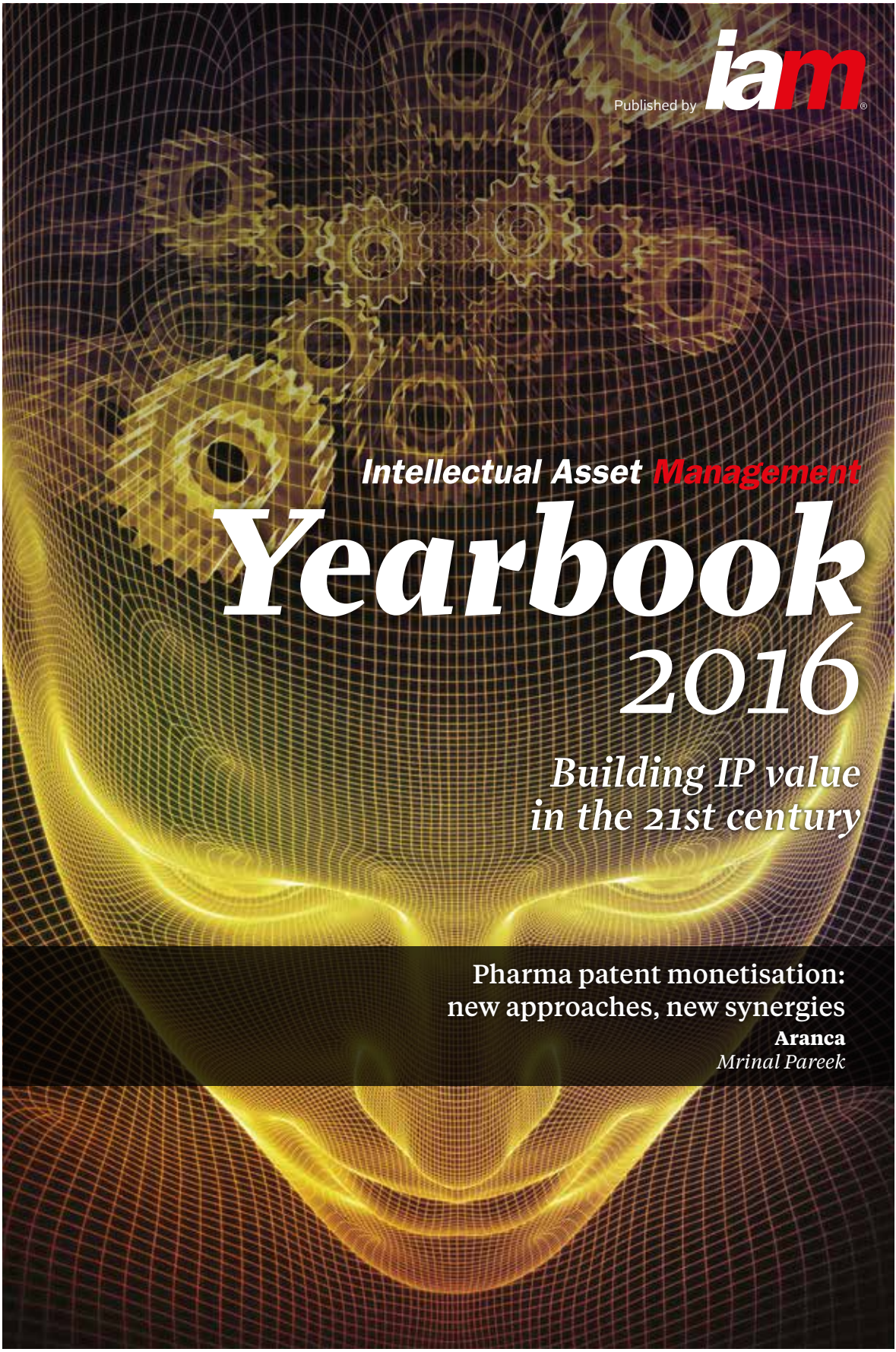
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Pharma patent monetisation: new approaches, new synergies
Aranca
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Pharma patent monetisation: new approaches, new synergies

By **Mrinal Pareek**, Aranca

Patents are undoubtedly the kingmakers in the life sciences industry. This fact was reinforced when certain pharmaceutical blockbusters came off patent in 2011.

Pharmaceutical giants had a massively fruitful run with some of their branded drugs. However, in the last four years the patent cliff has shaved off billions of dollars in revenue and pushed even the biggest drug makers to scramble to find ways to stem the revenue loss.

The most notable patent cliff appeared in 2011 when the patent for one of the most successful drugs ever, Lipitor, expired. Lipitor accounted for more than 40% of Pfizer's total profits and generated $115 billion in revenues since its release in 1997. In the three years following its expiry, revenues dropped by nearly $15 billion as generics flooded the market. Similarly, AstraZeneca's revenues plummeted following the expiry of Seroquel, as did Merck's following the expiry of Singulair. A number of patents for chemical drugs expired between 2011 and 2015. Further, the trend for biologics to go generic (which started in 2014) is projected to continue until 2019 (see Table 1).

Such steep patent cliffs and far fewer in-house breakthrough innovations in recent years have forced the pharmaceutical industry to re-examine its business models, and many companies have shifted focus away from primarily spending time, effort and money on finding the next blockbuster.

Many in the industry are keen to identify more symbiotic R&D alliances and leverage various patent monetisation strategies in order to avoid falling off the growth path while staying invested in the search for 'big tickets'.

As such, large pharmaceutical companies are more focused on looking outside of their organisations for innovations that might become the next big breakthrough. Small and medium-sized companies benefiting from exclusive, niche patents are looking to commercialise their innovations. Industry observations suggest that patent monetisation and commercialisation strategy should naturally take advantage of this convergence.

However, before the pharmaceutical decision makers can ascertain the right strategic approach to monetising their patents and optimising their alliances, the technology and patent portfolio must be clearly understood.

Table 1. **Top blockbuster patents expiring 2015/2016**

Year of expiry	Drug	Company	Revenues (billion)
2015	Abilify	BMS	$4.6
2015	Copaxone	Teva	$3.57
2015	Gleevec	Novartis	$4.26
2015	Namenda	Forest	$1.8
2015	Baraclude	BMS	$1.8
2016	Crestor	AstraZeneca	$6
2016	Benicar	Daiichi Sankyo	$2.5
2016	Humira	Abbott	$10

Source: IMS Health, EvaluatePharma

Table 2. **Pharmaceutical company and investor perspectives across product development stages**

Development stage	Pharmaceutical company			Investors		
	Monetary gains	Pros	Cons	Risk	Pros	Cons
Discovery – pre-clinical	Low	Early support and faster progress	Unclear valuation	High	Lower price for well-judged breakthrough innovation	High risk
Clinical – Phase I-II	Mid	Monetary support accelerates progress; opportunity for collaborative research	Few opportunities for research integration	Mid	Medium price for more established innovation	Medium risk
Phase III – post-approval	High	More monetary gain	Missed opportunities for collaborative and complementary gains from research; missed opportunities to 'make it big'	Low	Calculated risk and more clarity; opportunity to profit through commercialisation of approved product	Expensive

Table 3. **Top licensing deals of 2014**

Licensor/licensee	Product/technology	Status	Value (billion)
Edison/Dainippon Sumitomo Pharma	Extension/amendment of 2013 deal; joint research; equity investment for drugs targeting cellular energy metabolism; broadening of rights to EPI-589 (p1) + 10 new drug candidates for Japan and North America; EPI-743 (p2) in existing alliance	Phase I/II and earlier	$4.295
Merck KGaA/Pfizer	Joint development and commercialisation of MSB0010718C and combinations	Phase II	$2.85
Ablynx/Merck & Co	Nanobody candidates (including bi and tri-specifics) targeting immune checkpoint modulators	Discovery	$42.3
Nogra/Celgene	Licence to develop and commercialise GED-0301	Phase II completed	$1.525
Proteostasis/ Astellas	Collaboration to develop therapeutic candidates that modulate unfolded protein response	Discovery	$1.2
Newlink Genetics/ Genentech Roche	Licence for NLG919, IDO pathway inhibitor and next-generation IDO/TDO compounds	Phase I	$1.15

Source: Medius Deal Watch Annual Review 2014

The prospect of monetisation is founded on collaborative innovation. While all pharmaceutical companies continue to search for the next big blockbuster, some companies are also increasingly investing in smaller, yet more strategic innovations that play a key role in strengthening portfolio and product development. A prudent monetisation strategy is a correct mix of these two approaches – and it all begins with developing a clear understanding of the technology and patent portfolio.

Association with larger pharmaceutical players can be rewarding for smaller companies, exposing them to complementary technical and resource deployment. Correspondingly, larger companies get quicker access to niche innovations and developments that can be turned around for continued profits. Here, the trick is to find the right place and the right time.

In the life sciences industry, every decision becomes critically strategic because of the long journey from discovery to commercialisation. While a highly mature technology can swiftly generate revenue, associating at a late stage means risking missing out on early opportunities to tap greater benefits for lesser investments. Conversely, associating at an early stage means taking much longer to realise optimum monetary gains. See Table 2 for a comparison of the gains and risks for both pharmaceutical companies and investors for alliances across the product development stages.

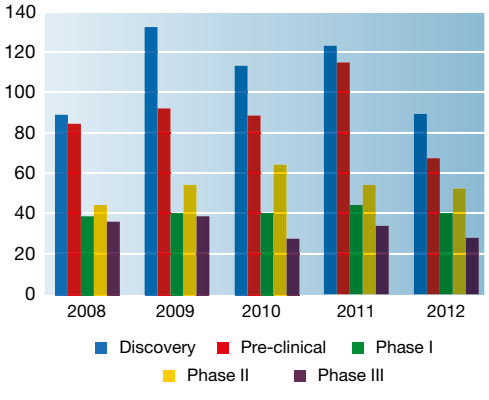
In fact, this focus on finding the right time to build collaborations is visible in the overall trends of the licensing deals that were agreed around the time that the patent cliff began to materialise in 2011 (see Figure 1).

Early stage – maximising gains by understanding breakthrough therapies

The increased impetus on forging alliances has altered industry dynamics and old blockbuster-based operating models have come crashing down. Newer business models, fuelled by various patent monetisation strategies, are scripting the new growth story in the life sciences industry.

Out-licensing is a critical strategic decision exercised by companies that own patents and technologies at the commercial stage, but lack the resources to manufacture internally; these companies forge alliances with key investors and pharmaceutical companies that are usually looking to commercialise such promising innovations.

Figure 1. **Number of licensing deals by development stage, 2008-2012**



Source: recreated from PharmaDeals® v4

Figure 2. **Number of industry-wide deals by therapeutic area, 2008-2012**

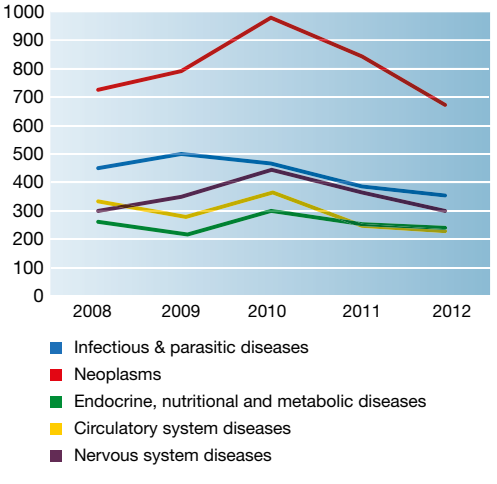


Table 4. **Acquisitions of early-stage technologies, 2014**

Target	Acquirer	Product/technology of target	Status	Headline (billion)
Idenix	Merck & Co	Hepatitis C assets, including IDX21437, a nucleotide inhibitor, to combine with Merck's MK 5172 (Phase1/2)	Phase I/II	$3.9
Alios Biopharma	J&J	Company acquisition includes antiviral therapies and AL 8176 for the treatment of RSV	Phase II	$1.8
Seragon	Genentech	Selective oestrogen receptor degrader (SERD) platform for hormone-dependent breast cancer ARN-810 (next-generation SERD)	Phase I	$1.7

Source: Medius Deal Watch Annual Review 2014

This strategy is used extensively by companies striving to monetise non-core, yet high-potential technologies that they do not plan to continue developing. This option helps to generate additional revenue and enhance the net worth of patents retained in the portfolio.

Previously, assessment of the market potential for out-licensing earlier in the pharmaceutical domain was skewed towards prevalent and obvious applications. However, perspectives have widened to include much broader, exclusive and uncommon application areas – thereby increasing potential opportunities.

Although companies usually prefer to do extensive assessments before striking deals (due to the long product development cycle, low success ratios and high risk owing to regulatory requirements), the out-licensing strategy is generally pursued at an early stage of product development.

These early-stage licensing deals are at molecule or pathway level related to new and challenging therapeutic areas such as oncology, neurology and immunology – including:

- Merck KGaA and Pfizer's deal for joint development and commercialisation of MSB0010718C (oncology);
- Ablynx and Merck & Co's deal which included nanobody candidates targeting immune checkpoint modulators; and
- Nogra and Celgene's deal to develop and commercialise GED-0301 for Crohn's disease.

As illustrated in Table 3, most of the high-value licensing deals signed in 2014 were at an early stage of product development.

For a large pharmaceutical company, mergers and acquisitions are part of a long-term strategy to enhance and improve its R&D activity and pipeline portfolio. Following the patent cliff, large pharmaceutical companies are more open to exploring this avenue, with the goal of benefiting from smaller players' innovations or collaborating with similar organisations.

Pharmaceutical companies are also looking for early alliances with biotechnology companies that have carried out extensive R&D in a complementary or niche domain (see Table 4).

Companies are increasingly using pay-per-programme deals (see Table 5). For example, Alexion paid $100 million to Moderna Therapeutics to buy 10 product options pertaining to the development and commercialisation of therapies using mRNA for rare diseases. Here, Moderna can develop the products and will in return pay royalties on sales, in addition to milestone payments.

Another example is the licensing deal between Immunocore and Eli Lilly for the co-discovery and co-development of cancer therapy based on T-cells. On successful advancement to pre-clinical stage, Immunocore must continue the co-development with Eli Lilly; otherwise, it will have to pay milestone payments and royalties.

Table 5. **Pay-per-programme deals, 2014**

Licensor/licensee	Product/technology	Financial details (million)
Discovery stage		
Immunocore/ MedImmune	Immune mobilising monoclonal T-cell receptor against cancer (ImmTAC) therapies for immuno-oncology targets	$320 per programme (including a $20 initiation fee)
Five Prime Therapeutics/BMS	Drug discovery against two undisclosed targets in immune checkpoint pathways including R&D funding, equity investment	$20 upfront plus $30.5 (equity plus R&D funding) plus $300 in milestones per programme
CytomX/BMS	Probodies for up to four immuno-oncology targets including CTLA-4	$50 upfront plus $298 in milestones per programme
Pre-clinical stage		
MacroGenics/J&J	MGD011	$700 ($50 cash plus $75 equity upfront)
Bionomics/Merck & Co	BNC375 programme	$526 ($20 upfront)
Dimension Therapeutics/Bayer	Gene therapy for haemophilia A based on AAV vector systems	$252 ($20 upfront)
Emergent BioSolutions/ Morphosys	MOR209/ES414, anti-PSMA/anti-CD3 bi-specific antibody for prostate cancer (worldwide, excluding North America); joint development/cost share	$183 ($20 upfront)
Phase I and II		
Edison Pharmaceuticals/ Dainippon Sumitomo	Extension of 2013 alliance/licence to EPI-589 to North America and Japan, plus collaboration to develop 10 further drugs	$4,295 ($10 + $50 equity upfront)
NewLink Genetics/ Genentech	Licence to NLG919 and research collaboration for discovery of next-generation IDO/TDO compounds	$1,150 ($150)
Cytokinetics/Astellas	Expanded collaboration for CK-2127107	$675 ($30 cash, $10 equity, $15 in milestones)
Array BioPharma/ Oncothyreon	ONT-380 (ARRY-380)	$300 ($20 upfront)

Source: Medius Deal Watch Annual Review 2014

Late stage – quick and risk-free benefits of established products

Big pharmaceutical companies are acquiring patents in late-stage products related to value-added capabilities, such as drug delivery devices (see Table 6). These technologies are valued high because they play a crucial role in improving therapeutics. The deal between Intarcia and Servier, one of the big deals of 2014, was driven by a breakthrough technology that provides consistent drug therapy for type 2 diabetes.

Co-development and co-commercialisation strategies are also seen at the late stage of product development. Examples include Bayer and Merck's deal to co-develop and co-commercialise Adempas and other soluble guanylate cyclase modulators for pulmonary hypertension; and Ophthotech and Novartis's deal to

commercialise and co-create a licence for Fovista (excluding the United States), in wet macular degeneration.

In the later stages, companies enter into cross-licensing deals while mutually respecting one another's IP rights. For example, in September 2011 Sartorius Stedim Biotech and GE Healthcare signed a cross-licensing agreement related to biopharmaceutical technologies.

Acquiring biotechnology companies based on their strong patent portfolios to strengthen R&D and the product pipeline works well for pharmaceutical companies at late stages of product development. This strategy enables biotechnology companies to monetise their mature and approved technologies and helps pharmaceutical companies to improve their product pipelines by accessing late-stage products.

According to the *Medius Deal Watch Annual Review* 2014, the acquisition of Cubist for $9.5 billion by Merck was the highest-value deal in 2014. InterMune's acquisition by Roche for $8.3 billion is another such example. Avanir's acquisition by Otsuka for $3.5 billion is another example – although it did not involve any big pharmaceutical company.

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Mrinal Pareek heads the life sciences function within the IP research practice at Aranca, a customised research and analytics organisation. She has an MS in biotechnology from the Indian Institute of Technology, Roorkee, and a management certification from the Indian Institute of Management, Kolkata.

With rich experience of close to eight years in patent research and analytics, Ms Pareek has worked extensively on various technology research and analytics projects in the pharmaceuticals, biotechnology and life sciences domains to support clients with the R&D strategy and techno-commercialisation aspects of their business. She has proven expertise in sequence and structure searches and analysis, and has trained and managed teams on various IP projects for Aranca's global clients.

Restructuring business models

Pharmaceutical organisations are increasingly forging alliances and leveraging patent monetisation strategies in order to counter the patent cliff and reduce future dependence on blockbusters. This is giving rise to new business models that are focused on long-term productivity and driven by varied strategies, including integrated models, patent synergies, semi-blockbusters and specialised solutions.

The paradigm shift in the acceptance of mergers and R&D collaborations is being seen as a catalyst to enhance portfolio productivity, as it is creating significant opportunities for better, robust and fruitful innovations. In fact, the first quarter of 2015 has already witnessed over 15 deals valued at approximately $10 billion.

With this shift, newer business models are being fuelled by new approaches to ensure long-term gains. Some of these key approaches are as follows.

Collaborations and partnerships

Companies are actively looking to associate with similar players and develop symbiotic relationships across the product development cycle. Companies are adopting various modes of associations (eg, licensing, co-development, co-commercialisation and mergers and acquisitions) in order to strengthen R&D and business alike.

Biotechnology

The industry is increasingly looking to reduce its dependence on blockbusters. To address complex disorders, more innovative and dependable platforms or pathway-based solutions are being created.

Table 6. **Drug delivery system-based deals, 2014**

Licensor or acquired/ licensee or acquirer	Product/technology	Status	Headline (million)
Intarcia/Servier	ICTA 650 (injection free GLP-1 agonist) for type 2 diabetes; global, excluding the United States and Japan	Phase III	$1,051 ($171 upfront)
Merrimack Pharmaceuticals/Baxter	MM398 nanoliposomal irinotecan for pancreatic cancer; global, excluding the United States and Taiwan	Phase III	$970 ($100 upfront)
Opko Health/Pfizer	Long-acting hGH-CTP for growth hormone deficiency in adults and children	Phase III	$570 ($295 upfront)
NuPathe/Teva	Company acquisition; Zecuity, an iontophoretic transdermal patch that delivers sumatriptan for migraine	Approved	$144-plus
Alpine Biosciences/ Oncothyreon	Company acquisition; protocells; nanoparticle technology for targeted delivery of nucleic acids, proteins, peptides and small molecules	Platform	$27

Source: Medius Deal Watch Annual Review 2014

Gene/biochip, genomics, proteomics and nanotechnology are among the fields being targeted for developing unique solutions.

Further, genotype-specific personalised therapeutic solutions are being created for patient groups with complex disorders. Major Food and Drug Administration approvals include the following:

- Trastuzumab (Genentech and UCLA) was developed in 1998 for breast cancer. In 2010 trastuzumab (Herceptin®) was approved for use in combination therapy for patients with HER2-overexpressing metastatic gastric or gastro-oesophageal junction adenocarcinoma.
- Erlotinib (Tarceva; by Roche, Genentech and OSI) for lung cancer was approved in 2013 as the first-line treatment of patients with non-small cell lung cancer having specific epidermal growth factor receptor exon mutations.

Niche approach

Once ruled by blockbusters, the industry is now increasingly associating with smaller, niche players seeking their breakthrough innovations.

These new business models and monetisation strategies do not depend on revenues from selling blockbusters. Instead, they are now largely using alternative approaches to commercialising patents across product development stages for long-term solutions and to continue on the growth path. *iam*

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