosis therapy, Zinbryta (daclizumab), has been given a green light for use in Europe – but what gap can this new drug fill in a crowded therapy space? Zinbryta received a positive recommendation from the European Medicines Agency’s scientific committee, the CHMP, following its April 25-28 meeting, based on data submitted from the Phase IIb SELECT and Phase III DECIDE trials of the drug in relapsing forms of MS (RMS). The CHMP noted that benefits of the drug are its ability to reduce the annualized relapse rate (ARR), as well as the risk of 24-week confirmed disability progression. However, analysts at Sagient Research’s BioMedTracker previously noted that while Zinbryta in the Phase III DECIDE trial did show efficacy superior to that of interferon beta-1a with regard to the annualized relapse rate and lesions, the drug was not associated with a significantly lower risk of disability progression.

R&D BITES
Heptares-Powered Sosei’s Incoming CEO Explains What Happens Next

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Japanese company Sosei conducted a master stroke last year when it acquired UK biotechnology company Heptares as its in-house R&D engine. Deal after quality deal has ensued, and Sosei’s share price has rocketed by more than 400%. *Scrip* Sukaina Virji spoke to Sosei’s COO – and CEO-elect – Peter Bains to find out what happens next.

After almost six years as a non-executive member of Sosei Group Corp’s board and one of the key architects of Sosei’s long-term strategic vision, Peter Bains was appointed Sosei’s COO at the start of April. If all goes to plan, he will take over the CEO role from company founder and chair Shinichi Tamura at the AGM in June this year.

**SCRIP:** What attracted you to the CEO role at Sosei?

**PETER BAINS:** I was brought in as a non-executive to strengthen the strategic and operational mix on the Sosei board almost six years ago. It was then a small company and today it’s still a small company. We have 110 people. In that context, the board plays quite a participative role. It’s not a million miles away from the coalface. I like to roll my sleeves up and get stuck into building business so it was attractive to me to join the Sosei board.

I was able to bring some of my experiences out of big pharma – GSK for 23 years – and experiences out of biotechnology companies, where I worked on the board of several companies. With the acquisition of Heptares I was the designated board member to oversee that, as I was with Allergan. The CEO and the board approached me several months ago to ask if I’d be interested in taking on the CEO role. My answer was that I’d be very interested. I was at that point the CEO of Syngene International Ltd., a contract research company in India. My contractual obligations to them were to build the company and list it in India and I had a contract that expired on March 31, so I had an evening off and then on April 1 I was in the COO role for Sosei. Because I was a non-exec and because of the nature of being a non-exec of a small company, I hit the ground running. I bring a degree of continuity and also a new outlook on what we need to do to achieve the vision.

**SCRIP:** What prompted the Heptares acquisition?

**PETER BAINS:** Sosei’s transformation began about five years ago when the Sosei board established a long term strategic framework. The aim was to build a leading global biopharmaceutical company in India. My contractual obligations to them were to build the company and list it in India and I had a contract that expired on March 31, so I had an evening off and then on April 1 I was in the COO role for Sosei. Because I was a non-exec and because of the nature of being a non-exec of a small company, I hit the ground running. I bring a degree of continuity and also a new outlook on what we need to do to achieve the vision.

Since the acquisition Heptares has comprehensively validated the underlying technology platform with a strong series of collaborations with some of the world’s leading companies in their fields. Immunology with AstraZeneca, migraine with Teva, neurology and Alzheimer’s with Allergan, and the discovery collaboration with Pfizer. That gives us enormous confidence going forward.

So what attracted us to Heptares fundamentally was the quality of the platform – we believe it’s world leading – and the scalability of that platform going forward, which we believe is practically almost unlimited.

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**SCRIP:** So what happens next at Sosei?

**PETER BAINS:** First and foremost our strategy is to look at organic growth focusing on Heptares. But that’s multi-layered. We are looking to strengthen our technology leadership. A good example of that is our participation in the consortium for the cryogenic electron microscopy. It’s highly complementary to our world leadership in X-ray driven high resolution crystallography and it’s particularly useful in complex proteins.

We will look to increase the number of STARs that we develop. From the STARs we get the crystals, from the crystals we get the candidates, and they then become opportunities for development.

**SCRIP:** Sosei’s share price has rocketed over the past 12 months so obviously investors are happy. Has Heptares lived up to your expectations?

**PETER BAINS:** When we looked at it just over a year ago we were very excited by what we saw as a world leading technology around GPCR targeted structure based drug design and receptor stabilizing technology. With stabilized receptors you get the very high resolution crystals and that is what you need to drive a pipeline of high quality candidates that can move into preclinical development and then into clinical development and beyond.

We saw a platform technology that we believed was world leading and had enormous scale opportunities ahead of it because the GPCR universe is very large. You can measure it. Including the sensory receptors, there are over 800. If you take those out it’s nearer 400. And while GPCRs have been the targets against 40% of industry’s drugs, many of those are suboptimal and only a quarter of the GPCRs have been drugged. So there is an enormous scope ahead of us. We can count the targets, and then you have agonist forms, antagonist forms, partial agonist forms. In a practical sense there is almost an unlimited opportunity. And what Heptares has delivered, from the first wave of assets it has developed over the past 12-14 months, we believe we can repeat again and again.

So what attracted us to Heptares fundamentally was the quality of the platform – we believe it’s world leading – and the scalability of that platform going forward, which we believe is practically almost unlimited.

Read the full interview at: http://bit.ly/1W8t5IX
One of the most difficult parts of the jobs of investors and analysts is to predict the future. This can prove tricky so we fall back on our experience by associating what has happened in the past with what is likely to occur in the future. In taking the temperature prior to the start of this year’s JP Morgan Healthcare conference I did not expect that almost every bearish prediction would come true and the stock price plummets that commenced that week would mark the start of one of the worst first-quarters for life science companies for many years.

Now that the first-quarter of 2016 is behind us, attentions turn to the rest of the year and at the Biotechs and the City event in London last week a former colleague mentioned her expectations for a further leg down in stock prices before we reach a bottom. While that weakness may still be the case, I am looking for any sign that the sector has reached the nadir and unfortunately, I have not yet seen many.

One of the supposed attractions of the sector to the generalist investor, and which partly catalyzed the seven-year biotech bull market that ended last summer, is the high level of merger and acquisition (M&A) transactions that punctuates the cycles of the sector. Medivation Inc. had a bad start to last week after receiving the ire of six members of Congress, including a presidential candidate, for the price of its lead oncology drug Xtandi (enzalutamide). However, Medivation’s stock price finished the week up about 10% after reports that it had appointed investment bankers to defend against takeover interest. The parties that are interested in acquiring Medivation must be thanking the senators for their intervention aimed at depressing Xtandi’s price and which also depressed Medivation’s share price prior to the 20% jump on the M&A reports. The acquisition of Medivation by a bigger pharmaceutical or biotechnology partner is eminently logical and has much in common with the acquisition of Pharmacysics Inc. by AbbVie Inc. last year. Both have growing oral oncology products with expanding indications – in Xtandi’s case, into earlier-stage prostate cancer and possibly a breast cancer subset – both agents are being investigated as components in combination therapies and both have a captive partner – Astellas Pharma Inc. in Medivation’s case – that might not be fleet of foot, or price insensitive enough to secure the acquisition of the full Xtandi rights and royalties.

Fortunately for most of the generalist investors who were once attracted to the sector for its M&A, but left it without seeing the expected transactions that their ironically price-insensitive buying prohibited, one swallow does not make a summer. However, the sell-side analysts, no doubt touting for the transactional business on behalf of their banking colleagues, were quick to point to the companies under their coverage as the next acquisition. In a fit of crying wolf, the analysts from Citigroup reeled off eight companies under their coverage (including Medivation) that are likely to be acquired in the next 12-18 months. This reminds me of a sketch from the BBC Radio series Old Harry’s Game where Satan bemoans the human race when asking which species proclaims humans as the most advanced species on Earth? Who says that the companies under coverage by an analyst will be acquired? The analyst covering the companies.

If the wilderness years after the 2001 biotech market correction are anything to go by, it took a series of acquisitions of companies whose share prices were half or less than their peak in a quiet tempo of transactions for the generalist investor to become interested in the sector. It is only wishful thinking for the sell-side to expect a transaction forte that prompts a quick return to the sector that generalists have only just rotated away from. In addition, since its peak last summer, the biotech sector is only off about 30%.

The other supposed attraction for investors new to the sector is the FDA’s more open-door policy on drug approvals. This has been tempered of late by the attention of members of the US senate on drug pricing but the reality of many new drug approvals is not a blockbuster panacea. Who can forget the commercial disasters of Omontys (peginesatide) from Affymax Inc. and Incivek (telaprevir) from Vertex Pharmaceuticals Inc. both of which were withdrawn and Afrezza (inhaled human insulin) from MannKind Corp, all recently approved drugs but none likely to ever recoup their development cost.

The chain of events illustrated by Medivation (but not Affymax, Vertex or MannKind) that looks like resulting in a profitable exit is positive clinical trials, FDA approval, billion dollar sales and acquisition by a bigger company. A very different scenario looks more likely to occur at Keryx Biopharmaceuticals Inc. While Keryx’s announcement of positive Phase III results for its lead product Auryxia (ferric citrate) resulted in about a 7% rise in its share price on the day, it finished the week about where it had started. Investors and analysts have increasingly come to recognize Auryxia – with sales last quarter of less than $6m after enacting an unpalatable 9% price increase – for its lacklustre attributes and a good dose of rationality suppressed Keryx’s share price. At least there is one rational sign that we are close to a bottom in biotech.

The Magna Biopharma Income fund holdings include Medivation.

Andy Smith is chief investment officer of Mann Bioinvest. Mann Bioinvest is the investment adviser for the Magna BioPharma Income fund which has no position in the stocks mentioned, unless stated above. Dr Smith gives an investment fund manager’s view on public life science companies. He has been lead fund manager for four life science-specific funds, including International Biotechnology Trust and the AXA Framlington Biotech Fund, and was awarded the Technology Fund Manager of the year for 2007.
Scrip's weekly Pipeline Watch tabulates the most recently reported late-stage clinical trial and regulatory developments from the more than 10,000 drug candidates currently under active research worldwide.

### Late-stage clinical developments for the week 22-28 April 2016

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<th>LEAD COMPANY</th>
<th>PARTNER COMPANY</th>
<th>DRUG</th>
<th>INDICATION</th>
<th>MARKET</th>
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<td><strong>REGULATORY APPROVAL</strong></td>
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<tr>
<td>AstraZeneca PLC</td>
<td></td>
<td>Bevespi Aerosphere (glycopyrrolate/formoterol fumarate)</td>
<td>chronic obstructive pulmonary disease (COPD)</td>
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<td>Servier</td>
<td>Taiho</td>
<td>Lonsurf (trifluridine/tipiracil)</td>
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<td>Exelixis Inc</td>
<td>Ipsen SA</td>
<td>Cabometux (cabozantinib)</td>
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<td>Collegium Pharmaceutical Inc.</td>
<td></td>
<td>Xtampa ER (oxycodone)</td>
<td>chronic pain</td>
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<td>Gilead Sciences Inc</td>
<td></td>
<td>Descovy (emtricitabine and tenofovir alafenamide)</td>
<td>HIV/AIDS</td>
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<td>Araelz Pharmaceuticals Inc.</td>
<td>FAES Pharma SA</td>
<td>Blexten (bilastine) tablets</td>
<td>seasonal allergic rhinitis and urticaria</td>
<td>Canada</td>
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<td>AbbVie Inc.</td>
<td>Enanta Pharmaceuticals Inc.</td>
<td>Viekira Pak (ombitasvir, paritaprevir, ritonavir tablets; dasabuvir tablets)</td>
<td>hepatitis C</td>
<td>US and EU</td>
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<td>Takeda Pharmaceutical Co.</td>
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<td>TachoSil (human thrombin/human fibrogen)</td>
<td>wound healing</td>
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<td>Swedish Orphan Biovitrum AB</td>
<td></td>
<td>Orfadin (nitisinone)</td>
<td>hereditary tyrosinemia type-1</td>
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<td><strong>FAST-TRACK STATUS</strong></td>
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<td>Advaxis Inc.</td>
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<td>ADXS-chER2</td>
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<td>CG100</td>
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<td>AM-Pharma BV</td>
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<td>reCAP</td>
<td>renal disease</td>
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<td>Novartis AG</td>
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<td>Illaris (canakinumab)</td>
<td>TNF receptor associated periodic syndrome, hyperimmunoglobulin D syndrome and familial Mediterranean fever</td>
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<td>Bristol-Myers Squibb &amp; Co.</td>
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<td>Opdivo (nivolumab)</td>
<td>head-and-neck cancer</td>
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<td><strong>COMPLETE RESPONSE LETTER</strong></td>
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<td>Otsuka Pharmaceutical Co. Ltd.</td>
<td>Proteus Digital Health</td>
<td>Abilify (aripiprazole) plus ingestible sensor and wearable patch</td>
<td>schizophrenia, bipolar I disorder and major depressive disorder</td>
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<td>Johnson &amp; Johnson</td>
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<td>Vermox (mebendazole)</td>
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<td>Relypsa Inc</td>
<td>Veltassa (patiromer)</td>
<td>hyperkalemia</td>
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<td>hepatitis B vaccine</td>
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<td>Zambon SpA</td>
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<td>Xadago (safinamide)</td>
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<td>Quillivant XR(methylphenidate)</td>
<td>attention deficit hyperactivity disorder</td>
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<td>Wellstat Therapeutics Corp.</td>
<td>BTG plc</td>
<td>Xuriden (uridine triacetate)</td>
<td>hereditary orotic aciduria</td>
<td>US</td>
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*Source: Sagient Research's BioMedTracker*
Finnish drug development company, Faron Pharmaceuticals, Ltd. has appointed Matti Karvonen medical director. Karvonen has a background in clinical neurology, and has previously served at several international pharma organisations, including Roche Holdings AG, Novartis AG and Biogen. He has also co-founded several commercial medical organisations and has participated in a number of clinical programmes, most recently in the pan-European launch of a new neurological drug.

GarmaMabs Pharma has appointed Martine J. George an independent board member. George joins the biotechnology company from Pfizer Inc, where she previously served as vice president global medical affairs, oncology. As a board-certified oncologist and gynecologist, she has previously held senior positions at GPC Bio tech and Johnson & Johnson, and has led the successful launch of drugs in multiple oncology indications.

UniQure N.V. has appointed Paul Firuta chief commercial officer. Firuta joins the company, which specialises in human gene therapy, from BioBlast Pharma, where he also held the post of chief commercial officer. He has 25 years of industry experience, previously serving companies such as NPS Pharmaceuticals, Inc. and Viropharma, Inc., where he held several senior leadership roles.

The genomic medicine company, Medogenics Inc., has appointed Michael Diem, former head of corporate strategy and corporate development at AstraZeneca PLC, senior vice president of business and corporate development. Prior to his time at AstraZeneca, Diem was head of business development at GlaxoSmithKline Rare Diseases, having previously acted as a partner in its corporate venture capital firm, SR One Ltd.

XBiotech Inc., the global biosciences company specialising in therapeutic antibodies, has appointed Scott Whitehurst chief financial officer. Whitehurst joins the business from Amgen, where he held the post of vice president of finance, operations for the past eight years. Prior to this, he spent 14 years at Hewlett-Packard Co before serving as chief financial officer at Novartis Animal Health.

Mylan has appointed Kenneth Parks chief financial officer (CFO). Parks has over 30 years of corporate finance experience, having previously served as senior vice president and CFO at Wesco International. Prior to this he held various senior roles at United Technologies Corporation, most recently as vice president, finance.

Abeona Therapeutics Inc. has appointed Christine Silverstein vice president of investor relations. Silverstein brings over 12 years of corporate communications experience to the role, having previously served as director of investor relations at Relmada Therapeutics and vice president of corporate development and investor relations at PlasmaTech BioPharmaceuticals, Inc.

UK-based biotech company Tiziana Life Sciences has appointed Dr Robert Evans vice president, clinical sciences. Evans joins the business from Glenmark Pharmaceuticals, where he was previously vice president, clinical development. Prior to this, he held a variety of scientific leadership roles at Regeneron Pharmaceutical, where he also worked alongside Tiziana’s current chief operating officer, James Tripp.
The balance of power behind the prescribing decision is changing: payers are ever more in charge. That means that insight into how payers make decisions – how they evaluate drugs, one against another – will be crucial to any successful drug launch.

RxScorecard objectively, authoritatively, and systematically assesses marketed and pipeline drugs in a therapeutic indication from the payer’s point of view. Developed by senior medical and pharmacy leaders from major payers and pharmacy benefit managers, RxScorecard delivers practical and powerful insight into your drug’s reimbursement potential and how you can maximize it.

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