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THE NEWSPAPER FOR THE CHEMICAL AND LIFE SCIENCE MARKETS

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The Future Lies in the Genome

As a Pure Life Science Company Bayer Steps up Investments into Health Care and Crop Science Businesses

Kemal Malik, board member for innovation at the German Bayer Group, sees many similarities in the genetic system of humans, animals and plants. This opens the door for synergies in R&D between the subgroups HealthCare and CropScience. It also facilitates new treatments for diseases. In an interview with Thorsten Schüller of CHEManager International Malik talks about the latest innovation activities of Bayer.

CHEManager: By spinning off the MaterialScience business under the new name Covestro Bayer is becoming a pure life science company. What is the reason behind this decision?

K. Malik: We found a lot of similarities between CropScience and the HealthCare business. If you look at Bayer, we had a very successful life science business over the last five years. We are one of the fastest growing large pharma companies in the industry. Also our crop science business has been growing very significantly over the last years. Both businesses have been driven by innovation in renewing products and bringing them to the markets. But innovations in pharma, crop science and consumer care require investments. As a consequence of this we need to invest further.

MaterialScience is different from this from the Life Sciences. But as our life science business needs strategic investments, we had to make decisions. We realized that we couldn´t make the level of investment in our material science business that it needs. So the best for both, Bayer and MaterialScience is to bring the material science activities to the capital market itself where it can raise the money it needs to have a successful future.

Looking on the weight of your health care and crop science businesses – what will be the split between them in the future?

K. Malik: From a sales point of view health care will stand for about 70%, crop science for about 30%. That split will be more or less the same for R&D as well where we plan to spend about €3.8bn this year.

The aim of Bayer is to grow mainly organically. Is this sufficient in order to be innovative and to compete in the global environment?

K. Malik: In terms of major M&A we made some pretty significant deals in the last two, three years. For our future growth we don´t see the need for another big merger or acquisition. We will continue to source innovation from a base we have. But we are always open to licensing agreements.

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Lanxess and Saudi Aramco to Form 50:50 Rubber JV

Germany's Lanxess has clinched a deal with Saudi Aramco Overseas Company, a subsidiary of the Saudi Arabian oil giant, to form a 50:50 joint venture that will own and operate the carved-out Lanxess synthetic rubber business units Tire & Specialty Rubbers and High Performance Elastomers.

Matthias Zachert, CEO, Lanxess

The new company with 20 production facilities in nine countries plus 3,700 employees and additional support staff will have annual sales of €3 billion and an enterprise value of €2.75 billion. Lanxess, which will consolidate operations financially, will appoint the CEO, while Aramco will name the CFO. The supervisory board will be chaired by Lanxess CEO Matthias Zachert.

To seal the deal, the Saudi company will pay the German chemicals and rubber producer around €1.2 billion in cash for the stake, after deducting debt and other unspecified financial liabilities. Following antitrust approval, the transaction is planned to close in Q1 2016. During a subsequent five-year lock-up period, the shareholder structure will remain unchanged.

Zachert said Lanxess will pump around €400 million of the proceeds from the share sale into expanding its well-positioned and less cyclical segments Advanced Intermediates and Performance Chemicals. An additional €300 million has been earmarked for further reduction of the company's financial debt position, about €200 million for a share buyback.

At the heart of the arrangement is security of feedstock supply to Lanxess, which despite being rubber market leader is not back-integrated. Once contracts with existing suppliers expire, Zachert said Aramco will serve as a "power network" to secure "attractive procurement agreements."

The future partners have also hinted at opportunities to share Middle East projects modelled loosely on Aramco's existing collaborations with French oil and petrochemicals player Total (Satorp) and US chemical giant Dow (Sadara). (dw) ■

EU Details New Proposal for TTIP

A detailed proposal to revamp the controversial Investor-to-State Dispute Settlement clause of the Transatlantic Trade and Investment Partnership (TTIP) still being negotiated with the US was presented by EU Competition Commissioner Cecilia Malmström in September.

Cecilia Malmström, Trade Commissioner, European Commission

The new plan building on input from the European Parliament, EU member states, national parliaments and feedback from the public calls for 15 internationally qualified and independent judges – five each from the US, the EU and a third country – to be appointed publicly to a new Investment Court System that would deal with complaints in first-instance and appellate tribunals.

Malmström said the ability of investors to take complaints to the tribunal would be precisely defined and limited to cases such as targeted discrimination on the base of gender, race or religion, or nationality, expropriation without compensation or denial of justice. National governments' right to regulate would be an integral part of the process and guaranteed in the provisions of the trade and investment agreements.

Taking account of European unease about disputes being heard outside regular court systems, the EU paper calls for proceedings to be transparent, hearings open and comments available online. Even with the changes, TTIP is certain to remain controversial among advocacy groups who fear multinational companies could use private arbitration rules to challenge European food and environmental laws.

The European chemical industry unequivocally supports TTIP, expecting benefits in the form tariff reduction, lowering of non-tariff trade barriers, and stimulation of the overall economy, as the German industry association VCI has stressed. (dw) ■

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CONTENT

Olin Shareholders Pass Dow Chlor-Alkali Merger

Shareholders of US-based Olin Corporation have overwhelmingly approved the issuance of new shares of common stock and the amendment of the company's articles of incorporation needed to complete the chlorine chain merger with Dow Chemical by the beginning of October.

The $5 billion Reverse Morris Trust tax-saving transaction foresees Dow merging its US Gulf Coast chlor-alkali and vinyl chlorinated organics and global epoxy businesses with Olin's relevant businesses, more than doubling Olin's scope.

An asset merger would create a low-cost industry leader with revenues approaching $7 billion, the companies said when announcing the plans at the beginning of April. Dow's shareholders will hold 50.5% of Olin shares, with existing Olin shareholders owning about 49.5% of the merged company.

The transaction includes $2 billion of cash and cash equivalents to be paid to Dow, along with an estimated $2.2 billion in Olin common stock, based on its value at close of Mar. 25, 2015. The new Olin is expected to assume around pension and other liabilities worth around $800 million. Annualized cost synergies of at least $200 million are forecast to be achieved within three years.

Current Olin CEO Joseph D Rupp will head the enlarged company, flanked by a senior management team made up of both Dow and Olin current employees. (dw) ■

Merck to Close on Sigma-Aldrich in Q4

German chemicals and pharmaceuticals producer Merck KGaA now expects to close its € 13.1 billion acquisition of Sigma-Aldrich some time during the fourth quarter following the sale of certain of the US company's solvents and inorganics assets.

Merck said it has obtained all necessary antitrust approvals, and negotiations with potential buyers of the assets the European Commission has mandated Sigma-Aldrich shed are in the final stages. However, the EC will require time to approve the buyers.

At the end of August, after completing its financing package for the acquisition with the placement of a € 2.1 billion bond, the Darmstadt-based company said it hoped to close the transaction in the third quarter. (dw) ■

Air Liquide and Messer "Swap" Assets in Turkey and Hungary

Two European industrial gases producers, France's Air Liquide and Germany's Messer Group, will acquire assets from each other. In Turkey, Air Liquide is buying Messer Aligaz Sanayi Gazlari, and in Hungary Messer is taking over Air Liquide Hungary Ipari Gáztermelő, a subsidiary of Air Liquide Eastern Europe.

With sales of around €9 million in 2014, Messer Aligaz supplies industrial, medical and specialty gases to a range of Turkish industries in the highly industrialized regions of the Marmara and the Aegean and is mainly focused on the Industrial Merchant segment.

The acquisition will position Air Liquide in Ankara, Istanbul and Izmir. The Turkish company owns and operates an air separation unit (ASU) for production of liquid oxygen, nitrogen and argon, along with three cylinder filling centers.

In Hungary, the Messer purchase — which is subject to antitrust approval — is being wrapped up through subsidiary Messer Hungarogáz. With it, the German group will take over more than 50 employees, along with tangible assets and customer relationships.

The Ipari Gáztermelő assets include an on-site air separation unit, two nitrogen generators, a filling plant for gas cylinders in addition to road tankers, customer tanks, and steel cylinders. (dw) ■

Corbion Purac Takes Lactic Acid Business

Corbion Purac has signed an agreement with Malladi Specialties Limited (MSL) of India covering marketing and supply of lactic acid and derivatives. Part of the Malladi group, one of India's leading pharmaceutical companies, MSL will retain the production assets and toll manufacture for Corbion. Financial terms of the deal were not disclosed.

The Indian producer supplies regional pharmaceutical, home & personal care, chemical and food industries with products including calcium lactate, sodium lactate and buffered lactic acid. The partnership will give Corbion a local production base while maintaining control over quality of supply, the Dutch company said.

Frank Goovaerts, regional vice president at Corbion Purac Asia Pacific, said that with this acquisition, his company will be able to expand its distribution network and customer service in India. (dw) ■

EU Approves Shell Takeover of BG Group

The European Commission has approved the acquisition of BG Group by Royal Dutch Shell, saying the buy would not give Shell a dominant share in markets such as oil and gas exploration, gas liquefaction and wholesale supply of liquefied natural gas (LNG). It added that Shell would be unable to bar competitors from access to liquefaction facilities supplying LNG to the European Economic Area (EEA) or from gas transportation and processing infrastructure in the North Sea.

As a number of strong competitors would remain active in these markets, the oil and petrochemicals giant could not influence prices. (dw) ■

Russia's Sibur to Buy Stake in China's Sinopec

Russian petrochemical giant Sibur is planning to acquire a stake in Chinese energy and petrochemicals giant Sinopec, with a stock handover to be completed by Dec. 1, following regulatory approvals.

While the two companies have declined to disclose the size or the value of the proposed stakeholding, Russian sources told the news agency Reuters that Sinopec could acquire more than 10%. The deal signed in Beijing during Russian President Vladimir Putin's visit would not substantially alter the Chinese company's shareholder structure, however.

Businessman Leonid Mikhelson, head of Novatek, Russia's second largest gas producer behind Gazprom, is expected to remain Sibur's largest shareholder. Other Sibur shareholders are tycoon Gennady Timchenko, regarded as an ally of Russian President Vladimir Putin, as well as current and former Sibur managers. (dw) ■

BASF and Gazprom to Complete Asset Swap

The asset swap between BASF and Gazprom first announced in 2012 and originally scheduled to take place at the end of 2014 is now set to be completed by the end of 2015. Following approval by the European Commission in December 2013, the plans were put on ice a year later at as tension over Ukraine reached its height.

With the swap, BASF will exit the gas trading and storage business while expanding its production of oil and gas. As before, the transaction will be financially retroactive to Apr. 1, 2013. Terms foresee BASF's oil & gas arm, Wintershall, receiving the economic equivalent of 25% plus one share of two blocks the Achimov formation of the Urengoy natural gas and condensate field in western Siberia.

The two blocks have total hydrocarbon resources of 274 billion cbm of natural gas and 74 million t of condensate, equal to 2.4 billion barrels of oil equivalent (boe). From 2018, an annual plateau production of at least 8 billion cbm of gas is expected.

In return for the exploration asssets, Wintershall will transfer its share in the currently jointly operated natural gas trading and storage business to Gazprom, including its 50% share of gas trading companies Wingas, Wintershall Erdgas Handelshaus Berlin (WIEH) and Wintershall Erdgas Handelshaus Zug (WIEE).

Gazprom will also take a 50% share in the activities of Wintershall Noordzee, which pursues oil and gas in the exploration and production in the southern North Sea (Netherlands, UK and Denmark). Together the activities contributed around €12.2 billion to sales and around €260 million to EBITDA of BASF group in 2014 and about €7.2 billion and €240 million respectively in the first half of 2015. The gas transportation activities will continue. (dw) ■

Ashland to Spin off Valvoline to Shareholders

US chemical producer Ashland has announced it will spin off its engine lubricants subsidiary Valvoline in a tax-free transaction to shareholders. The separation is expected to take at least a year to complete.

Going forward, the lubricants business will be publicly listed, and Ashland will consist solely of its Specialty Ingredients and Performance Materials segments, which had sales of around $3.6 billion in fiscal 2015, which ended on Jun. 30.

In a statement, the company to be headed by William Wulfsohn as chairman and current senior vice president Luis Fernandez-Moreno as CEO, said the spinoff is the final step in its decades-long shift from an oil refiner to a specialty chemicals manufacturer.

In July of this year, Ashland completed the sale of Valvoline's car-care products to Niteo, a subsidiary of private equity firm Highlander Partners. This business represented less than 4% of Valvoline's $2 billion annual sales.

In late May, Ashland announced plans to sell the industrial biocides assets – about 2% of the Specialty Ingredients segment's sales – to Troy Corporation, a global leader in microbial control products and performance additives. Financial terms were not disclosed. (dw) ■

Yara to Sell European CO_2 Business to Praxair

Norwegian fertilizer group Yara International has signed a non-binding agreement to sell its European CO_2 business to industrial gases producer Praxair for €218 million. The deal set to close in the first quarter of 2016 will also see the Norwegian company transfer its remaining 34% stake in the Yara Praxair Holding joint venture to its industrial gases partner for around €94 million.

"The CO_2 business has been an attractive and long-standing part of Yara's portfolio, but remains a relatively small part of the broader industrial gas industry, and where Praxair is well positioned to create additional value," said Svein Tore Holsether, CEO of Yara International.

Praxair CEO Steve Angel said the acquired business will complement his company's industrial gases activities in Europe and will also enhance the US group's presence in non-cyclical segments such as food and beverage.

In 2014, Yara's European CO_2 business with revenues of €112 million sold around 850,000 t/y of liquid CO_2 and 50,000 t of dry ice, primarily to the food and beverage industries. The company operates five CO_2 liquefaction plants, three large CO_2 shipping vessels, seven shipping terminals and six dry ice production facilities across the UK, Ireland, Scandinavia, Northern Europe and Italy. (dw) ■

Caldic Completes R2 Group Takeover

Dutch-based Caldic has completed its acquisition of R2 Group, based in Denmark. The acquired company is an independent distributor and manufacturer of food ingredients, material science and health and pharma products with a strong presence in the Nordic countries as well as in the Netherlands, Germany and Italy. (dw) ■

Ter Group Expands Italian Business

Effective Sept. 1, 2015, Ter Chemicals Distribution Group, based in Hamburg, Germany, transferred its Italian business with specialty chemicals into the recently founded company Ter Italia.

Oliver Zimmermann, CEO of Ter Chemicals, said: "The established presence in Italy will strengthen our long-term relationships with strategic principals as well as attract new reliable and competent ones." (rk) ■

Syngenta Plans Share Buyback and Seed Divestment

With a scheme to buy back more than $2 billion in shares and its plans to divest the company's vegetable seeds business, Swiss agrochemicals giant Syngenta, which recently emerged relatively unscathed from Monsanto's bear hug, has tossed a bone to shareholders who may have preferred it to be more open to a merger with the US rival.

The world's largest producer of chemical crop protectants said the vegetable seeds business is industry-leading, has high margins, a significant global footprint and a wide array of best-in-class varieties. Although it had revenues of only $663 million in 2014, Syngenta's chief financial officer John Ramsay told the news agency Reuters that "valuation multiples in vegetable seeds are quite easily" in the 3-6 times sales range.

In the midst of the Monsanto's pursuit of Syngenta, several other industry players, most notably BASF, had been seen as poised to take any activities a merged company might have to divest. In the event of a successful takeover, Monsanto was said to plan to divest the bulk of the Swiss company's seeds assets in exchange for antitrust approval.

The vegetable seeds arm is regarded as one of Syngenta's most profitable, with gross margins of well above 60% in 2015, compared with about 45% for all seeds. However, Ramsay told Reuters the company is "not getting proper recognition either by the market or by Monsanto's approach for the fundamental value of our vegetable seeds assets."

Some of the company's major shareholders still grumbling about the failed takeover, with some quoted by news agencies as saying Syngenta threw away "billions" in shareholders' money. According to reporters, the buyback and the sale plan may not pacify all sides. Some investors said they supported the buyback but did not understand why management wanted to sell a business with high margins and a global presence.

With the Monsanto struggle off the table for the present, board chairman, Michel Demare has promised a thorough review of Syngenta's portfolio and also hinted at plans to take on another the major investor on board if the company's efforts to boost profitability and market share fail. (dw) ■

Lubrizol Acquires Particle Sciences

US-based Lubrizol Corporation has acquired Particle Sciences, a compatriot contract drug developer and manufacturer headquartered at Bethlehem, Pennsylvania. Terms of the acquisition were not disclosed.

The Wickliffe, Ohio-based firm said the takeover of Particle Science will boost its pharmaceutical development capabilities in the life sciences, providing full service drug delivery solutions to the market across a variety of dosage forms.

Lubrizol is regarded as a global leader in complex formulations, including drug eluting device product development and sterile and particulate drug products. The company said the acquisition also will allow it to leverage its core polymer chemistry to deliver tailored solutions for novel implantable and dermal drug delivery systems for improved patient outcomes.

While being integrated into Lubrizol Advanced Materials, Particle Sciences will retain its company name. (dw) ■

Brenntag Continues Acquisition Spree

In September, Germany-based chemical distributor Brenntag continued its acquisition spree, buying US-based Cargill's small pack specialty business in food and pharma grade alcohol and agreeing to buy Turkish distributor Parkoteks, along with Singapore's TAT group.

The acquired Cargill business supplies customers in the cosmetics, pharmaceutical and food & beverages sectors in the Netherlands and Belgium. Brenntag said the buy was a further step in its strategy to expand its portfolio in life sciences. Istanbul-based distributor Parkoteks, with sales of €14.3 million in 2014, focuses on specialty chemicals in particular for the personal care industry.

Brenntag's takeover of industrial chemicals distributor TAT Group, subject to the approval of the company's shareholders and certain other conditions, is due to close in the fourth quarter. (dw) ■

Pharma Players Mostly

Increased R&D and a More Robust

Joseph Jimenez, CEO, Novartis

Severin Schwan, CEO, Roche

Andrew Witty, CEO, Glaxo SmithKline

Pascal Soriot, CEO, AstraZeneca

Olivier Brandicourt, CEO, Sanofi

Marijn Dekkers, CEO, Bayer

After a challenging second quarter and first half 2015 – once again marked by foreign exchange turbulence and the impact of acquisitions and divestments – the international pharmaceutical industry expects to close the year on a positive note.

On the basis of a strong operational performance, many chief executives in Europe and the US have adjusted full year guidance upward, on the strength of their R&D pipelines and enhanced sales potential of innovative drugs.

Barring any unexpected changes on the currency front, companies who report in euros will continue enjoying relief from a strong euro this year, while US companies will have to work harder to counter the influence of a firmer dollar.

Novartis with "Solid" Q2 Performance

After a "solid" performance in the second quarter and first half, Joseph Jimenez, CEO of Swiss pharmaceutical giant Novartis has left the 2015 outlook unchanged. Group net sales are expected to rise by a mid-single digit percentage figure adjusted for generic competition, expected to be at about the same level as 2014. Currency translations will likely have a negative effect. Core operating profit is forecast to grow ahead of sales at a high-single digit rate. Jimenez confirmed growth for pharmaceuticals in the mid-single-digit range, for generics arm Sandoz in the high single-digit range and for eye care subsidiary Alcon in the low single-digit range.

US dollar-denominated Q2 figures show net sales down 5% to $12.7 billion, operating income down 28% to $2.3 billion and core operating income down 7% to $3.6 billion, partially reflecting foreign exchange turbulence. At constant exchange rates, quarterly sales were down by 6% and operating income by 14%. Core operating profit was up 6%.

Roche Confident of Reaching 2015 Target

Based on a strong first half that saw sales growth in both Pharmaceuticals and Diagnostics, Severin Schwan, CEO of Swiss-based Roche, has expressed confidence the company will achieve its full-year targets for 2015. He said management was "very encouraged" by the strong Q2 uptake of new drug Esbriet for idiopathic pulmonary fibrosis, acquired last year from InterMune. Oncology drug Avastin was another growth driver.

From January to June, Roche sales rose 3% to 23.6 billion Swiss francs, but operating profit fell back 5% to 7.7 billion francs, and core operating profit by 2% to 9.2 billion francs. At constant exchange rates, sales added nearly 6%, with core operating profit up 2%. Pharmaceuticals sales were up 5.5% and Diagnostics up 6.6%

GSK on Track with 2015 Guidance

The UK's largest drugmaker, Glaxo SmithKline, is on track to achieve its 2015 guidance and remains confident for 2016, said CEO Andrew Witty. In the second quarter, sales grew 7% to nearly £6 billion on a reported basis and 2% on a pro forma basis, thanks in part to the inclusion of the former Novartis vaccines business swapped for GSK's cancer portfolio. New HIV drugs Tivicay and Triumeq also padded sales.

Operating profit and earnings per share in Q2 totaled £335 million, down from £1.1 billion. This reflected accelerated restructuring costs due to the Novartis transaction, ongoing restructuring in Pharmaceuticals and further adjustments related to ViiV Healthcare and Consumer Healthcare, along with litigation expenses. Core operating profit sank by 4% to £1.3 billion. In 2016, without this year's adverse impacts but with "more meaningful" synergy benefits from the portfolio swap, Witty expects a "significant" recovery in core EPS with percentage growth at constant exchange rates in the double digit range.

AstraZeneca Beats Analyst Forecasts

The second quarter performance of British-Swedish pharmaceutical producer AstraZeneca exceeded analysts' expectations, with both sales and earnings rising slightly on a constant currency basis. Although adjusted sales gained 2%, due to a strengthening dollar reported revenue was 7% lower at $6.3 billion, and core earnings per share 8% lower. Core operating profit was down 11%, reported operating profit down 17% and reported EPS down 13%.

CEO Pascal Soriot said Q2 marked "sixth consecutive quarters of top-line growth." Overall, management was "very pleased" with the performance, driven by the five growth platforms, in particular oncology. Efficiency schemes have begun to reduce costs, and pipeline growth has had "positive momentum across all key areas. Along with the strength of the growth platforms, Soriot said better R&D productivity reaffirm the company's confidence in its ability to make up for patent losses and meet revenue targets. To speed new drugs through the pipeline, research spending has been boosted from 22% to 23% of sales.

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Sanofi Profits from Euro's Weakness

French drugmaker Sanofi's Q2 business was boosted by the stronger US dollar. Sales rose 16% to almost €9.4 billion, with favorable foreign exchange contributing 11.2 percentage points. Business operating income, excluding the effects of acquisitions and divestments, increased nearly 20% to €2.6 billion. At constant exchange rates, the improvement was about 5%. Business EPS increased by 5.1% at constant exchange rates and by 20.5% on a reported basis.

New CEO Olivier Brandicourt said lower sales (down 4%) in the diabetes franchise were more than offset by gains in the Genzyme biotech unit (up 26.6%) and in the animal health division (up 14%). "In the second quarter, Sanofi delivered solid growth on both the top and bottom lines consistent with our expectations," Brandicourt said. A new organizational structure to be implemented from January 2016 "will simplify and focus Sanofi to optimize future growth."

Bayer HealthCare Earnings Pressured by R&D

Ahead of becoming a life sciences "pure player" in Q3, Germany's Bayer's HealthCare segment increased Q2 sales by 28% (8.3% on a portfolio and foreign exchange-adjusted basis) to just under €6 billion. CEO Marijn Dekkers attributed the rise largely to the "gratifying sales performance" of recently launched drugs such as the anticoagulant Xarelto, the eye medicine Eylea and the cancer treatments Stivarga and Xofigo. Reported sales of the Pharmaceuticals business rose 10.7% to €3.5 billion.

EBITDA before special items in Bayer's HealthCare segment rose 27.5% to €1.7 billion, including positive currency effects of around €110 million. Earnings were held back mainly by an increase in R&D expenses in the Pharmaceuticals division, Dekkers said. In the second half of 2015, HealthCare's EBITDA before special items is forecast to rise by a "low-20s" percentage.

Merck KGaA Profits Sink on Higher Spend

The Healthcare segment of German pharmaceutical and chemicals producer Merck KGaA reported organic sales growth of 1.5% in Q2. Including positive foreign exchange effects of 7.8%, net sales rose by 9.2% to €1.8 billion, driven in particular by drugs for diabetes (Glucophage), thyroid disorders (Euthyrox) and cardiovascular diseases (Concor). By contrast, the multiple sclerosis drug Rebif saw an organic sales decline of 12%, reflecting strong competition from oral formulations. Currency tailwinds of 11.3% kept Rebif sales remained stable at €461 million, however.

EBITDA pre-exceptionals of the German Merck Healthcare business

UK Health Agency Blesses Merck Cancer Drug

UK drug cost-effectiveness agency National Institute for Health and Care Excellence, NICE, has approved the use of US drugmaker Merck's Keytruda for treatment of certain cases of advanced melanoma.

First of a new category of so-called anti-PD-1 checkpoint inhibitors to reach the market, Keytruda harnesses the immune system to eradicate tumors by making cancer cells visible to the immune system and opening them to attack. Like other first-generation immunotherapies, however, it is said to have thus far proved effective in only a minority of patients.

The treatment was greenlighted by NICE only after Merck agreed to supply it to the state health service NHS at an undisclosed discount over the $150,000 per-patient, per-year charged in the US. Officials called the approval proof that the UK health service was keeping pace with the latest innovations in medical science despite pressure on budgets.

NHS's England division has announced plans to withdrawing funding from about 20 cancer drugs in an effort to curb soaring cost costs, saying that removing less cost-effective medicines would free up money in the budget to pay for more advanced treatments. To provide access to new cancer drugs that have been rejected by NICE as too expensive to warrant long-term funding, the UK government has created a special Cancer Drugs Fund. (dw) ■

Amgen Gets Nod for New Cholesterol Drug

Amgen has won US Food and Drug Administration (FDA) approval for Repatha, the second medicine in a new class of biologics recently greenlighted by the agency and claimed to reduce cholesterol more effectively than older statin drugs.

Prescribed for self-injection on a monthly or bi-monthly dosing schedule, the new drug is designed to meet the needs of patients who cannot control their cholesterol with existing drugs and treatments, specifically those with extremely high levels of low-density lipoprotein, LDL.

Recently developed drugs are claimed to lower LDL more powerfully and in a different way than statins, blocking a substance called PCSK9, which interferes with the liver's ability to remove cholesterol from the blood.

The California drugmaker has priced its new product at $14,100 per year, slightly below the $14,600 per year cost of Praluent, which is manufactured by Sanofi and Regeneron Pharmaceuticals and won FDA approval in July. Pfizer is also working on a PCSK9 blocker, which is currently in clinical trials.

Analysts expect Repatha to reach peak sales of about $3.5 billion by 2022, with the entire PCSK9 class of drugs reaching global sales of $10 billion by 2019. (dw) ■

Bristol-Myers to Buy Fibrosis Drug and its Developer

Bristol-Myers Squibb (BMS) will pay as much as $1.25 billion for the worldwide rights to a developing fibrosis drug as part of a deal that also gives it the right buy the product's developer.

The transaction includes an upfront payment of $150 million and allows the US drug major to take over Promedior, a clinical stage immunotherapy company pioneering the development of targeted therapeutics to treat fibrotic diseases.

Premedior's prime drug candidate PRM-151, a recombinant form of human pentraxin-2 protein, is currently at the mid-stage development as a treatment for the lung condition idiopathic pulmonary fibrosis (IPF) and the bone marrow disorder myelofibrosis (MF).

Phase 2 trials both for IPF and MF applications are due to start shortly, and BMS will be able to exercise its right to acquire Promedior upon completion of either of the trials. PRM-151, has already been granted fast-track status in the US and Europe for treatment of IPF. In multiple preclinical models, the drug has been shown to regulate monocytes and macrophages at areas of tissue damage to prevent and reverse fibrosis, including IPF, acute and chronic nephropathy, liver fibrosis, and age-related macula degeneration. (dw) ■

Merck and Pfizer Get FDA Orphan Drug Status

An alliance of Germany's Merck KGaA and US pharmaceuticals giant Pfizer has been granted US Food and Drug Administration (FDA) orphan drug status for its investigational cancer immunotherapy avelumab, recommended for treatment of Merkel cell carcinoma (MCC), a rare and aggressive type of skin cancer.

Avelumab is an investigational fully human monoclonal IgG1 antibody against programmed death-ligand 1 (anti-PD–L1). The two companies are currently conducting a Phase II study in Asia-Pacific, Australia, Europe and North America to assess its safety and efficacy in patients with metastatic MCC who have progressed after at least one prior chemotherapy regimen.

Altogether, Merck and Pfizer's clinical trial program for avelumab now includes more than 1,000 patients treated across more than 15 tumor types, but the orphan drug status applies only to MCC.

The FDA's orphan drug designation is granted to medications intended to treat rare diseases or disorders affecting fewer than 200,000 people in the US, or those that affect more than 200,000 people, but are unlikely to recover the costs of developing and marketing the drug.

Orphan drug status qualifies the sponsor for incentives provided for in the Orphan Drug Act. (dw) ■

Lift 2015 Guidance

Pipeline Boost Executives' Confidence

Karl-Ludwig Kley, CEO, Merck

Ian Read, CEO, Pfizer

Kenneth C. Frazier, CEO, Merck & Co.

Alex Gorsky, CEO, Johnson & Johnson

Giovanni Caforio, CEO, Bristol-Myers Squibb

John C. Lechleiter, CEO, Eli Lilly

declined by 2.8% to €480 million, due to higher investment in both marketing and R&D in the second quarter. CEO Karl Ludwig Kley said the company has "deliberately invested in research and development in order to drive important pipeline projects such as the anti-PD-L1 antibody avelumab."

Pfizer Hit by Currency Headwinds

In the US, market-leading drugmaker Pfizer – pressured by currency exchange rates – saw a quarterly 7% decline in reported revenue to $11.9 billion, despite a 1% increase on an operating basis. Adjusted income was down 6% to $3.5 billion, while adjusted diluted EPS was down 3% and reported diluted EPS was down 7%.

Even amid currency pressures, Pfizer's Q2 performance showed "continued business momentum, driven by solid execution of recent product launches in the innovative products business as well as established products," said CEO Ian Read, adding that the acquisition of Hospira will "meaningfully enhance" the established portfolio. Due to the strong quarterly operational performance, chief financial officer Frank D'Amelio has raised full year financial guidance for adjusted EPS by $0.04.

US Merck Raises Non-GAAP Forecast

US pharmaceutical producer Merck has upgraded its full year 2015 non-GAAP earnings per share (EPS) forecast and narrowed the range to $3.45-3.55, including the negative foreign exchange impact. The GAAP forecast has been lowered to $1.52-171 per share, reflecting both Venezuela-related foreign exchange losses and expected profits on the sale of certain migraine clinical development programs. At current exchange rates, CEO Kenneth C. Frazier expects sales revenue of $38.6a39.8 billion, including negative foreign exchange rates, along with $1 billion in net lost sales from acquisitions and divestitures.

Merck's worldwide sales in Q2 shrank by 11% to $9.8 billion, including a negative foreign exchange effect of 7% and a quarterly 7% net impact from last year's sale of its $2.2 billion Consumer Care business to Bayer last year for $14.2 billion. Non-GAAP earnings per share rose to $0.86 from $0.85, while GAAP earnings fell from $0.68 to $0.24 per share. Frazier said the US drugmaker made "significant progress" in its Keytruda and hepatitis C programs during the quarter.

Johnson & Johnson Adjusts Guidance Upward

Second-quarter results for US pharmaceuticals and consumer products specialist Johnson & Johnson show a sales decline of nearly 9% to $17.8 billion. Adjusted earnings before provision for taxes on income fell 4% to $6.2 billion and diluted earnings per share by about the same margin to $1.51. J&J's Pharmaceuticals segment saw sales improve 1% to $7.9 billion, thanks to gains across the portfolio of immunology, infectious diseases, neuroscience, oncology and cardiovascular drugs. The Medical Devices portfolio had sales of $6.4 billion, up 4.7%, and Consumer Products reported sales of $3.5 billion, up 2.3%.

"Our solid sales and earnings results reflect the strong underlying growth we're seeing across the enterprise," said CEO Alex Gorsky, adding that the robust enterprise pipeline "will drive our growth over the long term." The drugmaker has increased its adjusted earnings guidance for full-year 2015 to $6.10-6.20 per share, excluding the impact of after-tax intangible amortization expense and special items.

Bristol-Myers Squibb Has Good Quarter

Another US drug major, Bristol-Myers Squibb (BMS) posted a sales improvement of 7% to $4.2 billion for the second quarter. Adjusted for the foreign exchange impact, revenue advanced by 16%. The gross margin as a percentage of sales was 75.7%, up from 74.5% a year ago. The company reported an acquisition-related quarterly GAAP diluted earnings per share loss of $0.08 ($130 million in total) for the second quarter against a non-GAAP diluted EPS gain of 10% to $0.53 ($890 million).

BMS "had a very good quarter, with strong sales across the portfolio, encouraging results from clinical trials and important regulatory milestones," said CEO Giovanni Caforio, remarking that the company is "making the right strategic investments to capitalize on the full potential of our portfolio." For full year 2015, he has increased the GAAP EPS guidance range to $1.02-$1.12 and the Non-GAAP range to $1.70-180.

Lilly Poised to Return to Growth in 2015

US pharma player Lilly reported Q2 sales revenue of almost $5 billion – a rise of 1%, thanks to the inclusion of Novartis Animal Health and higher volumes for cancer drug Cyramza and diabetes drug Trulcity. But CEO John C. Lechleiter said growth was largely wiped out by unfavorable foreign exchange effects and patent expirations. The gross margin as a percentage of revenue was 75.5%, almost in line with the 2014 quarter. Operating income declined by 9% to $803 million, due to higher R&D spending as well as asset impairment, restructuring and other special charges – partially offset by lower operating expenses. Lechleiter said Lilly remains on track to return to growth in 2015, driven by a strong underlying business performance, including uptake of recently launched products. "Our innovation-based strategy will continue to provide the basis for solid growth in the years ahead," he predicted.

Dede Williams, freelance journalist

FDA Approves Mylan's Yasmin Copies

Following the green light from health regulator European Medicines Agency, the European Commission is expected to decide on a final approval for GlaxoSmithKline's (GSK) injectable asthma drug, Nucala, before the end of 2015.

The US Food and Drug Administration (FDA) is expected to give its decision on Nucala, which is being recommended asthma patients who don't respond well to traditional inhalers, by Nov. 4. The monthly injection is also being tested for treatment of chronic obstructive pulmonary disease (COPD).

Analysts said the new product could help boost GSK's respiratory franchise as demand weakens for its asthma drug, Advair. In monetary terms, the value of this market is calculated to be potentially in the multi-billion dollar range.

GSK and other drugmakers including AstraZeneca, Roche, Teva Pharmaceutical Industries and Sanofi, are also developing drugs that take a more personalized approach to asthma care. (dw) ■

Alvogen to Buy Four Pfizer Drugs

Alvogen has agreed to buy four of compatriot Pfizer's products the country's largest drugmaker must divest to meet conditions for closing its $17 billion acquisition of Hospira.

Assets for sale include three injectables and one inhalation solution. Clindamycin injection and Acetylcysteine inhalation solution are on-market products: the latter will continue to be marketed by Fresenius, with Alvogen receiving profit-sharing payments.

The other two products are pending abbreviated new drug applications (ANDAs), namely Voriconazole and Melphalan injectables. Alvogen said both are expected to launch as early as 2016. The company said it has more than 60 pipeline ANDAs of which 28 have first-to-file or first-to-market potential. (eb) ■

Siegfried Ready to Take Over BASF Sites

Siegfried Holding, the Swiss drug contract manufacturer, said it has completed all closing conditions for its acquisition of the custom synthesis business of BASF and parts of the German group's current active pharmaceutical ingredients (APIs), as announced in May.

Among the most crucial requirements, financing has been secured, and Swissmedic, Switzerland's regulatory agency for drugs and medical devices, has given the necessary clearance for the Evionnaz production site.

Transfer of the BASF sites in France, Germany and Switzerland is scheduled to take place on Sept. 30, as agreed. Siegfried is buying the assets for a total consideration of €270 million.

All of the more than 800 employees at the three BASF sites — Minden, Germany, and Saint Vulbas, France — in addition to Evionnaz — will transfer to Siegfried. Following the acquisition, the company plans to increase its total workforce to around 2,200 people at nine sites on three continents.

From BASF, Siegfried is acquiring APIs such as ephedrine, pseudoephedrine and caffeine, with annual sales of around €270 million, while the German group is retaining its excipient portfolio and selected APIs, such as ibuprofen, omega-3 fatty acids and polyethylenglycol (PEG).

With the acquisition, the Swiss company will reach the critical size to play a leading role in the supplier market as a recognized partner for the pharmaceutical industry, CEO Rudolf Hanko said when the deal was announced.

Over the past five years, Siegfried has been on the acquisition trial, taking over California-based AMP and German companies Hameln Pharmaceuticals and Hameln RDS. (dw) ■

Bayer Settles 2008 Fatal Plant Explosion Lawsuit

Bayer CropScience has paid $5.6 million to settle violations of US chemical accident prevention laws stemming from a 2008 explosion that killed two people at its Institute, West Virginia, production site for pesticides. The facility once belonged to now defunct US chemical producer Union Carbide.

In addition to a $975,000 civil penalty, the US arm of the German group, headquartered at Research Triange Park, North Carolina, agreed with the US Environmental Protection Agency (EPA) and the Department of Justice to invest $4.23 million in improving emergency preparedness and response at the West Virginia site as well as protecting the Kanawha River from chemical discharges.

Bayer also must spend $452,000 on safety improvements at chemical storage facilities in the US states of Texas, Missouri and Michigan, in addition to West Virginia. The majority of the mandated actions will have to be completed within three years.

The US Bayer subsidiary previously paid a $143,000 fine to the US Occupational Safety and Administration for citations stemming from the incident that occurred during the restart of the site's methomyl unit following a lengthy maintenance turnaround.

In its investigation, the US Chemical Safety Board (CSB) blamed the blast on a reaction inside a 4,500-gallon tank that broke down waste from the process to manufacture methomyl, used at the site to produce the pesticide Larvin. According to Bayer, methomyl is no longer produced at the site.

According to the CSB report, plant management withheld information from county emergency officials during the response. (dw) ■

BASF Faces Legacy Lawsuits from Engelhard

BASF is facing around 300 lawsuits in the US as a legacy of its acquisition of catalyst manufacturer Engelhard in 2006. In the suits, plaintiffs allege that talc used in wall board, joint compound and auto body filler is responsible for medical conditions ranging from mesothelioma to lung disease.

With the 2006 buy of Engelhard for $5 billion in 2006, the German group inherited the catalyst maker's liabilities but also the New Jersey-based industrial firm's legacy of dodging allegations.

At the heart of a revived suit against BASF, for which class-action status is being sought, are claims that Engelhard and its lawyers lied about the presence of the asbestos in the talc and hid evidence. The company owned and operated a talc mine in Vermont from 1967 to 1983.

In a court filing dating from May of this year, quoted by international news media, BASF said the plaintiffs "face serious obstacles in attempting to certify a class based on events that took place in thousands of different asbestos cases litigated in different courts and at different points in time by different lawyers."

The German group in 2009 settled a lawsuit brought by the family of a woman who attributed her mesothelioma to contaminated clothing worn by her father, a research scientist for Engelhard, and from visits to his workplace. Both father and daughter have since died of lung disease.

Some legal experts now believe that up to 10,000 asbestos-related cases could be reopened. With other lawsuits dismissed by the courts, companies and their insurers are said to have paid at least $70 billion to settle litigation up to 2005. (dw) ■

Aesica to Benefit from New Green Energy Plant in Northumberland

UK Green Investment Bank (GIB) and John Laing Investments Limited (JLI) have committed £50 million of equity to a new £137 million renewable energy facility in North East England, developed by Estover Energy. The biomass combined heat and power (CHP) plant in Cramlington, Northumberland, will generate 223 GWh of renewable electricity annually. It is expected to reduce greenhouse gas emissions by circa [56] kt CO2e annually, the equivalent of taking 25,000 cars off the road during its lifetime.

Aesica Pharmaceuticals, together with another pharma company, will benefit directly from its output, alongside the National Grid. Green electricity will be routed to Aesica's Cramlington site located in an adjacent industrial estate. The energy plant will also have the potential to provide 5 MW of renewable heat to neighbouring facilities.

GIB will make a £23 million investment in the project, with JLI investing in a stake worth £27 million. Barclays will provide the remainder of the funding as debt, 60% of which will be guaranteed by the Danish export credit agency Eksport Kredit Fonden (EKF).

The construction of the plant will be undertaken by a joint venture between Burmeister & Wain Energy (BWE) and Burmeister & Wain Scandinavian Contractors (BWSC). BWSC will operate the plant upon completion. Up to 250 jobs are expected to be created during the construction process, while 25 permanent positions will be maintained at the operational facility.

Fuel for the plant will be provided by Stobart Biomass Products Limited, plus local growers and forest industry suppliers. (rk) ■

Piramal Targets the Antibody Drug Conjugates Market

The Pharma Solutions division of Piramal aims at becoming the market leader in antibody drug conjugates (ADCs) contract commercialization over the next five years. This is based on the focused investments at its current site in Grangemouth, UK and its recent acquisition of Coldstream, a specialised ADC fill/finish site, in Kentucky, USA.

Piramal sees the market for commercial ADCs accelerating over the next few years and a steady increase in the number of potential drug targets entering into the clinical phase. Currently the CDMO only manufactures one commercial product but expects about eight drugs to move into its commercial production by 2020. Piramal stated that despite the increase in development targets for ADCs, the global contract manufacturing sector still remains significantly under resourced with only a small number of players with experience and even less with the required regulatory accreditations.

The company is now in its fifth year of production on the first ever commercial ADC in the market and is using this landmark to look ahead five-years to strengthen its position as a leader in manufacturing of ADCs.

There are currently two commercialized ADCs on the market but research on ADC targets shows that there will be at least a further 50 entering clinical work by 2020. Therefore, a wave of consolidations within the CDMO sector to acquire technology is likely over the next few years. (rk) ■

Valeant Teams with AstraZeneca on Psoriasis

Canadian drugmaker Valeant has said it will work with AstraZeneca on brodalumab, a potential treatment for psoriasis. The Canadian company is taking up the gauntlet from Amgen, which recently curtailed research on the same drug due to a link to suicidal thoughts and behavior.

Valeant said it is prepared to pay AstraZeneca as much as $445 million if the drug is successfully developed and approved and meets sales targets. The companies will also share profits. The companies plan to file for marketing approval in the US and the EU during this year's fourth quarter. The drug would be marketed it as a treatment for moderate to severe psoriasis.

Kyowa Hakko Kirin Co. owns the rights to brodalumab in Japan and some other countries in Asia. (dw) ■

Merck Streamlines Healthcare Management

German chemicals and pharmaceuticals producer Merck has streamlined its Healthcare management team to accelerate growth. The company said the new organizational structure will facilitate execution of its newly focused three-pronged strategy aimed at driving key pipeline projects forward as well as expanding in growth markets.

With effect from Sept. 30, a Healthcare executive committee comprising four business functions and three supporting functions has replaced the former Pharma Executive Committee. Belén Garijo, member of the group managing board, will continue as CEO of Merck Healthcare.

Simon Sturge has assumed the newly created role of chief operating officer, overseeing all commercial regions and countries. His responsibilities include the General Medicine franchise, consisting of drugs for cardiovascular diseases and diabetes, as well as Global Manufacturing and Supply. Sturge will also continue to lead the Biosimilars and Allergopharma businesses.

New on the Healthcare executive committee is Rehan Verjee, formerly general manager Canada. As chief marketing and strategy officer, he has charge of the business' global specialty franchises of Oncology, Neurology and Immunology, Fertility and Medical Devices as well as the global immuno-oncology alliance with Pfizer and various strategic functions including business development.

Luciano Rossetti will continue to lead Merck's gobal R&D function as a member of the Healthcare executive committee while another new committee member, Jitinder Saini, has assumed the newly created role of global chief of staff and head of the strategy realization office. (dw) ■

Bayer Cautions Winegrowers on Fungicide

Bayer CropScience has advised wine grape growers not to use its Moon Privilege (or Luna Privilege) fungicide, pending an investigation into a possible connection between spraying of the chemical compound and reported crop damage.

Some wine grape growers are said to have reported deformed leaves and lower yields from their crops this year, and according to the newspaper Schweiz am Sonntag, some Swiss growers, who blame the fungicide, are demanding compensation from Bayer.

In a notice on its website, Bayer pointed to "atypical symptoms" in vines where the fungicide has been deployed in 2014. "As long as the cause of this change in the grape vines remains unexplained, we recommend for precautionary reasons not to use Luna Privilege for wine growing," Bayer said, adding that it "regrets" the situation and is doing "everything necessary" to discover the cause.

Reports said Bayer had acknowledged in a letter to growers a "high probability" of a connection between the fungicide and damage to the 2015 harvest. It also quoted a viticulturist grower in the northern Swiss canton of Aargau as saying damage could run up to triple-digit Swiss franc sum.

Moon / Luna Privilege is used to protect grapes against Botrytis cinerea, or gray mold, Botrytis rot or gray mold-rot. The fungicide contains fluopyram, a chemical that is active against a number of plant diseases.

Agricultural scientists in Norway as well as in the US Midwest are said to have warned that there is a high potential for runoff several months after application of the product and a threat of surface water and groundwater contamination. (dw) ■

Starpharma in Drug Delivery Pact with AstraZeneca

Australia's Starpharma has signed a licensing agreement with AstraZeneca, giving the Anglo-Swedish company commercialization rights for oncology compounds directed at a defined family of targets using Starpharma's DEP drug delivery technology.

The collaboration centers on Starpharma's proprietary dendrimers that aim to enhance the dosing and efficacy characteristics of pharmaceuticals and is seen as part of AstraZeneca's drive to upgrade its oncology platform. The agreement focuses on novel compounds, rather than unmodified drugs in currently marketed formulations.

Under the terms of the deal, Starpharma, regarded as world leader in the development of dendrimer products for pharmaceutical, life-science and other applications, is eligible to receive signature and milestone payments on one or more of AstraZeneca DEP products if they progress through the development pipeline, along with milestone and royalty payments on any net sales of the resulting products.

AstraZeneca will also fund all development and commercialization costs under the agreement, including ongoing and future collaborative work conducted. Starpharma's other programs, in particular its wholly-owned DEP docetaxel product, are said to be "not negatively impacted" by the new arrangement.

At the signing, the life sciences company became eligible for a signature payment of $2 million. For the initial product, development and launch milestones could total up to $64 million, and sales milestones based on specified annual sales levels could total up to $60 million, the companies said.

The licensing agreement allows for additional products to be incorporated, with development and regulatory milestone payments of up to $53.3 million. Potential sales milestones based on specified annual sales levels for qualifying additional products could total up to $40 million. Any AstraZeneca DEP products would also attract tiered royalties on net sales.

"We estimate that each qualifying product successfully commercialized under this agreement could be worth, over its life, around $450 million to Starpharma and, depending on the range of indications and degree of commercial success in the market, potentially significantly more," CEO Jackie Fairley said. (dw) ■

First C8 Exposure Case Opened Against DuPont

A US court has begun hearing the first of several cases in what began as a class action suit against DuPont, in which plaintiffs claim the US chemical giant was to blame for their illnesses. The company has denied all allegations.

All of the estimated 3,500 cases center around discharges of perfluorooctanoic acid (PFOA or C8) from the chemical producer's Washington Works plant in Parkersburg, West Virginia. The case currently being heard was brought by an Ohio woman, Carla Marie Bartlett, who charges that the chemical found its way into drinking water supplies and caused her kidney cancer.

The Bartlett case is being regarded as an early test of potential liability for the discharges alleged to have persisted for several decades. A second trial is due to start Nov. 30.

While DuPont is named as the defendant in all of the cases, some of the liability has been inherited by Chemours, the July 2015 spin-off of the company's Performance Chemicals business segment. (dw) ■

Merck Serono Expands Biopharmaceuticals Lab

Merck Serono, the biopharmaceutical arm of Germany's Merck, has laid the cornerstone for a new €65 million laboratory at its Darmstadt headquarters. When completed in 2017, some 200 employees will work in the 16,000 m^2 building designed to accelerate innovation in R&D.

The research building will unite various functions within R&D Discovery Technologies at Merck, including Molecular Pharmacology; Medicinal Chemistry; Computational Chemistry; Molecular Interactions and Biophysics; Protein Engineering and Antibody Technologies, along with Protein and Cell Sciences.

The Germany-based group employs 2,000 scientific and clinical development professionals at its R&D hubs in Darmstadt, Germany, as well as Boston, Massachusetts, US, Tokyo, Japan, and Beijing, China. Core areas of focus at the four locations are oncology, immuno-oncolgy and immunology. (dw) ■

US Food Safety Group Sues Over Withheld GMO Information

US Food safety advocate group Center for Food Safety (CFS) has sued the US Department of Agriculture's Animal and Plant Health Inspection Service (APHIS), charging that it illegally withheld public information on GMO crops. The suit asks the court to declare APHIS actions unlawful and order the agency to produce the records by a date to be set by the court.

In particular, CFS contends that the USDA arm failed to respond as required to requests for records it said relate to many concerns about the crops. Thus, it violated the US Freedom of Information Act "dozens of times" over more than 13 years.

The advocacy group also accuses the agency of failing to respond to inquiries about the handling of experimental genetically engineered wheat found growing uncontrolled in an Oregon field in 2013 – an incident that reportedly led to lost US wheat export sales as foreign markets feared contaminated supplies.

Requests are said to have covered GMO wheat, rice, alfalfa, sugar beets, bent grass, corn and other GMOs.

Food safety groups as well as lawmakers have repeatedly have criticized US regulation of GMOs as being too lax. APHIS also has been cited in government auditing for oversight lapses. (dw) ■

A Wasted Chance

As Buying Market India is Not Yet on the Radar of Western Chemical Companies

For many European companies India is foremost an outlet market. As a buying market the chemical market in India is still underrated. Especially in the area of chemical semi-finished goods, Indian providers offer significant cost advantages in contrast to established Western producers. In comparison with other Asian markets, India offers high creativity and flexibility.

Joerg Strassburger, Go East Advisors

When people think of India, they see 1.25 billion people and the demand that arises from that population. One thinks of the economic growth and the possibility to participate. As a buying market India is not yet on the radar of Western chemical companies.

"A wasted chance," said India expert Dr. Joerg Strassburger. "India has numerous middle-class companies, which are not only able to produce cheaply. They have developed a good understanding for quality and deadline demands of Western companies and are definitely able to fulfill those demands accordingly."

Implementing Western Standards

Concerning production sites, reality does not conform to the clichés. As soon as one deals more closely with the topic, one will find modern production sites in India, which fulfill the highest demands. The administrational environmental specifications correspond with those in Europe or are sometimes even stricter. Furthermore, standards of quality and occupational safety are set high in many companies. And India, in comparison with other markets, offers a distinct cost advantage, which is essentially a result of two factors: Labor expense and investment costs of the plants in India are considerably lower than in other countries, but also the corporate structure influences the costs. Owner-managed companies in family property generally have lower overhead costs and lower profit expectations than listed companies. A further advantage is the fact that in these companies the hierarchical structures are more tightly woven. The customer will normally negotiate with the owner, and this can be swiftly concluded. Lingual barriers will not be a problem, as the negotiations will be in English.

Simply Buying or Toll Manufacturing — Everything is Possible

India is an interesting market for standardized chemical products of specialty chemistry, but also for specific products, which are made to the clients' specifications. Also more complex chemical production processes are profitable in India.

The engineers usually possess a good education and a large amount of creativity — a combination that offers promising results. This also shows that when together with the product the process details are transferred — these processes will also be optimized, generally with an unexpectedly positive result.

Purchasing in India is one thing, but for those who want to secure the Indian buying market long-term, contract manufacturing is an interesting option. For toll manufacturing many detailed arrangements and clear mutual terms can be made, in order to create a handmade solution for the client.

"It works out very well," is Dr. Strassburger's experience. He and his partner have already successfully negotiated and implemented many such cooperations in India. "In a time of focus on costs, contract manufacturing in India is a good possibility to reduce the real net output ratio and production costs in Europe. Companies gain new competitiveness and more flexibility."

Experts know: Indian companies are generally very interested in Western partners and are flexible concerning the design of the cooperation models — as long as it is economically reasonable. These models range from the pure contract manufacturing to the equity participation on the respective plants — a possibility the Indian liberal economic policy allows.

"The buying market India offers the chemical industry — in comparison to Europe — cost advantages of 20% and more," said Dr. Strassburger.

Long-term toll manufacturing agreements, if they are properly prepared and solidly negotiated, can achieve the highest savings. In the long term, more options may arise, which will exceed the pure purchasing phase. Investments in a plant as alternative to toll manufacturing may lead to a participation in the production plants of the local market. Considering the predicted very positive development of the Indian market, these are promising possibilities.

Choosing Partners Sensibly

Nevertheless, the Indian expert emphasizes that one should choose a partner selectively. It's important to differentiate between the well-managed companies, which have experience with Western demands, and those who cannot keep their commitment. The latter mostly have fundamental deficiencies, and it is not only a question of timely and technical possibilities; they lack understanding of the importance of Western demands, such as just-in-time delivery.

To avoid such providers from the beginning, it is wise to ask the help of experts who know the industry and the market participants and who make sure that the demands of the clients are adequately met.

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Sika Owners Claim Win in Saint Gobain Challenge

A federal administrative court in Switzerland has upheld the right of the family that controls Swiss construction chemicals producer Sika to sell its stake to France's Saint-Gobain for around $2.8 billion without consulting the remaining shareholders.

The feud between Burkhard family – which controls Sika through its Schenker-Winkler Holding despite not having a majority shareholding – arose late last year.

Large shareholders opposing the so-called opt-out clause allowing such a procedure included the Gates foundation trust of Microsoft founder Bill Gates and his wife, Melinda, along with Cascade.

Urs Burkhard, spokesman for the family related to Sika's founder Kaspar Winkler, said the court's decision strengthens the case for proceeding with the sale, which also has been opposed by Sika's board of directors and employees.

The Gates foundation trust and Cascade have said they will "continue to defend their shareholder rights and oppose the ill-advised planned transaction that was structured to serve only the interests of Schenker-Winkler Holding and Saint-Gobain."

Those opposing the deal maintain that the sale of the family-owned stake of 16%, which carries voting rights equal to 52%, would be tantamount to Saint-Gobain taking over the entire company.

The French rival has offered a 78% premium for the Burkard stake but has stressed that it does not intend to bid for the rest of the company's shares.

Due to the dispute, Saint-Gobain and the Burkard family have been forced to extend the deadline for completing the transaction from the end of 2015 to mid-2016. (dw) ■

Inovyn to Close German PVC Plant

Inovyn does not plan to restart its PVC plant at Schkopau, Germany, idled since the end of 2014.

After failing to come to terms with Dow Chemical on supply of feedstock VCM, the recently launched 50:50 joint venture of Ineos and Solvay said it will now "pursue a plan for permanent closure."

In return for the European Commission's clearance of the joint venture, Ineos had initially planned to divest the plant with a nameplate capacity of around 300,000 t/y; however, the final remedy package instead called for the divestment of the plant at Wilhelmshaven, Germany.

The slightly larger Wilhemshaven facility was acquired at the beginning of August this year of by International Chemical Investors Group (ICIG), which has made it a cornerstone of its new vinyls platform Vynova.During the EU's review of the Ineos-Solvay vinyls merger plan, another German PVC producer, Vestolit, currently in the hands of private equity investor Strategic Value Partners (SVP), had expressed interest in the Schkopau facility.

Inovyn said it will continue supplying customers by sourcing PVC from other production sites within its extensive network.

However, it did not rule out repercussions for other companies at the site built up by Dow in the 1990s. (dw) ■

Kraton Wins Race for Arizona Chemical

Kraton Performance Polymers has won the race to acquire privately held Arizona Chemical Holdings for $1.37 billion in cash. Both companies are based in the US.

Seller of the business is AZC Holding Company, LLC, which is principally owned by investment funds managed by American Securities.

The Houston, Texas-based Kraton, once part of the Shell group, said Arizona Chemical's high-value performance products and specialty chemicals derived from non-hydrocarbon, renewable raw materials are "highly complementary" with its own portfolio, particularly in markets such as adhesives, roads and construction, coatings and oilfield chemicals.

CEO Kevin M. Fogarty said his company' shareholder will benefit from pretax synergies of $65 million, expected by 2018. With adjusted EBITDA margins exceeding 20% over the past five years and an attractive cash flow profile, he said Arizona Chemical has a stable and attractive margin profile. Moreover, the acquisition will create new opportunities for Kraton to expand its presence in its core markets, where more than 50% of Arizona Chemical's sales are directed. (dw) ■

Measuring China's Importance

Chemical Quotient Quantifies Relative Status of Chinese Chemical Industry

In the past 10 years, we have gradually become accustomed to China's economic rise. In some ways, we are no longer as surprised by it as we should be. I realized this recently when looking at old forecasts. For example, a Deutsche Bank research report published in October 2005 gives China's global chemical market share as 8%, and continues with a forecast (which at that time was seen as rather bullish) of this share rising to 13% in 2015, an assumption based on the domestic chemical market growing by 10% each year. As we know, in 2013 the Chinese share of the global chemical market already reached 33%, and annual growth in the period of 2004 to 2013 was not 10% but 23%.

Dr. Kai Pflug,
Management Consulting — Chemicals

Of course, during this period, not only the Chinese chemical market but also Chinese gross domestic product grew substantially. So is the increase of China's chemical market share only a consequence of its GDP growth? To answer this question, it helps to look at the relative importance of the Chinese chemical industry compared with the rest of the world, and how it changed with time. I would like to introduce a new measure to facilitate such a comparison — the Chemical Quotient (CQ).

This CQ compares the global chemical market share a country has with its share of GDP:

CQ = (global chemical market share)/(share of global nominal GDP)

Thus a CQ value above 1 means the chemical market of a country has a higher importance than its share of GDP would suggest. Similarly, a CQ value below 1 means the chemical market of a country is below its expected value based on a country's share of global GDP.

CQ Values

So what are the CQ values for selected countries? Take a look at figure 1. It shows the CQ for those 27 countries with the biggest global chemical market share — in fact these are all countries with a global chemical market share of 0.5% or above. These 27 countries account for a total of 88% of the global chemical market.

The graph clearly shows that some countries — in particular, Taiwan, Korea and China — have a much higher contribution to the global chemical market than to global GDP. This means that these countries should be of disproportionate interest to chemical companies. Among these three, China is by far the most important because of its large absolute size. In fact, the high values of Korea and Taiwan are probably due to their close proximity to mainland China and the resulting high production of chemicals for export to China. China itself is still the global production hub, and most production processes require chemicals; the CQ reflects this.

Most of the other countries with a CQ above 1 are smaller economies, which for a variety of reasons have a disproportionately large chemical industry. Among these reasons:

- Central location, particularly with regard to shipping (Netherlands, Belgium, Singapore, with their ports and the petrochemical industry there)
- Access to raw materials (crude oil for Saudi Arabia and Iran, minerals for Chile, oleochemicals and oil for Malaysia)

In contrast, larger highly developed countries such as the US, Japan, France and the UK have CQ values substantially below 1, reflecting the fact that the service sector — while adding a large share to the GDP of these countries — requires few chemicals. Generally speaking, large segments of the chemical industry are quite mature and commoditized and thus rather cost-focused, leading to a preference for locations with low labor and investment costs and cheap raw materials rather than one with a highly educated workforce. Germany with its strong manufacturing sector and a CQ of almost 1 is somewhat of an exception. In contrast, the low CQ value of the UK is particularly striking. The country accounts for only about one-third of the global chemical market share to be expected based on its share of global GDP alone.

Rise Of China

How has the CQ developed in the past 10 years? Figure 2 gives some indications.

Clearly the rise of China as a global industrial power was accompanied by an even stronger rise of its chemical industry, as witnessed by the substantial increase of the CQ during this period. Almost all other bigger countries and regions — with the exception of South Korea with its close links to the Chinese economy — saw a corresponding decline in the CQ as they had to cede market share to the stronger Chinese competitors.

How will China's CQ develop in the future? An analysis of the past 15 years — though complicated by the lack of some data for global chemical market share during this period — indicates that it has likely reached its peak (Figure 3).

In other words, China's global chemical market share no longer grows substantially faster than its GDP, which will in the long run lead to a lower CQ. However, given the very high current CQ, it will take a very long time before China's CQ gets anywhere near the global average (which by definition is 1). Assuming zero growth for China's global chemical market share (which currently does not seem a realistic assumption as this market share has constantly increased in the past), China would have to approximately triple its GDP just to get to a world average CQ.

What does this mean for investment? China will remain a very important location for chemical industry investment. The reason is not only that China accounts for a larger and larger share of global GDP, but also that in a global comparison, China's chemical market share is proportionately higher than justified by its GDP size alone. So while there are many difficulties in profitably investing in China's chemical market, it is also almost impossible for global players not to do so.

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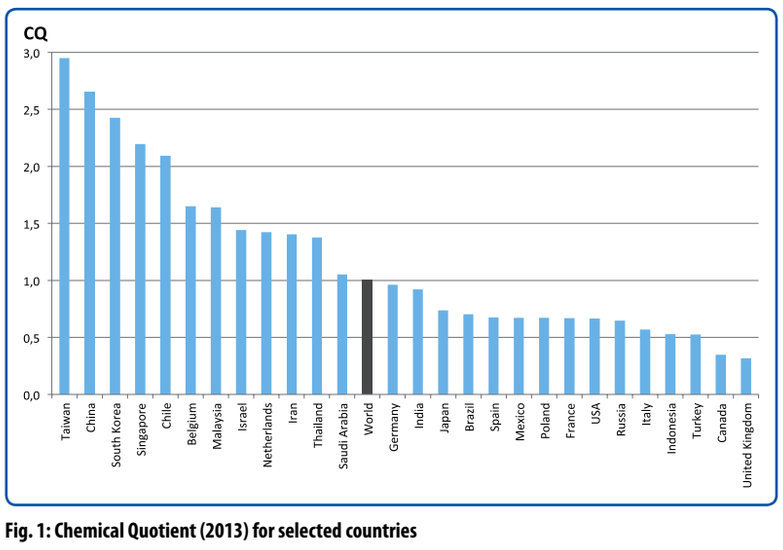

Fig. 1: Chemical Quotient (2013) for selected countries

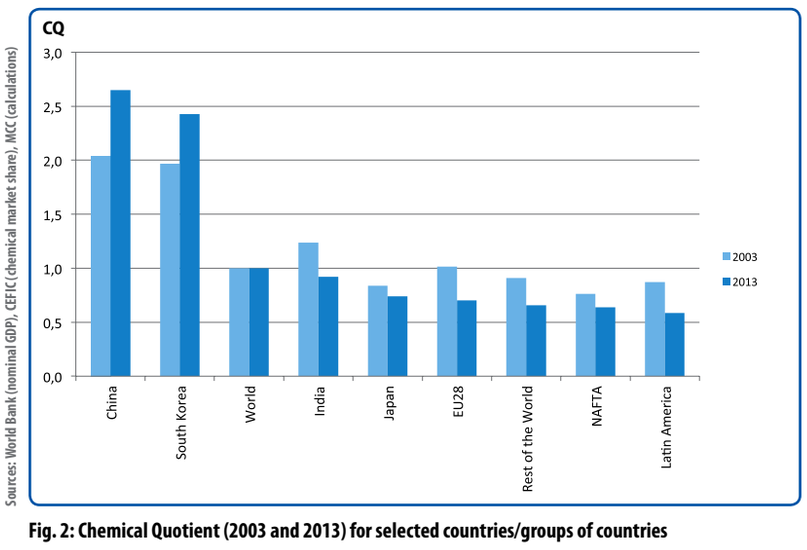

Fig. 2: Chemical Quotient (2003 and 2013) for selected countries/groups of countries

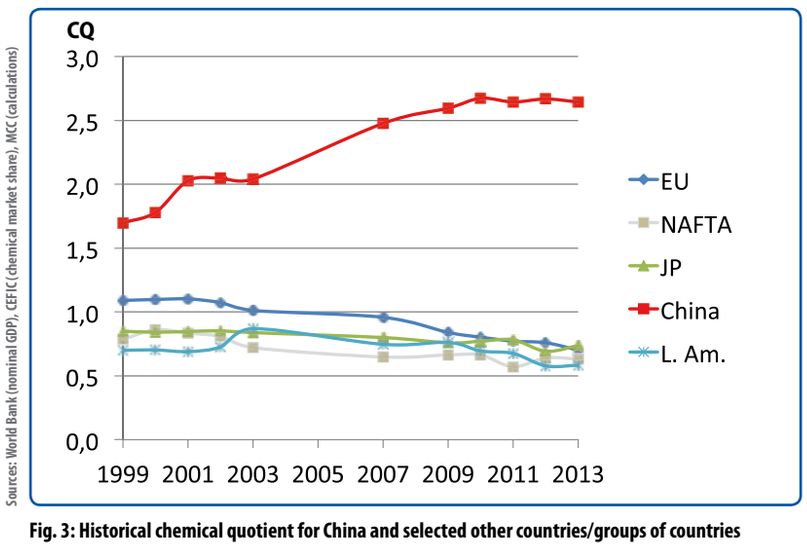

Fig. 3: Historical chemical quotient for China and selected other countries/groups of countries

Shell Starts New Singapore Plants

Citing increased demand in Asia, Shell has started up a new 140,000 t/y high-purity ethylene oxide (HPEO) purification plant and a new 140,000 t/y ethoxylates unit at its site on Singapore's Jurong Island, thereby doubling supply to local and regional customers.

The multinational oil and petrochemicals group delivers HPEO through an ethylene oxide pipeline grid to "over-the-fence" customers and its own expanded ethoxylation operations on Jurong Island. Feedstock comes from the group's ethylene oxide/mono-ethylene glycol plant, which is integrated with its ethylene cracker and refinery on Pulau Bukom.

Shell said Singapore continues to be an important refining and petrochemicals hub, with the new Jurong Island plants further deepening its chemicals footprint in Asia. The availability of both ethylene oxide and propylene oxide (PO) at the same location offers an advantageous value proposition for specialty chemical companies, who commonly use both of these intermediates to produce value-added products, it added.

As part of the same process, Shell increased polyols capacity by more than 100,000 t/y in 2013 and added new grades. In December 2014, it took 100% control of Ellba Eastern, the styrene monomer and propylene oxide (PO) joint venture with BASF, a move it said enabled integration with and optimization of Shell's existing assets on Jurong Island in a difficult cost environment. (dw) ■

AkzoNobel Expands Coatings in Vietnam, UK

AkzoNobel is doubling capacity for powder coatings facility at Dong Nai, Vietnam, and opening a new office in Ho Chi Minh City. The new production line, which will go on stream in November with a 20% increase in its workforce, will also supply customers across Southeast Asia, India, Australia and New Zealand.

Conrad Keijzer, AkzoNobel's executive committee member responsible for Performance Coatings, said Vietnam is strongly emerging as a manufacturing base in Asia, which continues to be an attractive growth market.

The Dutch company is the country's largest paints and coatings producer, with four manufacturing locations for both decorative paints and performance coatings.

In the UK, AkzoNobel plans to spend more than €1.3 million on a pilot plant for coatings resins to be built at its Performance Coatings site in Felling and scheduled to go on stream in the first quarter of 2016.

The new facility, part-funded by the UK government's "Let's Grow" regional growth fund. will initially provide resin samples for product testing and later is planned to be scaled up to commercial manufacturing dimensions. Felling is the business's largest R&D site worldwide. (dw) ■

BASF Starts First Chinese MDI Plant

BASF has started its first production of MDI at its new 400,000 t/y plant in Chongqing, China. Production will be ramped up gradually in line with market demand, the German group said. The plant's output will support key industries in China's western regions using the polyurethane feedstock in products for insulation, automotive parts and energy in buildings. MDI is also produced by BASF in Caojing, Shanghai, as well as in Antwerp, Belgium,Yeosu, South Korea, and Geismar, Louisiana, USA. (eb) ■

Hyosung Takes Unipol License from Grace

South Korea's Hyosung Corporation has taken its second license for the Unipol polypropylene technology now owned by US chemical producer W.R. Grace. The process will be used in the company's new 200,000 t/y plant scheduled to start up in at Ulsan, Korea in 2017.

Grace, which acquired the Unipol process with its $500m takeover of Dow Chemical's Polypropylene Licensing and Catalysts business segment in 2013, regards itself as a leading supplier of polyolefin catalyst technology. The company claims to have the broadest portfolio of any independent PE/PP catalyst manufacturer. (dw) ■

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Louisiana Cracker Boom Continues Unbroken

Thanks to its location on the US Gulf Coast with its booming shale gas industry and generous investment incentives to investors, the state of Louisiana is rapidly becoming a mecca for companies – in particular from Asia – seeking a low-cost location for new petrochemical and plastics production facilities.

In one of the latest projects to be announced, Thailand's Indorama Ventures (IVL), the world's largest PET producer, has purchased a mothballed cracker at Carlyss, near the Lake Charles chemical hub, from Occidental Petroleum and plans to revamp it to produce ethylene from shale gas-derived ethane and propane feedstock.

The $175 million project, which foresees output of 370,000 t/y of ethylene and 30,000 t/y of propylene from the end of 2017, is receiving a performance-based grant from the state of Louisiana worth $1.5 billion to cover infrastructure costs.

Through the family-backed Lohia group holding, Aloke Lohia, CEO of the Indorama group to which IVL belongs, is also said to own a stake in the defunct cracker, once part of Equistar, the former joint venture between Occidental, Milennium and LyondellBasell and now wholly owned by the latter group.

Lohia said the revamp will make Indorama the first Thai company to take advantage of the US shale gas boom, ahead of greenfield crackers under construction such as the tentative plans put forward by Taiwan's Formosa Petrochemical and South Korea's Lotte Chemical.

Formosa is mulling plans for a two-phase $9.4-billion complex in St. James Parish, Louisiana, which would include at least one new cracker and several downstream polyolefins plants as well as production facilities for ethylene glycol and other petrochemical products. The Asian group has been promised an incentive package that would include a $12 million grant.

In June of this year, South Korea's Lotte and US-based Axiall finalized agreements to build an ethylene cracker at Lake Charles using ethane feedstock. Definitive plans for the project are due to be revealed at the end of this year. CB&I has been awarded the engineering contract. (dw) ■

ENI Finds Gigantic Gas Field off Egypt's Coast

Italian energy giant ENI has discovered what it is calling a "super giant" gas field off the coast of Egypt. Once fully developed, what is believed to be the largest-ever gas find in the Mediterranean Sea could play a "major" role in meeting Egypt's natural gas demand for decades, CEO Claudio Descalzi said.

Claudio Descalzi, ENI

Using existing infrastructure, ENI will begin drilling more wells and installing pipelines next year and could see the first fruits of the project in about 2018, the CEO told the Italian daily newspaper La Repubblica.

The Italian group said it intends to make a final investment decision this year, with drilling likely to begin next year, and first gas production beginning shortly afterwards. ENI estimates peak output at roughly 65-80 million cbm per day.

Energy market analysts said the field, thought to be equivalent to 45% of Egypt's reserves, could also give Europe a new supply option, reducing its dependence on Russian gas imports. Depending on how much of the gas stays in the country, Egypt may not have to import any more gas for at least 10 years, Descalzi speculated.

Large oil and gas finds of this magnitude have become rare in recent years as companies have had to spend bigger sums on new technology to explore in hard to access deep water areas and other higher cost regions. Many of the market's major companies have been scaling back operations.

At ENI, however, "the exploration confirms the focus of our growth strategy," said Descalzi. In the past seven years, he said the Italian energy group has discovered 10 billion barrels of resources, including 300 million in the last six months. (dw) ■

Evonik Starts C4 Plants with New Technology

Chemical producer Evonik has started up new production plants for C4-based products at its Marl Chemical Park in Germany, using new technology that leverages flexible feedstock supply from BP the refinery at Gelsenkirchen, about 15 km away.

Johann-Caspar Gammelin, Evonik

For the process, which Evonik has labeled a "technological milestone," it is drawing FCC-C4 material streams from fluid catalytic cracking (FCC) through a pipeline and later will return byproducts it cannot use to BP by the same route.

The project emphasizes the significance of mineral oil processing for the supply chains of the chemical industry and is a good example for a cross-company cooperation that strengthens competitiveness, said Frédéric Baudry, the BP Europa executive board member responsible for the company's petrochemical business.

Johann-Caspar Gammelin, CEO of Evonik Performance Materials, said the new technology "significantly expands" the Essen-based company's raw material base, providing access to raw-material streams that so far have not been used for downstream chemical processing. While steam or naphtha crackers are the usual production base for petrochemicals, tapping the larger number of FCC crackers existing worldwide provides additional flexibility, he said.

Evonik's new German facilities, representing total investment in the triple-digit million euro range, are part of its Europe-wide capacity expansion for C4-based products, of which the company is a major producer. In addition to the expansion in Marl, the company has also invested in its C4 activities at Antwerp, Belgium, where new production facilities went on stream in the second quarter of 2015. (dw) ■

Ineos, Total and Cuadrilla Pick up New Shale Licenses

As part of its 14th offshore licensing round – the first in seven years – the UK government is selling exploration permits covering 2,700 km2 of land in Yorkshire and the Midlands. At least half of the exploration space is believed to contain shale gas.

Swiss-multinational chemical producer Ineos, as well as the UK subsidiary of French oil and petrochemicals group Total and Australia-headquartered Cuadrilla – the only company to have yet fracked in the UK – have already stepped up to buy additional stakes.

The first tranche of awards covers land not deemed to require further environmental assessment. Licenses for an additional 132 blocks covering parts of northwest England, including North Yorkshire and Lincolnshire, as well as Dorset in the south and the Isle of Wight are to be offered later, probably during the second half of this year.

Energy minister, Lord Bourne, said the license awards are part of the government's "long-term plan to build a more resilient economy, create jobs and deliver secure energy supplies." He said investment in shale could reach £33 billion and support 64,000 jobs "while providing a cost-efficient bridge to lower-carbon energy use."

As part of the UK's drive to emulate the US shale boom, the government in mid-August implemented a fast-track process to assess all applications systematically and quickly. Process would assure that local councils rule on the bids within 16 weeks or face having the decision taken out of their hands.

Environmental advocates already are up in arms about the fracking permits. Greenpeace said "hundreds of battles" are expected to spring up to protest destruction of rural landscapes. The Royal Society for the Protection of Birds said the 27 blocks currently being parceled out included 53 sites of special scientific interest and three nature reserves. (dw) ■

BASF and Genomatica Expand Renewable BDO Pact

German chemical giant BASF and US biotech firm Genomatica have expanded the scope of their license agreement for production of renewable 1,4-butanediol using Genomatica's patented process, adding countries in Southeast Asia to their initial agreement focused on North America.

Terms of the pact allow BASF to build a world-scale production facility for up to 75,000 t/y of renewable BDO, using the California company's process.

BASF is already offering commercial volumes of the renewable product to its customers for testing and commercial use. It says the quality is comparable to petrochemical-based butane diol. The group also has expanded its portfolio to include PolyTHF made from renewable BDO.

"We are happy to expand our license agreement with Genomatica to the dynamic Asia-Pacific region," said Stefan Blank, president of BASF's Intermediates division, He said the arrangement provides greater flexibility to respond to market requirements. (dw) ■

Grangemouth Biofuels Plant Gets £11 Million Grant

A new plant in Grangemouth, Scotland, to produce biobutanol from Scotch whisky byproducts has received an £11 million boost from the UK Department of Transport. Celtic Renewables, which would operate the plant, said it has already attracted investment and partners in the private sector to fund a demonstration plant that could be scaled up to industrial dimensions.

Production of biobutanol, used as an alternative fuel for automobiles and airplanes, would provide a clear contrast to the dominance of petrochemicals in the region. (dw) ■

Connected To Health

Internet of Things Nudges Life Sciences Industry Toward Reinvention

The Internet of Things (IoT), where smart devices, machines and people communicate and exchange information with each other, has the power to revolutionize the life sciences industry. What has begun with wearables such as fitness trackers or blood pressure monitors might eventually lead to connected patients, who provide real-time feedback on drug effects, and to a large new market of health-conscious individuals expecting "intelligent" treatments and completely new services.

Backed by a rather optimistic general business outlook, many industry players are currently in the process of planning or piloting IoT-related projects. Though some technologies already play an important role, it would be too early to call IoT the current megatrend of the industry. Rather, life sciences executives may not see IoT everywhere now, but they definitely see it coming.

This is the picture that emerges from the sixth Camelot Management Consultants Pharma Management Radar, a biannual survey that examines the general climate in the life sciences industry and additionally takes an in-depth look at a varying current management topic. In July and August, 30 executives from globally active life sciences companies based in 16 countries and spread over four continents participated in the online survey. The focus topic of the sixth Pharma Management Radar is the Internet of Things.

Positive Business Climate Continues

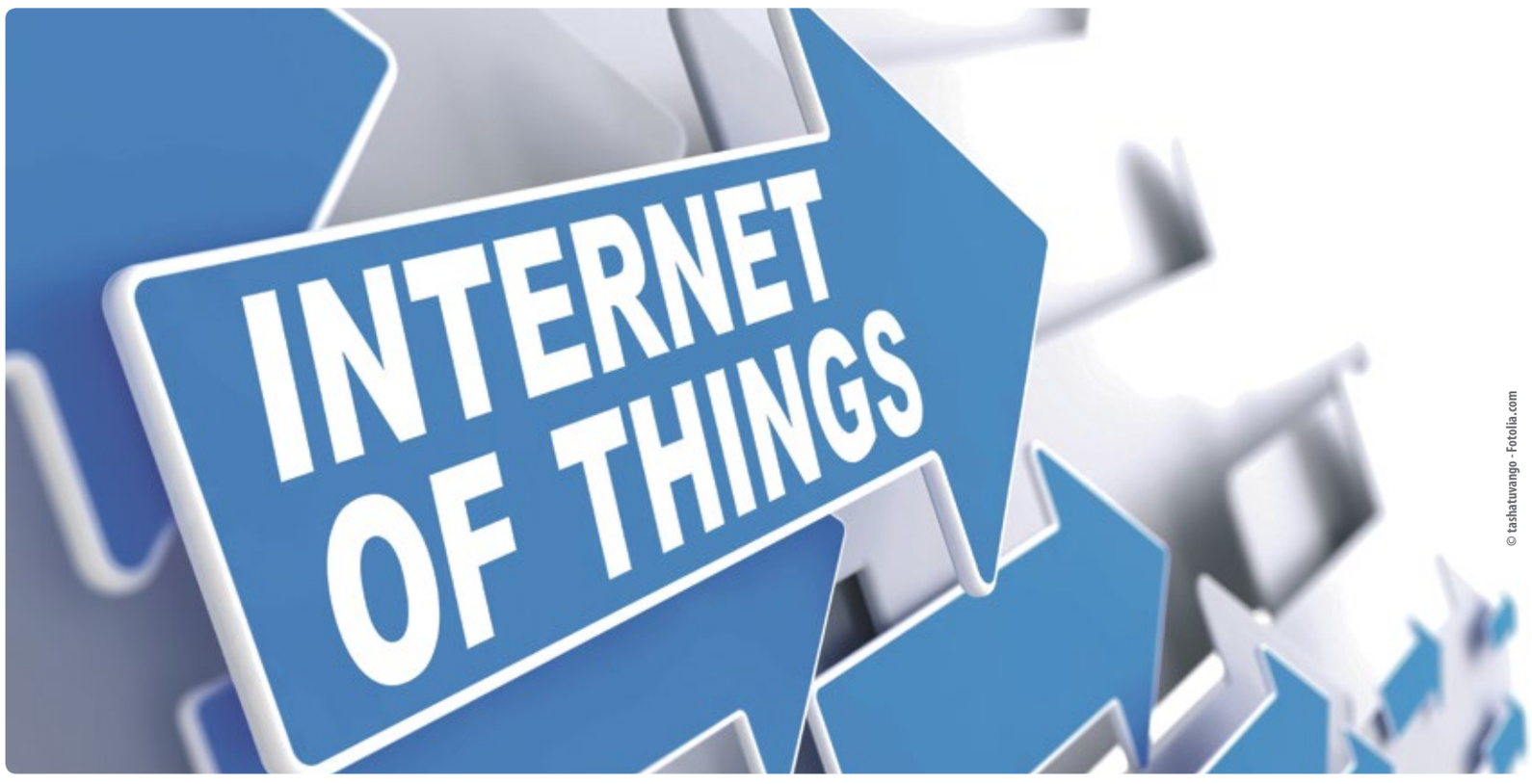
The executives' view of the business climate for the life sciences industry has further brightened since the Pharma Management Radar Survey half a year earlier. In accordance with their general industry outlook, most respondents are optimistic with regard to their own business development. Only 7% of them expect their global sales performance to deteriorate, while more than 90% anticipate revenue growth. When it comes to where this growth is expected to take place, China and North America hold the top positions. And Russia shows clear signs of recovery.

Most Important Markets for Investment: North America and China

These expectations are also reflected in many of the life sciences industry's regional investment plans for the next 12 months. North America has caught up with China as the most important market for investments. Southern Europe and the UK, which used to be considered quite attractive regions for investment, have obviously lost this status. Russia, on the other hand, seems to have regained some of the attractiveness lost during the political crisis.

Growing Employment Figures

In contrast to past developments, the will to invest and the general economic optimism are now accompanied by an expected growth in employment figures. More than three in four participants expect to keep their employment figures constant or to even increase staff. This development must not, however, be misinterpreted as a sign of lowered cost awareness regarding human resources. The contrary is true, which can be seen when asking for the evolvement of external sourcing volume. With more than 80%, the share of respondents planning to increase external sourcing has grown considerably since the previous survey (66%) conducted only six months ago.



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The Industry's Fears: Price Decrease and Political Risks in Growth Markets

The fear of revenue decrease due to patent expiry remains the major topic (48%) when it comes to the respondents' risk assessment — which clearly implies that for these respondents there will be important patents becoming obsolete in the near future. The second major risk has to do with the political and economic developments in various regions of the world: Further gaining relevance since the last survey (44%), political risks in growth markets are now sharing the top position with price decrease.

Industry Trends: Cost Reduction, Product Innovation, Offerings Beyond the Pill

In accordance with these results, cost reduction is considered the most important industry trend by three-quarters of respondents. Product innovation through research collaboration has also gained relevance among the respondents (1/2015: 26% vs. 2/2015: 44%). Another major trend reflected in the survey is offerings beyond the pill including e-connected devices. The relevance of these offerings has grown considerably since the last survey (13% vs. 44%) — which hints at the growing importance of the so-called Internet of Things.

Internet of Things Gaining Relevance — Slowly But Surely

The Internet of Things is definitely on the executives' radar, as can be seen from various questions dealing with the IoT. When asking for the functional area most strongly influenced by IoT within the next five years, most executives (60%) name supply chain and logistics. Sales and marketing comes second (45%), while figures are surprisingly low with regard to research. These near-term expectations are more or less in line with the current status of IoT in the industry where nearly 40% of respondents have IoT projects implemented in supply chain and logistics. Regarding sales and marketing, surprisingly just around 10% have realized IoT projects, though 50% have already planned or piloted IoT in this area — which allows for the interpretation that most companies are still in a trial-and-error phase.

IoT Expected to Gain Significance in the Next 15 Years

This assessment is backed by the fact that respondents are much more positive about IoT in all areas when extending the timeframe to 15 years. A similar phenomenon can be observed with regard to the individual technologies that are part of the IoT. While it is mainly sensor and communication technologies like NFC that stand out in terms of relevance for the near to medium-term future, two-thirds expect that other technologies such as nanotechnology, e.g., smart pills, and connected robotics will strongly influence the industry in 2030.

IoT in SCM and Logistics

Taking a closer look at the field of Supply-Chain Management (SCM) and logistics, more than 40% expect Track & Trace to be highly affected by IoT within five years. Environmental control ranks quite high as well, mainly among innovators. This might relate to the increasing share of biotechnology products, which require tougher environmental controls, in their portfolio. Consequently, these two areas of application show the highest shares of implemented IoT projects in the respondents' companies now. In other fields such as new services and reverse logistics, the general trend still swings between total reservation and first steps in the form of planned or piloted IoT projects. In the 15 years perspective, however, virtually all areas achieve high shares of strong or even very strong IoT influence expectations.

Main Push for IoT Technologies in SCM in Three to Five Years

The executives' high expectations for the longer-term future do not mean, however, that IoT will remain a lame duck until 2030. On the contrary, most respondents — especially those representing innovators — expect the main push for new IoT technologies in pharmaceutical SCM to happen in three to five years. Despite their rather distinct belief in progress, executives are also aware that an extensive range of hurdles and challenges will have to be overcome before IoT's complete breakthrough. While technological maturity and the question of the business case are two of the top answers, most other major hurdles require a lot of effort from the global life sciences industry and legislators: Immaturity of standards and lack of global legislation are considered particularly challenging when it comes to implementing IoT solutions.

Peter Holland, partner and head pharmaceutical value chain, and Andreas Gmür, partner and head of logistics practice, Camelot Management Consultants

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The Internet of Things has the power to revolutionize strategies, processes and organizations in life sciences.

Dr. Josef Packowski, managing partner, Camelot Management Consultants

In the next few years, sales and marketing and SCM and logistics will be the areas most fundamentally impacted by IoT.

Peter Holland, partner and head of pharma value chain, Camelot Management Consultants

Current public hype technologies such as drones are not yet expected to have a strong impact in the nearer future.

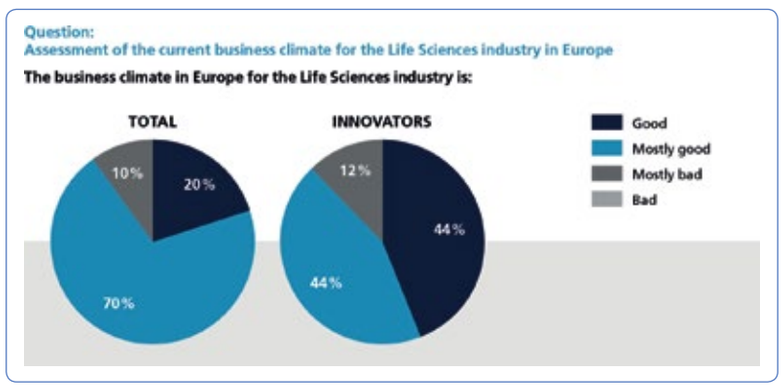
Andreas Gmür, partner and head of logistics practice, Camelot Management Consultants

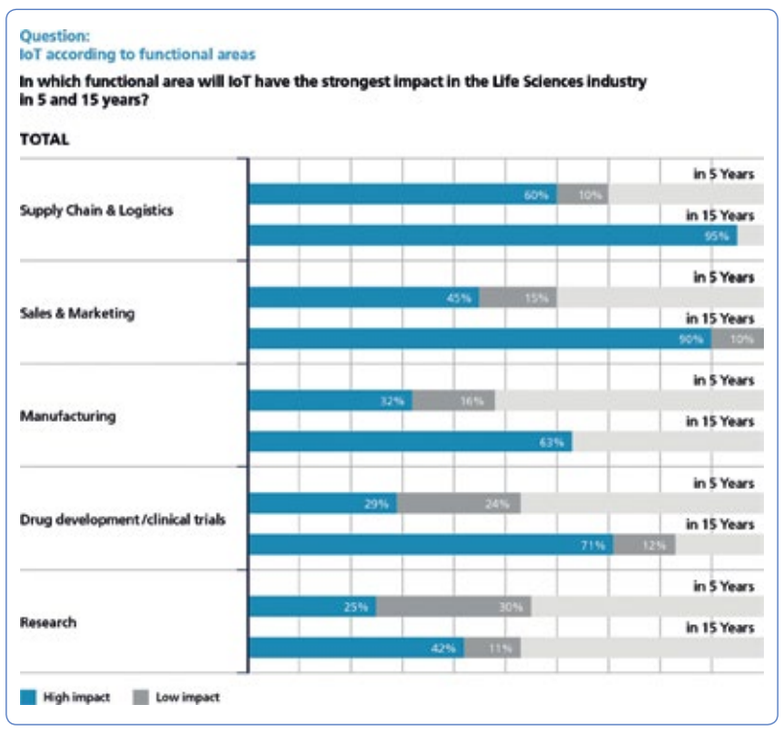
In supply-chain management, we expect the main push for IoT technologies in three to five years.

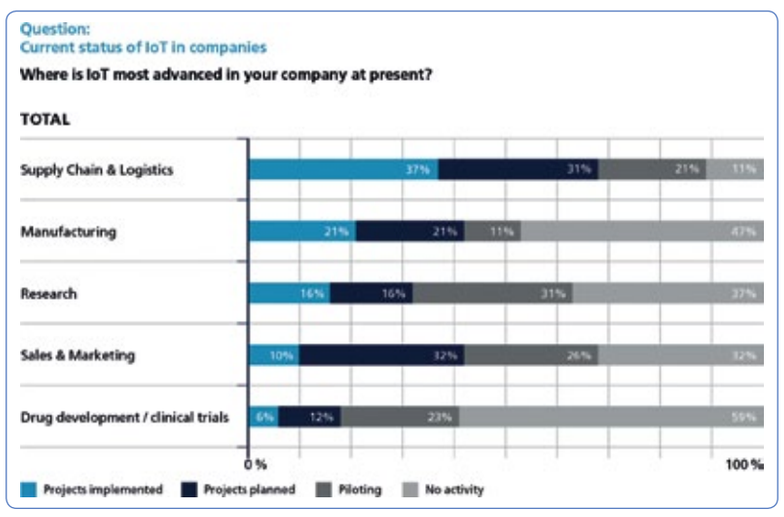
Jukka Pietilä, senior development manager supply chain, Orion Corp.

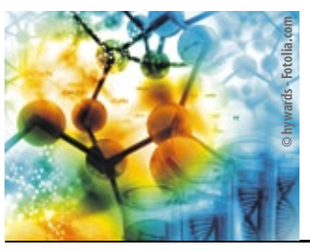
Technology, standards, legislation and internal know-how are the key challenges when it comes to leveraging the IoT.

Ann Merchant, president, Schreiner MediPharm









Drug Sales

The pharmaceutical industry is entering a period of sustained growth

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R&D Efficiency

Research-based pharma companies are committing to rising productivity targets

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Pharma Manufacturing

Bio on demand: paving the way for a new biopharma manufacturing paradigm

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Modified Peptides

The Importance of Protein Chirality

The folded structure of a protein defines its interactions with other molecules. Selective binding ligands could be, e.g., other proteins or peptides. A natural protein consists exclusively of L-amino acids and glycine, and its folded structure is chiral. The folded structure of a protein composed of D-amino acids is the mirror image of the all-L-amino acid protein molecule. Hence, for developing an all-D-protein ligand for a natural protein, the L-protein ligand has to be mirrored a second time (fig. 1).

Dr. Monika Mergler, Bachem

Dr. Michael Scholze, Bachem

The all-D-amino acid enantiomer of the target protein is prepared by total chemical synthesis and used as the target for phage display of a library of L-protein ligands. An L-protein, which binds to the all-D target with high affinity, is selected. Then, the corresponding all-D-protein is synthesized, which will bind to the native all-L-amino acid target protein.

Professor Stephen Kent from the University of Chicago, a pioneer in the chemical synthesis of proteins, evaluated this concept for its potential in drug development in collaboration with Reflexion Pharmaceuticals, a company he co-founded. Peptides and proteins consisting of D-amino acids resist degradation by proteases. Used as therapeutics, they combine an increased half-life with non-immunogenicity.

As an example for engineering a D-protein ligand to recognize an L-protein target vascular endothelial growth factor Type A (VEGF-A), an angiogenesis-inducing protein overexpressed in tumors, was chosen as the natural protein target. All-D VEGF-A was produced by total chemical synthesis using native chemical ligation.

Then, the laboratory of Professor Sachdev Sidhu at the University of Toronto used the all-D VEGF-A as the target for phage display of a library of small protein ligands, and the L-protein binding to all-D VEGF-A most efficiently was selected. The corresponding D-protein of the same amino acid sequence was prepared by total chemical synthesis and shown to bind to native VEGF-A and act as an antagonist preventing receptor binding.

Professor John Robinson's group from the University of Zürich works on synthetic protein epitope mimetics. The group has developed a type of macrocyclic peptides acting as β-hairpin mimetics. An L-Pro-D-Pro scaffold stabilizes the conformation of the loops. A β-hairpin-mimetic tetradecapeptide derived from the antimicrobial peptide protegrin I showed a vast increase in activity. It acted specifically against Pseudomonas species. Pseudomonas bacteria such as P. aeruginosa pose a grave problem, as they are often detected in hospitals and have acquired multi-antibiotic resistance. The peptide antibiotic POL7080 developed by Polyphor and recently out-licensed to Roche is the result of further optimization of Robinson's protegrin mimetic.

Well-Defined Glycoproteins and Glycopeptides

Chemical glycosylation is an innovative approach for the modification of peptides and proteins to improve drug properties such as pharmacokinetics, efficacy and solubility. The glycosylation of proteins is a most important post-translational process. Precise position and type of glycosyl residues are essential for the activity of the resulting glycoprotein. Glycoproteins are usually obtained by recombinant technologies employing mammalian cells, and the chemical synthesis even of simple glycopeptides is elaborate and cost-intensive.

GlyTech, a company in Kyoto, Japan, is a pioneer in the manufacture of glycoproteins and glycopeptides by chemical means. Professor Yasuhiro Kajihara from Osaka University and Dr Michael Haller from GlyTech described their approach to site-specific glycosylation. The synthetic approach developed by GlyTech allows choosing from a broad array of stable preformed glycan building blocks. It is perfectly suited for optimizing peptide leads and improving established peptide pharmaceuticals and for large-scale production. Their asparagine derivatives carrying linear or branched glycans are compatible with standard protocols of solid-phase peptide synthesis. Bromoacetylated glycans allow glycosylation of cysteine-containing proteins in solution.

Glycosylated proteins and peptides prepared by the method are well-defined compounds, more homogeneous compared with those obtained recombinantly in mammalian cells. Unambiguous structure is highly desirable for glycoproteins used in drugs and equal or improved activity could be demonstrated for glycoproteins obtained by GlyTech's approach. Multiple site-specific glycosylation of proteins can be a more biocompatible alternative to PEGylation. Not unexpectedly, glycosylation improves the water solubility of peptides and proteins. With peptides, dramatic effects can be induced: glycosylation of the somatostatin analog octreotide not only increased the half-life of the drug, but it also markedly changed the receptor-binding affinity, which came close to the behavior of native somatostatin.

Peptide-Based Anti-Alzheimer Vaccine

Misfolding and aberrant processing of proteins play an important role in neurodegenerative diseases such as Alzheimer's (amyloid β and Tau) or Parkinson's (α-synuclein). Such proteins are potential therapeutic targets. AC Immune is a company specializing in the development of therapeutics for neurodegenerative diseases including Alzheimer's disease (AD).

Professor Andrea Pfeifer, founder and CEO of AC Immune, considers the microtubule-stabilizing Tau proteins a promising target for a therapeutic vaccine for this devastating disease. Hyperphosphorylated Tau proteins form twisted fibers inside neuronal cells and build tangles, which are associated with the pathological conditions of AD and other neurodegenerative diseases. Pfeifer presented the company's platform SupraAntigen it used to obtain a peptide-based anti-pTau vaccine. During pre-clinical development, this vaccine showed reduction of phospho-Tau aggregates and total pathological Tau and improvement of clinical parameters. The vaccine is also characterized by very specific and T-cell independent immune response, which is an important feature of the SupraAntigen technology platform. The vaccine is being tested in a Phase 1b clinical trial.

The heavily modified short peptide T3, an essential component of the anti-pTau vaccine, was produced at Bachem. The development and optimization of the synthesis and purification of the tetrapalmitoylated phosphopeptide was presented by Ralph Schönleber, vice president research & development at Bachem. Various strategies for preparing a peptide containing two phosphoserine residues and five lysines, four of them modified by palmitoylation, could be conceived. Solid-phase peptide synthesis was the method of choice, but modification steps can be performed on-resin or in solution, after cleavage from the carrier.

Purification of tetrapalmitoylated T3 was the major challenge due to the low solubility of the peptide, which could be facilitated by improving the quality of the crude product. Eventually, the palmitoylation of the purified partially protected peptide was conducted in solution followed by deprotection of the fifth lysine and the N-terminus. As the non-palmitoylated peptide can be purified very effectively, the final purity of T3 could be increased to more than 95%.

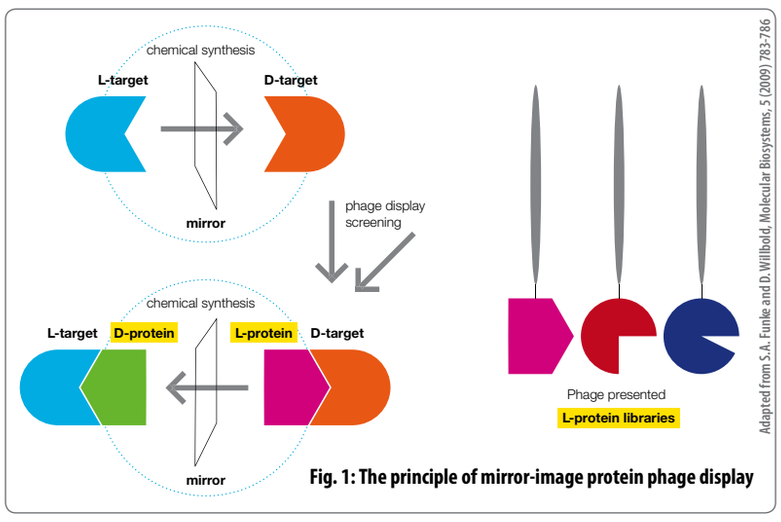

Fig. 1: The principle of mirror-image protein phage display

Symposia Dedicated to Peptide Research

In spring 2011, Bachem AG organized the first of a series of annual symposia dedicated to peptide research. The events were intended to bring together representatives from academia and industry, and each of them covered a specific topic. The fifth spring symposium was "Modified Peptides" in Basel, Switzerland, on April 23. Various aspects of the field were addressed in-depth by individual presentations, with an emphasis on the role of peptide modification or protein modification in drug development.

Dr. Monika Mergler, Marketing Specialist, and
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Leaving the Patent Cliff Behind

Global Pharma Increases R&D Productivity; Report Forecasts Prescription Drug Sales of $1 Trillion

The pharmaceutical industry is entering a period of sustained growth. Prescription drug sales are set to advance at almost 5% a year until 2020, while worldwide prescription drug sales are expected to reach almost $1 trillion by 2020. This is the conclusion of the World Preview 2015 report from EvaluatePharma, a specialist in life science sector analysis and consensus forecasts.

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The report, based on the company's coverage of the world's leading pharmaceutical and biotech companies and on consensus forecasts, says key prescription drug sales jumped 4.9% in 2014, driven by an 8.9% surge in US sales. In the same year, Europe returned to growth at 2.4%, while Japan slumped 2.6% in yen.

Increase in R&D Activities

In the view of the authors, the pharma and biotech industry is in very good shape. The patent cliff is firmly in the rearview mirror. Continued confidence in the sector is driven by a number of positive fundamentals including the recent increase in R&D productivity. The report mentions that worldwide pharmaceutical R&D totaled $141.6 billion in 2014, representing an increase of 3.1% on the previous year. Looking forward, R&D spend is forecast to grow 2% per year, compared with the compound annual growth rate of 3.4% between 2006 and 2014. The spend per new molecular entity (NME) was $2.7 billion in 2014, the lowest for at least the past seven years. This fall in spend per NME indicates increased productivity within the industry: Essentially, companies are containing R&D spend while achieving greater regulatory success.

EvaluatePharma highlights that this increased productivity has resulted in a big hike in drug approvals and the emergence of breakout drugs such as Gilead's Sovaldi franchise. Excitement surrounding new products including Merck & Co.'s Keytruda, Bristol-Myers Squibb's Opdivo and anti-PCSK9s from Amgen and Sanofi should ensure the sales momentum continues. The analysis company values the current total industry's R&D pipeline at $493 billion. Within this, Gilead's potential new combination hepatitis C product is seen as the most valuable drug.

The current industry feel-good factor has also been mirrored in the amount of money businesses are raising, the number of pharma and biotech companies floating on exchanges around the world, and the healthy appetite for M&A across the board.

The Biggest Players

EvaluatePharma finds that Novartis will remain the No. 1 pharmaceutical company through 2020 with total prescription drug sales of $53.3 billion, representing a 5.4% share of the entire world market. Actavis' prescription drug sales are forecast to almost triple between 2014 and 2020, primarily as a result of its acquisition of Allergan in March 2015 and Forest Laboratories in July 2014. Celgene is forecast to debut in the top 20, rising nine places, by 2020 with its anti-cancer therapeutic Revlimid and its immunosuppressant Otezla adding a combined $6.6 billion to its 2020 prescription drug sales. Overall, global prescription drug sales are expected to grow, on average, 5% per year between 2014 and 2020 and reach almost $1 trillion by 2020.

Encouragingly for drug developers, despite the increased number of drugs approved, the quality of new drugs did not slip. Eight of the top 10 drugs approved in 2014 are forecast to have sales of more than $1 billion five years after launch.

Biologics On Its Way

The industry as a whole is expected to enjoy the benefits of the move toward biological drugs. Despite setbacks from some approved and clinical biological drugs depressing the speed of change, the global sales contribution from biologic drugs is forecast to jump from 23% in 2014 to 27% in 2020.

EvaluatePharma says these drugs have traditionally enjoyed greater patent protection than their small-molecule relatives, but the landscape is changing with the approval this year of the first US biosimilar.

Zarxio was given the green light in March but has yet to make it into pharmacies thanks to ongoing challenges from originator Amgen. Industry and legal experts also believe that navigating a legal pathway through the less than perfect US biosimilars legislation could hold up launch for several more months if not years.

Given the legal wrangling that is set to occur for biosimilars, and unresolved issues around substitution, analysis continues to show that the effect on branded products will be much softer than that of small-molecule generics. Thus biologics remains an attractive space for drug developers.

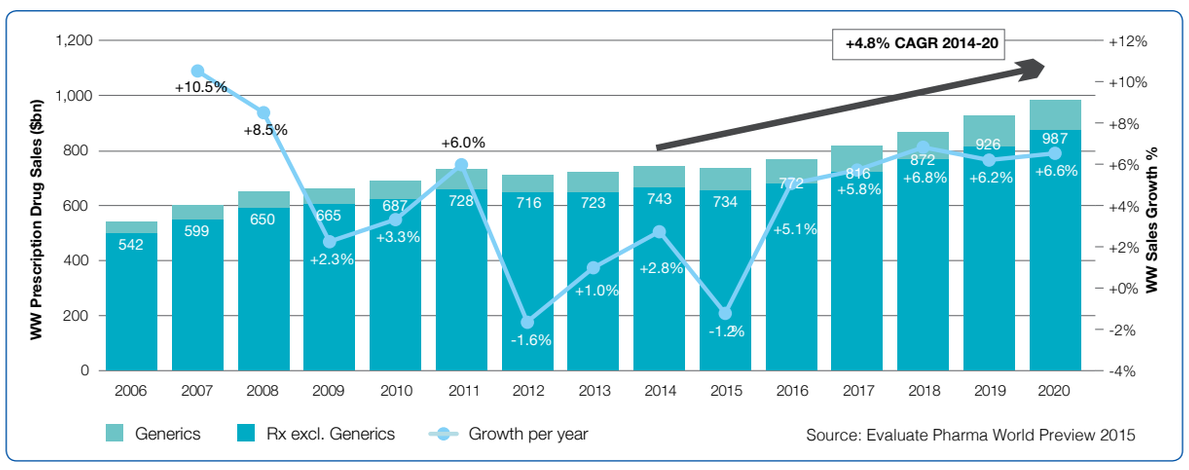

Fig. 1: Worldwide Total Prescription Drug Sales (2006-2020)

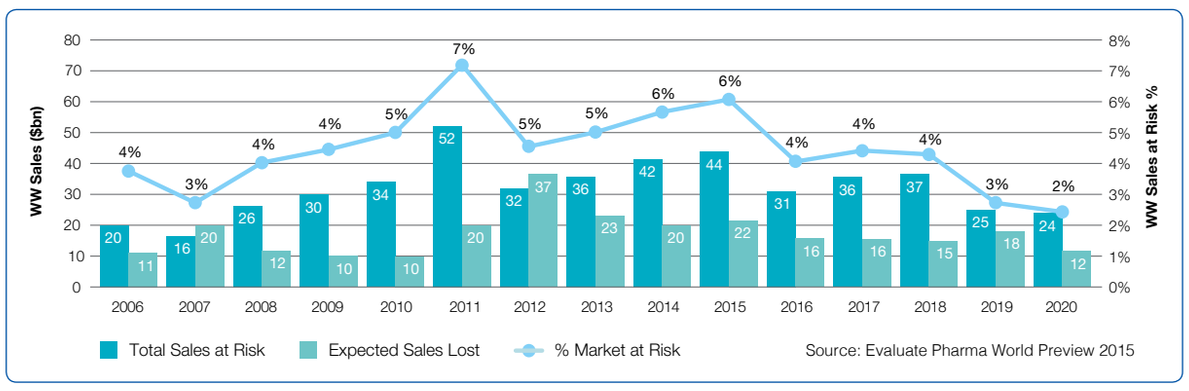

Fig. 2: Worldwide Sales at Risk from Patent Expiration (2006-2020)

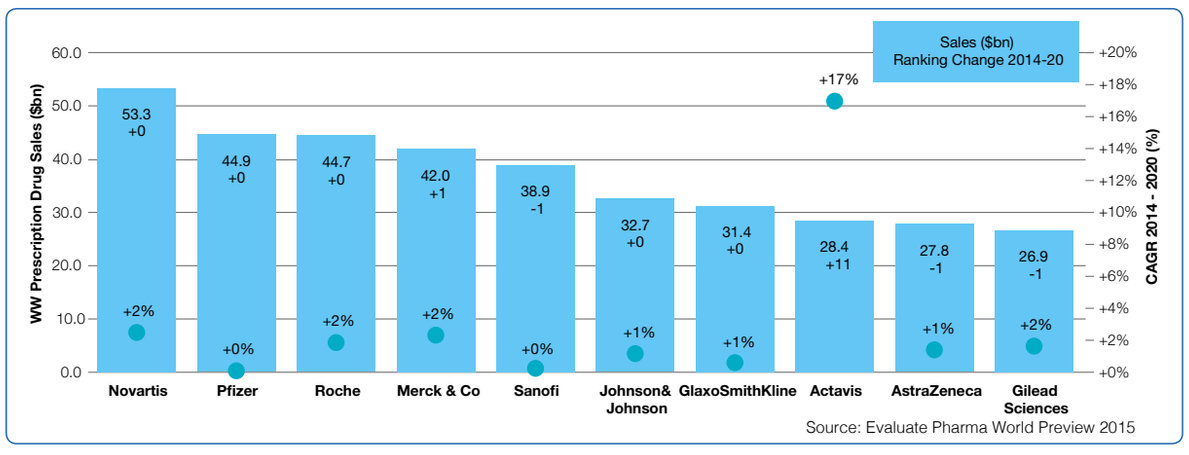

Fig. 3: Worldwide Prescription Drug Sales in 2020 of Top 10 Companies

Some Clouds

The only clouds on what looks to be a sunny horizon for pharma and biotech are global pricing and market access. With many predicting that for the first time the industry could produce a series of real cures for previously intractable diseases, it is clear that these innovative drugs will come at a price. What is also clear is the growing reluctance of both government and private health-care providers to fund very expensive drug treatment regimens.

Recent pressure from health insurers in the US has seen pricing ground lost in both diabetes and respiratory drugs, with both GlaxoSmithKline and Sanofi reporting reimbursement hits. Gilead has also seen insurers trim the amount they are willing to pay for its pioneering hepatitis C drug. All this has led some to ask if we are seeing the end of pricing freedom in the US.

If the industry is to keep up the impressive growth of the last couple of years, which is predicted to continue, it will either have to accept lower prices for its products or persuade those who hold the purse strings that its products are indeed game changers and their benefits outweigh the cost of disease.

Thorsten Schueller, freelance journalist, Grafing, Germany

Oncology Largest Segment

EvaluatePharma finds that oncology will remain the largest segment in 2020 with an expected annual growth of 11.6% per year, reaching $153.1 billion in 2020. Growth from in-line products, and potential new entrants such as drugs targeting the PD-1 pathway, is expected to more than compensate for a number of key patent expiries between 2014 and 2020. Anti-diabetes is forecast to be the second biggest therapy area with sales of $60.5 billion in 2020, less than half that of oncology.

Humira Remains Top-Selling Product

Based on the authors' opinion, AbbVie's Humira will remain the No. 1 worldwide product in 2020 with sales of $13.9 billion. However, the threat of biosimilars has tempered the growth of the product with sales forecast to peak in 2017 at $16 billion. While Sovaldi debuts at No. 2 with sales of $10 billion, Opdivo, Bristol-Myers Squibb's anti-PD-1 monoclonal antibody, leaps to third place in 2020 following its launch in 2014. Seven products currently in R&D are in the top 50, the biggest of which is Vertex's Orkambi, a combination product for the treatment of cystic fibrosis, which is forecast to have sales of $5.1 billion in 2020. Collectively, Gilead's hepatitis C franchise is forecast to sell $13.4 billion in 2020.

Sanofi Teams with Google on Diabetes Care

French pharmaceutical producer Sanofi has announced plans to cooperate with the life sciences team at Google to improve care and outcomes for people with type 1 and type 2 diabetes. Sanofi said the collaboration will pair its leadership in diabetes treatments and devices with Google's expertise in analytics, miniaturized electronics and low-power chip design. To improve diabetes care, the intention is to develop new tools to bring together many of the previously "siloed" pieces of diabetes management and enable new kinds of interventions.

Plans include new health indicators such as blood glucose and hemoglobin A1c levels, patient-reported information, medication regimens and sensor devices.

The goal of the collaboration is to make it easier for patients to successfully manage their diabetes, reduce the risk of complications, improve outcomes and ultimately lower costs. (dw) ■

Novartis and Amgen Partner on Alzheimer's and Migraine

Novartis has announced it will cooperate with US biopharmaceutical group Amgen to develop and sell neuroscience treatments for conditions such as Alzheimer's disease and migraine headaches. Under the terms of the arrangement, the two companies will share responsibility for development and commercialization of the Novartis BACE inhibitor program.

Novartis' oral therapy CNP520 – said to have potential to prevent, slow or delay symptoms of Alzheimer's – will be the lead molecule. Amgen will make an upfront payment and milestone payments as well as disproportional R&D costs for an agreed upon period, followed by a 50:50 cost and profit share arrangement.

For compounds in the migraine field, Novartis will receive global co-development rights and commercial rights outside the US, Canada and Japan to the investigative molecules in Amgen's migraine portfolio. (dw) ■

Heavy Reliance on Contract Manufacturing

View the Strengths of CMOs through the Eyes of their Customers

The results of ISR's 2015 Contract Manufacturing Quality Benchmarking study give insight into the outsourcing preferences and practices of 116 buyers of commercial manufacturing services.

The participants reported API manufacturing (51%), fill-finish (45%) and distribution (46%) are outsourced at the greatest frequencies (fig. 1); followed closely by chemical synthesis (43%), packaging & labeling (43%) and holding & storage (41%). An average of 39% of analytical testing / lab services and cold chain management is outsourced.

Outsourcing Practices

The majority of respondents, 50%, work for a drug innovator that manufactures its own products and uses contract manufacturers to augment its internal supply. Over two-thirds of respondents from large biopharmas (R&D $1 billion+) reported using CMOs to augment internally manufactured drug supply. Almost one-third of respondents use CMOs for all of their manufacturing needs; this practice is especially common among smaller companies. A small percentage use CMOs only when they have an emergency need for a product that they are unable to meet.

Heavy reliance on contract manufacturers has fueled the use of preferred providers, with half of respondents reporting the use of a preferred vendor list in 2015; two-thirds anticipate their company will use CMOs from a preferred provider list within three years. Among those with preferred vendor lists, the majority has one to three CMOs on their list. At the same time, a large portion of manufacturing work is still contracted on a one-off basis, but respondents anticipate this practice becoming less common over the next three years. About one-tenth of sponsor-supplier relationships fall into a single-source model. Respondents do not anticipate expanding use of the single-source outsourcing model over the next three years (fig. 2).

Geographic Preferences

When it comes to selecting suppliers, geography plays an important role. The data show a tendency for companies to outsource the greatest proportion of their commercial manufacturing to CMOs within their own geography. That is, companies with a North American headquarters send the highest proportion of outsourced work to CMOs located in the United States and Canada. According to survey participants, 40% of outsourced work is performed in the United States. Western Europe follows with 30%, and trailing in third, 12% of outsourced work is performed in India. A small percentage of outsourced work is conducted in China and South America (4% each); Eastern Europe, Asia-Pacific, Japan and Russia together comprise the remaining 10% (fig. 3).

Supplier Selection Criteria

A CMO's reliability, regulatory history and capacity are key selection criteria. Sponsors also look for a track record of meeting quality performance metrics and low cost as part of their top five criteria. Not only is it important to convey these attributes in order to win business, excelling across multiple areas is required to maintain business and develop loyalty. The research data show a disconnect between winning business and maintaining it, as respondents reported one favored set of CMOs for perceived leaders, proposal volume and use and a different set of leading CMOs based on performance metrics. This finding strongly reiterates the importance of using real customer feedback, not just industry perception, as part of supplier shortlist due diligence.

Supplier Preferences

When asked what measures are used to judge quality, respondents mentioned FDA compliance, QA/audits and previous experience with the company. Despite its position as a top of mind attribute, quality is particularly hard to judge and define; therefore, meeting expectations for this performance metric is tricky. The full report includes detailed service quality profiles based on 28 performance metrics for 19 contract manufacturers. These ratings evaluations are from recent customers who are either currently working with the CMO or have within the past 18 months, enabling users of the data to make educated contract manufacturing purchase decisions and for suppliers to present their true areas of strength to prospects.

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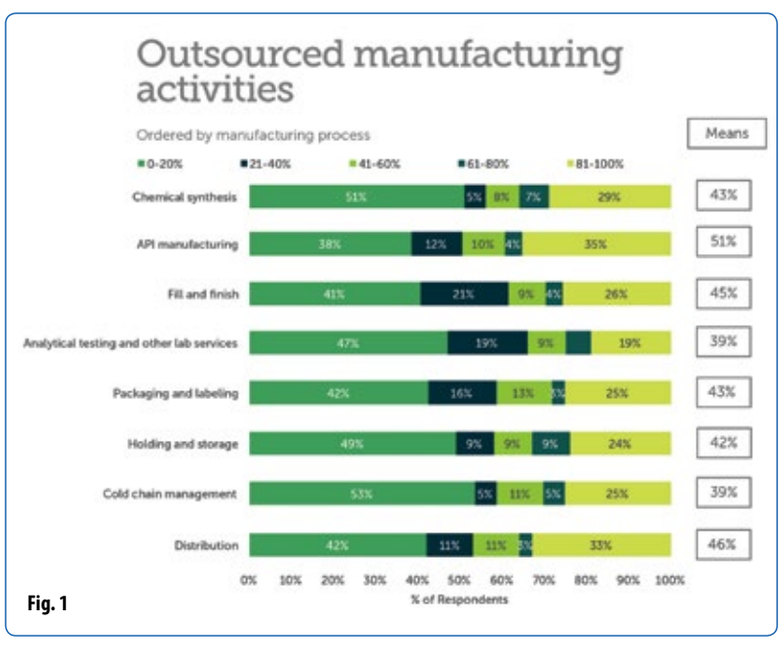

Fig. 1

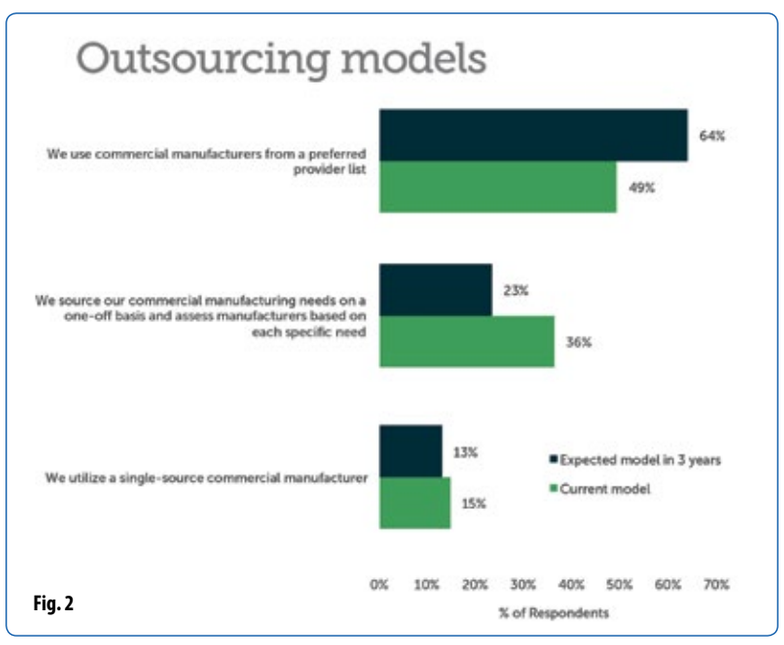

Fig. 2

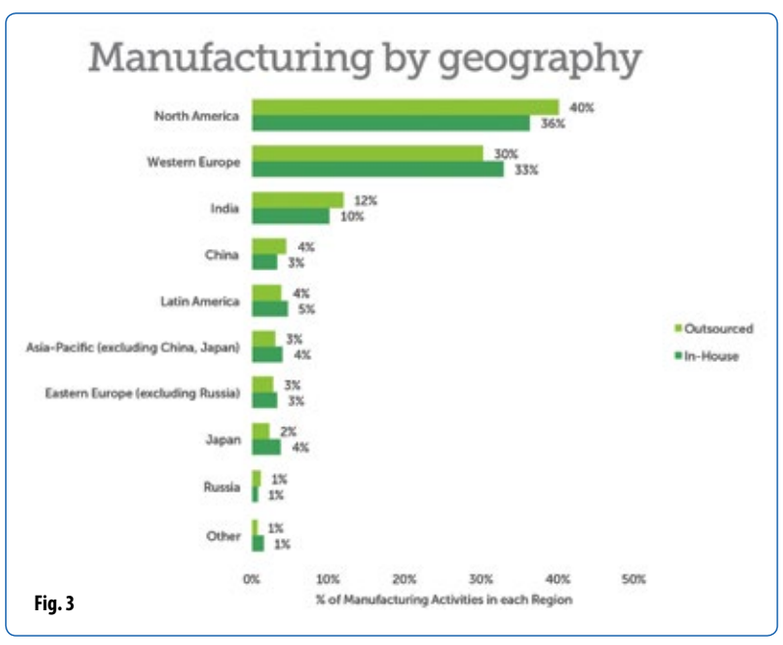

Fig. 3

Chances and Hurdles for Biosimilars

Follow-Up Drugs Hold Potential for Patients, Pharmaceutical Industry

With biosimilars the pharmaceutical industry and health-care business move into a relatively young discipline with high sales potential. The follow-up drugs of biopharmaceuticals are becoming more and more a cost effective alternative for the often expensive but very effective originator medicines. But the way to the market is armed with hurdles.

The age of biosimilars has finally dawned in the US after Zarxio (filgrastim-sndz), a cancer drug, was approved by the US Food and Drug Administration in March. Since September the copy of Amgen's Neupogen (filgrastim) has been on the market. With this the US, the world's biggest pharmaceutical market and often at the forefront of medical innovations, is jumping into the biosimilar business 10 years after Europe, Australia and India.

Biosimilars are much more than generics of off-patented originals. They are complex follow-up drugs, approved because they are highly similar to an already-existing biological product, a reference product. The biosimilar also must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference drug.

Revolution In Medicine

Since their introduction in the 1980s, biopharmaceuticals have revolutionized the treatment of serious diseases such as cancer, diabetes, rheumatoid arthritis or multiple sclerosis. As base material drugmakers usually use living species, such as plants, animal cells, bacteria, virus or yeast, which generally have been genetically modified.

Production of biopharmaceuticals is an extensive process, which has to be observed continually. About 250 in-process tests have to be carried out on biopharmaceuticals while small-molecule drugs need around 50 such tests. Because of the biologic origin of the base material, ensuring constant quality, efficacy and consistent results is extremely important. The final products are generally highly complex and consist of several thousand atoms.

As a consequence and in contrast to traditional generic drugs with their small-molecule structure, the development, production and approval process of biosimilars is difficult and requires a lot of expertise. The variability of the molecules makes an exact reproduction nearly impossible. This also refers to the originator products. Different batches of the same product can vary significantly.

Highly Dynamic Class of Drugs

Despite the complexity of the molecule structure and the development and manufacturing process, biosimilars belong to a highly dynamic class of drugs. Today eight of the top 10 drugs are from the biopharmaceutical sector, accounting for 81.9% of sales in that blockbuster field. Biopharma experiences a growth of 7% or 8% annually — double as much as the whole pharmaceutical market. Based on data of IMS Health, the worldwide market share of biopharmaceuticals rose from 11% in 2002 to 18% in 2012 and is expected to further increase to 20% by 2017.

Simultaneously more and more biopharmaceuticals go off patent. In Europe and the US about 12 biosimilars with the highest revenues will lose their patent protection by 2020, the German monitor Versorgungsforschung reported in 2013. Citi Research estimated that manufacturers of biopharmaceuticals would likely lose more than $360 billion in revenues over the next 10 years. In the same period a value of $110 billion will be transferred from innovators to biosimilars. Thomson Reuters, more conservatively, calculates that worldwide biosimilar sales will increase to $35 billion by 2020.

Big Deals and Small Caps

Coming from global sales of $1.3 billion in 2013, the industry thus has a huge growth dynamic.

"We believe that the market materially underestimates the magnitude and the timing of the impact on exposed innovator companies as well as the commercial opportunity for the biosimilar sponsors," according to Citi Research.

Other analysts call biosimilars one of the fastest growing segments of the pharmaceutical market.

Not surprisingly, Big Pharma extends its tentacles into the biosimilar business. Pfizer completed in September the $17 billion acquisition of Hospira, a global leader in biosimilars. Hexal, the generic unit of Novartis, has already built up a strong presence in biosimilars. And specialized biosimilar companies try to get a piece from the attractive pie, such as Pfenex, Epirus, Coherus or the German Formycon. The small company focuses on biosimilars that will come to market after 2020. It has three biosimilar candidates under development, two of them already licensed to the Santo Holding. One project will be entering clinical phase III trials soon.

Factors of Development for Biosimilars

The rise of biosimilars has several causes. One trigger is our aging society's need for more and better medical aid. As a consequence general health-care spending is continually rising.

Another important growth factor is cost. Because of their complicated manufacturing, biopharmaceuticals are about 20 to 50 times more expensive than chemical drugs. Depending on the therapy, total costs can amount to $200,000 per patient per year. AbbVie's rheumatoid arthritis drug Humira, for example, costs more than €5,200 per package in Germany and is one of the most expensive drugs ever.

Here biosimilars offer a significant cost reduction opportunity for the health-care sector.

Biosimilar commercial success is an important and necessary safety valve in allowing US and EU health-care budgets to continue to reimburse premium priced highly innovative therapies, such as cancer immunotherapies, in the wake of an aging population, according to Citi Research analysis. The German research institute IGES calculates with reduced costs between €11.8 billion and €33.4 billion from 2007 until 2020 in eight European countries.

Requirements For Approval

But the road to the market is not a fast-selling item for biosimilars. The hurdles are significant. In Germany, for example, the national pharmaceutical association VFA calls for detailed data on the quality of biosimilars as well as comparing non-clinical and clinical data for approval of biosimilars. The organization also calls for observational studies after approval of biosimilars, no automatic substitution in pharmacies, safeguarding of therapeutic freedom for the doctors and change of therapy based only on medical considerations and inclusion of the patients.

As a core criterion, national drug authorities require proof of similarity of the biosimilar to the reference product in clinical trials. Furthermore the legal approval criteria are an important factor for the development of biosimilars. This is evident in the different approaches in approval processes between the US and Europe. While that process in the US only recently got a legal base, Europe has had corresponding legislation since 2005. Therefore Europe with 19 approved biosimilars is well ahead of the US with just one.

Challenge "Interchangeability"

But this picture could change now. "In our view, the market underestimates the willingness of the FDA to approve competitive biosimilar entrants using extrapolation and interchangeability," according to Citi Research.

Especially the term "interchangeability" could become a challenge for the biosimilar industry. Ultimately, not only drugmakers of original products want to go further than biosimilars and try to achieve interchangeability. When the Affordable Care Act opened up a pathway for the FDA to approve drugs that mimic off-patent biologics, it created two tiers: products that are biosimilar — "highly similar to the original product... (with) no clinically meaningful differences" — and those that are interchangeable, which would be held to even higher standards.

The problem: So far no drug has met the standards for interchangeability. Hans Ebbers, a researcher at Utrecht University in the Netherlands and an expert on biosimilars, addressed whether the challenge of achieving interchangeability was an insurmountable hurdle.

The idea that an interchangeable biosimilar must perform the same in any given patient is part of what makes achieving interchangeability so tricky, because that's not exactly how studies on new biotech drugs work, Ebbers said.

"Such studies will only be able to address comparability on an aggregated (population) level," he wrote — not in every individual patient.

Beyond that, rules against exchanging a biosimilar for the original product "could be misinterpreted by prescribers to indicate that switching to a biosimilar might lead to unsafe situations," Ebbers and colleagues wrote in a Nature Biotechnology commentary.

How Will Physicians Respond?

This leads to the question of if and how doctors and patients will accept biosimilars. Doctor platform and community QuantiaMD surveyed 300 primary care physicians and specialists to find out how much health-care providers knew about the drugs. Of those polled, 78% said they were familiar with the term "biosimilar," but only 38% could name one under consideration for FDA approval that would be relevant to their patients, the magazine Medical Marketing & Media (MM&M) reports.

Only 17% of the doctors said they were "very likely" to prescribe biologics and, thus, the most likely to prescribe biosimilars in the future.

That's a problem for the biosimilar companies. Whether biosimilars pick up steam will largely depend on doctors and on their likelihood to order them for patients. At this point experts still see a lot of room for the drug companies to educate their clients.

Thorsten Schueller, freelance journalist, Grafing, Germany

Johnson Matthey Acquires Pharmorphix from Sigma-Aldrich

Johnson Matthey has acquired the Pharmorphix solid form research business from Sigma-Aldrich. This acquisition brings material science capabilities to Johnson Matthey's expanding European API and clinical supply services.

Pharmorphix is an established provider of solid form services, including polymorph studies, salt selection, co-crystallization, chiral separations and process scale up that are critical to successful drug discovery and development. This expertise also has valuable applications for process control, and can enable innovators or generics customers to find new forms for novel or existing pharmaceuticals.

"Pharmorphix serves an important niche area that complements our custom pharma solutions, API life cycle management offerings and existing US-based solid state science capabilities," said John Fowler, Division Director at Johnson Matthey Fine Chemicals, who also comments on the division's recent re-branding in an interview with CHEManager International on page 21 of this issue. "The acquisition adds further differentiating technologies to our advanced catalysis and complex chemistry capabilities, building on the expertise that our customers rely on to enable successful drug development and commercialization."

The Pharmorphix facilities and staff are located at the Cambridge Science Park, UK, where they will be fully integrated into Johnson Matthey's expanding Cambridge presence.

The sale of the Pharmorphix business by Sigma-Aldrich Corporation is not part of the conditions imposed by the European Commission (EC) in the context of the planned acquisition of Sigma-Aldrich by Merck, for which closing is expected within the next one or two months. (mr)

Pharma CDMO Vetter Embarks on a €300 Million Investment Strategy

Ravensburg, Germany-based contract development and manufacturing organization (CDMO) Vetter has announced that the company will invest approximately €300 million to expand and upgrade its manufacturing facilities over an estimated five-year period. The upgrades are being driven by a changing healthcare market that is affected by issues such as ever-more complex molecules, smaller batch sizes, and increasing regulatory requirements, the company says.

The first of the facility expansions are already ongoing at several of the company's German locations including its 'Ravensburg Vetter West' center for visual inspection and logistics. Structural work for the facility enlargement, which will offer more than double of its current capacity, is completed with the site being on schedule to become fully operational in 2017. In addition, the Ravensburg Vetter South production site has also been designated for significant enlargements as is another facility in the same town where initial construction activities began in 2013. All three site expansions will result in additional capacities for drug product manufacturing and logistic sevices.

A central technology element of the planned upgrades will be the implementation of an in-house made improved restricted access barrier system (RABS) concept which will contribute to increased operational excellence in aseptic manufacturing.

"We are continuously monitoring and reacting to a changing marketplace and are pleased that we are in the position to be able to make these strategic investments to further develop our sites and meet these challenges," said Vetter Managing Director Peter Soelkner. (mr)

Brazil's Pharma Market Value Will Approach $48 Billion by 2020

The Brazilian pharmaceutical market will expand in value from $29.4 billion in 2014 to reach approximately $47.9 billion by 2020, representing a strong compound annual growth rate (CAGR) of 8.5%, according to a report recently published by GlobalData. The report states that Brazil's increasingly elderly population, which will lead to a rising incidence of chronic and lifestyle-associated diseases, as well as the country's robust investment in healthcare, will be key drivers of market growth during the forecast period.

Joshua Owide, GlobalData's director of Healthcare Industry Dynamics, says that Brazil has emerged as a global manufacturing hub for pharmaceutical and biotechnology companies, with countries such as India investing heavily in the manufacturing sector after former Brazilian health minister, José Serra, invited investment from generic companies.

Owide comments: "As a consequence, Brazil is now one of the most attractive and promising pharmaceutical markets in the world. Indeed, its pharmaceutical market value has increased considerably over the past six years, having more than doubled from $14.1 billion in 2008."

The report also shows that Brazil's market for generic drugs is witnessing rapid growth, with almost all of the country's generics procured by the public healthcare system.

Owide continues: "Government initiatives, such as the People's Pharmacy program, have been responsible for the increased usage and availability of generics, further boosted by the announcement of $34 billion investment in the Brazilian healthcare sector in 2014."

According to the US Department of Commerce, approximately 80% of pharmaceutical companies in Brazil are domestic, and this number has been increasing since the Generic Law was introduced in 1999. However, multinational companies currently generate higher revenues than domestic companies." (rk)

The Biggest Side Effect of Making Medicine

How to Manage Intellectual Property and Patent Law

International intellectual property regulations are doing serious damage to the pharmaceutical industry and, by extension, to the health of people around the world. The core of the problem: growing global concern about how to ensure affordable access to medicine without damaging the initiatives that sustain pharmaceutical research. Attempts to address the issues have resulted in significant disagreement between developed and emerging economies about just how much protection should be available to companies that develop drugs.

Dr. Ralf Boscheck, IMD

Members of the World Intellectual Property Organization are trying to resolve their differences on how — and even whether — emerging market countries should move to a framework that offers greater IP protection, but the results to date are not promising. Access-to-medicine advocates propose measures based on national income levels; branded drug producers want a time-based transition schedule; others argue that patent protection should be linked with the UN's Human Development Index, which is a relative scale with frequently changing outcomes and policy incomes.

The Case for Strong Patent Protection

Developed countries, particularly the United States, usually try to commit emerging economies to more stringent intellectual property right rules in exchange for bilateral concessions in other areas of trade. These arrangements typically involve an extension of patent terms and data exclusivity as well as limits to parallel trade and accelerated marketing approval for generic producers.

Strengthening intellectual property rights, they argue, incentivizes research on diseases that are specific to developing countries and promotes technology transfer through the localization of R&D and production investments. This then contributes to improving typically inadequate health service infrastructures.

The Counterargument: Cost and Accessibility

For many observers in emerging economies, however, strict protections on IP translate into higher prices for life-saving drugs, delayed generic competition and weakened local production. As a result, countries like India have taken the lead in employing patentability criteria that may set new standards.

In 2005 India amended its patent law in line with the international agreement on trade-related aspects of intellectual property rights (TRIPS). However, it also inserted a provision preventing the patentability of substances including salts, esters and metabolites, and other derivatives and combinations of previously known compounds. It also banned the patenting of new uses of existing compounds.

This provision has since been used to deny drugs such as Sutent, Pegasys, Tarceva and Glivec the same patent protection available to them elsewhere.

Attempts to challenge the law as not being TRIPS-compliant failed, with India's supreme court ruling that the provision was, among other things, intended to ensure that the country's citizens had easy access to life-saving drugs and to prevent "evergreening" of patents.

However, research published last year casts doubt on just how effective this approach is, at least regarding the first part: A review of 184 drugs between 2000 and 2009 concluded that only 60% of the products in US markets were available to Indian patients by 2010. Half of the drugs had a launch lag of more than five years, while a quarter lagged by more than nine.

The Evergreening Debate

Evergreening is a series of techniques used by pharmaceutical firms to continue protecting their drugs after the initial patent expires in order to maximize their return on R&D investments. That is, they prevent or limit the manufacture of generic drugs for longer.

The specific approaches used are numerous but include continued differentiation of branding, dosing, formulation or mode of action; patenting active compounds or co-specialized delivery systems; and seeking to expand a compound's market through approvals for new indications.

Critics of evergreening argue that patients miss out on the benefits of cheaper generic drugs. However, they also usually neglect the existence of regulatory and market responses that limit the risk of abusive patenting.

For instance, patentability typically requires an invention to be novel, non-obvious and useful in the sense of capable of industrial application. The coloring and scoring of a drug may seem purely aesthetic, but if it can be shown to improve patient compliance, and therefore efficacy, that is novel and not obvious, and must therefore be patentable. In short, properly designed and implemented patent systems already deal with some common evergreening concerns.

Reverse Payments

Both the US and EU systems allow companies to legally challenge patents and potentially speed up generic substitution. In Europe, generic companies have nine months to revoke a patent through a process administered by the European Patent Office. In the US, the Hatch-Waxman Act offers producers of bioequivalent generics that certify not to be infringing any valid patent surrounding the original compound an abbreviated new drug application.

When this happens the patent holder has a choice: contest the application, with all the costs and uncertainty this involves; ignore it, and plan on losing up to 80% of its total sales within a year; or pay the generic manufacturer not to get involved for a defined period.

This last approach, known as a reverse payment or "pay for delay," can mean that a big pharmaceutical company that has already spent hundreds of millions of dollars developing a drug can find itself paying out millions more to another company to hold on to its own IP in what could be characterized as a form of commercial blackmail. Or, looked at the other way, big companies are using their financial heft to prevent competition that could lead to cheaper drugs for patients. However, if a settlement allows entry before any litigation would be terminated and patent expires — whichever comes first — the apparently anticompetitive agreement may actually improve consumer welfare.

For more than 15 years, pay-for-delay deals have extended the life of contested pharmaceutical patents, and given the indeterminate effect on consumer welfare, the US Supreme Court has been unwilling to take a definitive position either way. Just as in other areas of dispute between intellectual property rights and antitrust law, settlement deals present a substantial conceptual challenge to be translated into efficient regulatory standards. Such difficulty, however, does not justify a call for additional actions against evergreening of pharma patents or the use of any regulatory shortcuts.

Conclusion

Escalating health-care expenditures and the need to ensure access to affordable medicine in both emerging and emerged economies are fueling calls for containing evergreening practices around the world. But such practices are the necessary outcome of a system that responds to market incentives and is already sufficiently controlled by established patentability standards and policies to determine patent term extension. Even reverse payment arrangements may ultimately deliver consumer net benefits. They present a challenge for efficient rule writing and a reminder of the need for better and coordinated policy analysis.

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The Future Lies in the Genome

Continued Page 1

You are currently in the process of integrating the consumer care businesses of Merck & Co and Dihon Pharmaceuticals. How do these businesses fit into your strategy of a life science company with strong focus on innovation?

K. Malik: These are different levels of innovation. Innovation in our understanding is anything that is new and that has value for the customer. It can be a new scientific principal outcome of research in oncology. But it also can be a new formulation or new packing in consumer care. Both innovations may have much meaning for the end user, for the patients or consumers. In that context consumer care is a very important part of our Bayer family. We don´t want to be a pure pharma company. We don´t want to be a pure crop company. It is important to us to have a diversified portfolio within the life sciences.

You say that a kind of revolution that took place in life sciences during the last 10 to 15 years. Can you explain what kind of revolution this has been?

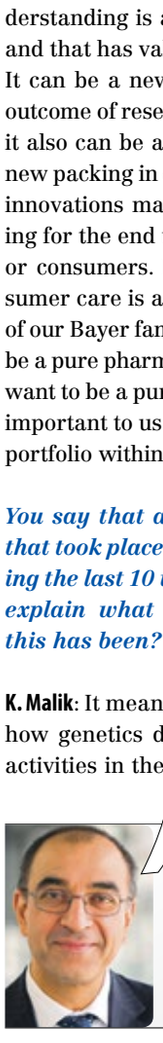
K. Malik: It means our understanding how genetics determine life. Many activities in the past 10 to 15 years laid the foundation to understand the genome of living species. Back in the early 1990, the Drosophila Genome Project was launched and it took ten years to complete. At that time it took five years and $70 million to sequence the genome of a plant called Arabidopsis. Today you can sequence the human genome for less than $1,000. So there has been an extraordinary explosion in terms of our technical capabilities of sequencing a complete genome. But now we also see new techniques on the markets coming from research in the area of analyzing and editing such information.

Will this revolution continue? Do you have an idea where we will be after the next 10 years?

K. Malik: The costs of the sequencing of the genome will come down further. This technique developed from an experimental endeavor to what is now a research tool and will becoming much more practice when you go to your doctor. In future he will be able to further determine your illness by analyzing your genome. Apart of this our capabilities of looking at the genome with new technologies and targeting and insertion and removal of genome sections will become more elaborated. I think this will open up a lot of new possibilities for new therapies principles.

In Oncology you see a high potential in immuno oncology. How can you realize this potential?

K. Malik: In oncology we brought over the last years significant innovation to the market, for example Nexavar for kidney and liver cancer. Stivarga is for treatment of colorectal cancer, and Xofigo which is for prostate cancer. Today we have a very healthy pipeline with innovative compounds and products. Currently there is a lot of noise in oncology how we can utilize the own immune system of bodies to fight cancer. A couple of agents are coming to the markets to unveil the tumor so that the body's immune system can fight against it. We are also active in this area. We have some important internal projects, but also a very significant partnership with the German Cancer Research Center. We are still very much in the early days of immune oncology. But I think there will be further ways to innovation.



> *It is important to us to have a diversified portfolio within the life sciences.*
>
> Kemal Malik, board member for innovation, Bayer

Will immuno oncology become an important field in the fight against cancer?

K. Malik: The immuno agents that are coming to the markets will be used in combination with other products, more traditional compounds such as small molecules. Cancer will be a more chronic disease and patients will take a cocktail of drugs as we have seen in HIV.

You mentioned the synergies between health care and crop science. How does this affect your R&D activities in these areas?

K. Malik: We always look for synergies across our businesses. As a consequence our technology platforms apply to all our activities. Our researchers look for similarities in our businesses and thus we realized that there is a lot of commonality between all our life sciences businesses and a lot of information to share. Our understanding of the genome helped us a lot to see the commonality of the genetic system between humans, animals and plants.

Can you give an example?

K. Malik: One example is the respiratory chain in cells. As Mitochondria are the cells' "powerhouse", new products from CropScience were able to treat fungi or nematode infections in plants by cutting this energy supply. So it can prevent them from destroying the harvest. This principle works also for dangerous lung or heart worms in animals. And the respiratory chain is also a target in oncology research as cancer cells are using a lot of energy. This is an example of how Bayer understands common pathways across species. Finally, this allows us to use our R&D money in a more efficient manner.

In one of your activities you promote the so called open innovation approach. Here you have projects as Grants4Apps or Grants4Targets. What is it and why are you doing this?

K. Malik: "Grants4Apps" is a new model of Bayer's open innovation approach in the area of digital health. We are looking for novel software, hardware, technologies, or processes that could improve health outcomes or pharmaceutical processes. We provide grants to health IT startup companies under our crowdsourcing program, offer office space for digital startups in our Grants4Apps Accelerator at our premises of Bayer HealthCare in Berlin. The startups in the Accelerator have 100 days to evolve their app-projects in the area of health. Our financial support is about €50.000. In addition, we provide senior manager support for the startups. We started this project last year in Germany, Denmark, Portugal, Belgium and the UK. We aim to further expand this in the world.

> *Today (in oncology) we have a very healthy pipeline with innovative compounds and products.*

This gives the impression that Bayer puts its strategy of generating knowledge on a new basis. Is this correct?

K. Malik: We have multiple ways of sourcing innovation. We have partnerships with biotech companies, startups and research institutions. Projects like Grants4Apps are another and a new source. We like to have this mix of sourcing. This doesn´t mean that we replace traditional licensing or mergers and acquisitions. These new sources are just another string to our bow.

As the responsible person for innovation at Bayer – how do you manage innovation? How do you bring all ideas and projects together?

K. Malik: If you look at the scope of innovation across Bayer we have three distinct parts. About a third what we do is quite routine, just stepwise in incremental innovation. Then you have about 50% or 60% of your activities that require more significant innovation. And finally we have 20% which is really breakthrough. We can´t just do breakthrough activities, that would be quite risky. So we have a mix of how we approach innovation. And we have a very systematic way of managing that. We have governance in place to ensure that we retain the capability for innovation.

Is it today more difficult to be innovative than some decades before?

K. Malik: Actually it is easier now than 20 or 30 years ago. Our understanding of disease biology and the information sharing is much greater now. Secondly, the focus around innovation is not limited to our company, but it´s the whole world. In many ways I have the best and easiest job in the company because everyone is interested in innovation. Everybody knows that this is the sustainable way for the company to grow.

You have another project called CoLaborator. What is this about?

K. Malik: We launched this project in 2012. We give startup companies in the life science area access to space on our campus. There they have access to our research environment and senior researchers. Currently we do this on two sites, in San Francisco and in Berlin. Our aim is to give these companies access to Bayer, but also to give Bayer access to the knowledge of these companies. This also has an effect on our culture. The entrepreneurship partnering brings a different atmosphere and changes the culture in our organization - it makes us a little bit more entrepreneurial.

Which are the most important innovation challenges you and we all are facing in life sciences, health care or crop sciences?

K. Malik: We have external pressure in terms how to feed the world and in medicines. We as a life science company have the responsibility to contribute to solving these challenges. The general question in health care is how we can utilize new technologies and platforms to move forward in innovation. There were two revolutions in the past. One was the advent of small molecules. The next were large molecules. The third one which is coming, are cell-based therapies. For the understanding of that area we need a key technology platform in the next years. ■

Bayer Realigns after Covestro Split

After shedding its plastics business Bayer MaterialScience – now trading as Covestro – the Bayer group is reorganizing its business structure, replacing the strategic management holding with an integrated organization that from January 2016 will have three divisions: Pharmaceuticals, Consumer Health and Crop Science.

The aim of the new structure, CEO Dr. Marijn Dekkers said, is to "provide the best possible support to Bayer's strategy as a leading life science company and to put ourselves in an even stronger position vis-à-vis our competitors. As the Bayer managing board in future will have responsibility for all business operations, the company has appointed the heads of the Pharmaceuticals and Consumer Health divisions of its Healthcare subgroup, Dieter Weinand and Erica Mann, along with the head of the CropScience subgroup, Liam Condon to the managing board.

When the HealthCare subgroup is dissolved, the radiology business will be assigned to the Pharmaceuticals division. In future, Consumer Health will comprise the present Consumer Care division. The CropScience subgroup will be known as the Crop Science division. The division's former Animal Health unit will report directly to Liam Condon.

Bayer said the divisions will focus on core competencies close to their businesses, including research and development, production, and sales & marketing. They will be supported by integrated functions such as Human Resources and Procurement and by global services. The existing Technology Services company will become the Engineering & Technology function. Bayer Business Services, the company bundling information technology and business support service, will remain a separate legal entity that is to see further expansion. (dw) ■

Turing Says it Will Cut Daraprim Price

Turing Pharmaceutical, the company that sparked an angry backlash for raising the US price of Daraprim (pyrimethamine), a drug for treating the deadly parasitic infection toxoplasmosis – in combination with a sulfonamide – more than 50-fold has said it will drop the price again, but did not disclose by how much.

After obtaining marketing rights to the drug in the US – the only country in which it has been approved – from Impax Laboratories in August of this year, Turing hiked the price overnight from $13.50 per pill to $750.

"The acquisition of Daraprim and our toxoplasmosis research program are significant steps along Turing's path of bringing novel medications to patients with serious disorders, some of whom often go undiagnosed and untreated," Martin Shkreli, CEO and company founder, said when announcing the rights acquisition.

"We intend to invest in the development of new drug candidates that we hope will yield an even better clinical profile, and also plan to launch an educational effort to help raise awareness and improve diagnosis for patients with toxoplasmosis," he added.

Shkreli told US media the new price would make the medication more accessible. "We've agreed to lower the price of Daraprim to a point that is more affordable and is able to allow the company to make a profit, but a very small profit," he said.

In particular because toxoplasmosis is most threatening to people with compromised immune systems such as HIV sufferers, as well as to pregnant women, the company has come in for sharp criticism from health professionals as well as the general public. Even presidential candidate Hillary Clinton weighed in, calling the hike "outrageous." (dw) ■

Sanofi and Lilly Settle Lantus Patent Row

France's Sanofi and US drugmaker Eli Lilly have resolved their patent dispute over insulin drugs. The settlement ends a US lawsuit brought by the French producer of Lantus SoloSTAR (insulin glargine) in response to its US rival's pursuit of regulatory approval for a competitive product. The two companies also agreed to discontinue similar disputes worldwide. As part of the agreement, Lilly will pay royalties to Sanofi in exchange for a license to certain Sanofi patents and will not sell its insulin glargine product on the US market before Dec.15, 2016. The agreement does not extend to Lantus (vial), Toujeo or combination products. (dw) ■

Bavarian Nordic Wins Janssen Ebola Subcontract

Bavarian Nordic, a Danish biotechnology company, has been awarded a €9 million subcontract from Crucell Holland, a group company of Johnson & Johnson's pharmaceutical subsidiary Janssen.

The primary contract was awarded by the US Biomedical Advanced Research and Development Authority (BARDA) to Janssen to support the advanced development and manufacturing of the Ebola prime-boost vaccine regimen which consists of Bavarian Nordic's MVA-BN Filo and Janssen's Ad26.ZEBOV. As part of the accelerated development program, Janssen has initiated multiple clinical studies of the prime-boost Ebola vaccine regimen in Europe and Africa. To date, Bavarian Nordic has produced and delivered the bulk equivalent of over 1 million doses of its vaccine. (dw) ■

Growth Amid Risk

Trends, Challenges and Regulatory Requirements Affecting the Biopharma and CDMO Industry

Interest in the biopharma industry continues to grow, making the development and manufacturing services of the biologic entities for both drug substance and drug product a more integral part of Patheon's business. We have seen a demand — specifically from small to mid-sized companies — for contract development and manufacturing organizations (CDMOs) to enter the biotech business (including biosimilars) from development through manufacturing and commercialization.

Dr. Stefano Chiaramonti, Patheon

However, moving into this industry comes with challenges. The biopharma industry is risky and expensive. For example, in the biosimilar world, the vast amount of data needed to compare these drugs with market-leading products makes the projects very costly. Additionally, many biotech products don't transition into Phase 3 clinical trials, with many of them not even surviving past Phase 1 because of toxicity or lack of efficacy. Lastly, projects are often delayed by the complexity of active pharmaceutical ingredients (APIs). The complexity of biotech products makes them difficult to handle during the manufacturing process and the related analytical testing. Their management indeed requires a high level of expertise.

Looking Beyond Cost

Although the biopharma sector is strewn with roadblocks, highly reliable CDMOs are expanding as demand continues to increase. Clients are becoming more selective when deciding which CDMO to partner with to develop their product. While cost has always been an important factor when considering a CDMO, clients have recently shifted to a much broader examination, focusing on reliability as the most important element.

Additionally, as the product and the industry landscape are constantly changing, flexibility and the ability to troubleshoot become critical traits that clients seek in a CDMO. Flexibility of the project management team is vital to creating a successful client-CDMO relationship, while problem-solving skills are just as important since clients typically not only have products that need to be developed but also issues to be analyzed. Other key characteristics such as quality, expertise and end-to-end services are what make clients so willing to pursue and commit to fully integrated CDMOs like Patheon, which can offer both drug substance and drug product services.

Patheon's Ferentino, Italy, site specializes in the development of sterile dosage forms.

Expertise On The Rise

Patheon is continuously proving itself as a leader in the CDMO industry, meeting clients' expectations regarding quality, technical expertise, and end-to-end services and project management. A commitment to quality and customer service permeates every aspect of our business. Our clients demand reliability and transparency, and our Right First Time and On-Time Delivery philosophy is ingrained in our company culture. This system, which also enables clients to follow the entire development life cycle of their product, fosters personalized and long-lasting partnerships.

Additionally, the regulatory environment for both the sterile development and commercial manufacturing businesses continues to become more tightly monitored. With these strict regulations in place, there is a high expectation — particularly for complex biotech products — to have the product fully characterized and evaluated, specifically for critical process parameters (i.e., the evaluation of the robustness of the lyophilization cycle), so that it is guaranteed to be of high quality by the time it reaches the registration and validation stages.

Finally, the technological expertise expected of CDMOs is drastically increasing, and sites are becoming more automated as machines like automatic loading systems and restricted access barrier systems (RABS) are being used more and more at manufacturing facilities to maximize efficiency and increase the sterility assurance effectiveness.

Simplified Services

A key differentiator for Patheon is its fully integrated offering, Patheon OneSource, an end-to-end solution focused on increasing simplicity, speed and quality by giving clients just one point-of-contact for all supply-chain services. Clients are becoming more and more interested in services such as this, as they drastically simplify the development process and supply chain.

To be valuable, a CDMO needs to be composed of the right people, the right processes and the right equipment, and if these important factors are not in place, target objectives cannot be met for clients and their patients.

The CDMO business serving the biopharma industry is changing quickly, and Patheon's Ferentino, Italy, site is a prime example of it. Within just two years, we have doubled the size of projects, number of employees and clients served by the site, an indicator of how quickly things are changing within the market. Being a reliable provider of high-quality drug development and delivery solutions brings more clients to partner with to develop and launch their products.

Dr. Stefano Chiaramonti, PDS, group director, Patheon, Ferentino, Italy

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Knowledge of Proteins to Guide Pharmaceutical Industry

Knowledge of the properties of proteins right down to atomic level is essential for making it easier and faster for the pharmaceutical industry to manufacture protein-based drugs in liquid form. Over the next four years, a joint European project, PIPPI, with Technical University Denmark (DTU) as the overall coordinator, is to develop a public database with cutting-edge knowledge about the properties of proteins in pharmaceutical formulations.

The average age of Europe's population is rising, which translates into financial challenges for the healthcare sector. Greater focus is also being devoted to manufacturing safe and risk-free drugs, while the requirements for evaluating new drugs and their possible side effects are becoming stricter. All of this has moved the pharmaceutical industry towards protein-based drugs, which have high specificity and relatively few side effects. But there is very little knowledge of the way these proteins behave in the solutions in which they are sold.

Together with a large number of partners from both the pharmaceutical industry, European universities, and other stakeholders, DTU has received DKK 30 million from Horizon 2020. This is for the development of a data base over a four-year period, which is to ensure more efficient development of the very extensive and protracted screening process that protein-based drugs, e.g. next generation insulins and growth hormones, undergo before being put on the market.

„Drugs as we know them from the pharmacy typically consist of an active substance such as paracetamol in painkillers. In addition to the active substance, there are other substances in the finished tablet, for example, excipients facilitating that the tablet is dissolved in the right way and stabilizes the active substances. Similarly, excipients are added to protein solutions to increase the stability of proteins. Today, the pharmaceutical industry carries out very extensive screening of all these excipients to test their performance with the active substance. It is this screening process that we hope to be able to streamline with this project," explains Pernille Harris, associate professor at DTU Chemistry, who is the overall coordinator for the entire project.

Few universities in Europe have formulation of biologics as a scientific subject. Consequently, the pharmaceutical industry is required to train hired scientists.

"We are proud to be part of a consortium comprising leading researchers in protein and pharmaceutical science in Europe. We have high expectations that PIPPI will help boosting the knowledge in the field. Furthermore, we hope that PIPPI will result in increased focus to the field, so that Europe can catch up with USA and Asia," says Jens Bukrinski, senior scientist at Novozymes.

While the substance paracetamol is a small organic molecule, which will keep for a long time in a tablet, protein-based drugs are more unstable, the challenge in respect of these drugs is, for example, to eliminate the risk of the proteins, in their aqueous solution, precipitating into the solution.

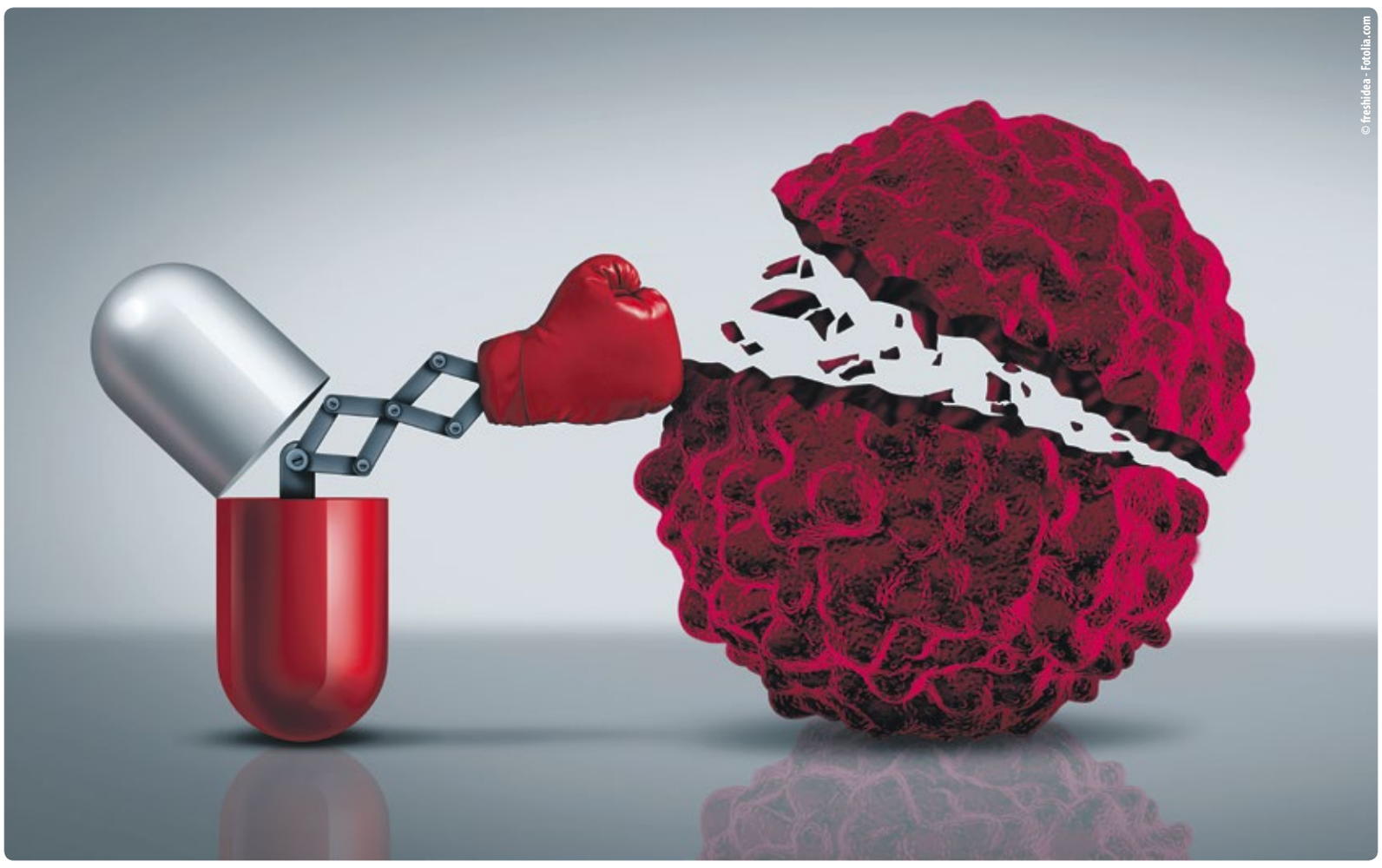
„Today, the pharmaceutical industry manufactures the drugs by testing and screening until they obtain a solution that keeps the active substance suspended in the liquid. The idea of the project is to establish as many as 15 PhD positions with the various partners in the project at the same time. Initially, a comprehensive protein library will be established, representing the different properties that proteins can have, for example in terms of size, whether they are positively or negatively charged, hydrophobic or flexible. Subsequently, their abilities to interact with various substances will be characterized and everything will be gathered in a database," explains Pernille Harris.

Ultimately, knowledge right down to the atomic level about the different types of proteins may make it easier to predict the behavior of a similar protein targeted for use by the pharmaceutical industry. The aim is for the protein to be stable in the solution, and although this result can be achieved today, getting there may be a long and hard process. (rk) ■

Innovative Medicine with Rising Productivity Targets

Current Challenges and Potentials for R&D Efficiency in the Pharmaceutical Industry

The need to get products quicker to market, to ensure greater regulatory compliance and to boost efficiencies while reducing operational cost is a challenging goal. Owing to the dynamic market environment, research-based pharmaceutical companies are committing to rising productivity targets.




Gerd Grimm, KPMG


Dr. Ralf Kaspar, KPMG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Dr. Andreas Ries, KPMG

The causes for rising productivity targets are manifold and related to factors such as patent expirations for blockbuster drugs, increasingly cost-constrained health-care systems or the development of cheaper generic drugs by other market participants. On the other hand, drug R&D costs of bringing a new biological or chemical product to market have significantly increased over the last decade. The increase also applies to R&D timeframes whose delay is due to more complex compliance and regulatory requirements.

The evaluation of the EU R&D Scoreboard 2014 revealed that pharmaceutical companies operating in biotechnology increased R&D by 20.4% (share of R&D investment) whereas the traditional pharmaceutical companies showed a slight decrease of 0.2%, which is mostly due to the fast development of biotechnology.

Innovation Versus Cost Optimization

After a decade of decline, innovation is on the rise for the pharmaceutical industry because of an upturn of approval rates, according to results from KPMG's Global Life Sciences & Development Survey in 2013. Innovation is the major strategic success driver, which has to be accompanied by a rapid market launch of the new product for generating profit. Nevertheless, ambitious productivity targets, which are often supplemented by cost optimization programs, have to be met. An exploitation of cost-cutting potential, however, may have a significant limiting or negative effect on companies' innovative strength if not carried out specifically. Adverse effects usually arise if cost reduction initiatives lead to the delay of programs, a lack of empowerment, delegation upward or frustrated scientific experts.

Smart Compliance Versus Bureaucracy

One of the main challenges regarding higher productivity is managing risk without restricting innovation. Hence, successfully achieving productivity targets means mitigating the risks that are connected to medical innovation processes. The pharmaceutical industry is faced with a higher-than-average level of R&D project risks, which is reflected by high attrition rates.

At the same time, pharmaceutical companies operate in one of the most heavily regulated industries and have to cope with high compliance and regulatory standards. As the price of failure places more and more at risk, there is a strong motivation to make more conservative research that may restrain the acceleration of drug discoveries. Similar reasons may also lead to additional testing on active ingredients with lower benefits. Both of these motives result in an increase of R&D costs as well as in an extension of the R&D timeframe, which is directly followed by a delay in market launch. Being only the second on the market behind a competitor can have severe consequences regarding painful profitability losses and a jeopardy of return on R&D investments.

Apart from balancing smart risk-taking and fulfilling complex compliance as well as drug safety and efficacy requirements, a missing coherence of scientific and business requirements is considered as another main challenge to productivity for R&D executives (compare fig. 1).

Barriers For Innovation

For enhancing R&D productivity within the drug development process, it is crucial to understand the underlying interfaces between inputs, outputs and outcomes (compare fig. 2). R&D efficiency outlines the ability of an R&D organization to transfer inputs (e.g., ideas, R&D investments or research effort) into tangible outputs (e.g., new active ingredient launches), whereas R&D effectiveness can be represented as the ability to provide outputs with certain intended and desired qualities (e.g., medical value to patients or physicians as well as a profound financial outcome). R&D productivity encompasses both R&D efficiency and R&D effectiveness.

For executives the main barriers for a successful improvement of R&D productivity are a lack of business training for R&D leaders, insufficient information flows between project organization and cost centers, an inadequate involvement of other neighboring functions and in particular excessive administrative work (non-project time) for scientists, which is hindering R&D potential. The presence of non-standardized processes as well as complicated approval and decision processes are considered to be further obstacles for a leaner drug development process.

Untapped Opportunities for R&D Productivity Enhancement

Considering what is needed for improving R&D productivity — several unexploited potentials in pharmaceutical companies should be examined. A large part of improvement potential still lies in complexity reduction of processes and interfaces. Some companies get stuck between cost-cutting initiatives on the one hand and the ramp-up for product launches on the other hand, which leads to frustration of experts and co-workers who have to implement both initiatives.

Overarching and unspecified percentage-cuts can work in opposite directions as it bears a high risk of disrupting the R&D flow and reducing the company value. For instance, inadequately aligned outsourcing initiatives have jeopardized data quality and cut through trusted and established networks.

Based on the fundamental premise that scientists should focus on science, it has to be secured that innovative research is not confronted with bureaucratic obligations, so that non-medical tasks (e.g., scheduling, resource management, administrational oversight) are in a right balance with the risk and complexity of research or clinical projects.

Admin and budgeting processes should be improved or centralized where needed and removed where possible. An activity-split-analysis helps to identify tasks with an administrative or transactional character that can be moved out from the processes/responsibilities of medical experts to a center of excellence with appropriate skills and economies of scope without disrupting the R&D flow. The positive result is more focus on customer and patient needs. The establishment of a medical center of excellence can reduce the workload of medical experts regarding project management; for example, a dispatcher coordinates the schedule and necessary interaction during the development and implementation of a study so that all participating functions are optimally aligned.

For an enhancement of R&D productivity the unspecific roll-out of standard operating procedure (SOP) trainings has to be changed to an SOP approach at the right time (when needed), with the adequate content (what is ahead in the next time period) and for the right medical experts (who in the department and who within a certain role description). The benefit is that SOPs take on real meaning for the reduction of risk instead of being treated only with half attention by clicking through the SOP training program.

Unnecessarily precise requirements regarding the business planning and budgeting of studies should be challenged in two ways. First, bottom-up planning without an appropriate guidance can lead to frustration of the involved medical experts because after a first budget proposal is created, top-down changes of senior management render the first draft obsolete and require a complete rework of the budget. Second, based on the effect that in early studies, the attrition rate is significant, a lot of work that goes into backups of business plans and approval templates can be saved through a lean approach whereas phase 2 and phase 3 studies should be planned with increasing details and requirements for precision as part of a smart risk-taking approach.

Figure 3 gives an overview of some potential strategies for boosting R&D productivity.

Nevertheless, the achievement of productivity targets strongly depends on further organizational key success factors. A coordinated approach with financial control of R&D productivity improvement is needed. Finance and Controlling should be involved from the beginning and maintain the overview of business cases and financial target setting. Change management has to be integrated while processes are simplified so that people experience quickly the added value of new structures.

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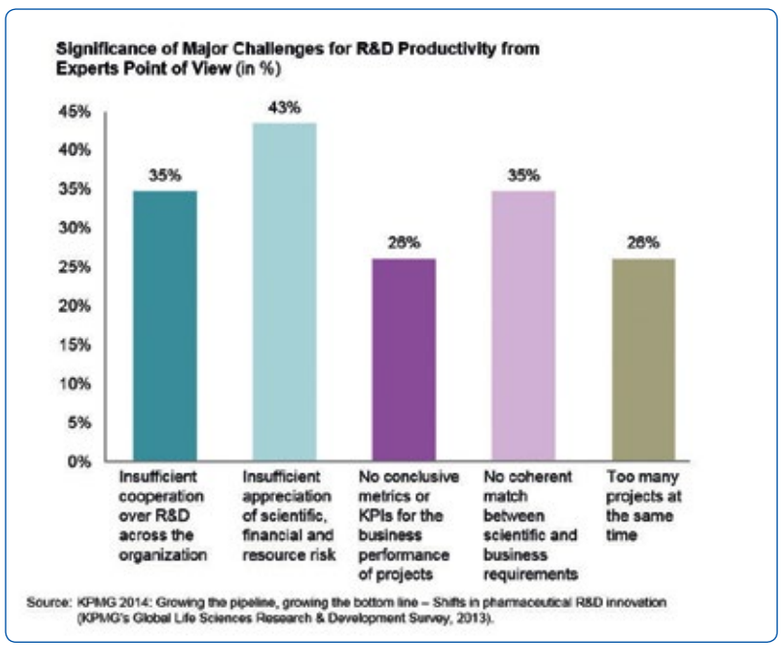


Fig. 1: Top Challenges for R&D Productivity

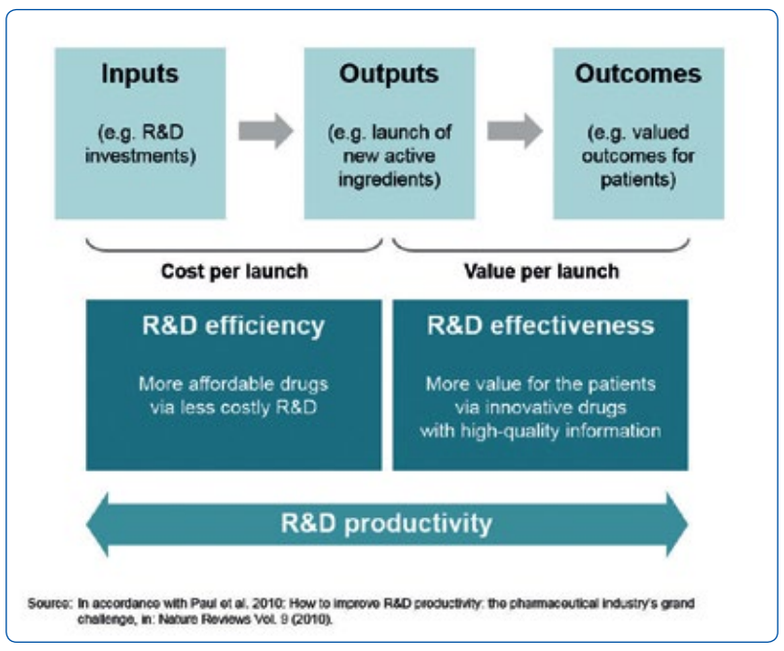


Fig. 2: Dimensions of R&D Productivity

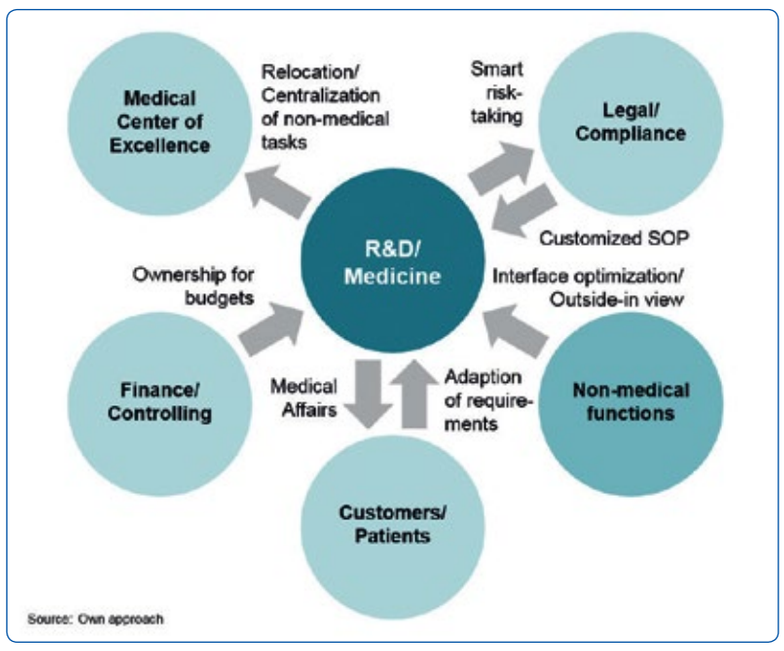


Fig. 3: Framework for R&D Productivity Enhancement

Easy Access

Johnson Matthey Rebrands Fine Chemicals Division as Key Part of a Customer-Focused Initiative

In late June, Johnson Matthey announced that it will divest its Alfa Aesar Research Chemicals business to Thermo Fisher Scientific. Following the divestment the company has unveiled a new branding for its Fine Chemicals Division that provides pharmaceutical customers around the globe with a range of services and solutions, including active ingredients, custom development services, catalysts and chiral technologies. The rebranding is seen as a key part of a customer-focused initiative to unite and realign these diverse fine chemicals capabilities and will enhance access for customers to the company's chemistry capabilities and technologies, according to John Fowler, Division Director at Johnson Matthey Fine Chemicals. Dr. Michael Reubold asked John Fowler to expand on the rebranding and provide a deeper insight into the strategy.

Manufacturing active pharmaceutical ingredients at Johnson Matthey's Riverside facility in the USA.

John Fowler,
Johnson Matthey Fine Chemicals

CHEManager International: After the completion of the Alfa Aesar divestment the Fine Chemicals division will have two principal business units left: API Manufacturing and Catalysis & Chiral Technologies. What are the strategic plans for both businesses?

J. Fowler: Our API Manufacturing and Catalysis & Chiral Technologies business units together provide our complete range of custom products and services for companies developing pharmaceuticals, agrochemicals and other specialty chemicals. Within these business units we have numerous specialized technologies and capabilities that our teams can draw upon. We work collaboratively across the ten different global sites within these business units to deliver customers' products and solve their complex chemistry challenges.

Over the past few decades, we have built the Fine Chemicals Division on a number of high quality brands that retained individual identities and operations. Recently, we have been realigning our service capabilities across the API Manufacturing and Catalysis & Chiral Technologies business units to develop a single, cohesive brand. The unified brand brings together our diverse chiral and catalysis technologies, our world-leading opiates and narcotics capabilities, and global API development, life cycle management and manufacturing facilities.

Strategically we will be focusing on growth markets where our technologies and capabilities provide us with sustainable competitive differentiation.

How will the rebranding change the structure and organization of these activities?

J. Fowler: The main purpose of the current rebranding is to simplify how we describe our businesses and activities, and enable our customers to recognize and value our capabilities and offerings more fully. We are highlighting our diverse services under four core customer-focused offerings: Custom Pharma Solutions, Controlled Substances, Catalysts, and APIs & Life Cycle Management.

We believe that this will help customers to understand more clearly the breadth and depth of Johnson Matthey Fine Chemicals technologies and capabilities, and how our offerings can support them to achieve their own business goals.

Which market trends do you see as most important for your businesses?

J. Fowler: The pharmaceutical industry remains under increasing pressure to discover and develop innovative products, and quickly bring these successfully to the market. We're finding that both innovator and generics companies require more R&D expertise and specialist chemistry capabilities from their partners, but very few companies can provide these in breadth and on a global scale. Customers come to us for our unique expertise in solving the most challenging chemistry and engineering scale-up problems to enable more innovative synthetic routes.

> ***Innovator and generics companies require more R&D expertise and chemistry capabilities from their partners.***

The ability to combine this with our large-scale, global manufacturing services is also important for accelerating project delivery. Having a partner that can provide development, scale-up and commercialization aspects of customer projects saves significantly on the time and complexity that would be required in switching to a new supplier. It also helps to reduce risk and protect IP, as well as maintain the integrity of the supply chain, which are all matters of increasing concern for fine chemicals companies.

Our core capabilities – especially in and around catalysis and sustainable technologies – are becoming increasing valued by affiliated industries such as agroscience and flavor & fragrances, as the technical challenges are often similar to those found in the pharma industry. We continue to see these industries as important sources of growth for our catalysts and chiral technologies.

Which customer requirements will the new structure cater to?

J. Fowler: As described above we will continue to supply pharmaceutical and biotech companies of all sizes. We do however recognize that these different custom segments in the pharma space have specific needs; for example the requirements of large pharma customers differ from small-mid pharma and the biotechs. So as we begin to focus on our core offerings we'll also be focusing on customer segments and how our capabilities and technologies can enable then to achieve their specific business objectives. Similarly so for agrochemicals and other specialty chemicals developers, worldwide.

Which activities will be emphasized under the new structure?

J. Fowler: As discussed, we have four core offerings. Custom Pharma Solutions is focused on enabling innovative pharma companies with their product development and commercialization. Controlled Substances has been a core offering for Johnson Matthey Fine Chemicals for 200 years, and we'll continue with our market leading position in the supply of scheduled products. In addition to this, we have an extensive portfolio of APIs and continue to add to our offering through our Life Cycle management services. Of course catalysis is also at the heart of Johnson Matthey and we'll continue to be a leading provider of homogeneous and heterogeneous catalysts and biocatalysts to the life science industries.

What advantages should customers expect as a result of the rebranding?

J. Fowler: Customers will continue to receive our standards of service and quality across all of their projects. One of our aims with the rebranding is to improve people's understanding of the scope of our services, and enable easier access for customers to any of our areas of expertise. The unified branding and positioning of the Fine Chemicals Division rely on great knowledge sharing between our teams in order to advance product development and bring significant value to customers' projects.

What will be the key technologies and key differentiators to position the new Fine Chemicals division in the market?

J. Fowler: The Fine Chemicals Division is built on a 200-year history that has always had technology and innovation at its core. Our advanced fine and specialty chemicals products and our API development services are supported through an extensive portfolio of differentiating technologies. They include chiral and catalyst technologies, with both chemocatalysis and biocatalysis platforms; significant experience in handling highly potent APIs and controlled substances; expertise in drug-conjugate and polymer-conjugate technologies; chromatography from small- to large-scale; and process and analytical technologies and solid form sciences.

We're known for our particular expertise in solving complex chemistry problems, from handling complex molecules that require lengthy synthesis to finding appropriate tools to solve new complex problems for customers.

Our infrastructure makes us an ideal commercialization partner: we have deep expertise in R&D, chemistry, and engineering but also large-scale capabilities – through our extensive global manufacturing infrastructure – supported by the firm financial base of the Johnson Matthey corporation.

Will the proceeds of the Alfa Aesar divestment be reinvested into the Fine Chemicals division in order to add new technologies?

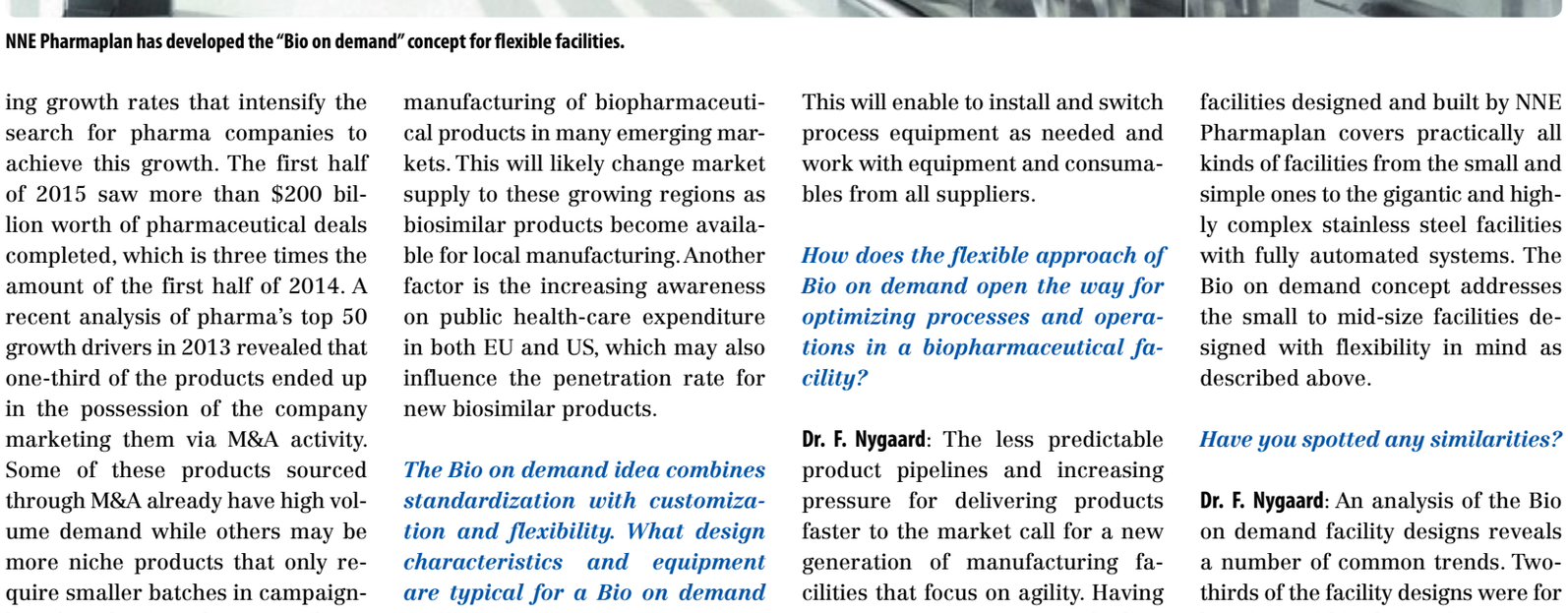
J. Fowler: We continue to invest across Johnson Matthey in areas that will differentiate and strengthen our technology offerings to customers, including within the Fine Chemicals Division. However, in the absence of any material acquisitions, there are other options, such as the return of excess capital to shareholders. ■

On October 1, Johnson Matthey announced the acquisition of the Pharmorphix solid form research business from Sigma-Aldrich. Read more about this deal on page 16. (mr)

Open For Evolution

Market Trends and Technological Concepts are Paving the Way for a New Biopharma Manufacturing Paradigm

The ability to rapidly deploy manufacturing capacity will be a strategic asset of the pharmaceutical industry in the future. NNE Pharmaplan has developed the "Bio on demand" concept for flexible facilities. According to the international pharma engineering company with an annual turnover of about 250 million, the concept allows drug manufacturers to bring products to market faster. Since 2011 NNE Pharmaplan has designed many Bio on demand facility projects for global pharmaceutical companies. Dr. Michael Reubold asked Dr. Frank Nygaard, senior technology partner, biopharmaceuticals at NNE Pharmaplan, about the current and future pharma production trends and the elements and benefits of the Bio on demand concept for next generation bioprocessing.



NNE Pharmaplan has developed the "Bio on demand" concept for flexible facilities.


Dr. Frank Nygaard, NNE Pharmaplan

CHEManager International: The design of most pharma production facilities is still dominated by traditional stainless steel reactors with fixed piping and tank layout. Will this manufacturing technology vanish in the near future?

Dr. F. Nygaard: The global capacity for commercial biopharmaceutical manufacturing is dominated by traditional stainless steel facilities with fixed piping and tank layout. These aging facilities were initially designed for single products, but are now widely undergoing upgrades to enable multiproduct manufacturing allowing more efficient facility utilization. Prior investment in existing capacity and/or a need for large-scale capacity might still favor manufacturing from traditional stainless steel facilities in the future. However, a clear trend for utilizing single-use systems for flexible manufacturing is seen as it is estimated that more than 80% of the new products being tested in early clinical trials are manufactured using single-use systems.

This widespread use of single-use technology for new product developments together with recent years of significant improvement in biopharmaceutical processes make single-use technology an attractive alternative to stainless steel. Some of the key risks associated with the introduction of new products are mitigated by significantly lower upfront investment costs, and a more seamless technology transfer from clinical to commercial manufacturing is expected. Therefore, we believe that the trend we see with increased use of single-use systems in clinical manufacturing will translate into commercial manufacturing as well.

What are the driving forces behind the growing need for flexible, multipurpose and more cost-effective pharma manufacturing facilities?

Dr. F. Nygaard: On the surface, the main objective for pharmaceutical manufacturing today remains to deliver on output targets. In spite of this, conditions for reaching these targets have changed significantly in recent years. With output targets more or less defined, the previous main task was to keep the facility running in a stable and efficient manner. Growing uncertainty and an overall faster pace have added a whole new dimension to achieve success within the pharmaceutical industry today. Growing concerns about, e.g., health-care expenditure and cost pressure, increased regulatory pressure, patent expiry and generic competition as well as pharma M&A all add to an increased level of uncertainty and change in the pharmaceutical industry.

Pharma M&A deals are chasing each other and are accelerating the market consolidation. On the other hand, personalized therapies will further drive the fractionation of the biopharmaceuticals market. How do these opposed trends influence manufacturing strategies?

Dr. F. Nygaard: Both trends — M&A and personalized therapies — are pushing for the need for flexible, multipurpose and more cost-effective manufacturing. The pharmaceutical industry has seen growing revenues for years, and the investors will continue expecting growth rates that intensify the search for pharma companies to achieve this growth. The first half of 2015 saw more than $200 billion worth of pharmaceutical deals completed, which is three times the amount of the first half of 2014. A recent analysis of pharma's top 50 growth drivers in 2013 revealed that one-third of the products ended up in the possession of the company marketing them via M&A activity. Some of these products sourced through M&A already have high volume demand while others may be more niche products that only require smaller batches in campaign-based production schemes similar to personalized therapies.

By 2016, five of the top 10 biopharmaceuticals are expected to be monoclonal antibodies, and biosimilar versions of these blockbusters will most likely become available in the coming years. Will this kick-start the demand for smaller batch sizes and campaign-based production schemes?

Dr. F. Nygaard: The competition from biosimilar versions of current blockbuster products will likely change the landscape for biomanufacturing over time, although at different pace depending on the geographical region. Short term, I think we will continue to see large-scale blockbuster originator products being manufactured for global supply from a limited number of sites. However, this large-scale global supply from few sites will gradually be challenged as the alternatives mature. There is an increasing demand for local manufacturing of biopharmaceutical products in many emerging markets. This will likely change market supply to these growing regions as biosimilar products become available for local manufacturing. Another factor is the increasing awareness on public health-care expenditure in both EU and US, which may also influence the penetration rate for new biosimilar products.

The Bio on demand idea combines standardization with customization and flexibility. What design characteristics and equipment are typical for a Bio on demand facility?

Dr. F. Nygaard: The core of the Bio on demand concept is built around single-use bioreactors — short: SUBs. Single-use technology decouples the process from the building, which gives a lot of flexibility. The implementation of single-use technology is generally maximized to the extent feasible from both a practical as well as a financial perspective. A Bio on demand facility design is therefore characterized by the absence — or only limited — complex distribution matrices for fluids as connections are flexible. A feature of the Bio on demand facility design is the ease of capacity expansion.

The progress of the single-use technology has expanded well beyond bioreactors, mixing systems and hold systems. Single-use transfer sets for chromatography and filtration are well-established and disposable chromatographic columns and single-use flexible fill & finish modules are also frequently implemented into Bio on demand designs.

How do you customize a Bio on demand facility to meet the technical, operational and regulatory requirements of each specific customer?

Dr. F. Nygaard: The Bio on demand facility is based on a configured-to-order idea. Although being based on a high degree of standardization, it is adaptable to customer needs, national and local requirements, site-specific conditions as well as international regulations. The standard facility is designed for an open process architecture, where process equipment from a full range of suppliers can be used to build the optimal process train. This flexibility is reflected in ample space for processing operations, reserved workflow routes and readiness for room classification changes. This will enable to install and switch process equipment as needed and work with equipment and consumables from all suppliers.

How does the flexible approach of Bio on demand open the way for optimizing processes and operations in a biopharmaceutical facility?

Dr. F. Nygaard: The less predictable product pipelines and increasing pressure for delivering products faster to the market call for a new generation of manufacturing facilities that focus on agility. Having access to smarter ways of planning and foreseeing future needs, smarter solutions for maintaining flexibility and methods to reduce complexity and risk of fast-track engineering projects will be key competitive parameters in future biopharmaceutical manufacturing facilities.

The Bio on demand standard facility concept is designed for easy configuration to company requirements and local conditions. That means that you can create your own company-specific standard facility, which can be deployed to a number of locations with only minor reconfigurations for local conditions. This standardization reduces risk and speeds up the facility project by applying proven project management methods for project realization.

Does the Bio on demand concept work for a revamp of existing facilities as well or is it predestinated for greenfield plants that are designed from scratch?

Dr. F. Nygaard: On-site construction offers the highest degree of flexibility and ability to shape a facility. This method offers few limitations in, e.g., ceiling height, floor loads and number of floor levels. However, converting an existing building space is also possible and could potentially be the fastest and most cost-effective route to biomanufacturing capacity. Time-critical activities such as various permissions may already be in place, and timelines for project execution can potentially be compressed by initiating parallel work in multiple sections of the facility independent of weather and seasons if roof and climate shell is established.

Which different types of facilities have you designed and built so far?

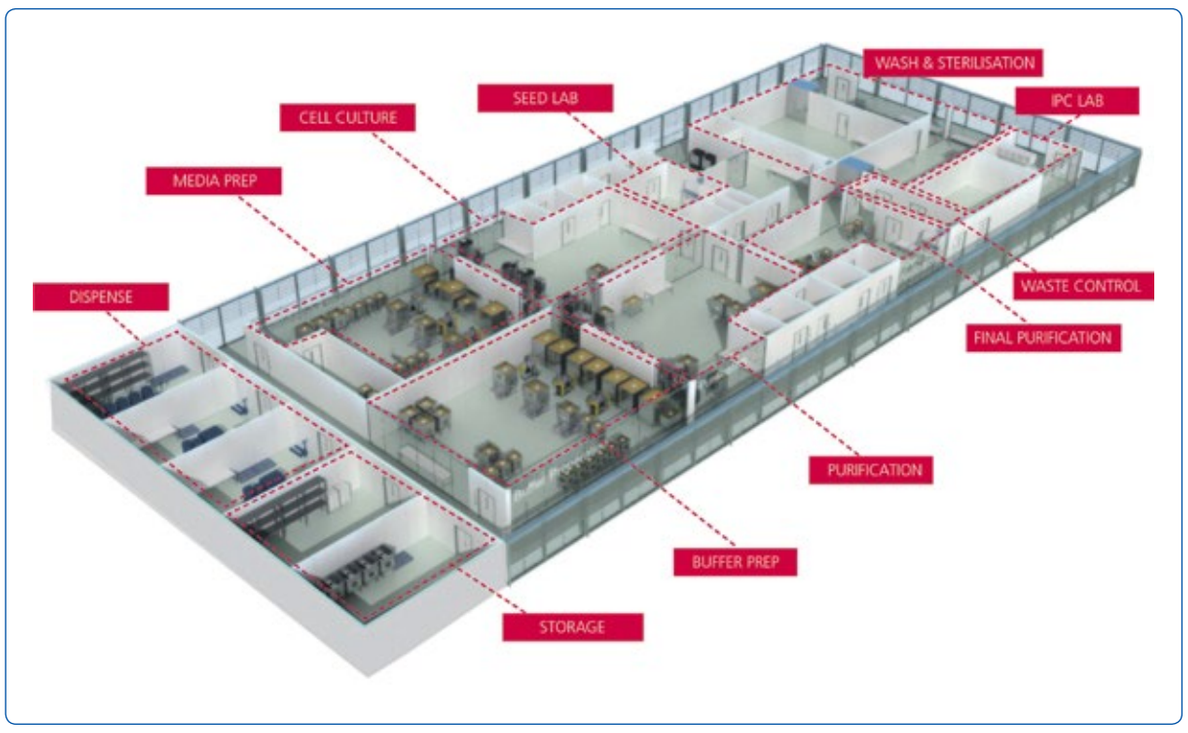
Dr. F. Nygaard: Being an engineering and consulting company focused on pharma engineering, the diversity of facilities designed and built by NNE Pharmaplan covers practically all kinds of facilities from the small and simple ones to the gigantic and highly complex stainless steel facilities with fully automated systems. The Bio on demand concept addresses the small to mid-size facilities designed with flexibility in mind as described above.

Have you spotted any similarities?

Dr. F. Nygaard: An analysis of the Bio on demand facility designs reveals a number of common trends. Two-thirds of the facility designs were for locations within the BRIC countries. All designs were made for manufacturing complex proteins including mAbs. All facilities were designed for clinical production initially, of which half of them were also designed for commercial manufacturing and one-fourth with manufacturing up to product launch. One-third of the commercial scale design also included an option to scale-out the batch size to up to 6,000 L. Although modular construction was evaluated in 10% – 20% of the concepts, we see that the construction designs for all Bio on demand facilities are stick built.

In general, we also see that facility designs for pilot scale and launch are using single-use technology for process and support — media and buffers — whereas the majority of the commercial designs are hybrid solutions with stainless steel systems for media and buffer preparation and the recovery using a centrifugation step. All Bio on demand facility designs are considering capacity expansion as part of the business strategy starting small and subsequently increase the capacity by, e.g., swapping equipment with larger systems, fitting out the manufacturing areas with additional systems and/or adding new manufacturing "blocks" to the existing manufacturing by preparing for this expansion in the early facility design. Nearly half of the designs also considered implementing continuous manufacturing into the manufacturing strategy.

We also see that half of the designs included a flexible fill and finish allowing end-to-end manufacturing. These flexible solutions we see in the Bio on demand designs are based on customer requests and the "configured-to-order" idea using a high degree of standardization and an open-process architecture as described above. ■



Example of a "Bio on demand" layout

People

Hubert Fink

Hubert Fink has been appointed to the Lanxess managing board effective October 1, 2015, increasing the number of board members from three to four. Head of the Advanced Industrial Intermediates business unit since 2011, Fink in future will have board responsibility for that segment with the Advanced Industrial Intermediates and Saltigo business units and for the High Performance Materials business unit. He also will oversee the Global Procurement & Logistics group function and the Production, Technology, Safety and Environment (PTSE) group function, which combines all production-related services. The German national joined Bayer in 1988 and became head of Global Operations Semi-Crystalline Products in the Bayer Polymers subgroup — predecessor of Bayer MaterialScience, now Covestro — in 2002. With the creation of Lanxess in 2004, he assumed responsibility for the same functions there.

Matthias Schönberg

Axalta Coating Systems has appointed **Matthias Schönberg** as Vice President of Axalta and President of its Europe, Middle East and Africa (EMEA) region. He will take up his position on October 1, 2015. Schönberg joins Axalta from Continental where he held numerous leadership positions including, most recently, as CEO of its ContiTech Fluid Technology business and Executive Vice President of Continental AG. During his 17 year tenure with Continental, he gained experience in dealing with multi-brand, multi-channel and distributor-oriented business models as well as working closely with automotive OEMs. Schönberg holds a Master of Business Administration, Corporate Finance and Tax from the University of Bayreuth, Germany.

Nicolas Cudré-Mauroux

Nicolas Cudré-Mauroux has been appointed as Solvay's group research & innovation general manager. He joins Solvay from DuPont where he began his international career in 1988 as a researcher in the United States. The positions he held at DuPont included that of EMEA regional business director for the Advanced Fibers and Nonwovens businesses. In 2011 he joined the DuPont-Danisco integration team and, in 2012, moved to Denmark to become the technology & innovation director for the Food Ingredient business formed following the acquisition of the Danish enzyme maker. A Swiss national born in Luxembourg, Cudré-Mauroux holds a MSc and a PhD in materials science from the Swiss Institute of Technology in Lausanne, Switzerland.

Andreas Maier

Andreas Maier, executive vice president, has been appointed as general manager of the newly formed business segment Consumer Care within the WeylChem Group with effect from September 1, 2015. This business segment includes the development, production and sales of performance chemicals for use in home and personal care applications. Furthermore, Maier will carry the responsibility for the companies WeylChem Wiesbaden GmbH and Nease Co LLC. He held various international positions in development and operations within theWeylChem Group and served as head of sales and marketing for fine chemicals since 2011. In addition, **Marcel Ijland** has been appointed global head of sales & marketing for fine chemicals effective September 1, 2015. He joined WeylChem in 2014 and has considerable experience in sales and marketing of specialty chemicals.

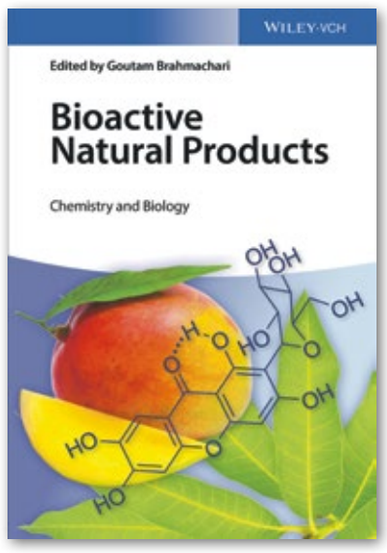
Heike Faulhammer has been appointed Vice President Sustainable Development for Arkema effective October 1, 2015, taking over from **Gérard Langlais** who is retiring. Faulhammer is a graduate from the Institute of Macromolecular Chemistry in Freiburg,Germany, and holds a PhD in Chemistry. Following a post-doctorate, she joined Arkema in 1997 at the Cerdato R&D Center, France, as R&D Engineer, and later Process Engineer. In 2001, she was given responsibility for a fine powder production line at the Serquigny plant in Eure, France. Faulhammer was put in charge of a business activity in 2006 and had been director Arkema's of the GRL Research Center since 2009, which comprises three areas of activity in thiochemicals and fine chemicals, polymers and additives, and mineral chemicals and adsorption.

Simon Sturge will assume the newly created role of chief operating officer at Merck KGaA with effect from September 30, 2015, overseeing all commercial regions and countries. His responsibilities will include the General Medicine franchise, which consists of drugs for cardiovascular diseases and diabetes, as well as Global Manufacturing and Supply. Sturge will also continue to lead the Biosimilars and Allergopharma businesses. **Rehan Verjee**, currently general manager Canada, will also join the Healthcare Executive Committee. As chief marketing and strategy officer, he will be in charge of the business' global specialty franchises of Oncology, Neurology and Immunology, Fertility and Medical Devices as well as the global immuno-oncology alliance with Pfizer and various strategic functions including business development.

Andre Becker (46) has been named by BASF as President of Human Resources, with effect from March 1, 2016. The executive who most recently served as President, Regional Functions North America, at BASF Corporation in the US, will succeed **Wolfgang Hapke** (59), who is due to retire at the end of February 2016. **Manfredo Ruebens** (52), President, Finance, Ludwigshafen, will succeed Becker from January 1, 2016. **Marc Ehrhardt** (47), Senior Vice President, Mobile Emissions Catalysts at BASF Corporation, will take Rubens' current position from December 1, 2015. **Dr. Beate Ehle** (52) will return from BASF Corporation in New Jersey to succeed **Dr. Ulrich von Deessen** (59) as President, Environment, Health & Safety, based in Ludwigshafen effective March 1, 2016.

Bioactive Natural Products

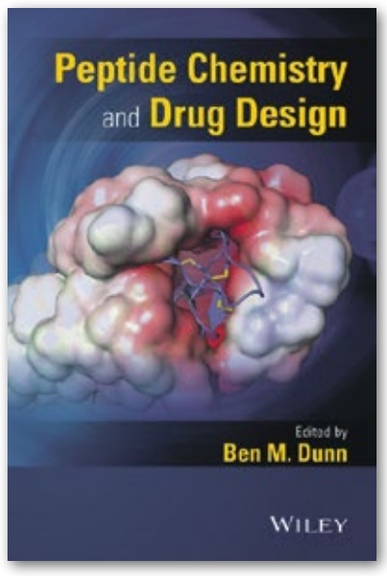
Natural compounds, which have evolved their function over millions of years, are often more efficient than man-made compounds if a specific biological activity is needed. This book by Dr. Goutam Brahmachari highlights the chemical and biological aspects of potential natural products with an intention of unravelling their pharmaceutical applicability in modern drug discovery processes. The synthesis, semi-synthesis and also biosynthesis of potentially bioactive natural products are covered. It also features chemical and biological advances in naturally occurring organic compounds. 40 expert scientists from around the world report their latest findings and outline future opportunities for the development of novel and highly potent drugs based on natural products operating at the interface of chemistry and biology.



▶ Bioactive Natural Products
by Dr. Goutam Brahmachari (ed.)
Wiley, 1st edition 2015
508 pages, hardcover, €159.00
ISBN 978-3-527-33794-1

Peptide Chemistry and Drug Design

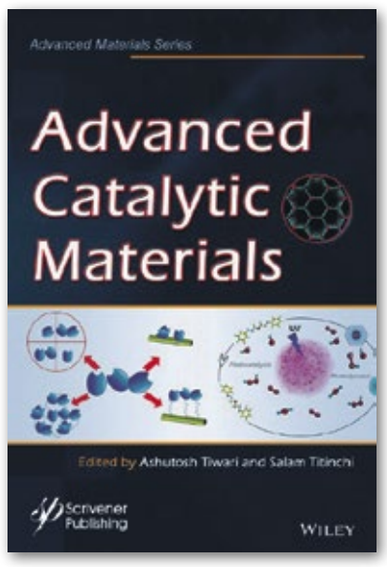
This book by Dr. Ben Dunn, a distinguished professor in the department of Biochemistry and Molecular Biology at the University of Florida, who has served on many NIH review panels, focuses on peptides as drugs, a growing area of pharmaceutical research and development. It helps readers solve problems of discovering, developing, producing, and delivering peptide-based drugs and identifies promising new areas in peptide drug discovery. The book includes chapters on discovery from natural sources, metabolic modification, and drug delivery as well as overviews on separation methods and techniques for analysis, bond formation, and purification.



▶ Peptide Chemistry and Drug Design
by Dr. Ben M. Dunn (ed.)
Wiley, 1st edition 2015
336 pages, hardcover,
€145.00
ISBN 978-0-470-31761-7

Advanced Catalytic Materials

The subject of advanced materials in catalysis brings together recent advancements in materials synthesis and technologies to the design of novel and smart catalysts used in the field of catalysis. Nanomaterials in general show an important role in chemical processing as adsorbents, catalysts, catalyst supports and membranes, and form the basis of cutting-edge technology because of their unique structural and surface properties. The book provides comprehensive coverage of the current literature, up-to-date overviews of all aspects of advanced materials in catalysis, and present the skills needed for designing and synthesizing advanced materials. It also showcases many topics concerning the fast-developing area of materials for catalysis and their emerging applications.



▶ Advanced Catalytic Materials
by Ashutosh Tiwari and Salam Titinchi (eds.)
Wiley, 1st edition 2015.
472 pages, hardcover, €189.00
ISBN 978-1-118-99828-1

Events

CPhI Worldwide, 13 – 15 October 2015, Madrid, Spain
CPhI (Convention on Pharmaceutical Ingredients) Worldwide — the International exhibition on Pharmaceutical Ingredients and Intermediates — is the leading networking event and exhibition dedicated to pharmaceutical developments, trends, products and services, including contract services, excipients, ingredients, APIs, machinery, finished dosage forms and packaging. The show hosts over 36,000 attendees from 140 countries and 2,200 exhibitors, representing every step of the pharmaceutical supply chain from drug discovery to finished dosage. First held in 1990, 2015 marks the 26th edition of this prestigious and industry leading event.
▶ www.cphi.com

International Bioenergy Exhibition and Asian Bioenergy Conference, 21 – 23 October 2015, Shanghai, China
The International Bioenergy (Shanghai) Exhibition and Asian Bioenergy Conference 2015 is the new leading conference and exhibition in Asia, an invaluable and influential international platform to discuss the role of bioenergy in the Asian context. The exhibition is open to industries, international organizations, research structures and organizations, specialized advisory services and consultancy firms, donors and professionals involved in the various sectors of biomass. The conference's main objective will be to promote synergy among markets, technologies and investments.
▶ www.ibsce.com

OLED World Summit, 27 – 29 October 2015, Berkeley, USA
The OLED (organic light-emitting diode) industry is display, lighting and materials leader. The OLEDs World Summit 2015 program will examine OLED strategies, including a look at new applications, emerging strategies and challenges from quantum dots. Designed to connect people from different sections, the congress will provide key insights into investments, markets and technology needed to take advantage of OLED's rapid advances towards widespread commercialization.
▶ www.oledsworldsummit.com

Chem Show, 17 – 19 November 2015, New York, USA
Since 1915, the Chem Show is one of the main showcases for the latest process equipment, products and services, bringing together manufacturers and innovative new suppliers with executives, process engineers, production teams and plant personnel throughout the chemical process industries (CPI). Held every two years, the 2015 Chem Show will celebrate its 100th anniversary by looking to the innovations that will drive the industry into the future.
▶ www.chemshow.com

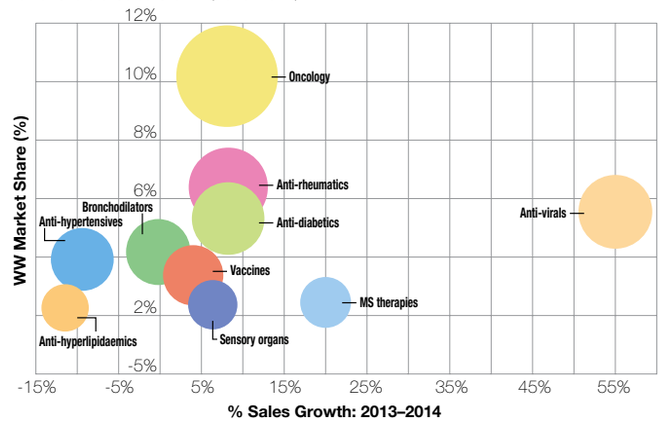
European REACh Congress, 24 – 25 November 2015, Duesseldorf, Germany
As with the 2014 event, the Congress encourages shared learning amongst industry, service providers, authorities and policy makers. It will facilitate great networking opportunities and allow participants to meet with key service providers from the chemical industry. The program will include a key note presentation from Jochem van der Waals (Ministry of Infrastructure and the Environment, Netherlands) on solutions to reducing the burden of REACh on SMEs.
▶ www.reachcongress.com

Informex, 2-4 February 2016, New Orleans, USA
The conference focuses on the innovation and commercialization of unique chemistry across all verticals and will play host to a global network of attendees and exhibitors in some of the most rapidly growing chemical markets including the broader energy field, pharmaceuticals, life sciences and agrochemicals. The event will also highlight innovative sub segments such as green chemistry, 3-D printing and electronic chemicals. Bringing together innovators with those that can commercialize, InformEx provides a unique platform to conduct profitable business. The event will feature enhanced opportunities to network with new and current suppliers, provide greater company exposure and facilitate connections with key decision makers. There will be dedicated educational content focused on growth markets as well as presentations on best business practices and innovative technologies through our innovation-focused show floor programming.
▶ www.informex.com

Pharma Industry's Feel Good Factor

Top 10 Therapy Sales in 2014 Fig. 1

Market Share & Sales Growth (2013–2014)



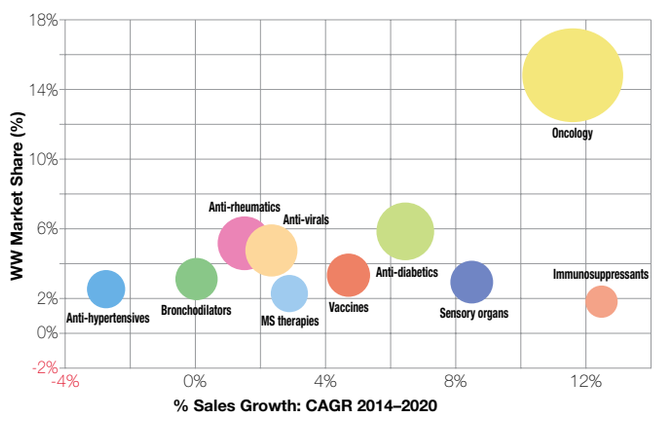
Source: EvaluatePharma World Preview 2015 © CHEManager International

Prescription Drug Sales in 2014

The pharmaceutical industry is entering a period of sustained growth. This is the result of the World Preview 2015 report, recently published by EvaluatePharma (see also our article on page 14), showing prescription drug sales are set to advance at almost 5% a year until 2020. In 2014 oncology remained the largest therapeutic category with sales growing by 8% to $79.2 billion and accounting for 10.1% of the total prescription and over-the-counter (OTC) drugs market (fig. 1). Antivirals expanded the most, by 55% to $48.8 billion, in 2014 largely due to recently launched hepatitis C products from Gilead and Johnson & Johnson, which collectively recorded sales of over $14.5 billion in 2014. The MS therapies segment also performed well with 20% growth over the year driven by products from Biogen and Novartis.

Top 10 Therapy Areas in 2020 Fig. 2

Market Share & Sales Growth



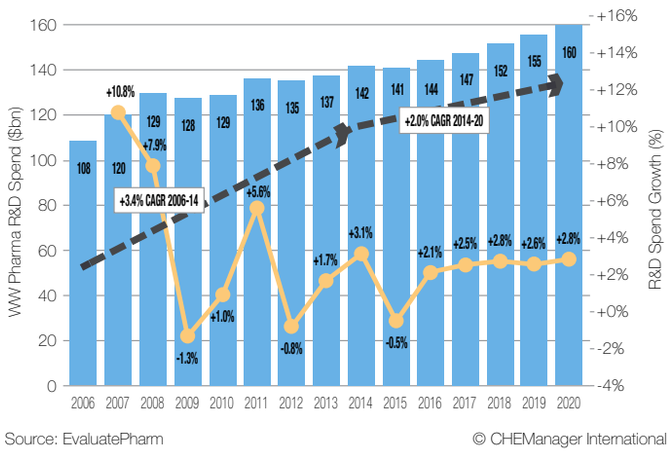
Source: EvaluatePharma World Preview 2015 © CHEManager International

Prescription Drug Sales in 2020

Oncology is likely to remain the largest segment in 2020 with an expected annual growth of 11.6% per year and reaching $153.1 billion in 2020 (fig. 2). Growth from in-line products and potential new entrants is expected to more than compensate for a number of key patent expiries between 2014 and 2020. Anti-diabetics is forecast to be the second biggest therapy area with sales of $60.5 billion in 2020, less than half that of oncology. Overall, the cancer market is expected to expand by an average 10% per year between 2014 and 2020 to $153.1 billion, with worldwide sales of the new PD-1 products accounting for over $17 billion, or 23%, of this growth. Although Roche is expected to remain the market-leader through 2020, the company's market share is forecast to decline by 14%, caused by competitor products and biosimilars.

Worldwide Total Pharmaceutical R&D Fig. 3

Spend in 2006-2020



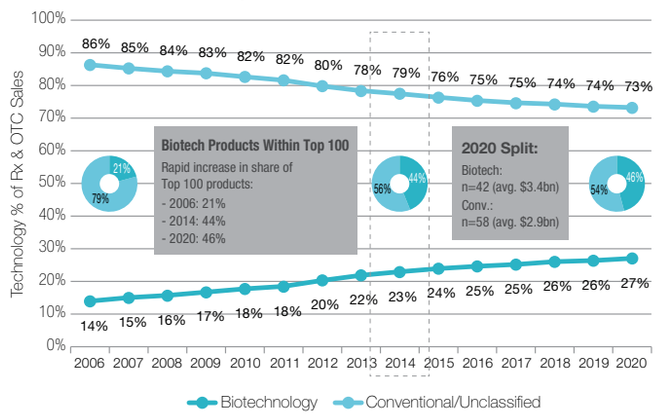
Source: EvaluatePharm © CHEManager International

R&D Spend by Pharma & Biotech Companies

Global pharmaceutical R&D totaled $141.6 billion in 2014, representing an increase of 3.1% on the previous year. Overall, total R&D spend is forecast to grow at a rate of 2.0% per year, compared with the compound annual growth rate of 3.4% between 2006 and 2014, reaching $159.8 billion in 2020 (fig. 3). The spend per new molecular entity (NME), based on a three-year lag period between R&D expenditure and NME approval, was $2.7 billion per NME in 2014. This fall in spend per NME indicates increased productivity within the industry. Novartis is expected to spend the most on research and development in 2020, with a spend of $10.5 billion in 2020. Of the top 20, Celgene is forecast to grow its R&D expense the most rapidly, with R&D forecast to increase 10% per year from $1.8 billion to $3.3 billion in 2020.

WW Prescription Drug & OTC Pharmaceutical Sales Fig. 4

Biotech vs. Conventional Technology (2006–2020)



Source: EvaluatePharma World Preview 2015 © CHEManager International

Biotech vs. Conventional Technology

Although the percentage sales from biotechnology products (bioengineered vaccines & biologics), within the world's top 100, is set to increase from 44% in 2014 to 46% in 2020, this is lower than the 52% predicted in last year's World Preview. This is partly due to a number of key biotechnology products falling out of the top 100 after suffering significant forecast downgrades over the course of the year. Concurrently, a number of conventional drugs have had their forecasts upgraded, thereby increasing their contribution to the total value of the top 100 drugs in 2020. In the broader market, sales from biotechnology products are expected to account for 27% of the world's pharmaceutical sales by 2020 versus the current share of 23% in 2014. (rk)

Space Oddity: Microgravity Single Malt

The Scottish whisky that spent three years aging aboard the International Space Station has finally returned to earth. The result, according to the Ardbeg distillery and aerospace company NanoRacks, is a whisky with a "noticeably different" flavor profile to a control sample matured on earth.

Ardbeg, located on the Isle of Islay off the Scottish coast, and NanoRacks set up the experiment to determine what effect microgravity conditions would have on terpene, a set of organic compounds found in whisky and other foods that give them a distinct flavor.

By sending unmatured whisky into space along with charred oak wood shavings—which were only brought together inside a sealed vial once in space—they also hoped to reveal the effect of microgravity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on the extraction of certain flavor compounds from the oak.

Three distinct analyses were conducted upon the whisky's return to earth: chromatography for volatile congener analysis (substances other than alcohol produced during fermentation that give it its flavor); high-pressure liquid chromatography (HPLC) for maturation-related congener analysis; and a taste test.

While the analysis of major volatile congeners demonstrated no significant differences between the two samples, there was a larger difference in the effect the oak shavings had on the maturation process.

The control samples back on earth extracted more flavor-active derivatives from the oak than the space sample, which Ardbeg and NanoRacks believe indicates that the conditions of microgravity inhibited their extraction from the oak.

The biggest difference was in the tasting, though. The ISS sample apparently had a very different scent and flavor profile and in the test conducted, almost all participants picked out a difference between the space whisky and the mundane earth-matured control. (rk)


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Under Construction – Barcelona's iconic basílica Sagrada Família, designed by Antoni Gaudí, attracts around three million visitors a year although it has not yet been completed. The startling edifice, due to be completed in 2026, is to benefit from innovative chemistry. AkzoNobel's Interpon products will be applied to several areas of the UNESCO World Heritage Site, where construction first began in 1882. The powder coating products will be used to protect several parts of the building, including the enclosures and the balconies of the high conic towers. The Dutch company's coatings can be found on other famous landmarks around the world, including Tower Bridge and the Shard in London, Burj Al Arab in Dubai, Petronas Twin Towers in Kuala Lumpur, Malaysia, the Shanghai Tower in China, and the Rijksmuseum in Amsterdam, the Netherlands.

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