Recent IMAP healthcare transactions

**Recipharm**
- **Recipharm AB**
  - Global Pharmaceutical CDMO
  - Stockholm, Sweden
  - Entered into a Long-term Supply Agreement and Acquired a Manufacturing Facility from a Novartis company
  - Manufacturing plant Taboa da Serra, Brazil
  - Represented the Seller

**Domes Pharma SA**
- Pharmaceutical industry and animal health
- Clermont-Ferrand, France
  - Acquired 100% of Business Operations of Léro Laboratories d’Etudes et de Recherche
  - Dietary supplements, vitamins and trace elements
  - Paris, France
  - Advised on Purchase of Company

**GWB**
- G.W Berg & Co Ab
  - Laboratory equipment, ind. weighing solutions
  - Vantaa, Finland
  - Acquired 100% of Business Operations of Latio Oy
  - Reagents and laboratory equipment
  - Vantaa, Finland
  - Advised on Sale of Company

**Sievried**
- **Sievried Group**
  - Primary and secondary production of pharmaceutical drugs
  - Zofingen, Switzerland
  - Acquired 100% of Business Operations of Elvita – Jaworzno III
  - Healthcare and diagnostics, occupational medicine
  - Jaworzno, Poland
  - Represented the Seller

**SBK Holding**
- **SBK Holding**
  - Turkey-based conglomerate
  - Istanbul, Turkey
  - Acquired 100% of Business Operations of Betasan
  - Manufacturer of bandages and plasters
  - Istanbul, Turkey
  - Represented the Buyer

**Domes Pharma SA**
- Pharmaceutical industry and human health
- Clermont-Ferrand, France
  - Acquired 100% of Business Operations of Precisa – Laboratorio Arias Stella
  - Pathology Lab Biopap and clinic lab
  - Acquired by Ve. Pa. Fin. S.r.l. (Ve.Di. Group)
  - Advised on Sale and Purchase of Company

**FENNO MEDICAL OY**
- **Fenno Medical Oy**
  - Medtech wholesalers
  - Malmön, Sweden
  - Acquired 100% of Business Operations of Mediplast AB / Addtech AB
  - Advised on Sale of Company

**LBnet Oy**
- **Labnet Oy**
  - Reagents and laboratory equipment
  - Vantaa, Finland
  - Advised on Sale of Company

**Sterling Partners**
- **Private Equity House**
  - Chicago, Illinois, United States
  - Acquired Business of Surgical Solutions LLC
  - Healthcare service provider for operating rooms
  - Henderson, Kentucky, United States
  - Advised on Sale of Company

**FIZAN BIS**
- **PZU SA Investment Fund**
  - Warsaw, Poland
  - Acquired Majority Control of Business Operations of Elvita – Jaworzno III
  - Healthcare and diagnostics, occupational medicine
  - Jaworzno, Poland
  - Represented the Seller

**SBK Holding**
- **SBK Holding**
  - Turkey-based conglomerate
  - Istanbul, Turkey
  - Acquired 100% of Business Operations of Betasan
  - Manufacturer of bandages and plasters
  - Istanbul, Turkey
  - Represented the Buyer

**Euromedic International**
- **Diagnostic services**
  - Milan, Italy
  - Acquired 100% of Business Operations of Ve. Pa. Fin. S.r.l. (Ve.Di. Group)
  - Healthcare services
  - Milan, Italy
  - Represented the Buyer in this Transaction

**CooperSurgical, Inc.**
- **Global medical device company**
  - Pleasanton, California, United States
  - Acquired 100% of the Equity
  - Advised on Purchase of Company

**Novartis**
- **Novartis**
  - Manufacturing plant Taboa da Serra, Brazil
  - Represented the Seller

**AstraZeneca**
- **Entocot**
  - Treatment of inflammatory bowel disease (IBD) owned by AstraZeneca
  - London, United Kingdom
  - Represented the Buyer in this Transaction

**Permira**
- **Pantheon Healthcare Group**
  - Services for hospitals and diagnostic centers
  - Reading, United Kingdom
  - Acquired a controlling interest in Ingegoria Biomedica Santa Lucia
  - Biomedical equipment and systems
  - Piacenza, Italy
  - Represented the Seller in this Transaction

**Pernova Pharma (Zeria Group)**
- **Pharma company focused on gastroenterology**
  - Rheinfelden, Switzerland
  - Acquired ex-US global rights for Entocort

**Permedia**
- **Public Equity Fund**
  - Sterling Partners
  - Chicago, Illinois, United States
  - Acquired Majority Control of Business Operations of Surgical Solutions LLC
  - Healthcare service provider for operating rooms
  - Henderson, Kentucky, United States
  - Advised on Sale of Company

**Sievried**
- **Sievried Group**
  - Primary and secondary production of pharmaceutical drugs
  - Zofingen, Switzerland
  - Acquired 100% of Business Operations of Elvita – Jaworzno III
  - Healthcare and diagnostics, occupational medicine
  - Jaworzno, Poland
  - Represented the Seller

**Elements Behavioral Health**
- **Provides behavioral health care programs**
  - Long Beach, California, United States
  - Acquired 100% of Business Operations of Park Bench Group
  - A drug & alcohol treatment center
  - Northfield, New Jersey, United States
  - Advised the Seller on Buyside
For the Pharma and Biotech industry, the year 2015 can be summarized in just three phrases: Pfallergan, Clinton’s Tweet and CRISPR-Cas9. In what was an exceptional year, these terms describe what moved the industry: merger mania, price pressure in the US and accelerating innovation.

“Pfallergan”, the combination of Pfizer and Allergan, is one of the largest M&A transactions ever and caps a two-year period of intense deal-making (see pages 4-6). Valuations of large deals increased dramatically during this time, driven primarily by tax inversions but also by a sentiment of “land-grabbing” amongst large players. Many believe that Pharma companies need to slim down and differentiate. Page 10 illustrates what drives the emerging 4 Strategic Archetypes and on page 14 we look at how Pharma companies extend their franchises by doing large portfolio deals rather than company M&A.

“Clinton’s Tweet”, posted in September, sent biotech and pharma stocks prices down 4.5% in just a few hours. In her message, the presidential candidate announced she would lay out plans to counter “price gouging” in the specialty Pharma industry. The tweet targeted Turing Pharmaceuticals but also hit-out at other companies known for increasing prices of old drugs following their acquisition, such as Valeant. The ongoing political debate confirms that the climate in the US regarding drug pricing is fundamentally changing, which will have profound effects on the global industry which finances most of its R&D with profits gained in the US market.

“CRISPR-Cas9” epitomizes the big hope which Biotech carries: novel technologies that allow the development of new groundbreaking treatments. The CRISPR-technology combines an enzyme with a targeting sequence (see cover picture) to specifically change the genome of an organism and may be used to cure hereditary diseases. While it will still take years to see the full impact of CRISPR in practice, we look at business models emerging from another recent wave of innovations: genomics and next-generation sequencing (pages 14-16).

We hope you enjoy reading our report.

Truly yours,
Large deals dominate Pharma M&A

The year 2015 saw a continued high level of M&A activity in the Pharma and Biotech industry. As we show in our long-term view (see Graph 1), deal volumes, the number of deals and average multiples are still at a very high level as compared to the mid-term past.

The word of the year in the Pharma industry – and among deal makers at large – is probably “PfAllergan”, a merger of “Pfizer” and “Allergan”. Allergan was the only target large enough to enable Pfizer to move its tax domicile through an acquisition (a so-called “inversion”), after the US-based giant was rebuffed by AstraZeneca in 2014. Ironically, Allergan, previously Actavis, has been Irish since only 2013 when its precursor Watson Laboratories changed its legal seat in a tax inversion involving Warner Chilcott.

In our analysis, building on data sourced from global deal database MergerMarket, we compare announced deals over the last three years. The number of deals increased from 371 in 2013 and 438 in 2014, to 494 last year. The cumulative deal values almost doubled from US$ 226bn to US$ 415bn – largely due to the announced acquisition of Allergan by Pfizer. With a deal value which is in excess of US$ 183bn, the Pfizer / Allergan merger makes up more than 40% of the sum of all deal values and skews the statistic significantly. However, even without this huge deal, deal activity in 2015 was at a very high level. With its US$ 40bn sale of the generics drug portfolio, Allergan also accounts for the second largest transaction in 2015 (see Graph 2). Other large transactions included further generics consolidation deals (Endo / Par and Pfizer / Hospira), Baxter’s split, and pipeline acquisitions by AbbVie, Alexion, Shire and AstraZeneca.

Looking at inter-regional transactions (buyer and target in different regions), most of the money was spent, as in the past, on acquisitions between the US and Western Europe (see Graph 3). However, putting aside the huge Pfizer / Allergan deal (a US firm buying a “European” target), much less money was spent on targets located in Western Europe in 2015 compared to 2014 (see Graph 4). This is a consequence of the wave of tax inversion deals in 2013/2014. The acquirers in those deals, formerly US-based, now have tax domicile seats in Europe and continue to spend on acquisitions. They generally acquire targets based in the US,

**GRAPH 1 / PHARMA M&A IS ARGUABLY AT ITS ALL-TIME HIGH, WITH UNPRECEDENTED VALUATIONS**

Worldwide M&A Transactions with Pharma and Pharma-related targets, 2010-2015

Note: Pharma deals with reported revenue multiples <20x and deal size >US$ 10m: n=607; bubble sizes represent deal size.
Source: IMAP analysis based on data from MergerMarket.

**M&A TIMELINE 2015**

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

- Shire acquires NPS for US$ 5bn
- Valeant picks up Dendreon assets for US$ 495m
- Tekmira buys OnCore for US$ 376m
thereby exploiting their tax-efficient set-up.

Valuations have been persistently high and TEVA’s acquisition of RIMSA, a branded generics provider in Mexico, was one example of a very expensive deal (10x revenues). Pfizer is also paying a considerable amount for ALLERGAN (14x revenues), as did BAXALTA for Sigma Tau’s oncology pipeline deal.

sometimes, high revenue multiples may have been justified by large synergy effects or strongly growing profits. In other cases, the valuation drivers are not so obvious and may be a result of an ongoing pressure to consolidate. Our long-term analysis of EBITDA multiples in the pharma industry (see Graph 5) shows a strong increase in valuations for larger deals (deal size bigger than US$ 2.5bn) in the last two years.

In the last quarter of 2015, the climate cooled down considerably and some insiders expected markets to crash during a brief time. What happened? When TURING Pharmaceuticals multiplied the price of an old but essential product, the resulting public backlash caused analysts to review the long-term implications.
prospects of serial acquirers Valeant, Mallinckrodt and Horizon Pharma. The huge valuations these companies had been able to pay were partly recouped with dramatic price increases of the target’s old products, an operational tactic which appeared unsustainable after the public debate caused by Turing. The demise of these companies, in particular of Valeant, was a much discussed drama towards the end of the year.

In parallel, the IPO market – which also extended its boom from 2014 – went through a “soft landing”, as hedge funds and other general investors pulled out of pre-IPO and IPO-financing. Valuations of privately held and IPO-ready Biotech firms are likely to suffer in the near future, however, industry insiders do not believe that the IPO and financing machinery will come to a standstill as they did after the dot-com crash. Too much money has been raised by investment funds which needs to be deployed.

What else is to be expected? The changing political climate and more importantly, the scarcity of eligible targets for the usual tax inversions – which are based on ownership ratios post-transaction – means that the wave of purely tax-driven billion-dollar deals will soon come to an end. Another type of tax inversion based on financial ratios between acquirer and target is likely to become an avenue for smaller companies to change tax domicile. If this will play out still has to be seen.

Fundamentally, the industry is still far from being organized. Large deals such as the Pfizer/Allergan merger, for example, will lead to divestments and spin-offs as the organization is too diverse and complex to be manageable in the long term. Even though Pfizer’s long-expected spin-off of its generics business has been delayed, it will certainly be implemented. At the same time, a number of companies which came under pressure by recent consolidation waves, such as Johnson & Johnson in the OTC/Consumer Health space, may use their accumulated “war chest” to pursue “transformational” acquisitions. Thus, we expect that deal activity will remain high, but the nature of deals will shift from multi-billion dollar deals which are financially driven, to comparatively smaller transactions which fundamentally improve the acquirer’s strategic position in a given market sub-segment.

GRAPH 4 / CUMULATED DEAL VALUES BY TARGET REGIONS

GRAPH 5 / PHARMA EBITDA MULTIPLES OVER THE PAST 10 YEARS

Note: Median EBITDA-multiples of Pharma transactions from the trailing twelve months (TTm) preceding quarter shown. Only data points with a minimum of 10 transactions (resp. 6 transactions for the category >US$2.5bn) in the TTm are shown.

Source: IMAP analysis based on data from MergerMarket.
In an all-time record year for global M&A, acquired US-based companies accounted for approximately US$ 2tn or 46% of global deals across all industries in 2015. The healthcare industry, dominated by Pharma, was the most active deal arena, accounting for 15% of all M&A activity in the US. This M&A-enthusiasm was in part supported by economic growth and low interest rates.

The past year was again a seller’s market for US-based companies: excluding the Allergan-related mergers, 73% of the total global deal value originated from US-based targets, similar to in 2014. On the other hand, almost half (46%) of the global deal value originated from buyers located in the US (compared to 21% in 2014). Interestingly, the average deal size involving US-based targets was more than double the global average. This high activity involving US-based targets is, to some extent, also a secondary effect of the tax inversion wave which peaked in 2014: Pharma companies with new, tax-efficient domiciles deploying capital for acquisitions in the USA.

Most notable transactions in 2015

Allergan was responsible for the two largest and most prominent transactions in 2015 – Allergan being a result of various mergers over the past five years; of Forest, Actavis, Warner Chilcott and Watson, amongst other companies. In July, Teva acquired Allergan’s generic business for over US$ 40bn (paying 6x revenue), followed in December by Pfizer’s proposed merger with the other part of Allergan for US$ 183bn (paying 14x revenue, including an R&D pipeline and a biosimilar program). The transaction resulted in the creation of the world’s largest drug maker. Pfizer needed to prop-up its weak pipeline (similar to their acquisition of Wyeth in 2009) and deploy its capital, however, more importantly for this deal were the tax motives, including the realization of an expected US$ 21bn one-off tax savings by Pfizer.

Another notable deal in 2015 was AbbVie’s acquisition of Pharmacyclics for US$ 19bn, winning a hotly contested bid against J&J. This deal was a strategic move to access Pharmacyclics’ hematologic oncology portfolio, including its recently approved flagship product Imbruvica, an innovative BTK-inhibitor to treat B-Cell Malignancies, expected to deliver peak sales of US$ 7bn. Finally, Pfizer’s acquired specialty injectables provider Hospira for US$ 16bn earlier in the year, made it one of the top five US generics drug manufacturers. In addition, the deal gave Pfizer access to a biosimilar platform complementary to that of Allergan.

Outlook

For 2016, we expect few, if any, large “bigger is always better” deals, but instead the reemergence of strategically more precise transactions. On the one hand, such large deals will be dominated by spin-offs and carve-outs of businesses, particularly by those that went through major transformations recently, such as Pfizer/Allergan. On the other hand, we expect large acquisitions initiated by certain Big Pharma, which have been rather passive (or unsuccessful) in the recent consolidation waves. This includes J&J, with a US$ 18bn cash pile, as well as also other US-based Big Pharma companies with big war chests such as Merck&Co or Gilead Sciences. Furthermore, since the tax inversion wave has passed, which mainly involved European targets, we expect the US, the major source of BioPharma innovation (with around 80% of global R&D spending in the past years), to continue to be the location of most of the Biotech and Pharma M&A targets in the years to come.

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Western Europe

In the year 2015, the Western European Pharma market was a sellers’ market, a result of global high deal activity. Valuations in the Pharma sector in 2015 appeared to be holding up at an average of 17x EBITDA (compared to 2014). The average revenue multiple in 2015 increased from 2.5x to 3x.

Most notable transactions in 2015

The largest deal by size was Endo’s acquisition of Par Pharmaceutical. Endo used its “acquisition platform”, i.e. its new tax domicile in Ireland which it gained through an inversion via its acquisition of Paladin Pharmaceutical in 2013, to acquire Par Pharmaceutical from a group of private equity investors. The deal valued Par at US$ 7.4bn, representing a multiple of 21x EBITDA and 3x revenues. With the acquisition, Endo gets access to Par’s generic business which includes a line of high barrier to entry generics, as well as some niche innovative brands. The Par portfolio includes 100 products and a pipeline of more than 200 ANDA. The resulting combination has created a leading specialty pharmaceutical company, with a fast growing generics business which is now one of the top 5 industry players in the USA by revenue. The drivers for the deal were to give Perrigo the ability to leverage Omega’s strong and established commercial, regulatory and distribution platform. The acquisition allows Perrigo to expand its markets across Europe and to achieve critical mass across the European OTC market place.

Perrigo, also with legal and tax domicile in Ireland (since its acquisition of Elan in 2013), made a big step into OTC by acquiring privately held Omega Pharma in Belgium. Omega in turn had been a prolific acquirer of local OTC brands in Europe. The deal amounted to US$ 4.7bn, representing an EBITDA multiple of 13.5x and a revenue multiple of 2.9x. The combination of Perrigo and Omega makes Perrigo a leading global healthcare company, a top 5 global OTC player and the world’s largest manufacturer of OTC products. Perrigo has great hopes for its OTC business which it plans to expand by repositioning old, prescription-only branded drugs as OTC medicine (“Rx-to-OTC switches”). The key drivers were to give Perrigo the ability to leverage Omega’s strong and established commercial, regulatory and distribution platform. The acquisition allows Perrigo to expand its markets across Europe and to achieve critical mass across the European OTC market place.

Concordia Healthcare (US) bought out Amdipharm (UK) for US$ 3.5bn, which included the assumption of US$ 1.4bn of debt. A substantial element of the purchase price is in the form of an earn-out contingent on future performance of the target. Revenues for Amdipharm for 2015 were circa US$ 530m. With no published EBITDA numbers on Amdipharm we are estimating that the deal value represented a revenue multiple of circa 3.5x to 4x (adjusting for the earn-out and the debt). The driver for the deal was to increase Concordia’s global footprint and also adds a diversified and attractive portfolio of 190 complementary niche pharmaceutical products.

Outlook

There is evidence that the Pharma M&A market was cooling towards the end of 2015. The number of deals announced in the 4th quarter was down on prior quarters. M&A lawyers are now starting to question whether the Pharma M&A juggernaut is slowing. However, whilst there will likely only be one or two more “super mergers” (e.g. Pfizer/Allergan) in the coming years there will continue to be an appetite for mid-sized deals. This will be partly fuelled by major US players with significant war chests who are looking for international growth or an expansion of their product pipelines (e.g. J&J and Gilead) and by mid-tier European Pharma companies acquiring product portfolios and looking at their own exit strategies.

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Latin America

2015 saw a sharp decline in M&A transactions in the pharmaceutical market, from 24 reported transactions in 2014 to a meager number of only 9 announced deals. Deal activity in Brazil and Mexico decreased by 60%. While in Brazil several deals had been called off due to the deteriorating macroeconomic situation, foreign investment in Mexico slowed down, probably triggered by the unstable security situation in the country. The focus in 2015 had been on fully integrated pharmaceutical businesses where 6 out of the 9 transactions took place. Two transactions were closed in the CMO area and one in the distribution market. Five transactions were closed by regional buyers (Eurofarma, Cristalia, Hertape, Biotoscana and Raia Drogasil), three by large pharma corporations (Teva, Valeant and Perrigo) and only one by an international medium-sized pharma group (Lupin). Regional buyers were clearly on the move to consolidate their strong position in the market of branded and non-branded generics.

Most notable transactions in 2015

The transaction sizes express the cautious attitude of investors; there was only one billion-dollar-deal recorded, but 8 deals below US$ 100m. The largest transaction was closed by TEVA who acquired RIMSA in Mexico for US$ 2.3bn, thus ending a 5 year period of courting potential investors by the RIMSA owning families. Atypical is the acquisition of a Patheon manufacturing site in Mexico by Perrigo; however, Perrigo had been looking for softgel manufacturing technology for the group for quite some time, eventually finding it in Mexico. Also unusual, is the re-purchase of 50% of its own shares by Hertape, a leading Brazilian Veterinary provider, from the Spanish Calier Group.

Outlook

For 2016, we expect an overall increase of M&A transactions driven by Brazil and Argentina. Targets in Brazil have become more affordable due to a more realistic exchange rate. An endless political crisis combined with the toughest recession in 25 years, however, will ensure that investors move very cautiously. Argentina is likely to attract more foreign investors following the liberalization measures adopted by the new government to stimulate the economy. Colombia may also attract new investors as a side effect of the envisaged peace treaty. In Venezuela, some large pharma corporations may consider options to dis-engage.

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4 strategic archetypes for pharma companies

**STRATEGIC ISSUES**

US$ 1.4bn average expenses for 1 new molecule, incl. failed programs. Driven by: Better than the Beatles problem: need to be better than standard of care; Evidence-based medicine: increasing requirements to show efficacy and safety.

**DEAL DRIVERS**

Pipeline deals
Mega-mergers

**DEALS IN 2015**

- **AstraZeneca**
  acquired 55% of **Acerta Pharma**
  for US$ 4.0bn for an oral BTK inhibitor

- **AbbVie**
  acquired **Pharmacyceis**
  for US$ 6.8bn to access an I&I portfolio

- **Cologyne**
  acquired **Receptos**
  for US$ 19bn to access the product Imbruvica

**DEALS IN 2014/15**

- **Immunogenetics**
  acquired **Idexx**
  for US$ 19bn to access the product Imbruvica

- **Novartis**
  acquired **Alcon**
  for US$ 6.8bn to access an I&I portfolio

**ORIGINATORS**

**THERE MISSION**

Find, develop and launch novel treatments.

**WHAT THEY EXCEL IN**

Selection and funding of best R&D projects; influencing regulations and reimbursement policies.

**SIZE**

Huge and global; US$ 10bn revenues or more.

Originators complement portfolio (e.g. oncology) and/or salvage sales (e.g. PPI inhibitors)

**LOW-COST PROVIDERS**

Generics, Biosimilars

**THERE MISSION**

Deliver quality products at low prices.

**WHAT THEY EXCEL IN**

Capacity utilization along value chain; combining cost-efficiency with quality.

**SIZE**

Huge and strong in each market in which they are present.

Generics try to escape low margins

Rx-to-OTC sw: convert Rx products to consumer brands

Point-of-Call specialists do R&D for US$ 40.5bn to enhance its generic business

**DEAL DRIVERS**

Consolidation (local and global)

**DEALS IN 2015**

- **Teva** (incl. Allergen Generics)
  for US$ 4.0bn to enhance its generic business

- **Novartis** (Sandoz)
  for US$ 2.7bn to become #5 US generic company

- **Mylan**
  for US$ 2.3bn for their Latin American generic business

Source: EvaluatePharma, 2015; IMAP research.

**TOP GLOBAL GENERIC DRUG MANUFACTURERS BY SALES, 2015**

- **Teva** (incl. Allergen Generics)
- **Novartis** (Sandoz)
- **Mylan**
- **Sun Pharma**
- **Aspen**
- **Pfizer** (Hospira)
- **Sanofi**
- **Fresenius**
- **Lupin**
- **Others**

**NEW DRUG AND BIOLOGICS APPROVALS AND R&D SPENDING**

Source: Tufts Center, 2014; IMAP research.
DEALS IN 2015

- **Almirall** acquired **POLICHEM** for US$ 386m to strengthen the dermatology franchise.
- **Axilas** acquired **DERMATOLOGY** for US$ 724m to strengthen the dermatology position.
- **Synageva** acquired for US$ 8.3bn for a rare disease product portfolio.

DEAL DRIVERS

Adjacent acquisitions
Portfolio complementation

STRAEGIC ISSUES

Generitization of franchises; Innovation threats from originators.

POINT-OF-CALL SPECIALISTS

**THEIR MISSION**

Provide comprehensive solutions for an indication or therapeutic area.

**WHAT THEY EXCEL IN**

Network to decision makers, portfolio beyond drugs.

**SIZE**

Large enough for dominant market share in therapeutic area.

OTC firms complement categories (e.g. cough & cold)
Point-of-Call Specialists add brands (e.g. dermatology)

OTC / CONSUMER HEALTH

**THEIR MISSION**

Market consumer products with medical claim.

**WHAT THEY EXCEL IN**

Consumer branding, channel management.

**SIZE**

Large in the relative market (indication in a geography); in the long term: global scale.

OTC firms complement categories (e.g. cough & cold)
Point-of-Call Specialists add brands (e.g. dermatology)

DEALS IN 2014/15

- **Sanofi** acquired **Boehringer Ingelheim Consumer Health** for US$ 7.4bn to build up consumer care business.
- **MSD Consumer Care** acquired **Novartis Consumer Health** to form a leading consumer health Joint Venture (US$ 10bn revenue).

DEAL DRIVERS

Consolidation (local and global)

STRAEGIC ISSUES

Channel strengthening: pharmacy chains consolidate; globalization of consumer preferences (such as personal care brands).
Central and Eastern Europe (CEE)

With 29 transactions and a total deal volume of €1,120m, healthcare M&A in CEE saw fewer deals but a similar volume as in the previous years (2013: 41 transactions and €1,208m deal volume; 2014: 37 and €995m). Valuations were between 7.0x and 23.3x EBITDA. Fifteen transactions were domestic and 14 cross-border. Poland was the center of investors’ interest, where twelve transactions took place, five of which were acquisitions by foreign entities. Four companies were acquired in Russia, one by domestic strategic and financial buyers and three by strategic investors from India and the UK. Romania saw three transactions (two domestic and one foreign private equity buyer) as did the Czech Republic (two private equity deals and one strategic consolidation). The acquisition of Regina Maria of Romania by Mid Europe Partners for €135m was the highest valued transaction of the year; two transactions were domestic consolidations.

With four fifths of all deals, strategic buyers dominated financial acquirers. Three key observations stuck out: firstly, private investors, composed almost exclusively of PE funds, were interested in the acquisition of healthcare providers (incl. clinics) and drug producers. Secondly, two medical manufacturers acquired producers of technical products with the aim of increasing the scope of their operations. Thirdly, several of the other transactions were motivated by consolidating market shares.

Most notable transactions in 2015

Regina Maria, a Romania-based company that owns and operates a network of healthcare clinics was acquired by the UK-based private equity firm Mid Europe Partners for an estimated €135m, thus the highest valued acquisition of a healthcare entity in 2015. Walmark, a Czech Republic-based manufacturer, distributor and seller of nutritional supplements and drugs employing over 700 people agreed to sell the remaining 50% stake to Mid Europe Partners. The PE house became the sole owner of Walmark. Bovital, the vitamin product portfolio of Bayer AG was acquired by eGIS, a Hungary-based listed Pharma company. The acquisition of Bovital is in perfect correlation with eGIS’ continuing strategy of strengthening its presence in the Polish market in the vitamin supplement segment.

Outlook

We expect deal activity in 2016 to remain at the same low level as in 2015. The capital outflow, due to potential increases in US interest rates together with slowing economic expansion, may have a negative effect on general M&A activity in the CEE region. In the case of more stringent lending policies, the EBITDA multiples may decrease to levels which were seen prior to the period of quantitative easing; this will reduce the willingness of owners to sell their companies. The situation in Russia is particularly complicated with the collapse of oil prices and local currency. Regardless of the implications of the macroeconomic factors on M&A in the CEE region, the healthcare sector is very attractive for financial investors, often providing the possibility of attractive returns. Therefore, the industry is likely to continue to attract investors during 2016. However, the question is: at what rate?

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2015 saw an increase of 340% in total value of cross-border M&A transactions, but the overall activity fell 30% to US$ 3.7bn. Outbound deals contributed US$ 2bn and inbound deals US$ 1bn. The reason for a surge in outbound activity was the consolidation in the US generics market. However, this was not enough to offset the effects of decreasing domestic consolidation. Currently, large cap pharma companies in India are trading at an average EV/EBITDA multiple of ~19x and P/E multiple of ~27x.

Most notable transactions in 2015
One of the most remarkable deals seen was when Indian pharma major Lupin acquired US based Gavis Pharmaceuticals and Novel Laboratories for US$ 880m. This is the largest buyout of a foreign pharma company by an Indian firm. Gavis specializes in niche dermatological and psychiatric segments. The deal value represents an EBITDA multiple of ~16x by CY15 management estimates. The acquisition offers a number of synergies: first US manufacturing plant, controlled substances and derma capabilities. Lupin expects Gavis to contribute ~US$ 300m in revenues by FY18 as based on estimated ~50 approvals (66 pending ANDAs) in the next 3 years. Another large Indian generic drug manufacturer, Cipla, acquired InvaGen Pharmaceuticals and Exelan Pharmaceuticals, two US based generic manufacturers, for US$ 550m. This values the deal at 2.4x TTM June 2015 revenue. With the acquisition of InvaGen, Cipla will gain scale in the US generics market and a complementary product portfolio in cardiovascular, anti-infective, anti-inflammatory, antidiabetic and anti-depressant therapeutic areas with various dosages. While InvaGen adds US-based manufacturing and a strong near-term revenue potential (given 40 approved/ 30 pipeline ANDAs, with 5 FTFs), Exelan will provide Cipla with access to incremental business channels, including to the US government. The most prominent inbound deal of 2015 was the acquisition of Famy Care’s female healthcare business by global generics company Mylan for US$ 750m plus contingent payments of up to US$ 50m. As a result, Mylan will gain access to a wide range of women’s health products and a dedicated hormone manufacturing unit. This will also provide an entry into the Indian female contraceptive and healthcare markets. Famy Care and Mylan had a prior exclusive partnership since 2008, where Famy Care supplied OTC drugs to Mylan for the US and other regulated markets. This deal also complements Mylan’s acquisition of Abbott’s women’s health products for non-US developed markets.

Outlook
Indian pharma companies, with strong financials and access to additional capital, are in a prime position to evaluate acquisitive growth opportunities in 2016. Indian companies are expected to make further inroads into generic markets by forward-integrating, particularly to the US. They are also expected to expand their presence in other regulated markets through acquisitions, targeting complex generics and niche therapeutic areas. Increased consideration will also be on moving up the value chain and enhancing focus on complex biosimilars, branded portfolio and OTC drug segments.

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Welcome to the age of portfolio deals

April 2014 saw a stellar day for strategic deal making. The multiple swaps of GSK and Novartis (and Eli Lilly), which in one stroke strengthened Novartis’ position in oncology and GSK’s in vaccines; created a global giant in OTC and relieved Novartis of its stepchild animal health. The transactions left Novartis focused on the dynamic, high-profit parts of the conglomerate and most importantly, less complex and more competitive in all markets in which the firm plays. Novartis clearly gave the industry an example of strategic deal making: in a phase where many players, in particular US-managed companies, still believe that “bigger is just better”, more sophisticated companies realize that only a strong position in the relevant market will secure the future prospects. These companies look for “portfolio deals”, i.e. sell sub-critical businesses to players better suited to own and manage them, or vice versa, look for such sub-critical portfolios which they can acquire. Since Novartis’ famous deal day, less spectacular portfolio deals have been signed by Pharma companies (see table overleaf). Some of them, such as Boehringer and Sanofi at the end of last year, found a way to “align the many stars” (as called by the Novartis executive who led the “deal day”) required to enable an asset swap. Some companies completely reshaped their core and future with business portfolio deals: AstraZeneca is acquiring assets in respiratory, an indication which is dominated by few large players and is one of three core areas for the UK firm, while systematically selling all non-core legacy drugs (such as its GI product Entocort®, a deal led by IMAP Switzerland). However, most spectacularly relative in terms of the size of the company, was Almirall’s refocusing from an aspiring player in respiratory to a dermatology company: first selling its product franchise and late-stage pipeline to AstraZeneca including transferring over 700 staff (a deal which, given the organization’s self-understanding, amounted to open heart surgery); and then acquiring PoliChem to bolster its dermatology portfolio. We expect strategic consolidation in specific business areas to be a sustainable driver for transactions over the next few years.

1 / Concordia becomes global with US$ 3.5bn AmCo buy
2 / Amgen buys Dezima for US$ 1.6bn
3 / Cipla buys InvaGen for US$ 500m
### Example of Portfolio Deals - Selling / Buying Business Units Between Pharma Companies

<table>
<thead>
<tr>
<th>WHEN</th>
<th>DEAL</th>
<th>SIZE</th>
<th>RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEC 15</td>
<td>Sanofi animal health and Boehringer Ingelheim’s consumer health.</td>
<td>US$ 19.7bn</td>
<td>Boehringer had been looking for a solution for its OTC division for some time and strengthening its core animal health franchise makes sense.</td>
</tr>
<tr>
<td>DEC 15</td>
<td>AstraZeneca acquiring Takeda’s respiratory business, including 200 staff.</td>
<td>US$ 575m</td>
<td>Takeda was sub-critical in respiratory treatments which in turn comprises one of three core areas for AZ (see further deals below).</td>
</tr>
<tr>
<td>NOV 15</td>
<td>Astellas selling its global dermatology business to LEO Pharma.</td>
<td>US$ 724m</td>
<td>Gives dermatology specialist LEO more products (atopic dermatitis, acne and skin infections) and access to China and Russia, while Astellas can use funds to accelerate innovation in its core areas.</td>
</tr>
<tr>
<td>JUL 15</td>
<td>Boehringer Ingelheim exiting US generics by selling Roxane to Hikma.</td>
<td>US$ 2.7bn</td>
<td>Hikma massively increases foothold as one of the key generic players in the USA, becoming sixth largest generics provider. Boehringer can focus on its innovative platform.</td>
</tr>
<tr>
<td>JUL 15</td>
<td>Teva buys Allergan’s generics drug business.</td>
<td>US$ 40.5bn</td>
<td>Divesting the generics business makes Allergan a pure originator – and attractive target for Pfizer.</td>
</tr>
<tr>
<td>JUN 15</td>
<td>Baxter to spin-off its biopharmaceutical business.</td>
<td>US$ 17.9bn</td>
<td>Baxter spin-offs its biopharma business unit newly called Baxalta, which then becomes an attractive target for Shire. Baxter to focus its core business around hospital supply.</td>
</tr>
<tr>
<td>MAY 15</td>
<td>SigmaTau divests OncoSpar to Baxter (Baxalta).</td>
<td>US$ 900m</td>
<td>Divesting the oncology business and merging its European sales with Alfa Wassermann splits SigmaTau in two parts.</td>
</tr>
<tr>
<td>JUL 14</td>
<td>AstraZeneca acquires Almiralls’ respiratory business.</td>
<td>US$ 875m</td>
<td>Almirall had great hopes for its respiratory drugs, but found competition was too strong and sold it to AstraZeneca, for which respiratory is one of three core businesses.</td>
</tr>
<tr>
<td>JUL 14</td>
<td>Mylan acquires Abbott’s ex-US developed markets generics business.</td>
<td>US$ 5.3bn</td>
<td>Almost pure generic player Mylan is a better owner for slow-growing and low-margin generic drugs in established markets than Abbott – who is in MedTech and hospital supply.</td>
</tr>
<tr>
<td>MAY 14</td>
<td>Merck &amp; Co. sells their OTC drugs to Bayer.</td>
<td>US$ 14.2bn</td>
<td>Bayer’s stated goal to become the world’s largest OTC supplier meant it had to buy the legacy drugs from Merck, most of them former Schering brands.</td>
</tr>
<tr>
<td>APRIL 14</td>
<td>Novartis vaccine business to GSK. (October: influenza business to CSL).</td>
<td>US$ 5.3bn US$ 275m</td>
<td>In a big strategic reshuffle, Novartis and GSK combined their vaccine businesses (now owned by GSK), oncology division (now owned by Novartis) and OTC drugs (pooled in a JV), while Novartis sold its animal health business to Eli Lilly. Result: all units with substantially better relative market shares.</td>
</tr>
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**JANUARY**

- Teva acquires Mexican branded generics business RIMSA for US$ 2.3bn

**FEBRUARY**

- Roche acquires Adheron for US$ 105m

**MARCH**

- Recipharm buys Nitin majority for US$ 103m

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Mining DNA: businesses built on genomics

Over the past decade, DNA sequencing costs have been collapsing exponentially. Today, there is an abundance of sequencing facilities and having a person’s full genome sequenced now only costs US$ 1,000 (see Graph 1). The pace of technology development was so fast that corporate stars rose and fell swiftly, with one wave of disruptive innovators following the other and a sizeable number of high-profile corporate failures. Challengers continue to emerge, which again may reshape the market for sequencing instruments (see Box 1); however, the main instrument providers seem more or less set.

Already here: personalized medicine

Today, DNA-sequence based tests (or molecular diagnostics) are an integral part of medical practice. For example, molecular diagnostic tests (e.g. for EGFR and KRAS) can determine for certain cancers whether a patient will benefit from a specific, highly targeted treatment. It is now common that companion diagnostics are developed together with new cancer drugs. These are the prime examples of “personalized medicine”.

There are many other areas in which molecular diagnostics supports medicine. For example, testing the predisposition of a patients’ body to clear the drug substance from the blood helps physicians to adjust dosage. This is highly relevant if drugs are taken over an extended period of time, such as in psychiatry, pain management, or for cardiovascular conditions. For certain cancer patients, a DNA test can help decide whether they should undergo chemotherapy after surgery. Establishing whether a person has inherited a predisposition for a disease enables the physician to have an informed discussion on preventive measures. All these applications bring a great medical and health economic benefit and increasingly health insurances are rewarding the development of tests with reimbursement.

Consumer genomics in a changing environment

The early success and big media attention enjoyed by 23andMe, one of the first consumer genomics companies, showed that there is great demand from consumers to learn about their genetic makeup, be it to answer relatively minor (ear wax type), personal (ancestry) or serious (cancer risk) questions. However, the regulatory requirements for consumer genomic testing are not yet clear: in late 2013, FDA stopped 23andMe from providing medical information.

Another determinant for the future market of consumer genomic testing are legal restrictions for the access to and the use of genomic data, as Ellen Matloff points out when speaking to us. Ellen is a renowned cancer genetics expert and CEO of My Gene Counsel, a US-based firm providing digital tools to ensure accurate understanding of genetic test results. Prior to the Genetic Information Nondiscrimination Act (GINA) of 2008, she points out that it was not uncommon for patients to use aliases and pay cash for genetic testing, out of fear of potential insurance or employment repercussions in case...
of adverse results. Despite certain loopholes, such as not covering life insurance, long-term care or disability insurance, GiNA has alleviated the fears of many genetics customers. Thus, consumer-driven genomic tests are here to stay, as there is clearly a demand. However, it is likely that they will be offered as a package together with counselling, as done by Kailos Genetics (see Box 2), a combination which may even become mandatory under certain legislations.

Building the Google of genomics

The revolution in DNA sequencing is also the basis for a long-term vision: to build and mine large-scale genomic databases to find new links between genes and medical conditions. However, there is still a lot of work to be done before such visions become reality. The reason for this is that most diseases are complex long-term processes, involving multiple genes (to varying degrees) and dependent on such factors as lifestyle, nutrition and the environment.

In order to convert genomic data to knowledge about disease mechanisms, three challenges need to be met: i) sequencing of a massive number (hundreds of thousands) of complete genomes; ii) collection of data on medical conditions and relevant traits of each sequenced individual; and iii) development of powerful algorithms and computational methods to process and integrate the various data types. There are several ongoing efforts to create large-scale genomic databases, both privately (deCODE, Invitae) and publicly funded (100,000 Genomes Project of Genomics England). One of the most prominent examples is, again, 23andMe (mentioned above).

<table>
<thead>
<tr>
<th>BOX 1 / SEQUENCING TECHNOLOGY PROVIDERS</th>
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<tbody>
<tr>
<td><strong>Criteria</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Accurate reads</td>
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<tr>
<td>Long reads</td>
</tr>
<tr>
<td>Single molecule</td>
</tr>
<tr>
<td>No complicated optics (fast and robust)</td>
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<tr>
<td>Low price</td>
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<tr>
<td>Wide selection of instruments</td>
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<tr>
<td>Handheld</td>
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<table>
<thead>
<tr>
<th>BOX 2</th>
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<tr>
<td><strong>KAILOS GENETICS – A SERVICE PROVIDER EXAMPLE</strong></td>
</tr>
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</table>

As the medical applications of molecular diagnostics are more widely used, new types of businesses emerge. Privately held Kailos Genetics, based in Alabama USA, for example, could be described as a “genome analysis service provider”.

Kailos performs tests to predict patients’ responses to common drugs, such as antidepressants or birth control treatment. Even though consumers drive the demand for testing, Kailos’ CEO, Brian Pollock, emphasizes that physicians and other medical professionals are closely involved in the entire process, from approving each test to interpreting and discussing the results. “Sequencing today is a cheap commodity” he tells us.

“Sample preparation and data analysis are really value-adding”. Kailos simplified the wet lab component by developing a one-step sample enrichment method, TargetRich.

The company’s Kailos Blue analysis software is based on open source algorithms and tools such as Broad Institute’s Genome Analysis Toolkit (GATK), and can be used with sequencing data from any platform, in contrast to other software.
The company, fittingly backed by Google (the prime collector of massive amounts of data), cleverly marketed its genetics tests to customers. This allowed 23andMe to collect huge amounts of data – its database currently contains genomic information (albeit not full genomes) of approximately one million people. In addition, 23andMe has managed to create a highly engaged user community, which regularly responds to questionnaires and provides additional information. To exploit that trove, the company has partnered with a number of pharma companies for specific diseases and is building up capabilities to start in-house drug development.

The continued interaction with its customers allows the 23andMe team to constantly adjust their hypotheses and to probe for new gene/trait connections.

While 23andMe has developed an excellent method to collect data, other initiatives focus on developing sophisticated algorithms to extract the knowledge from the data glut, including both open source projects such as Bioconductor and private entities (Sophia Genetics and Veritas Genetics). The key question for owners of commercial large-scale genomic databases is how to protect their knowledge. It is not clear how intellectual property regarding variant-trait combinations will be handled. For example, genes cannot be patented, as the outcome of the epic battle against Myriad Genetics’ BRCA patent (the famous "breast cancer gene") has shown. Ownership of personal data will also be a point to consider, particularly in Europe. Both issues set boundary conditions on how the “Google of Genomics” can develop.

### On the back of the sequencing revolution, an evolving system of business models

The speed of technical development in DNA sequencing remains high, but the competitive field of instrument providers will more or less remain stable (see Box 2), although Illumina will probably lose part of its 70% market share as the market matures. Sequencing technology has laid the basis for the evolution of a variety of down-stream business models, including test service providers such as Kailos, big data-collectors such as 23andMe, data miners such as Switzerland-based Sophia Genetics and of course, a large number of novel diagnostic tests. Which model will get the highest share of the value created remains unclear and will be interesting to follow.

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