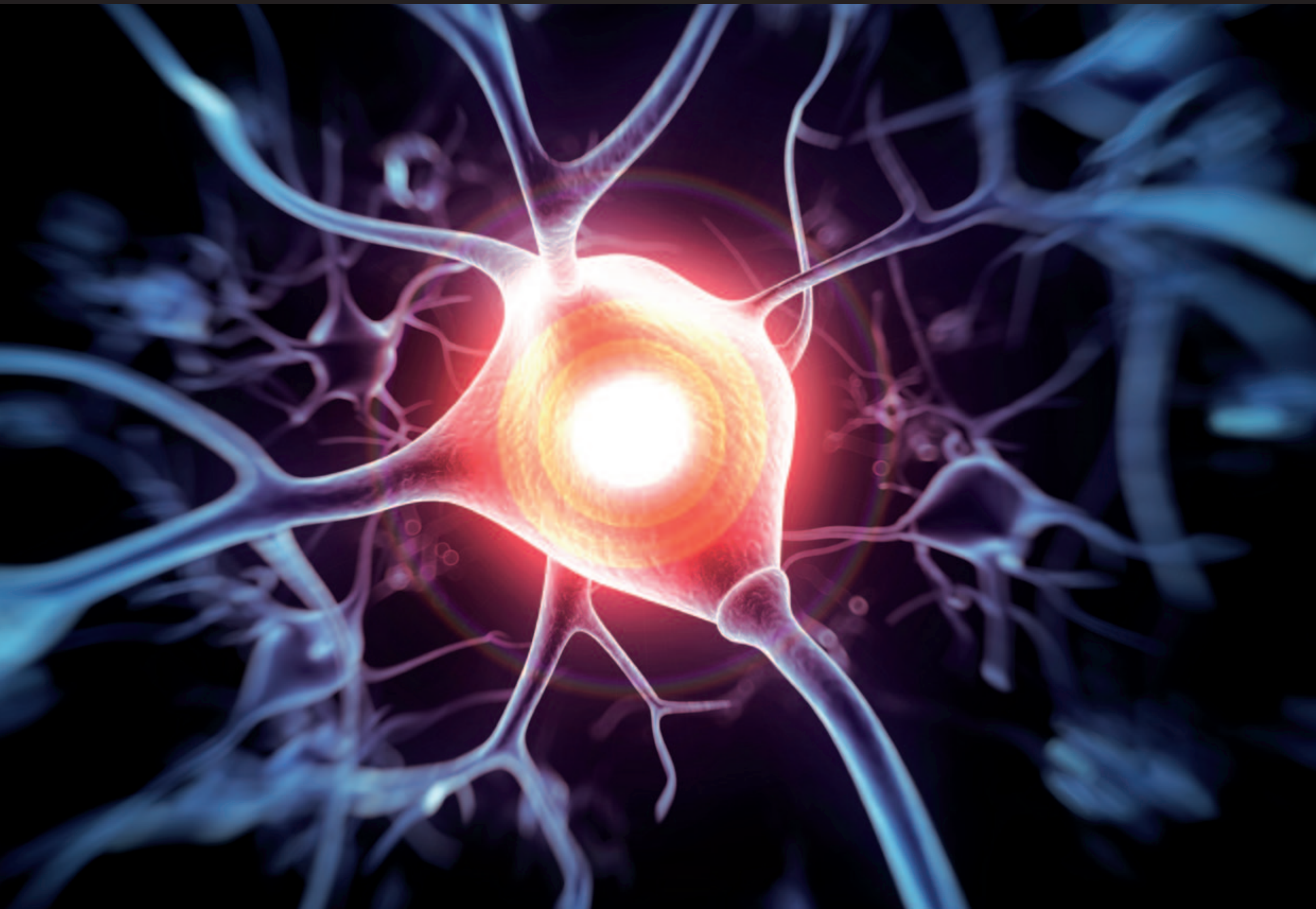
AN IMAP INDUSTRY REPORT

GLOBAL M&A REPORT
PHARMA / BIOTECH 2015



IMAP healthcare transactions in 2014

Siegfried Group
The company is active in both the primary and secondary production of pharmaceutical drugs
Zofingen, Switzerland
Acquired 100% of Business Operations

hameln pharma
Specialist for the contract manufacturing of parenteral solutions and suspensions
Hameln, Germany
Represented the seller in this transaction

Petrus AS
Family office
Oslo, Norway
Provided Funding

Auris Medtech Europe Limited
Medical devices
London, UK

GE Healthcare
Technology, services, research for healthcare sector
Chalfont St Giles, Buckinghamshire, UK
Acquired Majority Control of Business Operations of

Finnamore Ltd
Consultancy services to UK Healthcare sector
London, UK
Advised on Sale of Company

AccessOne Consumer Health, Inc.
Discount medical plan provider
Greenville, SC, US
Acquired Minority Ownership Position of

AccessOne Consumer Health, Inc.
Discount medical plan provider
Greenville, SC, US
Advised on recapitalization of Company

Fort Mobile
High net worth individual looking for new platform
Greenville, SC, US
Acquired 100% of

Quality Mobile X-Ray
Mobile x-ray service provider to nursing home
Winston Salem, NC, US
Advised on Purchase of Company

BIOVENDOR
Supplier of in-vitro diagnostics products
Brno, Czech Republic
Acquired Part of Business of

Merebit s.r.o.
R&D of laboratory equipment
Pohorelice, Czech Republic
Advised on Sale of Part of the Business

LDC backed management team
UK-based private equity house
Birmingham, West Midlands, UK
Acquired 100% of Business Operations of

Prism UK Medical Ltd
Moving and handling equipment manufacturer
Wakefield, West Yorkshire, UK
Advised on Sale of Company

Undisclosed Private Investors
Private investor
Switzerland
Provided Growth Funding for

Vital Solutions Swiss AG
Development & sale of natural OTC ingredients
Tägerwilen, Switzerland
Advised on the Placement of Equity

Silver Peak Partners
Private equity firm
Denver, Colorado, US
Adquired 100% of Business Operations of

MedSource Incorporated
Sales and distr. of durable medical equipment
Layton, Utah, US
Advised on Sale of Company

BENU Ceska republika a.s.
Pharmacy chain, part of PHOENIX Intl.
Prague, Czech Republic
Acquired 100% of Shares of

VEROPHARM a.s.
Pharmacy chain
Ceske Budejovice, Czech Republic
Advised on Sale of Company

ICICI Venture
Alternative asset managers
Mumbai, India
Equity Investment & Stake Purchase of IBOF Stake in

Krishna Institute of Medical Science
Healthcare Services
Hyderabad, India
Advised the Sellers and the Company On the Placement of Equity

Fiba Saglik Yatirimlari A.S.
Fiba Group company engaged in operating hospital
Istanbul, Turkey
Acquired Investment Interest in Seller's Business

Florence Nightingale Hastaneleri
Turkish health group
Istanbul, Turkey
Advised on Sale of Company

Fagron BV / Arseus NV
Pharmaceutical compounding
Rotterdam, Netherlands
Sold remaining 49% stake of

Unit Dose Packaging BV
Innovative medical unit dose packaging
Einhoven, Netherlands
Advised on Sale of Company

Abbey Pharma Ltd
Supplier of niche pharmaceutical medicines
Maidenhead, Kent, UK
Acquired 100% of Business Operations of

Peckforton Pharmaceuticals Ltd
Speciality pharmaceutical company
Crewe, Cheshire, UK
Advised on Sale of Company

EMKA TECHNOLOGIES
Instruments for medical research
Paris, France
Acquired 100% of Business Operations of

SCIREQ
Respiratory research equipments
Montreal, Canada
Advised on Purchase of Company

Laczay Family
Majority owners of target company
Budapest, Hungary
Acquired 25% Shares from the Minority Owner

Lavet Kft.
A leading veterinary producer and distributor
Budapest, Hungary
Advised on Sale of 25% shares of the Company

Cambian Group plc
Provider of specialist behavioural health services
London, UK
Acquired 100% of Business Operations of

Ansel Ltd.
Specialist personality disorder services
Nottingham, UK
Advised on Sale of Company

Undisclosed HNW Individual
Finantial investor
Paris, France
Acquired 100% of Business Operations of

FLAMARC
Distribution of consumables to dental labs
Vendôme, France
Advised on Sale of Company

Mediplast AB
Distribution of disposable medical products
Malmö, Sweden
Acquired 100% of Business Operations of

ErgoNordic AB
Distribution of disposable medical products
Stockholm, Sweden
Advised on Sale of Company

Vitabalans Oy
Privately owned pharmaceutical company
Helsinki, Finland
Acquired 100% of Business Operations of

Birger Ledin AB
OTC Pharmaceutical supplier
Skövde, Sweden
Advised on Purchase of Company

LDC backed Management Team
UK-based private equity house
Birmingham, West Midlands, UK
Acquired 100% of

Prism Medical UK Ltd
Moving and handling equipment manufacturer
Wakefield, West Yorkshire, UK
Raised Debt Funding

IndiaVenture Advisors
India-focused private equity fund
Mumbai, India
Provided Growth Funding

Baroda Medicare Private Limited
Multi-speciality hospital chain
Baroda, India
Advised on Placement of Equity

TPG Growth
Global private investment firm
Mumbai, India
Provided Growth Funding

Sutures India Private Limited
Manufacturer of surgical sutures
Bangalore, India
Represented TPG Growth on Buyside

Contents

Christoph Bieri
Chair, IMAP Healthcare Group
IMAP in Switzerland / Kurmann Partners

Editorial

The year 2014 witnessed an intense phase of M&A in the Pharma industry. While the number of transactions was comparable to 2013, the cumulated total transaction volumes more than doubled due to the larger number of multi-billion dollar deals (see pages 4 and 5). The higher M&A intensity was felt in all regions, as our healthcare experts report (pages 6-12). The buoyant mood also extended to the innovation motor of the industry: The number of IPOs of Biotech companies (91), and the money they raised (US$ 6.4bn), reached an all-time high.

In our in-depth analyses of this report we look at two fundamental deal drivers: First, tax inversions by US-based Pharma companies, which were often cited as key motivation for deals and as driver for valuations, with the failed attempt of Pfizer to acquire AstraZeneca as the most prominent example (see page 13). Second, the reorganization of Pharma manufacturing and the concomitant consolidation in the CMO segment, which progresses with less publicity, but which will have deep consequences for the whole industry (see page 16).

In April, Novartis created a veritable "Big Bang" by simultaneously announcing four large transactions (three with GSK and one with Eli Lilly) which leave the giant focused on its areas of strengths. We think Novartis' strike may be the first of a wave of transactions amongst Pharma companies in which businesses are swapped to build critical mass.

With its combination of M&A experience, global reach, local presence and deep industry expertise, IMAP's healthcare group provides outstanding support. Please contact us for a discussion on your plans and needs.

Truly yours,

C. Bieri

M&A is heating up

At the end of 2013, many industry observers thought that M&A in the Pharma & Biotech industry had reached a high plateau. They were wrong: 2014 showed a consistently higher deal activity in terms of value in all regions (+130% higher sum of total transaction values), albeit not in terms of number of deals (more or less flat at around 600). In addition to the already high IPO activity, the IPO boom continued, with 91 companies going public in 2014, raising overall US$ 6.4bn in the process.
Most notably, 2014 was a year of many mega-mergers. There were eleven transactions bigger than US$ 5bn (up from four in 2013), including four with transaction values higher than US$ 10bn - in 2013, there was only one such large transaction.

Geographic shifts

As in 2013, most of the money was spent on targets located in the USA, whereas Western Europe and Canada have seen most activity in terms of the number of deals (see figure 1). Deal value of US-based targets quadrupled in 2014 vs. 2013. This was the result of the large mergers with US-based targets.
Looking at where the money came from (the location of the acquirer) however shows a distinct shift from the US to Western Europe: Most of the transactions of 2014 by value and by number of deals involved acquirers located in Western Europe, in contrast to 2013, when most of the deals and money involved US-based acquirers. This is not the result of a strategic shift but rather the result of transactions driven by tax inversions, which some of the acquirers used to create "tax-efficient M&A platforms" (see also page 13).

Global deal drivers

The benefits of a lower tax rate were major deal drivers in 2014, but the strategic rationales of the largest transactions in 2014 were gaining scale (such as Actavis, which is now a true Big Pharma company), consolidation of the businesses a company covers, and adding complementary products to the core business areas.
The prime example of refocusing a business was Novartis. In April, the giant initiated a series of transactions to dispose of business where it was in a sub-critical position. Thereby Novartis and GSK engineered an innovative deal in which they swapped businesses, achieving their goal in one stroke: GSK and Novartis now co-own (under GSK's leadership) one of the global leaders in OTC; Novartis increased its oncology footprint by acquiring GSK's business and pipeline; and GSK increased its position in vaccines by acquiring Novartis' non-influenza vaccine assets. The same day, Novartis' animal health unit went to Eli Lilly.
We believe that a major pruning of product and business portfolio will be seen in the next few years particularly by the companies who went through acquisition sprees such as Actavis, Perrigo or Mylan. For these companies, the critical question will be how they can combine OTC, generics and originator businesses, with their totally different constraints and challenges, or whether they have to spin off assets which do not fit their core competences.

TABLE 1 DEALS IN 2014 BY TRANSACTION SIZE

	2014		2013	
RANGE	TTV	DEALS	TTV	DEALS
Bigger than US$ 5bn	158'827	11	39'440	4
US$ 1bn to US$ 5bn	40'175	16	26'132	13
US$ 50m to US$ 1bn	31'304	117	32'060	109
Smaller than US$ 50m	2'412	173	3'235	214
Unknown	0	259	0	274

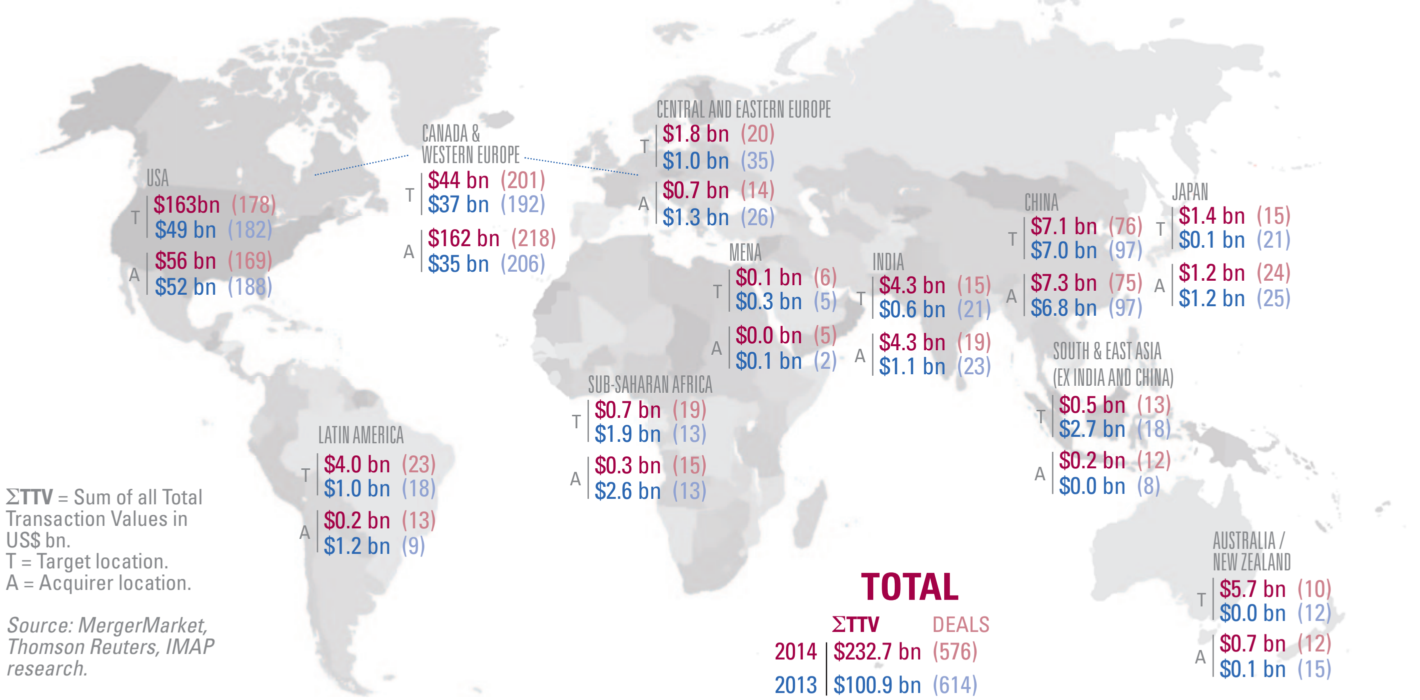
TTV: Sum of transaction values in US$ bn. *Source: MergerMarket, Thomson Reuters, IMAP research.*

M&A TIME LINE 2014

JANUARY FEBRUARY MARCH APRIL MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

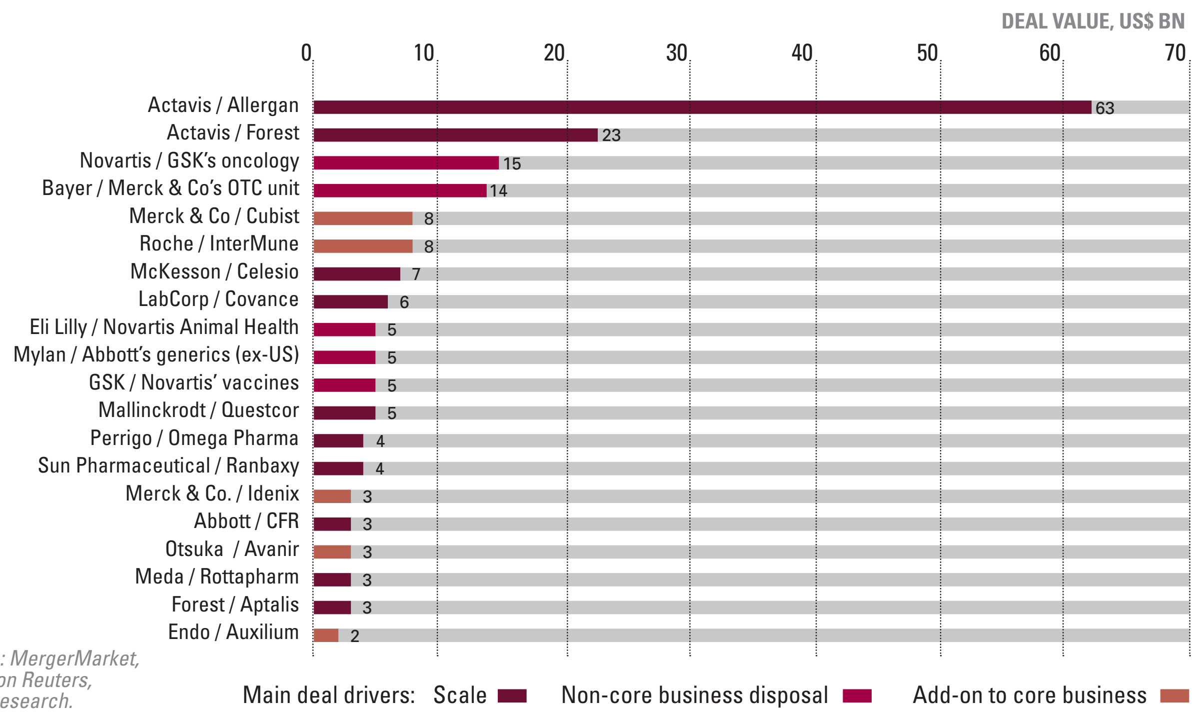
- **Alnylam acquires Sirna and its siRNA assets from Merck & Co. For US$ 192m**
- **Lotus acquired Alvogen's Korean and India assets for US$ 162m**

FIGURE 1 **DEALS BY LOCATION OF TARGET AND BY LOCATION OF ACQUIRER**



Source: MergerMarket, Thomson Reuters, IMAP research.

FIGURE 2 **TRANSACTIONS WITH A DEAL VALUE LARGER THAN US$ 2BN**



Source: MergerMarket, Thomson Reuters, IMAP research.

JANUARY **FEBRUARY** MARCH APRIL MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

/ **Forest acquires Aptalis for US$ 2.9bn**

/ **Elanco purchases Lohman Animal Health for US$ 600m**

USA

Growth prospects drive valuations

It is our expectation that Pharma Biotech activity in 2015 will continue the strength shown in the last 3 quarters of 2014 which saw consolidation of core businesses, partnering on strategic goals, and divestment of non-core assets.

Many of the prior concerns, such as patent expirations, implementation of the Affordable Care Act (ACA), and higher R&D costs, appear to have been offset by the current strategy of focused growth and increased M&A. Specialty Pharma transactions saw a significant rise in debt/equity financing ratios and extremely positive post transaction guidance by management, resulting in higher valuations and stock prices. This continued re-fueling will spur activity along with an aging population, new technological treatment discoveries, and continued corporate cost consolidation.

While hurdles exist going forward such as rising interest rates, increased regulatory effects of the ACA in 2015, lack of suitable acquisition targets, and new treasury regulations effecting tax inversions, these do not seem to be an overall concern at this time.

Most notable transactions of 2014

Announced in February, **Actavis**' US$ 25bn deal for **Forest Laboratories** is one of several transactions the company has taken advantage of in recent years to move away from its generic roots and into higher margin branded drugs. The acquisition provides Actavis with additional branded product depth headlined by the antidepressant Viibryd and the blood-pressure treatment Bystolic, while Forest teams up with a deep-pocketed industry powerhouse.

Bayer has repeatedly said its goal is to become the world's OTC leader. When word got out that **Merck** might be ready to shed some of its business units to narrow their strategic focus, Bayer was very interested, as were a few others. Ultimately it came down to a contest between Bayer and Reckitt Benckiser, however Reckitt unexpectedly dropped out just as the competition intensified and Bayer came away the winner at a price of US$ 14.2bn. As part of the deal, the two companies have entered into an agreement to jointly develop and market a group of cardio drugs known as sGC modulators, including Bayer's new pulmonary artery hypertension drug, Adempas. The acquisition consolidates a business that generated US$ 7.4bn in combined 2013 sales, with Merck's unit contributing US$ 2.2bn of that.

Roche Holding AG agreed to buy **InterMune Inc.** for about US$ 8.25bn in cash, gaining access to Pirfenidone, what may be the first drug in the U.S. for a lung disease that can be fatal within five years of diagnosis. Analysts predict Pirfenidone will generate US$ 1bn in global sales by 2019. The treatment targets idiopathic pulmonary fibrosis, a disease that causes tissue deep in the lungs to become thick and scarred over time. This acquisition will help Roche, the largest maker of cancer drugs, strengthen its global pulmonary franchise and offset the halt in development of diabetes and heart disease drugs in recent years as the company works to develop markets outside of oncology.

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JANUARY FEBRUARY **MARCH** APRIL MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

- **Myriad acquires Crescendo for US$ 245m**
- **Mallinkrodt purchases Cadence for US$ 1.2bn**
- **Thermo Fisher off-loads assets to GE Healthcare for US$ 1.1bn**

Latin America

A busy 2014

2014 has been a busier year in terms of number of transactions than 2013 with an increase of reported transactions from 17 to 24, according to our count. Not surprisingly, the majority of transactions took place in Brazil (9 vs. 5) and Mexico (5 vs. 2).

There are several trends which have become more prominent over the past years. First, the consolidation in the Pharma wholesale business continues as reflected by the acquisition of **Profarma** by **AmeriSourceBergen**. Second, there is an increasing number of transactions to be observed from companies with PE shareholders. **Invekra (Sanfer)**, the Mexican based Pharma group, now partly held by General Atlantic, is a good example for a more dynamic growth strategy through acquisitions (**Labinco** in Colombia now part of **More Pharma** in Mexico would be another one). Third, the animal health sector is undergoing a consolidation process as seen with **Nutreco Brasil** acquiring **Brnova Sistemas Nutricionais** and following a global trend set by **Merck's** divestment of its animal health business to **Merial (Sanofi)**. Fourth, some major players have been implementing strategies whereas they focus on core technology and share (divest?) other assets with third parties. A good example may be the divestment of **Novartis**' solids manufacturing in Brazil to the local pharmaceutical company **União Quimica**. Furthermore we have also noticed increasing acquisition intentions from major international CMOs in Brazil and Mexico.

Most notable transaction of 2014

By far the largest transaction in 2014 took place in Chile where **Abbott** acquired **CFR** (Recalzine) for the amount of US$ 3.4bn. This transaction appears to be a unique move rather than a trend as we have not observed any other Big Pharma player acquiring a regional branded generics business of this magnitude.

Several major regional champions have been facing difficulties in growing any further as their national antitrust authorities are reluctant to grant permission to acquire smaller national competitors. As a consequence, we have been observing an increasing amount of investments in North America and Europe by these groups or their wealthy shareholders. Despite the efforts of national governments to incentivize R&D, there are limited resources going into this area with the exception of biosimilars development, although it is yet unclear if these projects will be concluded successfully.

Outlook

For 2015, we expect a deal activity in the range of 2014 despite a rough economic climate in Brazil, Venezuela or Argentina and to a lesser degree also in Mexico and Colombia. It may be a good investment climate for long term investors, both, strategically or financially driven, as acquisition prices may be more affordable.

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JANUARY FEBRUARY MARCH **APRIL** MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

- **McKesson combines with Celesio for US$ 6.8bn**
- **Novartis acquires GSK's oncology business for US$ 14.2bn**
- **Lilly gets Novartis' animal health unit for US$ 5.4bn**
- **GSK gets Novarts' vaccines for US$ 5.3bn**
- **Sun relieves Daiichi Sankyo from Ranbaxy at US$ 4bn**

Western Europe

Generic consolidation is driving deals

Despite facing significant challenges, including rising customer expectation, the generics market has experienced substantial growth in the last decade. It remains a volume business – even though intensely competitive and highly consolidated – with many companies looking to improve margins either by optimising their operations or by diversifying into products with higher margins. This means the trend of consolidation is likely to continue.
As an example, in the latest in a string of acquisitions, **Actavis** will purchase **Allergan** in a deal worth a reported €54.7bn. The merger will create one of the top 10 largest Pharmaceutical companies in the world and will solidify Actavis as the world leader in generics. Also, Asian companies continue to build their international capabilities by expanding their presence in Europe where they are underrepresented.
For example, in April this year Indian generic Pharmaceutical company **Aurobindo Pharma** acquired certain commercial operations in Western Europe from **Actavis** plc, for €30m.

Most notable transactions of 2014

One notable transaction this year was **Bayer AG**'s €10.2bn acquisition of the Germany headquartered consumer health business of US Pharmaceutical company **Merck & Co**, proving that the over-the-counter (OTC) space continues to be a desirable area for consumer good companies looking to develop or extend their range of consumer brands. The transaction, which included Merck's existing OTC business comprising brands Claritin™, Coppertone™, Dr. Scholl's™, MiraLAX™, and Afrin™, significantly enhances Bayer's OTC portfolio and gives the conglomerate the global number two position in non-prescription medication, behind **Novartis** and **GlaxoSmithKline** (who announced their joint venture earlier this year) and Johnson & Johnson.
In October 2014, Swedish drug maker **Meda AB**, who is seeking to double its size within the next 2 years, acquired Italian Pharmaceutical company **Rottapharm** for an enterprise value of €2.3bn. Earlier this year Rottapharm had planned to publicly list its shares on the Milan stock exchange however aborted the IPO due to unfavourable international market conditions. Meda, who rejected a takeover approach from US generic-drug maker Mylan Inc. back in April 2014, reportedly chose Rottapharm from a short list of 10 targets, believing the company to be the "most interesting" target for them. The acquisition will strengthen Meda's consumer health care business expanding their global presence and product portfolio.
Another noteworthy transaction was the €160m acquisition of UK based **Penn Pharmaceuticals Services Ltd** (Penn), by US based Pharmaceutical packaging company, **Packaging Coordinators, Inc**. (PCI). The deal provided an exit for UK mid-market private equity firm, **LDC**, who took a significant stake in the business in April 2007. Penn, a Pharmaceuticals manufacturer providing a selection of CDMO services to some of the world's leading Pharmaceutical and Biotech companies, is assisting PCI's growth in the areas of clinical trial and commercial supply services, and helping expand their product portfolio.

Outlook

We expect 2015 to mirror 2014 M&A activity in the Pharmaceutical sector, as payers will look to source and procure low cost medicines, and look to negotiate heavy discounts on new drugs. Patent expiry exposure will impact top line sales of Pharma companies negatively, especially those that have a weak portfolio of medicine products, this will drive further consolidation in the mid market. The current financial climate appears friendly, with the market awash with cash from private equity investors. Combined with a strong debt market this will make 2015 an exciting and potentially prosperous M&A year.

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JANUARY FEBRUARY MARCH APRIL **MAY** JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

- **Santen acquires Merck & Co.'s ophthalmology products for US$ 600m**
- **Galderma acquires Valeant's injectable aesthetics for US$ 1.4bn**

Central and Eastern Europe

The level of M&A activity in the CEE region was somehow subdued by the negative political and economical situation in its Eastern European part (Ukraine crises) which led to economic sanctions of Russia. These events and the slump of petrol prices by 50% in the second half of 2014 sent the Russian economy into recession. With 37 disclosed transactions in 2014 (TTV €1.2bn) the year was higher in terms of deal value, but just slightly below the record of 41 deals in 2013 (TTV €1.06bn).

Most M&A activity happened concentrated in three countries: Poland and the Czech Republic both seeing ten deals, and Russia eight. All the other countries within the region have seen only one or two transactions per country. Out of 37 transactions only ten (or 27%) were international, which is a steep decline to the previous year, when 60% of all deals were cross-border. In both the Czech Republic and Poland, the M&A activities were mainly about consolidation of some sectors, e.g. outpatient & medical centers and medical services (45% of all deals). Private equity participated in one-third of transactions. The consolidation spree has driven prices up towards very high multiples for even small companies – approaching EV/EBITDA multiples of about 10x.

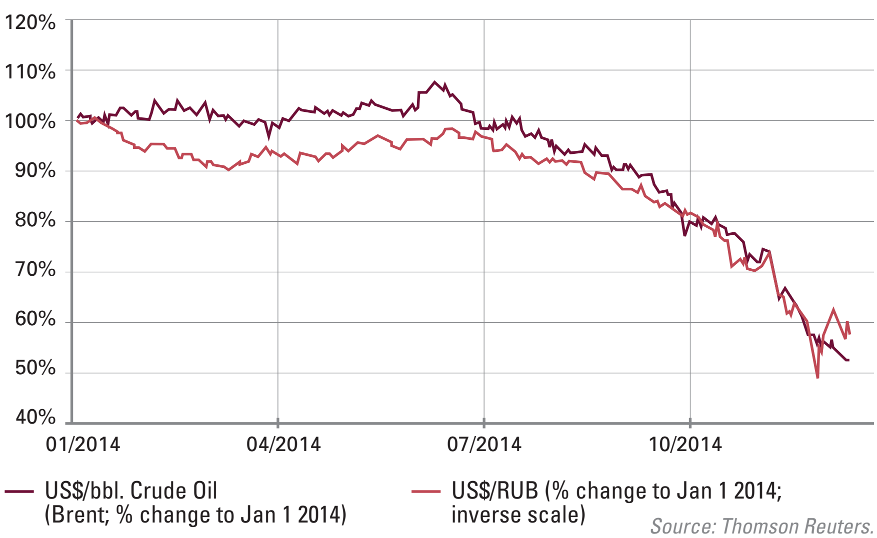
Most notable transactions of 2014

Veropharm OJSC, a Russia-based producer of generic and oncology drugs and medical plasters, was bought by US-based **Abbott Laboratories**, for €463m. The transaction will give Abbott a manufacturing presence in Russia and adds a portfolio of more than 100 products well aligned with its areas of focus. Veropharm should also contribute US$ 150m to Abbott's revenues in 2015. Abbott paid 2.9x revenues or 26.5x earnings.

Russia-based **CJSC Biocad**, active in gynecology, urology, oncology and neurology, was acquired by Russia planner company **Pharmstandart OAO** (taking 20%), and by **Millhouse LLC** (acquiring 50%), the Russia-based investment holding of Gazprom Bank. The total consideration was €512m.

Another notable deal was **Hartenberg Capital**, a Czech PE house, who has acquired **5 Czech medical companies**: Gennet Archa (healthcare services), Prvni Privatni Chirurgicke Centrum (medical centre), Iscare Clinical Centre (medical centers) Gyn Centrum (gynecological clinic) and Reprofit International (IVF clinic).

OIL PRICE DECLINE SHATTERING THE RUSSIAN ECONOMY



Source: Thomson Reuters.

Outlook

While the consolidation play in the segment of small and mid-sized companies should continue in Poland and the Czech Republic in 2015, the situation in Russia and Ukraine will be subdued as risks are high and owners will be reluctant to sell companies on low valuations based on low pre-crises multiples and low profits, when calculating from local currency to hard currencies. Conversely this negative development may initiate some fire-sale opportunities from indebted local investment groups and holdings.

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REDBAENK

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JANUARY FEBRUARY MARCH APRIL MAY **JUNE** JULY AUGUST SEPTEMBER OCTOBER NOVEMBER DECEMBER

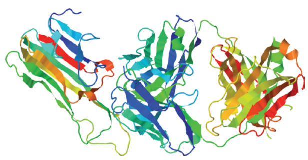
- **Teva acquires Labrys and its migrain pipeline, pays US$ 825m**
- **Abbott acquires Veropharm for US$ 631m**
- **Lundbeck purchases Chelsea for US$ 542m**

Top 30 drugs by

FABIAN WEBER AND BISSERA DIMITROVA

1. ADALIMUMAB

Humira®

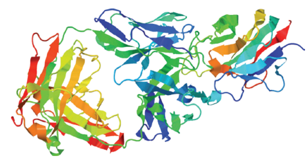


TNF inhibitor

2013:US$ 11.0bn vs 2011: +US$ 3.1bn (+39%)

2. INFLIXIMAB

Remicade®

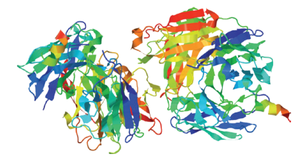


TNF inhibitor

2013:US$ 8.9bn vs 2011: +US$ 0.0bn (+0%)

3. RITUXIMAB

Mabthera®

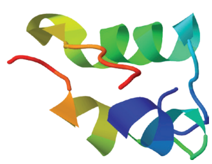


CD20 antibody

2013:US$ 8.6bn vs 2011: +US$ 1.8bn (+27%)

7. INSULIN GLARGIN

Lantus®

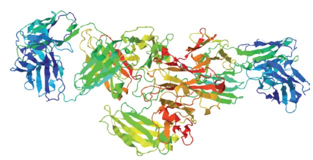


Insulin analogon

2013:US$ 7.6bn vs 2011: +US$ 2.1bn (+39%)

8. BEVACIZUMAB

Avastin®

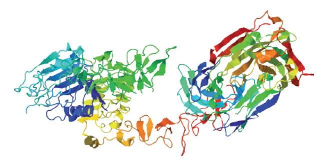


Angiogenesis inhibitor

2013:US$ 6.7bn vs 2011: +US$ 0.1bn (+1%)

9. TRASTUZUMAB

Herceptin®

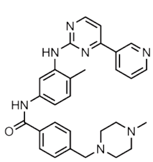


Her2-receptor antibody

2013:US$ 6.6bn vs 2011: +US$ 0.6bn (+11%)

13. IMATINIB

Gleevec®

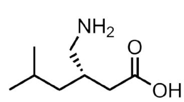


Tyrosin kinase inhibitor

2013:US$ 4.7bn vs 2011: +US$ 0.0bn (+1%)

14. PREGABALIN

Lyrica®

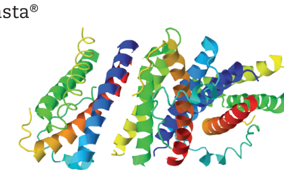


Binds voltage-dependent calcium channel inhibitor

2013:US$ 4.6bn vs 2011: +US$ 0.9bn (+24%)

15. PEGFILGRASTIM

Neulasta®

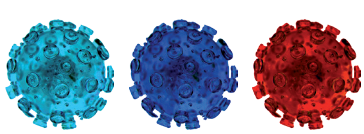


Granulocyte colony-stimulating factor

2013:US$ 4.4bn vs 2011: -US$ 0.8bn (-16%)

19. PNEUMOCOCCAL CONJUGATE

Prevnar®

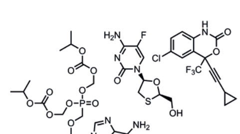


Pneumococcal vaccine

2013:US$ 4.0bn vs 2011: +US$ 0.3bn (+9%)

20. EMTRICITABINE / TENOFOVIR / EFAVIRENZ

Atripla®

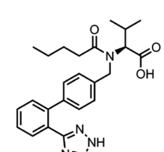


Reverse transcriptase inhibitors

2013:US$ 3.6bn vs 2011: +US$ 0.4bn (+13%)

21. VALSARTAN

Diovan®

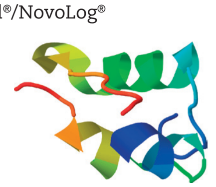


Angiotensin II receptor antagonist

2013:US$ 3.5bn vs 2011: -US$ 2.1bn (-38%)

25. INSULIN ASPART

NovoRapid®/NovoLog®

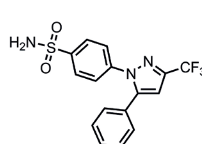


Insulin analogon

2013:US$ 3.0bn vs 2011: +US$ 0.6bn (+25%)

26. CELECOXIB

Celebrex®

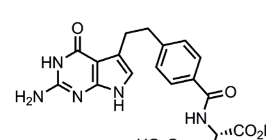


COX-2 inhibitor

2013:US$ 2.9bn vs 2011: +US$ 0.4bn (+16%)

27. PEMETREXED

Alimta®



Folate antimetabolite

2013:US$ 2.7bn vs 2011: +US$ 0.2bn (+10%)

worldwide sales

WWW.PHARMA-POSTERS.ORG

4. ETANERCEPT

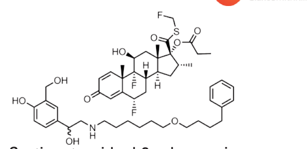
Enbrel®

TNF inhibitor

2013:US$ 8.3bn vs 2011: +US$ 1.0bn (+13%)

5. FLUTICASONE /SALMETEROL

Seretide®

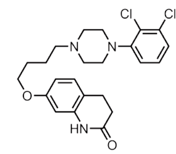


Corticosteroid + b2-adrenergic receptor agonist

2013:US$ 8.2bn vs 2011: +US$ 0.1bn (+2%)

6. ARIPIPRAZOL

Abilify®

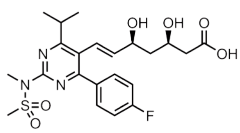


Atypical antipsychotic

2013:US$ 8.2bn vs 2011: +US$ 0.8bn (+11%)

10. ROSUVASTATIN

Crestor®

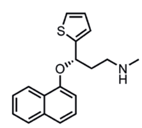


HMG-CoA reductase inhibitor

2013:US$ 5.6bn vs 2011: -US$ 1.0bn (-15%)

11. DULOXETINE

Cymbalta®

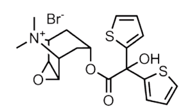


Serotonin-norepinephrine reuptake inhibitor

2013:US$ 5.1bn vs 2011: +US$ 0.9bn (+22%)

12. TIOTROPIUMBROMID

Spiriva®

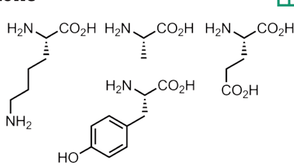


Muscarinic receptor antagonist

2013:US$ 4.7bn vs 2011: +US$ 0.3bn (+7%)

16. GLATIRAMER ACETATE

Copaxone®

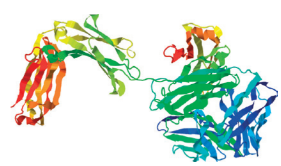


Decoy for immune system

2013:US$ 4.3bn vs 2011: +US$ 0.2bn (+4%)

17. RANIBIZUMAB

Lucentis®

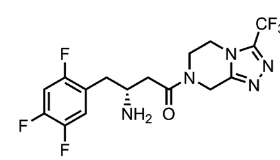


Binds to endothelial growth factor

2013:US$ 4.2bn vs 2011: +US$ 0.4bn (+12%)

18. SITAGLIPTIN

Januvia®

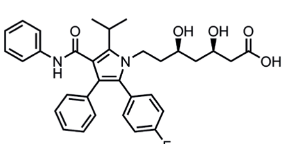


Dipeptidyl peptidase-4 inhibitor

2013:US$ 4.0bn vs 2011: +US$ 0.7bn (+20%)

22. ATORVASTATIN

Lipitor®

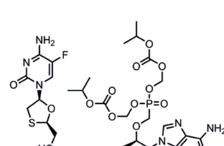


HMG-CoA reductase inhibitor

2013:US$ 3.3bn vs 2011: -US$ 7.5bn (-70%)

23. TENOFOVIR/ EMTRICITABINE

Truvada®

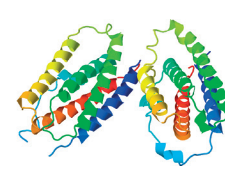


Reverse transcriptase inhibitors

2013:US$ 3.1bn vs 2011: +US$ 0.3bn (+9%)

24. INTERFERON BETA 1A

Avonex®

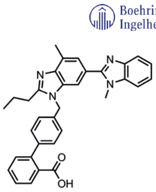


Activates immune system

2013:US$ 3.0bn vs 2011: +US$ 0.3bn (+12%)

28. TELMISARTAN

Micardis®

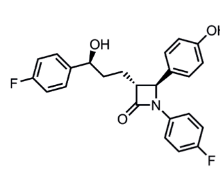


Angiotensin II receptor antagonist

2013:US$ 2.7bn vs 2011: -US$ 0.4bn (-13%)

29. EZETIMIBE

Zetia®



Decreases cholesterol absorption in the intestine

2013:US$ 2.7bn vs 2011: +US$ 0.2bn (+9%)

30. INSULIN LISPRO

Humalog®

Insulin analogon

2013:US$ 2.6bn vs 2011: +US$ 0.2bn (+10%)

Sources: Company websites & annual reports. Comments, additional information and a poster format with the 150 top drugs are available at pharma-posters.org.

China

The Chinese healthcare market has been in a prolonged period of fundamental upheaval. The anti-corruption trials of the government hit foreign and domestic companies hard. Change of pricing and tender models will cause tectonic shifts in the competitive space. On the other hand, China started to heavily invest into the development of own biosimilar competences, and the lift of the IPO ban on domestic stock markets led to 11 IPOs in the healthcare space and considerable deal making. There was also a pronouncedly increased level of Chinese companies and VCs investing in development-stage drugs abroad, a trend we expect to increase in the coming years.

M&A activity was mainly driven by domestic consolidation. We counted 57 transactions with Chinese participation (excl. financial investors) and with a transaction volume higher than US$ 10m, with a cumulated total transaction volume ("TTV") of US$ 6.6bn for 2014. Thereof, 51 deals (TTV US$ 5.2bn) were between Chinese firms, four involved Chinese firms acquiring foreign targets (outbound) and only two were inbound: **Bayer'**s acquisition of **Dihon Pharmaceuticals** for US$ 580m and **Alliance Boot'**s acquisition of **Nanjing Pharmaceuticals** for US$ 91m.

Key transactions in 2014

One of the key domestic deal makers was **Fosun Pharma** which formed an industry-changing joint venture with **Sinopharm** to build a nationwide drug and medical devices distribution network, with an initial investment believed to be worth US$ 1bn. Sinopharm is China's leading (and the world's fourth-largest) Pharma distributor. Fosun, who already owns a 30% indirect stake in Sinopharm, holds a 60% stake in the JV. The new venture plans to build up 20 logistical and 30 distribution centers covering 10 different regions in China and is aimed at flattening the way-to-market of China's multi-level and fragmented dealer structure.

Luye Pharma is the other big consolidator in China. The company, which recently went public, acquired a controlling stake in Beijing Jialin for US$ 590m in September 2014. **Beijing Jialin** owns a portfolio of late-stage cardiovascular and cancer drugs which are scheduled to be launched in 2015, and the leading atorvastatin generic sold in China ("A Le").

Shenzen Hepalink closed its US$ 337.5m acquisition of US API manufacturer **Scientific Protein Laboratories** in January 2014. With the acquisition, Hepalink broadens its distribution network, as both companies are in the business of producing the anti-coagulant heparin. Later in November, Shenzhen Hepalink announced its second outing in the USA, by acquiring 13% of the US Biopharmaceuticals company **Cantex Pharmaceuticals** for US$ 30m.

The largest deal closed in 2014, both on the cross-border and domestic deal front, was Bayer's acquisition of Dihon Pharmaceuticals for US$ 580m in November 2014. Dihon Pharmaceuticals, with 2,400 staff, specializes in OTC and TCM products, in dermatitis, acne, recurrent oral ulcer, hyperosteogeny and endometriosis, with sales worth US$ 168m in 2013. With the acquisition of Dihon, Bayer complements its global OTC strategy in the wake of its acquisition of Merck & Co's global healthcare products business for US$ 14.2bn.

Compared to the meager inbound M&A in 2014, partnership and licensing to engage with the Chinese increased. Out of 32 prominent in-licensing deals made in 2014 that are known to us and we reviewed, twenty deals involve the Chinese partner not just to commercialize the drugs, but also to invest actively in some sort, either in R&D, co-development, and / or clinical trials in China. This is a seismic shift from earlier years where Chinese companies were focused on licensing products which could be commercialized in China within two years.

Outlook

We expect especially domestic M&A activity to further increase in 2015 as the local Pharma landscape must further consolidate. Certainly, in- and out-licensing activities between non-Chinese and Chinese Pharma companies will further accelerate in 2015, but it remains uncertain if larger non-Chinese Pharma companies will bring up an appetite for major deals. Many multi-national companies are currently streamlining their own operations rather than making large moves on domestic competitors.

Contributed by IMAP in China

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Franc Kaiser
(franc.kaiser@imap.com)

Note: This overview is a summary of an in-depth analysis which can be retrieved from the author.

/ **Actavis acquires Forest for US$ 23bn**

/ **Mylan gets Abbott's non-US generics for US$ 5.3bn**

/ **Forest acquires Furiex for US$ 1bn**

Tax inversions - a major deal driver

US-based Horizon Pharma's acquisition of Ireland-based Vidara Therapeutics, Mylan's acquisition of one part of Abbott's generic business, and Pfizer's proposed acquisition of AstraZeneca. These deals of 2014, even though not all of them successfully closed, had one major objective in common: tax savings by shifting the US Company's headquarters to a different country with a more favorable tax system. These transactions involving a so-called corporate tax inversion have been a much discussed topic and a major driver of global M&A throughout 2014, particularly in the Pharmaceutical industry.

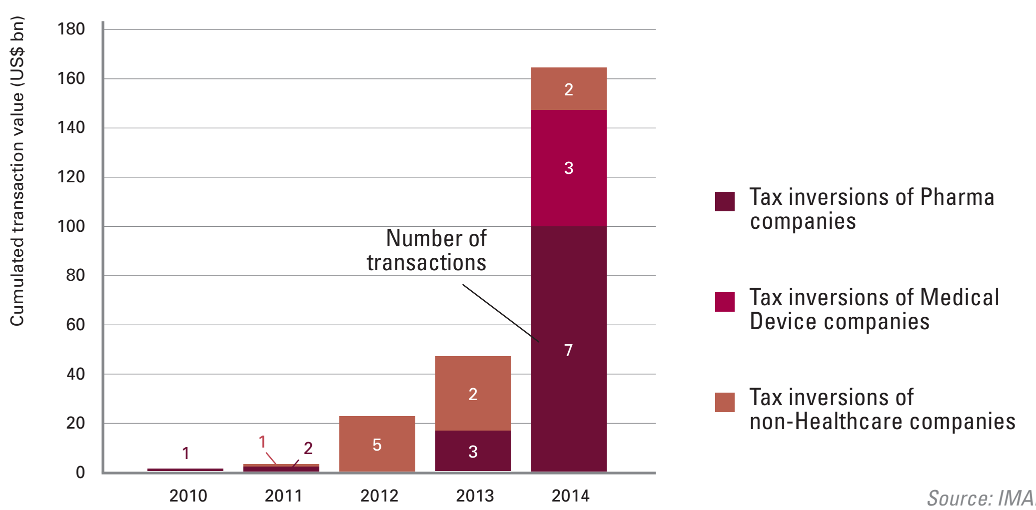
Three decades of tax inversions

Transactions by US companies leading to tax inversions have been performed since a long time, but in the recent years, their frequency increased dramatically. Between 1984 and 2004, there were 28 transactions which involved a tax inversion (on average 1.4 per year). Since 2004, there have been 47 inversions (almost 5 per year), thereof 22 in 2012-2014 (7 per year). In the last two years, there were ten transactions by Pharma companies which included an inversion, or were done by an acquirer which recently had done an inversion, amounting to a total volume of US$ 117bn (see figure 1).
Why are transactions involving inversions accelerating? And why are those transactions particularly attractive for US Pharma companies?

Drivers for corporate tax inversions

The combined corporate income tax rate (combined federal rate and average rate of US states) of US-domiciled corporations has stayed between 39% and 40% since 1993, while the comparable tax rate of all OECD countries declined steadily over the years (see figure 2). The US corporate tax rate today is the highest amongst all OECD countries. Thus it has become more and more alluring for US companies to move their tax domicile abroad.
Moreover, the US taxes foreign incomes of US-domiciled companies as soon as these earnings are repatriated (applying the incremental rate between the US and foreign tax rate). Trying to avoid these taxes made US corporates leave cash in their foreign subsidiaries, piling to an amount across all industries of US$ 947bn, according to Moody's, a rating agency. Other estimations amount to US$ 2tn. Performing an acquisition abroad using these monies means that the tax for repatriation can be avoided: an immediate benefit of any inversion, and certainly a driver of valuations of US-based companies purchasing foreign targets.
The Pharma industry is disproportionally exposed to this cash pile phenomenon. Moody's estimates around 15% of global ex-US cash piles of US domiciled

FIGURE 1 **TRANSACTIONS INVOLVING TAX INVERSIONS OR COMPANIES HAVING INVERTED RECENTLY, BY INDUSTRY**



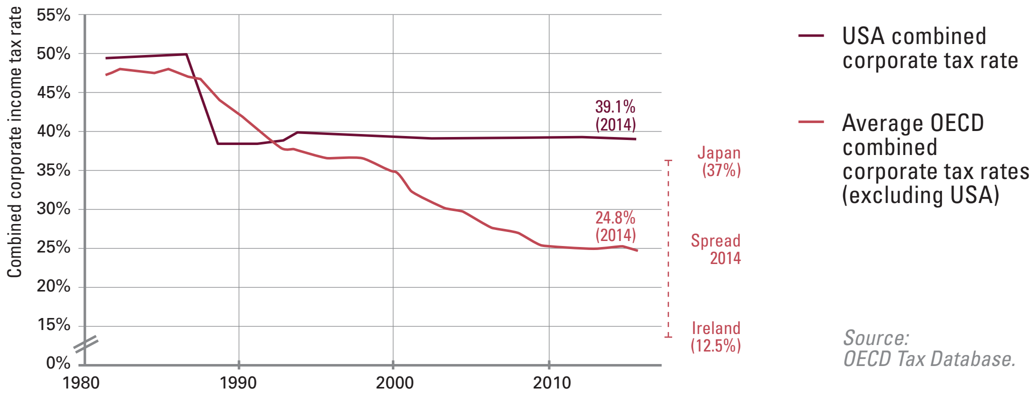
Source: IMAP research.

/ **Merck & Co purchases Idenix for US$ 3.5bn**

/ **Endo swallows DAVA for US$ 575m**

/ **Mallinkrodt acquires Questcor for US$ 5bn**

FIGURE 2 **COMBINED CORPORATE TAX RATES**



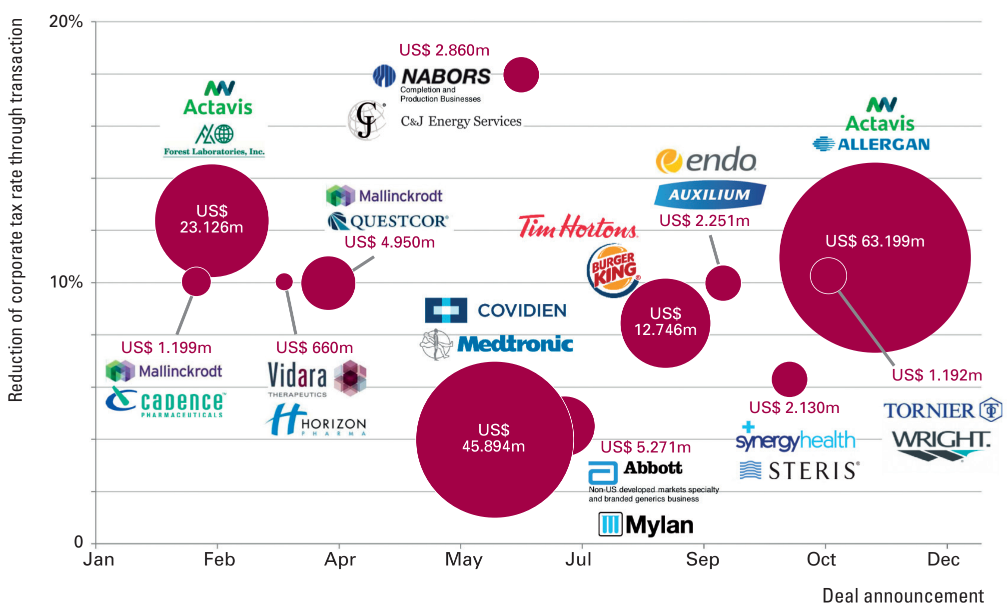
Source: OECD Tax Database.

companies are owned by Pharma companies, compared to an estimated 2.9% contribution of this industry to the total US economy.

2014 – The year of tax inversions

The year 2014 saw 12 high-profile tax deals leading to inversions or deals by companies which had done an inversion very recently, thereof seven in the Pharma industry and three in MedTech, accounting for a cumulated transaction volume of US$ 160bn (see figure 3). The merged entity's corporate tax rate fell around 8.9% compared to the tax rate of the acquiring or merging US Corporation before the transaction (weighted average).
However, throughout the year 2014, public resistance against tax-moving deals increased. AbbVie's US$ 53bn bid for Shire and Pfizer's US$ 116bn bid for AstraZeneca both came to a halt, at least partially due to the US Treasury's new rules on tax inversions

FIGURE 3 **NOTABLE TRANSACTIONS IN 2014 INVOLVING TAX INVERSIONS, OR ACQUIRERS WHICH INVERTED BEFORE**



Notes: Bubble sizes represent relative deal size; top logo is merging non-US company; bottom logo is merging US-company.

Source: Thomson Reuters, Bloomberg, MergerMarket.

JANUARY FEBRUARY MARCH APRIL MAY JUNE JULY AUGUST **SEPTEMBER** OCTOBER NOVEMBER DECEMBER

- **Abbot enters Chile with CFR buy for US$ 3.3bn**
- **Roche buys Intermune for US$ 7.5bn**
- **J&J acquires Alios for US$ 1.8bn**

issued in September 2014. This is to be expected, when the bottom line impact is considered which tax inversion transaction cause for the US tax system. Table 1 shows the estimated pre- and post-transaction corporate tax rates and annual tax savings (using the pre-tax profit of the previous fiscal year) resulting from selected healthcare deals in 2014. Of importance, this calculation does not take into account tax savings from the possibility to invest overseas cash piles without repatriation. The total loss for the US tax systems from these inversions amounts to billions of dollars.

TABLE 1

TAX SAVINGS OF SELECTED TRANSACTIONS OF PHARMA AND MEDTECH COMPANIES IN 2014

US COMPANY / NON-US COMPANY	TAX RATE US-COMPANY, PRIOR TRANSACTION	TAX RATE US-COMPANY, POST TRANSACTION	ANNUAL TAX SAVINGS (US$ M)
Allergan / Actavis	26%	15%	190
Mylan / Abbott (non US markets)	25%	21%	33
Medtronic / Covidien	20%	16%	148
Questcor / Mallinckrodt	35%	25%	44
Forest / Actavis	28%	16%	10

Source: IMAP research.

The strategic advantage of a lower tax base

Obviously, lowering the company's tax burden is desirable per se. In the context of deal making, which is such a central part of any Pharma company's strategy, a low tax base is also a key competitive advantage. Pfizer's CEO Ian Read emphasized the point when he stated that, due to taxes, Pfizer is "at a tremendous disadvantage" because it cannot pay the same prices for target companies.

Furthermore, one of the objectives of some tax inversion transactions involving Pharma companies, was building a "tax-efficient acquisition platform". Several post-inversion transactions of 2014 exemplify the point: Mallinckrodt, since recently based in Ireland, acquired Cadence Pharmaceuticals (US$ 1.2bn) and subsequently Questcor Pharmaceuticals (US$ 5bn); Actavis, an Irish company since 2013, acquired Forest Laboratories (US$ 23bn) and subsequently Allergan (US$ 63bn). On a smaller scale in 2014, Horizon Pharma started to build an M&A platform with its US$ 660m acquisition of Ireland-based Vidara Therapeutics, officially with the aim to establish a tax-efficient corporate structure for future acquisitions.

Arguably, Actavis' huge acquisitions past year may not have been possible without the lower Irish tax base it enjoys. Ironically, through its mergers, Actavis is now one of the few targets for Pfizer which would qualify as a target for a tax inversion.

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Christoph Bieri
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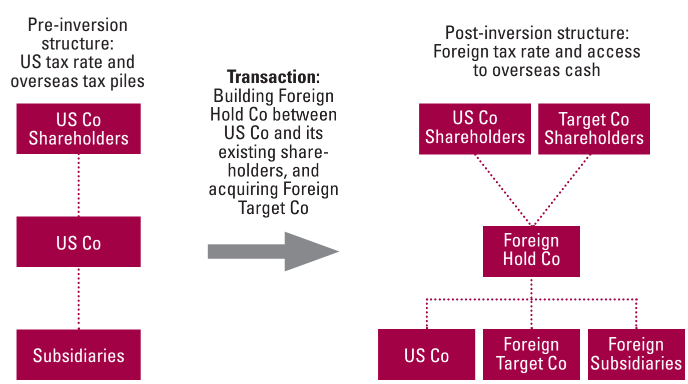
HOW DOES A TAX INVERSION WORK?

In a typical tax inversion transaction, a new non-US holding corporation ("Foreign Hold Co") which is based in a favorable tax system (e.g. in Ireland) is "built" in between existing shareholders ("US Co Shareholders") and the US Company ("US Co") through a "reverse triangular merger".

This structure at the same time acquires a foreign target ("Foreign Target Co", typically based in the same jurisdiction as the Foreign Hold Co) by way of a "cancellation scheme arrangement". The pre- and post-transaction structures typically look as outlined on the right side.



/ **Bayer acquires Merck & Co's OTC unit for US$ 14.2bn**

/ **Endo purchases Auxilium for US$ 2.3bn**

/ **Meda combines with Rottapharm for US$ 3.1bn**

M&A in Pharma manufacturing

The Pharma industry's transformation affects not only drug development and marketing, but also and increasingly so manufacturing. Changing regulatory frameworks, cost pressure, and an efficiency gap compared to other industries will lead to a fundamental reshaping of the manufacturing networks (in-house and outsourced) in the next few years, mainly through M&A.

Fundamental changes ahead

What is to be expected? Pharma manufacturing shares fundamental features with the automotive industry. Both are large, complex and heavily regulated industries with multilayered value chains. In the automotive industry, car manufacturers had to cope with ever more stringent environmental regulations. As a result, car manufacturers and suppliers were forced to innovate, leading to leaps in fuel efficiency technologies. Other noticeable outcomes include consolidation and a broader scope of outsourcing or collaboration. Surprisingly, today, many suppliers are more profitable than some brand owners: Hyundai Mobis, Continental or Bosch have EBIT margins between 6% and 10% and ROCEs between 12% and 20%; leaving no profitability gap with the top car manufacturers (e.g. BMW). Thus, the maturation rearrangement of the manufacturing value chain led to a redistribution of the value captured.

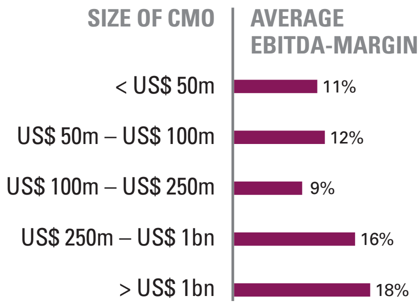
In Pharma manufacturing, we observe trends which may lead to a similar result. First, there is an increasing consolidation pressure among the contract manufacturing organizations (CMOs). Second, outsourcing by Big Pharma increasingly involves selling own manufacturing sites to CMOs to operate them.

In a fragmented CMO market…

While contract manufacturing may appear to be a reasonably profitable business, there are large variations (see figure 1). The large CMOs generate substantial margins. Catalent for example has built a very strong position in advanced technologies (softgel, ODT) and delivers an attractive 20% EBITDA. Smaller CMOs, many of them local and without technological specialization, often do not generate enough profit to cover necessary investments. They are increasingly exposed to changes in customers expectations and in the regulatory environment (serialization, upgrade of ERP systems). Thus, many of the CMOs with less than US$ 25m revenues will disappear in the mid-term.

In a still fragmented market (see figure 2), there are few truly global players, but globalization is under way. Western European CMOs typically operate close to their historic base. To some extent they are looking at relocating some of their business to Central or Eastern Europe to offer a low cost base for commoditized services such as manual packaging. Increasingly, European CMOs aim at setting up operations in North America, preferably in the USA. CMOs based in emerging markets have aso become active in expanding geographically to Europe or to the USA.

FIGURE 1



Source: IMAP research.

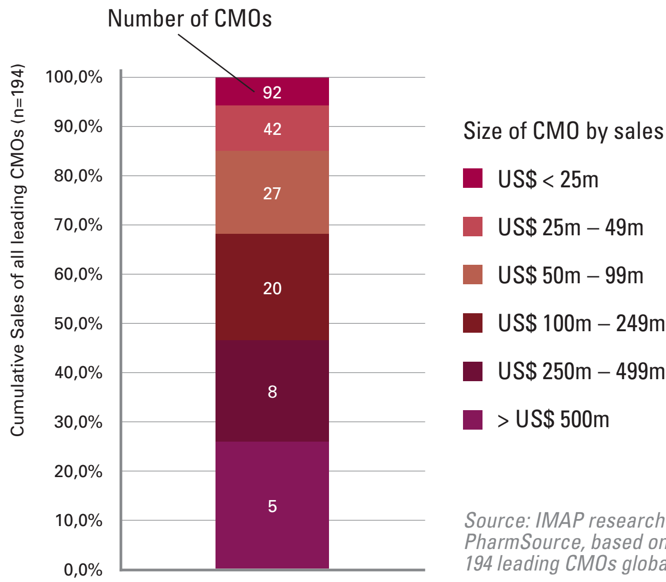
… maturation forces to differentiate

Such a market structure – not truly global, large spread in profitability and size – is predictive for consolidation. Leading CMOs are developing acquisition or differentiation strategies, based on three pillars: reinforcing their customer base, selectively expanding their geographic reach and broadening their capabilities (technology, services and development). Recipharm's acquisition of Corvette in 2014 is a good illustration: gaining access to a new customer base with little overlap, acquiring a strong geographical presence in Italy with experience serving emerging markets, and strengthening lyophilization capabilities. Mid-sized CMOs like Aenova, Corden Pharma, Delpharm or Fareva energetically expand this way. Other mid-sized players aim at building strong positions in technical niches. Siegfried's acquisition of Pharma Hameln, for instance, makes them a globally leading service provider of sterile filling of injectables.

JANUARY FEBRUARY MARCH APRIL MAY JUNE JULY AUGUST SEPTEMBER OCTOBER **NOVEMBER** DECEMBER

- **LabCorp becomes CRO with Covance buy for US$ 5.6bn**
- **Perrigo gets OTC with acquisition of Omega Pharma for US$ 4.5bn**
- **Actavis relieves Allergan of Valeant threat, pays US$ 63bn**

FIGURE 2 **FRAGMENTATION OF THE CMO MARKET**



Source: IMAP research / PharmSource, based on 194 leading CMOs globally.

The perspective of Pharma companies

Consolidation has left many large Pharma companies with sprawling, inefficient manufacturing networks. One key step for the networks' rationalization is the sale of operating plants. Unfortunately, these disposals are often treated as real estate transactions, not as sale of an ongoing business system intertwined with the seller's strategy. On the other hand, sellers' valuation expectations reflect the value as a "fit for purpose" business asset. This misalignment of M&A approach and financial goals leads to unsatisfactory results, or to the premature termination of the selling process.

Stakeholder alignment

At the outset of a sale of an operating plant, senior management needs to be aligned to realistic expectations. The result of a disposal is a combination of the price paid by the acquirer, the manufacturing agreement (costs and terms of manufacturing), and the supply certainty (business continuity, compliance, etc.) provided by the buyer. These three dimensions typically affect different line managers at the seller who have to be aligned.

In the past, Pharma companies were too often forced to refinance the acquirers of their plants. They now pay much more attention to the overall profile of candidate buyers (quality record, financial stability). CMOs, on the other side, had to learn hard lessons, ending with loss-making sites due to unrealistic expectations regarding new business, performance or cultural improvements and underestimated capital investment needs. We observe that acquisition prices for plants rather decrease than increase as a consequence.

Deal value is one parameter only

Transaction prices have to be assessed independently from historic investments in the plant. Obviously, there is a trade-off between the transaction price and future cost savings for the seller: lower manufacturing costs convert to a lower acquisition price. Our experience is that CMOs are relatively flexible to adjust the terms, applying a relatively transparent mechanism, which opens interesting opportunities to optimize the value for both sellers and buyers. Less obvious are the trade-offs between shorter duration of the manufacturing agreement and the acquisition price for the site. By co-developing an investment and business plan, buyers and sellers can also make this interdependence transparent and find mutually satisfactory solutions.

Outlook

We believe that the maturation of the CMO market and the ongoing pruning of the manufacturing network of Pharma companies will lead to a steady flow of transactions. They need to be shaped as long-term partnerships, similarly to some of the strategic alliances between Pharma companies and CROs. Scale and operational excellence combined with technical specialties may enable CMOs to capture an increasingly large part of the value, leading to a similar end-game as observed in the automotive industry today.

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JANUARY FEBRUARY MARCH APRIL MAY JUNE JULY AUGUST SEPTEMBER OCTOBER NOVEMBER **DECEMBER**

/ **Otsuka acquires Avanir for US$ 3.2bn**

/ **BTG purchases PneumRx for US$ 475m**

/ **Merck & Co acquires Cubist for US$ 8bn**

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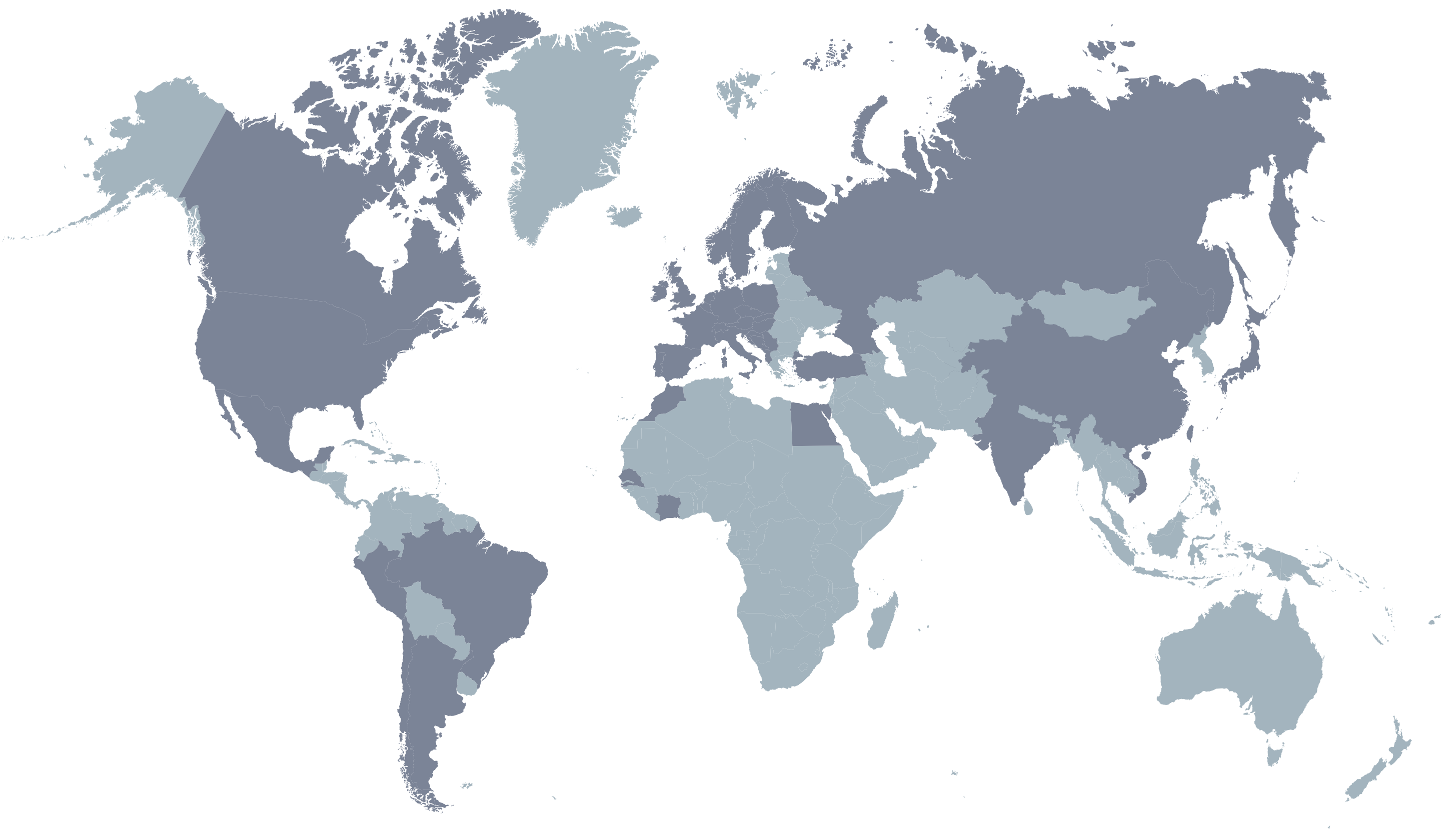

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