termsheet

PharmaVentures
Experts in deals and alliances

July 2016 Issue 18

Heads of Terms

Brexit will not directly affect M&A and Licensing in the UK and EU

British voters have just opted to express their view that the UK should leave the EU. I say 'express their view' because the referendum only delivers the preference of the voters and as such is advisory, not legally binding. Brexit may not even happen.

However, the UK parliament is now obligated to carry out the wishes of the voters. As David Cameron has stepped down, the next Prime Minister who will negotiate the UK's exit, will be elected by the ruling Conservative Party. The new Prime Minister is expected to be announced on the 9th of September.

So, as yet, we do not know what the final negotiated exit terms will be. Furthermore, the process will take at least 2 years from the official announcement and in the meantime the UK will remain in the EU.

Whatever the terms of Brexit, or whether the UK will actually leave the EU, there will be no change to the needs nor the opportunities that drive M&A and licensing. A significant amount of deal making is across borders and PharmaVentures has significant experience in completing this cross-border activity. Indeed, over 80% of our assignments are outside the UK and have been for over several decades.

Dr Fintan Walton
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industry insight

Bugs as Drugs

Microbiome Dealmaking Poised to Take Off

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Probiotics, prebiotics, medical food and supplements have been commercially available as OTC products for some time. These products claim to support human health by restoring the balance of the gut microflora in favour of 'beneficial' bacteria, most notably lactobacilli and bifidobacteria. With the growing understanding of the numerous biological processes that are influenced by the 100 trillion microorgansims that make up the microbiome of an individual, there is an increasing number of Biotech and Pharma companies seeking to capitalize on this research to develop therapeutic, microbiome-based agents to treat disease. The sector is still in its early stage with no drugs approved as yet but with a number of therapeutics in clinical development, the level of activity from early stage companies, and deals emerging involving big pharmaceutical companies, this could be a rapid and high growth area.

Big pharma, government agencies, venture firms and small biotechs are all investing significant amounts of capital and resources in the discovery and development of microbiome based therapeutics that seek to beneficially influence health outcomes across a range of diseases and conditions. Success in fecal transplantation for repeated Clostridium difficile infection pointed towards gastrointestinal conditions such as inflammatory bowel disease (IBD) as early areas to exploit. Clinical research is now spreading into other disease areas, particularly autoimmune diseases but even as far as cancer. This wide applicability is one of the drivers behind bigger company interest and thus igniting the dealmaking flame.

Janssen Biotech and Pfizer have invested significant biodollars in deals with emerging companies that are pioneering the clinical utility of modulating the microbiome. Other companies have declared their involvement indirectly, with Novartis and Danone investing into Seventures Partners' €160 million microbiome focused Health for Life Capital Fund. The Fund recently followed its money in a €14.5 million Series C funding of Enterome, alongside Nestle and Lundbeckfond Ventures. Likewise, it is believed that AstraZeneca, Roche, BMS and Merck & Co. are all in active discussions with a view to building a position in the Microbiome space through dealmaking.

Microbiome Deal Trends

An analysis of dealmaking, involving assets categorised as either 'probiotic' or 'microbiome', deal activity was low and slow through most of the first decade of this millennium. 2010 saw the first indication that something was changing, with 3 deals completed compared to a single deal in each of the preceding 5 years. Just two years later in 2012, a record 15 deals were closed. Although fluctuating, it does appear that 2012 was an anomaly with a further 21 deals signed up by the end of 2015. This year, 8 deals closed in the first 5 months suggesting 2016 could see the most deals of any year to date.

Probiotic and Microbiome Deals per Year, 2001-2016*

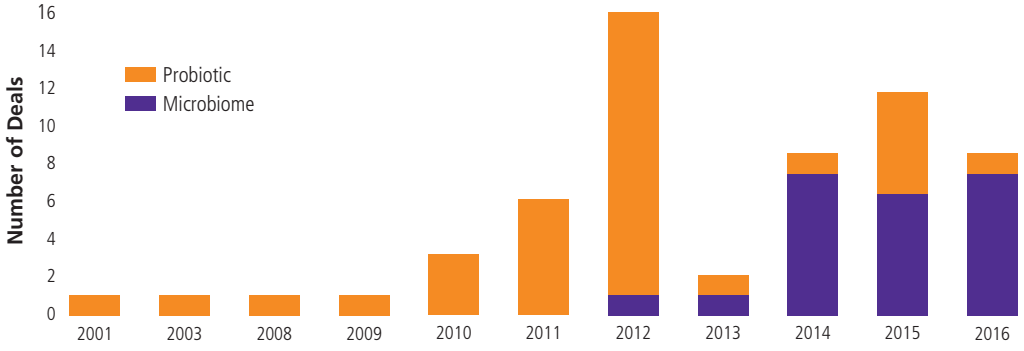

Figure 1

* PharmaVentures Analysis, data from Thomson Reuters Recap IQ

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Bugs as Drugs

The deals themselves are also changing, driven by the greater understanding of microbiome biology. Up to 2012, 93% of deals concerned probiotic assets and the vast majority of these were for distribution (75%) of mature probiotic assets, and only 14% of deal activity involved licensing. Even though activity and interest in the microbiome space was growing, the availability of tangible tradable assets had yet to reach a level which would drive dealmaking. Thus, the record deal year (to date) of 2012 was still characterised by deals for probiotics, with only one microbiome deal, concerning a research alliance between Harvard and UCB.

2013 marked a change in the balance of deal making activity. From 2013 onwards, the balance has favoured microbiome deals over probiotics, with 72% of deals concerning the microbiome. This shift reflects the increasing appreciation of the microbiome and deepening understanding of its role in disease and ties in with an increase in the sophistication of the research occurring in the sector. Microbiome-based research has evolved to include active microbiome therapeutics (drug candidates) rather than just beneficial bacteria for ingestion and restoration of gut flora, along with sequencing of bacterial genomes and the delineation of biological pathways and the crossovers between bacteria and human physiological systems. This laboratory based revolution is stimulating deal activity with 62% of deals since 2013 having been for enabling platform technologies as well as microbiome pharmacological agents, while 35% were research alliances/awards aimed at driving research in the sector forward.

Microbiome First Movers for Deals – 2013-2016

2013 onwards has seen an upsurge in microbiome licensing deal activity. In line with dealmaking in general, disclosure of financial terms is limited and with such low deal numbers so far, it is too early to carry out any meaningful analysis. Of those deals where financial terms have been disclosed, the largest to date is Janssen Biotech's 2015 licensing agreement for Vedanta Biosciences' lead microbiome candidate, VE202 for the treatment of IBD. Whilst the upfront payment value was undisclosed, Vedanta are set to earn up to $241 million in development milestones plus undisclosed sales milestones. Other deals where financials are disclosed are all in the low single digit millions.

Vedanta originally received funding from J&J Development Corporation in 2013 as part of a collaboration with the J&J Innovation centre in Boston. The collaboration supported the development of therapies that modulate the interaction between the microbiome and the human immune system.

Microbiome and Probiotic Deal Types, 2013-2016*

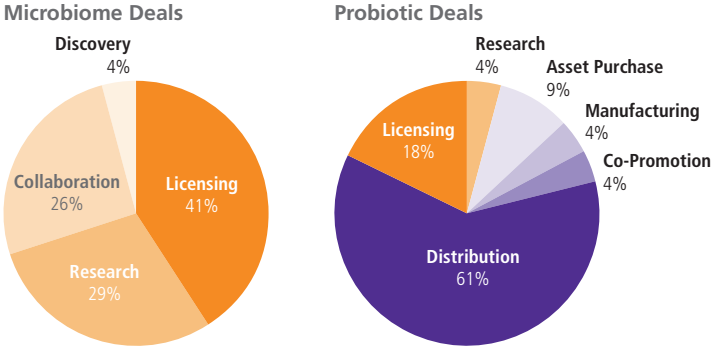

Figure 2

** PharmaVentures Analysis, data from Thomson Reuters Recap IQ*

Janssen Biotech is leading the way for Big Pharma on the deal front. In addition to the Vedanta asset, Janssen Biotech signed a deal with Second Genome in 2013 to license their discovery platform to characterise the role of bacterial populations in ulcerative colitis and develop therapeutics based on the discoveries. Data from EvaluatePharma shows that Johnson & Johnson, of which Janssen Biotech is a part, currently has only one microbiome modulator in their pipeline, VE202. These two deals suggest that J&J is keen to jump start its microbiome pipeline with a preclinical therapeutic, but is also planning to invest internal resources on developing new therapeutics from scratch. The Janssen deals represent the first "toe-dip" by a Big Pharma into this space but with the level of financial investment and activity from small biotechs suggests deal activity will grow significantly.

Another forerunning biotech company, Second Genome, has been aggressively leveraging its proprietary discovery platform to unveil new targets with collaborators and licensees, as well as in-licensing existing assets. This approach is similar to Janssen's; padding the pipeline as well as developing new therapeutics. In 2015 Second Genome signed two deals, an agreement with Evotec focused on in-licensing undisclosed Evotec assets, as well as a small molecule based discovery and development collaboration to screen microbiome related targets. Evotec is eligible for preclinical, clinical and regulatory milestones as well as royalty payments related to commercialisation. In the second deal, the company is collaborating with University College Cork on advancing therapies that prevent and treat inflammatory bowel disease.

More recently, in April 2016 Second Genome secured $42.6 million in Series B funding from 10 investors including Pfizer Venture Investments, Roche Venture Fund and the Mayo Clinic. In October 2014, the Mayo Clinic had entered into an extensive research collaboration with Second Genome, which included an equity investment component. The partnership is focused on discovering therapeutic candidates for inflammatory bowel disease, metabolic disorders, and colorectal cancer. The Mayo Clinic will supply human clinical samples from patients, while Second Genome will use its proprietary discovery platform to identify biological pathways in these diseases.

Over the period 2013-2016, the Mayo Clinic and Enterome Bioscience were the most active licensors. 2014 was a busy year for Enterome Biosciences as they signed an out-licensing agreement with AbbVie, centred on Enterome's proprietary metagenomic biomarker portfolio and technologies to develop non-invasive monitoring tools of the gut microbiome in Crohn's disease. This year Enterome has started to move away from the discovery and development of diagnostic tests and focus more on the development of therapeutic agents as indicated by their deal with Takeda, which again leveraged the core technology of its metagenomic platform. This is a prime example of how smaller biotechs are driving forward development in the microbiome space; hungry for the international reach and development infrastructure larger pharma's can provide. Enterome received an undisclosed upfront payment and 3-years R&D funding, and is eligible to receive additional payments for each molecule discovered through the collaboration in the form of option exercise, development, regulatory and commercial milestone payments. On top of which, Enterome will receive tiered royalties on the net sales of any products that are commercialized by Takeda.

The microbiome field is presently in a very dynamic state, in a few short years it has shifted from distribution deals for probiotics, to licensing and research collaborations concerning microbiome assets. This has been driven by a shift in the sophistication of microbiome research undertaken, which in turn has driven up the clinical and economic value of microbiome assets. Deals have already started to move from research collaborations and deals that validate microbiome biotechs' platforms and data, to more conventional structures with upfronts, milestones and royalties geared around commercial exploitation of active therapeutics. From a clinical and thus therapeutic perspective however, microbiome-based drug development is still in its infancy; the most advanced therapeutics being based on fecally-derived microbiota, in Phase II clinical trials for Clostridium difficile and ulcerative colitis. Despite its nascent state, the pace of development is being robustly driven forward by primarily smaller biotech's, which are hungry for recognition and on the search for bigger deals with more established pharma.

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meet the team

Alice Nettleton
Business Analyst

Alice holds a BSc in Biomedical Sciences from King's College London with a focus on Pharmacology, Neuroscience and Regenerative Medicine, and a MSc in Business Creation and Innovation in Biomedicine from Gothenburg University. Her master's thesis focused on current valuation practices for licensing in pharma. Previously to joining the PharmaVentures team, Alice worked at IP Pragmatics where she gained experience with intellectual property management and early-stage technology commercialisation. She is also member of the Licensing Executives Society.

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"Is this a typo? It says here the EU Phase III trial took place in whales?"

inside view

FCA
FINANCIAL CONDUCT AUTHORITY

PharmaVentures Capital Ltd

FCA authorised and regulated

PharmaVentures is pleased to announce that we recently received approval of our application to become authorised and regulated by the Financial Conduct Authority. All regulated business will be conducted through our subsidiary company PharmaVentures Capital Limited.

industry insight

Is Latin America a Merger Mystery?

Insights into South American Deal Activity

Valeria Uribe
Advisor

The global merger mania

The pharmaceutical and biotechnology industry are still deep in merger mania. A transformation of the industry in which companies fuse, split and re-merge has been taking place for the last few year, peaking in 2015.

According to the Global Pharma/Biotech M&A Report[1], the number of transactions went from 371 in 2013 to 438 in 2014 and 494 in 2015. The Allergan Pfizer deal, had it completed, would have almost doubled the total deal value from US$226bn to US$415bn for the year. Even without this transaction, 2015 experienced a significant increase in the number of mergers and acquisitions and their cumulative deal values.

2016 has seen a continuation of this merger mania. During the first week of January 2016 alone, there were 18 M&A transactions totalling US $37.3bn[2] and Between May 13 and May 20, 12 M&A transactions were announced and 6 were closed[3].

The merger mania was kicked off by looming patent expiries for major players forcing companies to merge or acquire in order to replenish turnover and pipelines. R&D and Business Development are the two means through which pharmaceutical companies can generate growth and expand their product portfolio. In recent years, due to the increasing costs and risks of R&D and pressure from investors, Business Development has played a key role through a strong M&A and licensing activity.

The merger wave has spread globally, but one of the emerging markets that has been a gold mine for international companies is Latin America. Compared to the slow growth of the pharmaceutical market in the United States and Europe, Latin American countries represent fast growing markets that have attracted a surge of investment.

Mergers and Acquisitions in Latin America

Whilst bigger Pharmaceutical companies have focused more on complex M&A transactions and asset swaps, others have sought to strengthen their presence in emerging markets. In 2014 Global Data reported an increasing M&A activity in the Latin American market, with totals reaching US $12.7 bn. This activity has been characterized by significant transactions between international and small to medium size local pharmaceutical companies. Grunenthal, Abbott, Endo and Teva among others, have been very aggressive with their Latam M&A activity.

In 2014 Grünenthal acquired the Chilean Laboratorio Andromaco and also the local affiliate of Almirall in Mexico in 2016, one of the few cases of affiliate acquisition in pharmaceutical history. One of the most publicized deals in Chile, was the acquisition of CFR, a Chilian generics player, by Abbott Laboratories. These transactions placed both Grünenthal and Abbott among the top four companies in Chile's pharmaceutical market.

Other healthcare related companies have also been active in the region. Alliance Boots, the UK pharmacy giant, acquired Farmacias Ahumada, a retail pharmacy chain. The company gained control over a distribution

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1 IMAP in 2016
2 Insight Bourne Partners Week of January 11, 2016, Vol. 5, Issue 2
3 Insight Bourne Partners Week of May 23, 2016, Vol. 5, Issue 21

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Is Latin America a Merger Mystery?

network of 1,400 pharmacies in Chile and Mexico representing US $1.4 bn of revenues.

Cross continent deals are not the only activity with local players also actively seeking acquisition opportunities. Laboratorios Sanfer, a leading Mexican pharmaceutical company, sold a minority stake to the private-equity firm General Atlantic LLC. Following an ambitious expansion strategy, Sanfer has acquired several regional players since 2008. More recently, the company has used the deep pockets of General Atlantis to fund acquisitions in Colombia and Mexico as well as in the veterinary space. In 2015 five regional players, Eurofarma, Cristalia, Hertape, Biotoscana and Drogasil also closed local deals.

What drives the value of M&A in Latin America?

The US $2.3 bn transaction between Teva and the Mexican company Represetanciones e Investigaciones Médcas, S.A. de C.V. (Rimsa) was certainly the highlight of 2015. The Teva – Rimsa transaction raised a few eyebrows amongst observers as Rimsa reported revenue of US$227 mn in 2014 with an annual growth, year over year of 10.6% since 2011 meaning Teva was willing to pay around 34 x EBITDA to secure the deal. The transaction places Teva, which until this point only had a small presence in the country, as one of the leading Pharmaceutical companies in Mexico. With Mexico being the second most important market in Latin America after Brazil and within the top five emerging markets worldwide, there was a clear strategic driver for Teva.

One reason for the explosion of international companies battling to enter the pharmaceutical Latin American market, is that it is expected to double from USD $73bn in 2014 to $124 bn by 2018 according to IMS health. Meanwhile, mature markets such as Europe and the US are almost stagnant. The drying up of the pipelines and the challenges of developing innovation for growth in mature markets, has forced the drug companies to turn their heads to emerging markets, where incremental innovation is still profitable.

Large multinational companies have made commitments to their stockholders to enter developing markets and they are willing to pay a high price. In the case of Latin America, there are very few large players left and a large number of buyers aggressively looking for opportunities with local know-how.

Abbott took a strategic decision to retain the CFR identity in Latin America in order to take advantage of its local market presence and knowledge. The transaction not only allowed for the expansion of its branded generics portfolio and placed the company on the top 10 of the pharmaceutical companies in Latin America, but it also provided a key understanding of the region.

There is only a relatively small number of strong local players, but they have been able to steal market share from the big multinationals by employing a successful incremental innovation strategy. Whilst big pharma have focused on developing thousands of new molecules and a small number of blockbusters, the small local players have implemented hundreds of thousands of smaller incremental innovations to maintain their portfolios and grow market share.

Improving an existing drug in order to maintain its competitive position ensures the continued quality of health care. Drugs based on incremental innovation deliver advantages related not only to safety and efficacy, but also dosing alternatives that contribute to patient compliance. In addition, these drugs allow physicians to treat a broader group of patients. From an economic point of view, incremental innovation provides competition within the same market, driving decreases in drug prices.

Most local Latin American pharmaceutical companies, which don't have the resources to invest in the development of new molecules, make incremental innovation a strategic competitive strength through the launch of branded generics. The brand is linked to a certain level of quality, which physicians perceive as positive and for which, patients are willing to pay a premium price. In developed markets, where growth is driven by pure innovation, drugs are reimbursed and the only distinction of generics is their price, this strategy is not applicable in Latam.

International as well as local players are keen to consolidate their position in the Latin American countries. Moreover, they are willing to pay high sums of money for local companies, even though their targets don´t have the capacity to develop blockbusters. It is yet to be seen whether this model is expandable and to which markets, but for the time being this strategy is likely to keep the merger wave going.

2016 has seen an increase in M&A activity. According to a review from Kurman Partners, future transactions are expected to be driven by Brazil and Argentina as the economic difficulties in these countries and exchange rate effects have resulted in acquisitions becoming more affordable. In addition, the new government in Argentina is likely to attract more foreign investment in order to stimulate the economy.

The Latin American countries and their governments seem to have learned a valuable lesson from Korea, where local companies have received incentives to invest in development. As a result, Korean corporations are successfully exporting incremental innovation, and in some cases even new molecules, to foreign markets.

In Mexico, President Peña Nieto has announced his commitment to triple the R&D budget from 0.5% to 1.4%. In addition, the Centro Nacional de Ciencia y Tecnología (CONACYT) recently created a fund, Inovación Ciencia y Tecnología para el Desarrollo Empresarial (INCIDE). Its purpose is to provide incentives for R&D to be conducted by local companies. It is still yet to be seen if Mexico will achieve its goals, but it is clear that there is increasing awareness and involvement in the R&D sector.

With the exception of Venezuela, where, due to the economic and political situation, big pharma and local players have started to retract from the market, the surge of companies interested in investing in Latin America does not seem as though it will lose momentum any time soon.

Big pharma who have traditionally played in the developed markets are facing the risks of lack of productivity in R&D and further patent expiries. This combined with the growing potential of emerging markets, and the need of Big Pharma to reinforce its presence in markets in which important players are scarce, has driven M&A transactions in Latin America to values that would have never been expected a few years ago.

Who would have predicted that R&D from developing countries would become so sought after by Big Pharma!

Forthcoming Conferences

Nordic Life Science Days
14-15 September, Stockholm

16th Annual Biotech Investor Forum for Global Partnering and Investment
27-28 September, Zurich

CPhI Worldwide
4-6 October, Barcelona

AusBiotech (International Biofest) 2016
24-26 October, Melbourne

Bio-Europe
7-9 November, Cologne

Medica
14-17 November, Dusseldorf

Genesis 2016
1 December, London

J.P. Morgan 2017
9-13th January 2017, San Francisco

To meet with PharmaVenture's experts at any of these conferences, please contact Danielle Parker-Smith: danni@pharmaventures.com

Or

To arrange an interview with PharmaTelevision, please contact Matthew Royan: matt@pharmaventures.com