



Deal Watch: 2011 Annual Review



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Medius Associates

The Annual Review of deals by
the Medius Deal Watch Team



47 Upfield
Croydon
CR0 5DR
U.K.

Tel: +44 (0) 20 8654 6040

Email: info@medius-associates.com

Crystal Ball Retrospective

In our annual deal watch report last year (covering deal trends and activities in 2010), we anticipated that major pharma would continue their hunt for products and discovery platforms to bolster flagging portfolios, through adoption of creative acquisition strategies, as well as more traditional licensing strategies and partnerships. This trend has been demonstrated with a number of deals using contingent value rights (CVRs) to try to mitigate against regulatory hurdles and commercial challenges; in its acquisition of Genzyme, Sanofi has up to \$4bn to pay in CVRs if Lemtrada hits its manufacturing and regulatory milestones.

Over the year we have also commented on the therapeutic area partnerships that are being set up to enable big pharma to work together in a certain therapeutic area, looking for synergies between their products rather than going head to head and potentially destroying value. In May 2011, Merck and Roche announced an alliance in the Hepatitis C field.

Roche and Bristol-Myers Squibb (BMS) have announced that they are collaborating in the study of combination therapy in advanced skin cancer. This combines Roche's verumrafenib with BMS's ipilimumab to treat metastatic melanoma in a Phase 1/2 study to determine the efficacy and safety of the combination. In a slightly different direction, Merck struck a \$720m strategic deal with Hanwha (South Korean petrochemicals group) to build a biosimilars platform.

We also questioned whether large pharma's trend for streamlining their R&D activities whilst maintaining options for scale-up would continue. There have been a few examples of this including Pfizer's \$2.4bn divestment of its Capsugel Business to KKR in April, as well as its divestment of an Irish biologics manufacturing plant to Biomar, for \$48.5m. In another example of rationalisation, GSK is in the process of divesting its non-core OTC assets and in December 2011 announced that Prestige Brands Holdings was acquiring the US and Canadian rights for \$660m. Perhaps the most notable streamlining activity is Abbott's autumn announcement that it is spinning out its pharmaceutical business from the medical devices business with a \$18bn price tag, a move which reflects the differing visions and roadmaps seen for both businesses.

Another area we forecast would see significant activity was in the numbers of deals done between Western and Chinese and Indian companies. In the past the trend has been inward-investment into Asian markets by US and Western European companies looking to get a foothold and take advantage of the lower cost structures, in addition to gaining access to the burgeoning healthcare markets in the region.



In 2011 we saw this trend continuing with large and mid-sized pharma investing in China (i.e. GSK / Nanjing MeiRui, SciClone Pharma / NovaMed Pharma, Nycomed / Guangdong). There are said to be 5,000 pharmaceutical companies in China and it is estimated that 98% of them produce generics. Therefore, not surprisingly we are also seeing an increasing level of consolidation within China (i.e. BioStar Pharmaceuticals / Shaanxi Weinan Huaren) as companies seek to benefit from economies of scale and to develop the profile to move outside China and participate on the global stage.

As part of this evolution, Chinese companies are beginning to look at investing in / partnering / and even acquiring Western companies (following the Japanese model several decades before); an example is 3SBio's acquisition of EnzymeRx's pegsiticase product for development in China with the intention of developing a global product.

The final prediction we made was that the number of deals in 2011 would exceed those seen in 2010 due to the continued shortage of differentiated new products and the fact that large pharma are looking to expand into new areas such as biosimilars, generics and orphans.

According to Medtrack data, in absolute numbers, the number of deals (preclinical to pending approval) done in 2011 was 4% lower than in 2010. However, there were four deals with price tags over \$10bn: J&J's acquisition of the orthopaedics company Synthes for \$21.3bn; the Sanofi / Genzyme \$20.1bn deal at the start of the year; Takeda's acquisition of Nycomed for \$13.7bn; and Gilead's \$11bn acquisition of Pharmasset announced in November.

The predictions about the focus of the deals were well founded and

biosimilars have featured in several deals e.g. Samsung's recent JV with Biogen Idec and its \$266m deal with Quintiles, to contract manufacture biosimilars in oncology and autoimmune diseases. The numbers of generics deals have been particularly high – led by Canada's Valeant and Paladin, with Teva and Par Pharmaceuticals also participating. There have also been several deals for companies and assets with orphan indications; Sanofi's acquisition of Genzyme is the largest, but other companies are continuing to make acquisitions and gaining access/rights to products in orphan indications.

Corporate M&A and Product Acquisitions

This section focuses on some of the interesting trends noted in corporate M&A during 2011 and particularly the activity relating to regional access, generics and OTC drugs, and in the dermatology area. In addition, we saw a number of acquisitions relating to individual product assets and product portfolios.

After merging with Biovail in 2010, Valeant Pharmaceuticals has been one of the most acquisition hungry companies of the year, closing transactions to acquire six companies. These exclude its failed bid to acquire Cephalon and the immediate rejection by ISTA Pharmaceutical's Board, in December 2011, to its offer of \$327m to acquire the specialty pharma company. Valeant's strategy has been both in consolidating its position and expanding its geographical footprint. The company has extended its geographic outreach in generics and OTC and also acquired two established dermatology companies; these deals are featured in the following sections.



Regional Access

We have already made reference to the numbers of deals being done in China but there have been several other noteworthy deals relating to gaining access to regional businesses as illustrated in Table 1.

Table 1 : Regional Access Deals 2011

Acquirer	Acquiree	Key Product/ Technology	Headline Value US\$M
Takeda	Nycomed	Company acquisition (excl Derm business) – to gain access to Nycomed’s channels in Russia and Eastern Europe	13,700
Reckitt Benckiser	Paras Pharmaceuticals	OTC company in India	721
Watson Pharmaceuticals	Specifar Pharmaceuticals	Acquisition of a Greek generic company	562
Valeant Pharmaceuticals	Pharma Swiss	Generics company acquisition with strong presence in Eastern Europe	481
Valeant Pharmaceuticals	AB Sanitas	Generics company acquisition with strong presence in Eastern Europe	441
Amgen	Bergamo	Acquisition of Brazilian company with oncology focus	215
Recordati	Frik Ilac	Acquisition of prescription pharmaceutical distributor company in Turkey	130
Shionogi	Victory Pharmaceuticals	Acquisition of CNS and anti-infective assets in US	127
SciClone Pharmaceuticals	NovaMed Pharmaceuticals	Acquisition of a Chinese pharmaceutical company	105
Cambrex	Zenara	Acquisition of an Indian generics company	20

In one of the largest transactions of 2011, Takeda’s acquisition of Nycomed (excluding the Dermatological business) gives Takeda extended geographical reach into Eastern European markets and Russia, where Nycomed is strong, and provides the Nycomed business with new life blood for its flagging pipeline. Amgen’s acquisition of Bergamo in August reflects the increasing importance that the Latin American market is having and will increasingly have, as Brazil is expected to become the 5th biggest pharmaceutical market by 2015.

As part of its strategy to enhance geographic outreach, Valeant bolstered its generics portfolio through the acquisitions of PharmaSwiss with its Eastern Europe generics business for \$481m and Lithuanian-based AB Sanitas for \$441m, to gain a further foothold in nine Eastern European markets.

Generic and OTC-Based Acquisitions

During 2011 we also saw further activity in acquisitions focused on generics as well as OTC – both of companies and product assets. A selection of these deals is summarised in Table 2.

Table 2 : Selected Generic and OTC Deals 2011

Acquirer	Acquiree	Key Product/ Technology	Headline Value US\$M
Valeant Pharmaceuticals	iNova	Australian Rx and OTC company acquisition	686
Prestige Brand Holdings	GSK	Non-core OTC brands in North America	660
Watson Pharmaceuticals	Specifar Pharmaceuticals	Acquisition of a Greek generics company	562
Perrigo	Paddock Labs	Acquisition of generics and OTC company	540
Par Pharmaceuticals	Anchen Pharmaceuticals	Acquisition of generics company	410
Hikma Pharmaceuticals	“Promopharm”	Acquisition of Moroccan Société de Promotion Pharmaceutique du Maghreb SA (Promopharm) with its branded generic and in-licensed product portfolio	174
Acino Holdings	Cephalon / Teva	Generic product businesses for Middle East and Africa, Latin America and Asia, R&D and production facility and Mepha “brand”	123
Hikma Pharmaceuticals	Baxter (generic injectables business)	Acquisition of US generic injectable products and facilities “Multi Source Injectables”	112
Valeant Pharmaceuticals	Afexa Life Sciences	Canadian OTC company	76
Pfizer	Akorn-Strides	Acquisition of product rights to 22 ANDAs for US from Indian partner	56



Another of Valeant’s deals in 2011 was the \$686m acquisition of Australian iNova completed in December 2011 with its Rx and OTC portfolio sold in Australia, New Zealand, Southeast Asia and South Africa. In its acquisition of the fellow Canadian OTC company Afexa Life Sciences for \$76m, Valeant will consolidate its position in the home OTC market. Interestingly, Afexa was wrestled from Paladin Labs as shareholders preferred Valeant’s offer. Paladin itself acquired Labopharm and its ailing modified release drug delivery business in August for \$20m, with significant tax losses that can be offset against future profits.

Before finally being acquired by Teva (after ousting Valeant as a suitor), Cephalon was also focused on acquisitions. In February it signed an option to acquire all of Alba Therapeutics Corporation's assets relating to larazotide, which is in Phase 2b trials for the treatment of coeliac disease, for \$15m. In March 2011, Cephalon announced plans to acquire oncology-focused Gemin X Pharmaceuticals for up to \$525m. The Gemin X pipeline comprises targeted cancer therapeutics based on reinitiating programmed forms of cell death (including apoptotic and autophagic cell death), based on the inhibition of metabolism in cancerous cells. Its lead product candidate, obatoclax, is a pan Bcl-2 inhibitor and is currently completing a Phase 2b trial in more than 160 patients with extensive stage small cell lung cancer (ES-SCLC).

Continuing its spending spree, and only a week after the acquisition of Gemin X was publicised, Cephalon announced it was acquiring all the outstanding shares in ChemGenex, an Australian biotech also focusing in oncology, for approximately \$163m.

M&As frequently trigger subsequent divestment activity and the acquisition of Cephalon by Teva is no exception. In October, Acino Holdings acquired the Mepha Middle

Eastern and African business from Cephalon (the Mepha range was acquired when Cephalon bought the Merckle family business). In a subsequent deal in December, Acino acquired from Teva the Latin American and Asian Mepha businesses, together with the R&D and manufacturing site in Switzerland. The total value of the combined transactions was \$123m. Earlier in the year, in its continued quest to become a global pharmaceutical company with branded and generic franchises, Teva completed its acquisition of Theramex, bringing a branded women's health product range.

Following on the Middle East and African theme, Hikma Pharmaceuticals, the fast-growing Jordanian multinational pharmaceutical group, has been busy on the acquisition trail; completing its \$112m acquisition of Baxter's generic "Multi-Source Injectables" products and facilities in May.

In December Hikma announced that it had acquired 63.9% of Moroccan Société de Promotion Pharmaceutique du Maghreb SA (Promopharm) for \$111m and would launch a mandatory tender offer for the remaining 36.1% of the company, valuing the whole company at \$174m.

Dermatology Focus on Acquisitions

In terms of therapeutic trends in the M&A and product acquisition deals announced in 2011, we saw deals in the following therapeutic areas: dermatology, CNS, ophthalmology, metabolic, gastrointestinal, cardiovascular, women's health, anti-infectives, anti-inflammatory and oncology. The number of dermatology-focused deals was an interesting feature and these are illustrated in Table 3.

Table 3 : Dermatology Deals 2011

Acquirer	Acquiree	Key Product/ Technology	Headline Value US\$M
Shire	Advanced BioHealing	Company acquisition – Dermagraft for diabetic foot ulcers	750
Medicis	Graceway Pharmaceuticals	Acquisition of assets (dermatology and women's health) following bankruptcy auction	455
Valeant Pharmaceuticals	Dermik (ex Sanofi)	Acquisition of US dermatology company with plant in Canada	425
Meda	Novartis	Product acquisition - Elidel for atopic dermatitis (US rights to Valeant)	420
Valeant Pharmaceuticals	J&J's Ortho Dermatologics	Acquisition including rights to Retin-A Micro and Renova	345
Allergan	Vicept	Development company with a product to treat rosacea	275

Shire announced its intention to acquire Advanced BioHealing for \$750m in May 2011 – just one day ahead of the latter’s planned initial public offering. Advanced BioHealing’s lead product is Dermagraft, a bio-engineered skin substitute used to treat diabetic foot ulcers. The acquisition will become the focal point of Shire’s new regenerative medicine unit. In July, Allergan acquired Vicept Therapeutics, a development company with a product to treat rosacea, paying \$75m upfront with an additional \$200m payable upon achievement of certain milestones.

Valeant inked two deals in the dermatology space; the first in July 2011 when it announced the deal to acquire J&J’s Ortho Dermatologics for \$345m, gaining the prescription medicines Retin-A Micro and Renova for acne and Ertaczo for fungal infections. Valeant’s second acquisition of Sanofi’s US Dermik business unit (including a manufacturing plant in Canada) for \$425m, brings the acne treatment Benzaclin, wrinkle therapy Sculptra, and Carac for skin growths, and is expected to fortify the company’s position in the US dermatological space.

Both these deals were cleared by the FTC in December 2011, but conditions of approval were that Valeant must sell manufacturing and marketing rights to two drugs for acne and pre-cancerous lesions to Mylan, and it also must sell marketing rights for a wrinkle treatment to Spear Pharmaceuticals. It is interesting to note that Valeant was also indirectly involved in Meda’s acquisition of Novartis’ Elidel for atopic dermatitis (for \$420m), as the licensee of the US rights.

Platforms and Discovery Deals: Feeding the Pipeline

Early in 2011, Burrill & Company published an annual report on the status of the industry with a key conclusion that the M&A activities between large pharmaceutical companies over the last 10 years have not delivered on their goal of growing businesses. This loss in value is

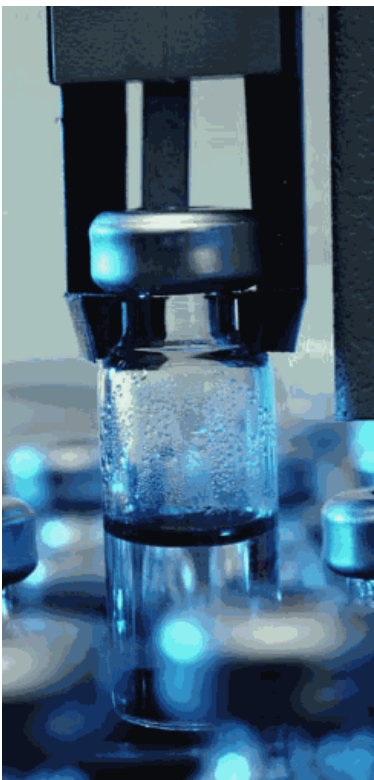
attributed not only to patent expiry of previously very successful drugs but also to the poor R&D productivity of the larger companies.

Burrill & Company comments further that while large pharma have been struggling to produce new compounds, smaller companies have delivered innovative drugs far more cost effectively. It is not too much of a surprise, therefore, to see a continuation of a theme noted in 2010, that there were a significant number of platform and discovery deals in 2011. Also, not unexpectedly, many of these transactions focused on biologics, with antibody-based therapeutic deals being ever popular and the majority of targets being in oncology. We will look at the hot therapeutic fields for deal activity later in this article and oncology is certainly one of them!

A selection of these early stage deals is illustrated in Table 4. The headline values for some of them are certainly impressive. However, it should be borne in mind that these transactions may comprise multiple targets, or multiple therapeutic entities against one receptor target, with each new molecule potentially commanding its own set of R&D funding and milestone payments. Furthermore, these deals will no doubt be back-loaded with the largest payments based on meeting later stage clinical milestones when the new therapeutics are considerably de-risked.

Of the deals illustrated in Table 4, Pfizer certainly seems to have gone on a spending spree, having signed up to two antibody deals and an RNAi deal with combined potential funding and milestones of up to \$1.45bn. Merck Serono comes in a close second with the F-star and Domain Therapeutics deals with a combined headline value of \$955m.

Typically for many early stage deals, the payments include initial technology access fees and R&D funding as well as licence fees, development, regulatory and commercialisation milestones and royalties on product sales.



The ability to attract R&D funding in this way is a potentially attractive option for biotechs that are starved of VC funds and looking for other approaches to generate income.

It is unusual for the royalty rates to be disclosed for platform/ discovery deals and, as the asset is at an early stage, it might be expected that the royalties would be single digit. However, it is interesting to note that some of the royalties noted in Table 4 are tiered up to double digit figures, which may well be when net sales reach a predefined high level.

For companies that are wishing to retain more of the value for themselves downstream, these discovery deals can provide a flexible framework in which to build specific elements to meet this objective. For example, the transaction between Ablynx and Merck Serono, which is the third agreement they have entered into, is focused on co-discovery and co-development of

Nanobodies® against two targets in osteoarthritis. Under this agreement, Ablynx received an upfront payment of \$28m and would then be responsible for all activities and costs for each programme, up to the delivery of a preclinical package that forms the basis of an IND or equivalent filing. The Ablynx costs exclude manufacturing costs and costs relating to certain *in vivo* models.

Merck Serono's acceptance of the preclinical packages will trigger a further approximately \$21m milestone for each programme. At this point Ablynx has the option to continue with Merck Serono on a 50:50 co-development and profit sharing basis or to convert the collaboration into an exclusive, worldwide licensing deal with milestone payments and tiered royalties. This provides the flexibility for Ablynx to decide downstream if it wishes to retain a larger share of the returns from the programmes by committing to a 50:50 share of clinical development costs.

Table 4 : Platform and Discovery Deals 2011

Licensor	Licensee	Platform/ Technology Comment	Headline Value (Upfront) US\$M
Micromet	Amgen	BiTE® antibodies – 3 solid tumour targets, 2 programmes	888 (13m) (+ dev costs) + up to double digit royalties
F star	Merck Serono	Modular Antibody Technology (antibody engineering to enhance activity) – 3 inflammatory disease targets	708 + undisclosed royalties
Epizyme	GSK	Small molecule therapeutics targeting histone methyltransferases (HMTs) (epigenetic enzymes) oncology & other diseases	650 (20) + up to double digit royalties
Theraclone Sciences	Pfizer	I-STAR antibody discovery and development - up to 2 infectious disease and up to 2 oncology targets	632 + undisclosed royalties
Santaris Pharma	Pfizer	Locked Nucleic Acid (LNA) Drug Platform - up to 10 RNA targets	614 (14) + undisclosed royalties
Aveo Pharma	J&J	Antibodies targeting the RON receptor – oncology	555 (15) + tiered, double digit royalties
ImmunoGen	Lilly	Maytansinoid Targeted Antibody Payload (TAP) technology with Lilly monoclonal antibodies to develop novel ADCs – oncology (\$200m potential milestones for each programme)	220+ (20) + undisclosed royalties
Seattle Genetics	Pfizer	Development of antibody drug conjugates (ADCs) to a single oncology target	208 (8) + undisclosed royalties
Zymeworks	Merck & Co	Azymetric™ platform for the development of new bi-specific antibodies - certain exclusive therapeutic targets	187 + undisclosed tiered royalties
Domain Therapeutics	Merck Serono	Metabotropic glutamate receptor 4 (mGluR4) Positive Allosteric Modulator (PAM) drugs for Parkinson's Disease & other CNS diseases	178 (3) + undisclosed royalties
Ablynx	Merck Serono	Co-discovery and development of Nanobodies® (antibody fragments) against 2 osteoarthritis targets (comprises option for Ablynx at point of delivery of preclinical package to continue on 50:50 co-develop / profit share, or to convert to exclusive, worldwide licensing deal with milestone payments and tiered royalties)	69 (28)

Therapeutic Trends

Oncology

In looking back over the trends for the year, this review would not be complete without giving some consideration to the hot therapeutic fields and the deal activity that has taken place. Oncology is a perennial hot area for deals and 2011 is no exception.

We have already reviewed some of the early stage discovery deals featuring oncology (Table 4); Table 5 covers a selection of transactions for specific products, most of which are for clinical stage assets or beyond.

The highest value deal was that between Astellas and Aveo Pharmaceuticals for tivozanib, which has commenced Phase 3 clinical studies in patients with clear cell RCC (kidney cancer) with prior nephrectomy. With a headline value of \$1.4bn, Aveo received \$125m as an initial payment which comprised a \$75m licence fee and funding for R&D of \$50m. The subsequent milestones amount to \$575m for clinical and regulatory events and a further \$780m in commercial milestones. The North American rights are shared for both development and commercialisation with a profit share. Outside the US, Astellas will pay double digit royalties, Kyowa Hakko Kirin retain rights to Asia.

In this table we have also seen the recovery of assets – similar to those noted later in this review. With a headline value of \$220m, Merrimack reacquired the European and Asian development and commercialisation rights to MM-398 (PEP02), which rights had been granted to the Taiwanese company PharmaEngine.

Merrimack had previously retained the US rights. For an upfront of \$10m plus \$210m (development, regulatory and commercial) and tiered royalties, Merrimack now has a global position. MM-398 is in Phase 2 in pancreatic cancer having completed Phase 2 in gastric cancer.

Restructuring is another feature where companies find that a negotiated settlement is preferable to litigation! Onyx and Bayer elected to restructure their agreement for Nexavar (sorafenib) to take account of Onyx's dispute with Bayer over the ownership rights to regorafenib, another multikinase inhibitor of angiogenic and oncogenic receptor tyrosine kinases. Onyx argued that regorafenib is a variant of Nexavar and as such should be treated under the companies' joint Nexavar project. Regorafenib, is in Phase 3 clinical development for gastrointestinal tumours and other cancer indications.

As part of the settlement, Bayer has bought out the Onyx royalty rights to Nexavar in Japan for a one off payment of \$160m, which means royalties in that territory cease at the end of 2011. In addition, Onyx will receive a 20% royalty on future global sales of regorafenib in oncology and co-promotion rights in the US. This arrangement gives weight to Bayer being the most obvious potential acquirer of Onyx in the future.



Table 5 : Oncology Deals 2011

Licensor	Licensee	Agreement	Product / Technology	Status	Headline Value US\$M
AVEO Pharmaceuticals	Astellas	Licence	Tivozamib worldwide excl Asia for Renal Cell Carcinoma	Phase 3	1,400
Pharmacyclics	J&J Janssen	Licence	PCI-32765, (Btk) inhibitor for NHL, CLL and multiple myeloma	Phase 2	975
Array BioPharma	Genentech	Discovery – oncology	Checkpoint kinase 1 (ChK-1) programme	Phase 1	685
Five Prime Therapeutics	Human Genome Sciences	Licence	FP 1039 for multiple cancers	Phase 1	495
Innate Pharma	BMS	Licence	PH 2102 antibody for cancer treatment, lead indication AML	Phase 1	465
Allos Therapeutics	Mundipharma	Licence	Folotyn outside USA for T cell lymphoma	Marketed	361
Merrimack	PharmaEngine	Recovery	Full rights to develop and commercialise MM-398	Phase 3	220
Seattle Genetics	Abbott	Collaboration	Antibody drug conjugate for oncology target	Preclinical	208
Epizyme	Eisai	Collaboration	EZH2 epigenetic enzyme for lymphoma	Preclinical	206
Onyx Pharmaceuticals	Bayer Healthcare	Renegotiation - dispute resolution	Regorafenib - oral multikinase inhibitor	Phase 2-3	20% royalty
Onyx Pharmaceuticals	Bayer Healthcare	Renegotiation - dispute resolution	Nexavar for kidney cancer - for Japan royalty stream	Launched	160
Ziopharm	Solasia Pharma	Licence/ collaboration	Darinaparsin in cancer for pan Asia markets	Phase 2	90
CureTech	Teva	Investment	Additional investment in CureTech for mAb CT 011 in large B cell lymphoma	Phase 2	69
Pfizer	Puma Biotechnology	Licence	Neratinib an inhibitor of ErbB1 (EGFR) HER 2 HER 4 in breast cancer	Preclinical	55
Infinity	Mundipharma	Funding	Mundipharma provide additional funds for oncology programmes	Phase 1	50
Yakult Honsha	Aeterna Zentaris	Development & commercialisation	Perifosine oral PI3K/Akt inhibitor in cancer for Japan	Phase 3	50
Marina Biotech	Debiopharm	Partnership	Programme for non-muscle invasive bladder cancer using RNAi drug discovery	Preclinical	25
Chroma Therapeutics	Cell Therapeutics	Licence	Tosedostat an oral aminopeptidase inhibitor for AML	Phase 1	10

In a busy year for Servier the company announced a strategic alliance to develop novel small molecule therapies for cancer with Galapagos. Compared to some other deals this is notably back-loaded with upfront research access payments of \$3m, but up to \$380m in milestones plus royalties. Servier will fund the development and commercialise whilst Galapagos retains the rights to the US. As Servier does not have a sales presence in the USA, this is an effective model for the company's partnering activities. This builds on the previous strategic alliance between Galapagos and Servier to develop new therapies in osteoarthritis (OA) in July 2010.



Also in the oncology space, Pfizer has licensed the worldwide commercial rights of Neratinib a Phase 2 pan-HER inhibitor (potent irreversible tyrosine kinase inhibitor) in the neoadjuvant, adjuvant and advanced settings in HER2/ErbB2 positive breast cancer, to Puma Biotechnology. Pfizer will receive undisclosed milestone payments and royalties. Pfizer also inked a \$340m deal for access to GlycoMimetics' GMI-1070 in Phase 2 for vaso-occlusion associated with sickle cell disease.

Diabetes

Perhaps one of the most notable deals of this period is the announcement of the strategic alliance between Boehringer Ingelheim (BI) and Eli Lilly. The alliance is in the hugely competitive diabetes field, in which 11 major deals were reported in 2010. The agreement covers four drugs, two from Lilly and two from BI. From the BI side are two oral diabetes agents; one a DPP-4 inhibitor (linagliptin), filed in US, EU and Japan, and the other a SGLT-2 inhibitor, in Phase 3, which could be

first in class. From Lilly come two basal insulin analogues, both due to enter Phase 3 in 2011. Also covered by this deal is the option to co-develop and co-commercialise Lilly's anti-TGF-beta monoclonal antibody. Lilly paid BI an upfront of \$387m. BI can receive up to \$808m in success-based regulatory milestones for its products and Lilly \$650m for similar milestones on its two basal insulin analogues. Should BI elect to exercise its option on the anti-TGF-beta monoclonal antibody, Lilly could receive an additional \$525m in milestones.

In this way the companies are playing to their strengths; Lilly providing the expertise in the disease and BI some much needed muscle to beef up Lilly's pipeline to provide a credible presence in a key disease area. This collaboration is by no means the first of its kind; GSK and Pfizer have set up ViiV to combine efforts in HIV and AstraZeneca and Merck recently embarked on a landmark partnership to develop a combination therapy for cancer, with each contributing an investigational compound to the mix. It is likely that we will see more of this type of creative big pharma partnership.

Continuing the theme of the non-traditional pharma business model, June 2011 saw Royalty Pharma acquire Prosidion's patent estate and associated royalty stream relating to the use of dipeptidyl peptidase IV (DPP-IV) inhibitors for the treatment of Type 2 diabetes for a total cash payment of \$609m. Prosidion was acquired as part of Astellas' acquisition of OSI Pharmaceuticals in June 2010. Interestingly, Prosidion retains two drug candidates in development for diabetes and obesity, until Astellas completes its review of strategic alternatives for these assets.

Other deals of note are BI's deal with Zealand Pharma for rights to its ZP2929 - GLP1 receptor agonists (against Type 2 diabetes and obesity), which are at the preclinical stage of development.

However, it was not all constructive in the diabetes field. The 2010 deal between Diamyd Medical and Ortho-McNeil-Janssen Pharmaceutical (OMJP), for the GAD65 gene-based therapy, Diamyd®, for the treatment and prevention of Type 1 diabetes and associated conditions, was terminated following the failure of the Phase 3 study to meet the clinical efficacy endpoints. OMJP had paid a non-refundable upfront of \$45m, which Diamyd retains with its rights to the product.

In addition, in July there was the sale by Astellas of a family of medical use patents for DPP-IV inhibitors for the treatment of Type 2 diabetes patents to Royalty Pharma, at a value of \$609m. In the case of Astellas, the patents had been acquired as part of the OSI acquisition in June 2010.

Not to be excluded from the deal activity, Servier signed a \$163m alliance with Intercept Pharmaceuticals for the discovery and development of novel agonists of TGR5 (a cell-surface receptor that is regulated by bile acids) for the treatment of Type 2 diabetes and other metabolic indications. The deal provides Servier access to Intercept's proprietary bile acid analogue chemistry platform and expertise in targeting TGR5 and other bile receptors. As usual for Servier, the rights exclude the US and Japan, which are retained by Intercept. Although Intercept and Servier will jointly support the discovery phase, Servier alone will be responsible for all costs associated with global development, regulatory approval and commercialisation of any compound selected.

Table 6 : Diabetes Deals 2011

Licensor	Licensee	Agreement	Product / Technology	Status	Headline Value US\$M
Eli Lilly	Boehringer Ingelheim	Co-development, commercialisation	BI10773, LY2605541, LY2963016, Ondero	Phase 3 - MAA Filed	1,844
Zealand Pharma	Boehringer Ingelheim	Exclusive licence	ZP2929 GLP1 receptor agonists in Type 2 diabetes obesity	Preclinical	588
Evotec	MedImmune	Licence	Insulin producing beta cell regeneration	Preclinical	349
Euroscreen	Ortho-McNeil-Janssen Pharma	Development, Licence, Research	ESN-JJ Type 2 diabetes	Platform	197
Intercept Pharmaceuticals	Servier	Discovery & development collaboration, ex US, JP	TGR5 agonists for diabetes and metabolic Type 2 diabetes, other metabolic indications	Discovery	163
Boehringer Ingelheim	Depomed	Commercialisation, Development, Licence	Acuform drug delivery for combinations of metformin	Approved	13

CNS

One of the most notable deals reported this year in the CNS field was that of Lilly and Medtronic. This collaboration combines a biologic approach to the disease with a new drug delivery system for the brain. Lilly intends to use the Medtronic implantable drug infusion system to deliver a modified form of glial cell derived neurotrophic factor directly into targeted regions of the brain. Last year Lilly acquired Avid Radiopharmaceuticals for \$800m to gain access to its new diagnostic system.

Reflecting the high amount of activity in CNS, the return by Merck & Co of the metabotropic glutamate receptor 4 programme rights to Addex Pharmaceuticals was seen positively by the company which remains committed to this development in Parkinson's disease. Citing pipeline prioritisation, Merck returned rights to intellectual property including the know-how. On a positive note, it is far preferable that the rights to a project are returned rather than seeing development languish due to lack of commitment by the partner; however re-partnering can prove to be a challenge.

Lundbeck was back in the headlines this year with its strategic partnership with Proximagen. Lundbeck made an investment of £10.3m (\$16m) in Proximagen with the aim of cooperating on several fronts – in epilepsy, pain

and inflammatory disorders. In return for its investment, Lundbeck will receive certain negotiation rights emanating from these programmes.

Shortly thereafter there was the next announcement of the long term deal to co-develop two Otsuka late stage products (Aripiprazole depot and OPC-34712, both of which are in Phase 3) and up to three Lundbeck early stage CNS products. As noted further below in this report, there seems to be no royalty, with the companies instead electing to profit share via sales and development and commercialisation costs. Lundbeck has rights to the products in the Americas, Europe, Australia and some other countries. Assuming a good long term working relationship, these two deals together should bolster the Lundbeck pipeline.

As seen in other therapeutic fields, Heptares signed an exclusive option to a worldwide licence with Shire for its adenosine A2A antagonist, which is in preclinical development. Inhibition of the A2A receptor has been proved to be clinically effective in treating symptoms of Parkinson's disease and this reflects a new approach to this GPCR target. Although not disclosed, Heptares received an upfront payment and will, on exercise of the option, be eligible for milestone payments and royalties. Of course the exercise will be dependent on good preclinical studies and there is no guarantee that the option will be exercised.

Table 7 : Selected CNS Deals 2011

Licensor / Licensee	Agreement	Product / Technology	Status	Financials US\$M
Otsuka / Lundbeck	Development and commercial alliance	5 CNS products	Phase 3	1,800
Evotec / Roche	Re-licensing	Originally licensed for another indication - EVT 302 in Alzheimer's	Pre-PoC	10 upfront, 820 in m/s and tiered double digit royalties
ITI / Takeda	Collaboration	Selective type 1 PDE inhibitors in cognitive impairment	Preclinical	750 of which 500 development and 250 sales based m/s with tiered royalties
PTC Therapeutics/ Roche	Licence	Spinal muscular atrophy programme including 3 products	Preclinical	30 upfront with 460 in m/s
Impax / GSK	Licence	ER carbidopa-levodopa ex US Parkinson's disease	Phase 3	187
MAP Pharma / Allergan	Co-development, Co-promotion	Levadex in migraine US	Phase 3	157
Durect / Zogenix	Licence	Long acting injectable risperidone to combine with Zogenix needle free system	Preclinical	106
Proteostasis / Elan	Investment	Discovery and development of small molecules and diagnostics	Platform	50 of which 20 in equity and 30 collaboration funding
Proximagen / Lundbeck	Investment	£10+m equity investment into Proximagen		16

Deal Structures

Terminations

In the ongoing need for news flow, an interesting aspect has been the advent of pre-closure announcements where deals are formally announced but noting of course that not all of these deals then proceed to closure. Some examples from 2011 include the planned acquisition of Newron by Biotie as well as the attempt by Paladin to purchase Afexa. The reasons for the deal not proceeding to completion can be varied; in the latter case with Paladin this was a hostile bid which was superseded by a friendly acquisition made by Valeant which proved to be successful.

As due diligence is normally running closely in parallel with the final negotiations, it is not surprising that issues may emerge which alter the previously agreed value or risk profile and hence push the deal into non viable territory. As there are so many areas where there is subjective interpretation of different data sets, there is significant scope for disagreement.

This in turn introduces a new component into the negotiations – the non completion fee, which in the case of Newron and Biotie was not insignificant at €1.5m and

which will go some way towards the due diligence costs incurred by Biotie. Not proceeding with this deal leaves Newron with its lead asset safinamide rejected by its original partner, Merck Serono and very dependent on showing good results from its two Phase 3 studies to revive the fortunes of the company. The termination by Merck Serono represented a material adverse effect allowing Biotie the right to withdraw from the deal.

Another merger which failed to materialise was that between Allos Therapeutics and AMAG Pharmaceuticals. Valued at some \$686m this share-based deal, which gave AMAG 61% ownership of the new entity, was vetoed by the AMAG shareholders. Originally announced in July the acquisition triggered an unsolicited offer of \$378m backed by key investor MSMB Capital Management to purchase the company in order to prevent the merger going ahead. As with the Biotie – Newron situation, AMAG made a \$2m payment to Allos in recognition of the expenses incurred in the run up to the transaction.

Other notable agreement terminations are included in Table 8 below.

Table 8 : Deal Terminations 2011

Licensor / Licensee	Rationale	Product / Technology	Initial Financials US\$M
Addex Pharmaceuticals / Merck	Pipeline rationalisation	Metabotropic glutamate receptor 4 programme ex USA/CA in Parkinson's	Dec 2007 - 3m upfront, PC m/s of 250k & 500k . Up to 107m in research and up to 61m for 2 nd and 3 rd products
PTC Therapeutics / Genzyme	Failure of P2b study in muscular dystrophy	Ataluren in Duchenne muscular dystrophy ex US/CA rights returned, option to other indications	100m in 2010
Amylin / Lilly	Phased hand back of commercial rights in settlement of outstanding litigation	Exenatide in diabetes	One off payment of 250m plus future revenue sharing of 15% of global net sales to max of 1.2bn plus interest

With being acquired by Sanofi, portfolio reviews would always be a potential break point and hence Genzyme was able to revisit the terms of its agreement with PTC Therapeutics for ataluren. In a similar vein, Addex fell foul of pipeline rationalisation by Merck leading to the recovery of the rights to its metabotropic glutamate receptor 4 programme.

The Amylin-Lilly Affair

Finally putting to bed a more acrimonious issue, after some 10 years of a successful partnership on Byetta, Amylin closed the chapter with agreeing to disengage from the original co-development and co-promotion agreement with Lilly. When Lilly signed up with Boehringer Ingelheim (BI) in a broad pipeline deal in diabetes, Amylin took issue that the degree of commitment to Byetta might be at risk. This concern was seen through the commencement of legal action, which through this termination agreement is now resolved. Originally signed in 2002 when Byetta was in Phase 3 clinical studies, Lilly entered into a development and commercialisation agreement with Amylin. With initial non refundable payments of \$80m, Lilly also agreed to purchase stock of \$30m at a price of \$18.69 per share (current price \$11) and pay up to \$85m in milestones convertible at Lilly's option. A further \$130m contingent on global commercialisation was due and US development costs were to be shared equally, with ex-US development costs being shared 80:20 Lilly: Amylin. The deal also included a \$110m convertible loan by Lilly to Amylin.

Some ten years on, in the strategic alliance between BI and Lilly mentioned above, Lilly agreed to make an initial one off payment to BI of \$387m, with \$808m in regulatory milestones for linagliptin and BI10773. Lilly became eligible to receive up to \$650m in regulatory milestones on its two basal analogue insulins. Furthermore if BI opted-in to the Phase 3 development and potential commercialization of the anti-TGF-beta antibody, Lilly would be eligible for up to \$525m in opt-in and success-based regulatory milestone payments. Ongoing development costs would be shared equally.

The dispute between the Amylin and Lilly centered on promotional efforts with Amylin's suit seeking to stop Lilly

using the dedicated Byetta sales force to promote BI's linagliptin. It is difficult to predict who will be the loser here; it will be interesting to see the impact on sales with the market sector being so dependent on share of voice; replacing the Lilly sales resource will not be easy. Financial terms for this termination include a one off payment of \$250m plus future revenue sharing of 15% of global net sales to a maximum of \$1.2bn plus interest. A significant sunset payment!

Options

In keeping with the risk averse economic climate, the re-emergence of options has been very evident during 2011. The Medtrack deals and alliances database included 43 deals (out of nearly 3700) in 2011 where an option was a main element.

According to Elsevier's Strategic Transaction data reported at BIO in June 2011, the number of option based deals, where an option was a main component, increased from 14% of total big pharma and big biotech deals in 2008 to nearly 20% in 2009 and 2010. Note this analysis is restricted to big pharma and big biotech and, more importantly, is based on deals where "an option was a main component" of the deal. This is often difficult to identify. Nearly every licensing deal has some option element. Often, if it is a biotech company, it seeks to retain an option to co-promote its licensed product in its home country. If it is a co-development collaboration, the licensee will usually seek an option to follow-on compounds.



The deals where an option is a main component are usually those where a potential licensee seeks to retain an exclusive position for a period of time while due diligence or a feasibility study is undertaken. It is these types of deals that are said to be increasing as licensees seek to hedge their bets whilst further data become available. For a cash constrained biotech company seeking immediate income, an option deal is not as satisfactory as a licensing deal because the values are usually lower and the biotech company is restricted in what it can do with the asset until the option period expires.

Table 9 below shows some of the option based deals captured during our analyses of 2011.

Table 9 : Selected Option Agreements 2011

Licensors / Licensee	Agreement	Product / Technology	Headline / Financials US\$M
Aires Pharmaceuticals / Novartis	Option to acquire company at end Phase2	Exclusive worldwide rights to Aironite, an inhaled nitric oxide prodrug for the treatment of pulmonary arterial hypertension	Up to 250m
Audion / Sanofi	2 year collaboration with option to license	Treatments for hearing loss—optimisation of small molecules using regenerative medicine	Financial terms not disclosed
Gedeon Richter / STADA	Option to extend distribution licence	Trastuzumab biosimilar	Financial terms not disclosed
pSivida / Pfizer	Option to license at end Phase 2	Implant for SR latanoprost	Initial payment of 2.3m; option exercise fee 20m; up to 146m m/s + double digit royalties
Xencor / Amgen	Late stage preclinical development collaboration with exclusive option to global exclusive licence at end Phase2	XmAb 5871 an Fc engineered monoclonal antibody dually targeting CD19 and CD32b in autoimmune diseases	Option exercise fee with upfront and early m/s of 75m; up to additional 425m subsequent m/s + tiered royalties

Each of these deals addresses a different risk issue. In the Aires Pharmaceuticals agreement with Novartis, if the product reaches the end of a Phase 2 clinical study to treat pulmonary arterial hypertension successfully then, rather than be held to licence terms, Novartis has the option to acquire the company. Presumably this will be at a pre-agreed price, which gives the company the security of access and supply to a new product. The transaction value could reach approximately \$250m including the initial acquisition payment plus potential additional regulatory and sales milestone payments.

The Sanofi – Audion deal represents a standard research collaboration arrangement over a period of two years with Sanofi retaining an option to any new small molecules. Similarly, the pSivida-Pfizer and Xencor-Amgen deals also cover off the risk that the technology may not prove to reach its anticipated value, with the licensee partner company being able to exercise its option when the technology has proved its worth. Successful completion of Phase 2 appears to be the agreed point for risk mitigation. When the technology or science is unproven, this is a sound approach to secure access with limited exposure to the risk.

The distribution deal between Gedeon Richter and STADA uses options in a different way – allowing the licensor to determine if the licensee is an appropriate partner before extending the collaboration to other products, in this case trastuzumab. Of course, this cuts both ways, as it usually ensures that other related products are not given to another licensee thus allowing the original licensee to build its franchise.

Making a welcome return to the deal scene was the arrangement between Merck Serono and Ono Pharmaceutical representing a geographical quid pro quo. The first agreement grants Merck Serono worldwide (outside Japan) exclusive rights for Ono's ONO 4641 in Phase 2 development for the treatment of multiple sclerosis. The upfront due to Ono for Ono 4641 is \$17.8m; no other financial terms were disclosed. In return, Merck Serono grants Ono co-development and co-marketing rights in Japan for Stimuvax, an immunostimulant used in cancer treatment which is in Phase 3 for non small cell lung cancer. Stimuvax was originally licensed from Oncothyreon. The upfront fee for this deal was \$6.35m, as before no other financial terms were disclosed.

Creative Deal Structures

The reason option deals are popular with licensees is because it is a way of managing, and possibly reducing, risk. Another way of managing risk is to devise a creative deal structure. Some interesting deal structures are shown below. The 2011 licensing deal with the highest headline value was Lundbeck's deal with Otsuka announced in November.

Table 10 : Creative Deals 2011

Licensor	Licensee	Agreement	US\$M
Otsuka	Lundbeck	Co-development of 2 Otsuka late stage and up to 3 Lundbeck early stage CNS products	1,800
Xoma	Servier	Co-development and commercialisation of anti-inflammatory drug in multiple indications	800

The Otsuka / Lundbeck deal shares not only development risk but also commercialisation risk. Whilst Lundbeck pays \$200m upfront and a further \$1.6bn in development, regulatory and sales milestones to Otsuka, there appears to be no royalty component and instead the companies have decided to "share sales as well as development and commercialisation costs". Lundbeck has rights to the products in the Americas, Europe, Australia and some other countries. Lundbeck's share of sales booked by Otsuka (and promotion costs) is shown below:

Table 11 : Lundbeck Sales Share 2011

Product	EU(5) + Nordic + Canada	US	Other countries
Aripiprazole depot - Phase 3	50%	20%	100%
OPC-34712 – Phase 3	50%	45%	100%

Where Otsuka sets up a sales organisation in a Lundbeck territory, it will have the rights to participate in the promotion of the product. Otsuka will supply bulk product at a price represented as a percentage of sales. This percentage cost of goods mechanism for the licensee is becoming increasingly important given Governments' pressure to reduce reimbursement prices. This is an innovative deal which for success will rely heavily on a good working relationship down to grassroots level.

The interesting aspect of the Xoma / Servier deal is that Xoma has retained an option to reacquire the development and commercialisation rights to the diabetes and cardiovascular indications in the US and Japan, areas where Servier's commercialisation capability may be less strong than other companies. Xoma can re-acquire the rights (and the right to license out to a third party) by paying an option fee and partial reimbursement of incurred development expenses. In addition, the milestones reduce from \$800m to \$470m.

Financial Aspects

2011 was a momentous year in terms of both natural and man-made events. The tsunami in Japan and the Arab spring had profound effects on the countries concerned and elsewhere in the world economy. In Europe the sovereign debt crisis and the ineffectual response by Euro zone Governments resulted in the change of Governments in Greece and Italy and continues to create an uncertain business environment for 2012. For the pharmaceutical and biotechnology industry, and as we have noted above, 2011 was pretty much a continuation of the trends from 2010, such as growth in emerging markets, development of biosimilars and so on. However the financial climate for the industry has become a lot colder and is likely to remain so for at least another year.

VC Funding declining

In February 2011 PWC reported a substantial decline in VC funding in 2011. This trend seems to have continued in 2011. Medtrack reported in December 2011 that venture financing to the end of 3rd quarter 2011 was \$5.1bn compared to \$6.7bn, \$7.8bn and \$10.8bn in the years 2010, 2009 and 2008, respectively. It seems that the venture finds set up by the big pharma companies have not filled the gap left by the reduction in funding from the traditional VC funds.

Small Biotech response

Obtaining funding from Government and NGOs

One reaction of the private biotech and SME companies to the decline in venture funding has been to seek funds from other sources such as charities and other NGOs and Governments where over 100 deals have been announced in 2011. Although Government agencies such as the National Institutes of Health dominates the number and value of deals, there seems to have been a significant increase in funding by charities. For example in 2011, the Michael J Fox Foundation, which claims to be the largest NGO funder of development of drugs to treat Parkinson's disease in 2011, committed over \$50m in new money and this funding has been increasing year on year since inception in 2001 reaching \$279m cumulative. The funding is provided to academic institutions and mainly small companies to develop new and 'repositioned' molecules and new formulations with novel drug delivery.

During 2011 new funding was announced for companies including Trevena and Civitas (US, December), Sapiens (Germany, November), AFFiRiS (Austria, October), Prana (Australia, August) and Melior Discovery (US, August), Impax Labs and Envoy Therapeutics (US, July), BioFocus (UK, July) and Zymes (US, February). While the amounts are often less than \$1m and therefore only make a difference to smaller companies, some companies are also able to attract funds from other similar sources. For example Sapiens received \$0.4m from Michael J Fox Foundation but in addition \$4.4m from The Wellcome Trust and \$8.25m from the Dutch Government.

Table 12 : NGO Funding Deals 2011

NGO	Company	Project	US\$M
Bill & Melinda Gates	Beijing Tiantan Biological	Oral polio vaccines	23.7
Michael J Fox Wellcome Dutch Government	Sapiens Steering Brain Stimulation	Electrophysiological treatment of Parkinson's Disease	13.0
Wellcome Trust	PTC Therapeutics	Small molecule drugs to treat multi-drug resistant bacteria	5.0
PATH	Merck & Co	Maternal health technologies	2.5
Michael J Fox	AFFiRiS	Parkinson's disease vaccine	1.5

Surprisingly perhaps, it is not only the small companies that collaborate with NGOs. In December Merck & Co signed a \$2.5m partnership deal with PATH “to identify game-changing technologies with potential to save the lives of women during pregnancy and childbirth in low-resource settings”. PATH is perhaps better known for its work to develop treatments for malaria. In June PATH signed a three-way deal with Crucell and GSK to develop a second generation malaria vaccine. Although the amounts contributed to specific projects and companies may be small, the total amounts contributed by NGOs in any year can be enormous. The Bill and Melinda Gates Foundation provided \$1.5bn in funds for healthcare projects in 2010. The Wellcome Trust, which also has an alliance with Merck & Co, spent a total of \$1bn.

Larger biotech Response

The larger biotech and drug delivery companies faced with difficulty raising equity or loan finance have, over the past few years, cut back their costs to the minimum levels by reduction in infrastructure costs and shelving of non-core programmes. Cutting costs works in the short term but at some point the companies have to generate or increase their income. In 2011 we have seen a continuation of the usual non-dilutive short term cash generation methods such as re-negotiation of licensing deals to request licensees to fund a greater share of R&D.

The other option of monetising royalty streams seems to have declined considerably in spite of bullish comments from the royalty buying companies. In fact the deals reported in 2011 are in effect divestments rather than long term sharing of royalty streams by companies requiring short term cash. Royalty Pharma made two new deals in 2011. The largest deal for \$609m was fundamentally a divestment of a non-core diabetes patent estate and

royalty stream by Astellas arising from the acquisition of OSI in 2010. [6 months later Prosidion gave Astra Zeneca an option to the Phase 2 product – see below.] The second deal for \$487m was to acquire the rights to royalties on Lexiscan and Cubicin from an undisclosed seller. The seller may have been the hedge fund TPG Axon Capital which originally paid \$185m to CV Therapeutics (now part of Gilead) in April 2008 for 50% of Lexiscan royalties in the US payable by Astellas. Dendreon undertook a similar deal to Astellas by selling for \$125m royalties linked to Victrelis IP, acquired in 2003, to CPPIB Credit Investments. Dendreon made a net loss of \$376m in the 9 months to end September but had \$568m in cash so the \$125m would fund a further quarter at current burn rates. The number of royalty monetisation deals with companies may be declining because the biotech companies are more nervous of the constraints e.g. pledge on the IP, that these deals place on future corporate transactions such as mergers or divestments.

Table 13 : Royalty Monetisation Deals 2011

Company	Royalty Company	Product / IP	US\$m
Prosidion Astellas	Royalty Pharma	Patents and royalty stream for DPP-IV inhibitors for type 2 diabetes	609
Not disclosed	Royalty Pharma	Lexiscan and Cubicin royalties	487
Dendreon	CPPIB Credit Investments	IP and royalties relating to Victrelis for treating chronic Hepatitis C	125

If all else fails or there is a better value than a licensing deal...seek a trade sale

For those biotech companies unable to raise cash or generate income from divestment or licensing deals, the options are few. Some have managed to sell the company or the company's assets (Lectus to UCB) and others have merged with other biotech companies often based on an all paper deal (Lipoxen acquisition of Symbiotech). On the other hand M&A is a favourite strategy for big pharma to bolster sales and reduce costs when under pressure from patent expiries (Pfizer and King), to buy a pipeline (Gilead and Pharmasset), or to increase geographic coverage (Takeda and Nycomed).

2011 started and finished with a major acquisition. At the start it was Sanofi's acquisition of Genzyme for \$20bn and at the end Gilead's acquisition of Pharmasset for \$11bn. One financial aspect of the M&A deals where the target is a public company has been the share price premium paid by the acquirer. The table below shows the prices paid by each acquirer and the annual net profit or loss of the target for the year prior to the acquisition. The average share price premium for 15 deals excluding the Gilead deal is 42%. Most of the 15 deals were for profitable companies and yet Gilead paid an eye-watering 89% share price premium for Pharmasset, a company without any products on the market and making a loss. Gilead will take on \$6bn of debt to fund the deal. So what is Gilead acquiring that justifies such a high price? Basically Gilead is buying a pipeline. The latest stage product in the Pharmasset pipeline is an oral Hepatitis C vaccine that is due to start Phase 3 clinical trials in 2012 with a second version in Phase 2b. A third Hepatitis C vaccine in Phase 2 is partnered with Roche. Only time will tell if the Gilead deal justified such a premium.

Table 14 : Share Price Premiums

Target	Annual Net Profit US\$Bn	Acquirer	Purchase Price US\$M	Share Price Premium %
Genzyme	0.42	Sanofi	20,100 + CVR	41%
Pharmasset	(0.09)	Gilead	11,000	89%
Cephalon	0.43	Teva	6,800	44%
King	0.10 est	Pfizer	3,600	40%
Afexa	(0)	Valeant	90	30%

Predictions for 2012

Keeping our crystal ball close at hand, what do we expect to see in the deal making world during 2012? There are some obvious trends which are likely to continue from 2011 such as biosimilar deals, several of which were announced as 2011 came to a close, e.g. the transactions between Amgen and Watson; Momenta Pharmaceuticals and Baxter; and Samsung and Biogen Idec. This area remains an interesting challenge both technically and commercially. We also anticipate more deals in China and other emerging markets, as once companies establish operations this will be followed by the need for product flow.

Within Europe and other developed markets, as companies move away from running primary sales forces, there will be a need for promotional effort for primary healthcare products and this could well be an area of activity. We would also expect to see more deals with big headline values; investors still like large numbers even when on closer analysis these deals are very often heavily back loaded to take account of the risk. It is likely that there will also be more renegotiations and asset recoveries either due to changing economic conditions or changing pipeline priorities.

In any event – a busy time for the Business Development community!

With best wishes for a successful and prosperous New Year!

The Medius Deal Watch Team

This review is based on publicly available information covering the top deals reviewed every month in our regular deal watch series. The views expressed in this article are those of the authors.

AUTHOR BIOS :**Sharon Finch**

Sharon has over 25 years' experience in business development working with Wellcome, Medeva and Ono Pharmaceutical. Sharon works primarily on partner searches and transactions. She is the Editor of the Business Development and Licensing Journal as well as a member of the Editorial Board for the Journal of Commercial Biotechnology. In addition, Sharon is the Course Director for the MSc in Pharmaceutical Business Development & Licensing which is run by Manchester University. She is also past President of the European PLG Council and past Chairman of the Pharmaceutical Licensing Group UK.

**Jill Ogden**

Jill has over 24 years' commercial and R&D experience in the biopharmaceuticals and healthcare industries and provides our biologics and drug delivery expertise. She has led and been involved in a wide range of product and technology deals.

**Roger Davies**

Roger works with Medius as a consultant in pharmaceutical licensing and business development. Having personally completed over 80 deals he specialises in valuations, deal structuring and negotiating licensing and acquisition deals. He is the former Chairman of the UK Pharmaceutical Licensing Group, the professional association of licensing and business development executives and is the Finance module leader for the Business Development MSc at the University of Manchester.

**Bridget Lacey**

Bridget has over 16 years of corporate finance and business development experience from the Healthcare industry in Pharmaceuticals, Vaccines and Life Sciences roles in the UK, Singapore and Japan. She has experience across a wide range of transactions including leading company and product acquisitions, business divestments and licensing deals, with a focus on due diligence and valuations.

Medius Associates

47 Upfield
Croydon
CR0 5DR
U.K.

Tel: +44 (0) 20 8654 6040

Email: info@medius-associates.com



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