termsheet

PharmaVentures
Experts in deals and alliances

January 2016 Issue 16

Heads of Terms

Are Asset Swaps better than Mega Mergers?

Mega mergers of the past helped to shape the industry as we see it today. However, rather than entering mega mergers, pharma has discovered the power of asset swaps. These avoid the huge disruptions associated with mergers and help companies focus their resources, leveraging certain parts of their businesses, typically consumer healthcare, vaccines or animal health, into dominant market positions. Since these sectors are highly competitive, with lower margins than typical prescription drugs, asset swaps provide an opportunity to cut costs.

A recent example of this play is the proposed transaction between Boehringer Ingelheim and Sanofi, where the latter's animal health business (Merial), with an enterprise value (EV) of €11.4 billion, would be swapped for Boehringer Ingelheim's consumer healthcare business, with an EV of €6.7 billion, with the difference in EV being closed through a gross cash payment from Boehringer Ingelheim to Sanofi of €4.7 billion. This deal would project Sanofi's consumer healthcare business into the number one position globally and help Boehringer Ingelheim become a global player in animal health.

This above transaction mirrors another recent asset swap completed back in March 2015 when GSK acquired Novartis' global vaccines business (excluding influenza vaccines) for an initial cash consideration of $5.25 billion while at the same time creating a new world-leading Consumer Healthcare joint venture with Novartis in which GSK would have majority control. As part of the deal GSK divested its Oncology business to Novartis for an aggregate cash consideration of $16 billion.

In the same theme, back in January 2015, Novartis completed the divestment of its Animal Health Division to Eli Lilly for approximately $5.4 billion. While in October 2014 Merck completed the sale of the Merck Consumer Care (MCC) business to Bayer

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industry insight

Anti-Microbial Resistance
and the search for New Antibiotics

Christopher Berry
Associate, PharmaVentures Limited

The 'antibiotic crisis' is rarely out of the news, with headlines issuing dire warnings that the rise in resistance to anti-microbial drugs could result in a return to the medical dark ages. In order to tackle this problem, various initiatives have been proposed on both sides of the Atlantic, to incentivise research into novel antibiotics. Here we give an overview of how governments and the pharmaceutical industry are responding to this 'ticking time-bomb', and the current status of R&D in new antimicrobials worldwide.

Challenges for industry

Despite the recognised need for new antimicrobials for clinical use, only two new classes of antibiotics have been brought to the market in the last 30 years, and many major pharmaceutical companies have left the field. What is most worrying is that the majority of compounds that do come to market are among existing drug classes. Moreover, the number of multinational pharmaceutical companies working in the field dropped from 18 in 1990 to 4 in 2011.[1] There are several reasons for this decline; firstly, among all drug classes, antibiotics are known to have among the lowest risk-adjusted net present value (NPV) – around $100 million; compared to an estimated $300 million NPV for cancer drugs or $1.15 billion for drugs treating musculoskeletal conditions.[2] This is due in part to the short treatment duration, days rather than years, short life cycle management due to appearance of resistance after wide use, and the tendency of infectious disease physicians and public health experts to hold new antibiotics in reserve to avoid fostering rapid emergence of resistant bacteria, a practice that leads to "slow commercial uptake" and limits the potential market for new antibiotics.[3]

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deal update

PharmaVentures advises Stericool on sale to Sweden's Getinge Group

PharmaVentures is pleased to announce that it acted as advisor to Stericool on its sale to Sweden's Getinge Group, a global leader in infection control and contamination prevention solutions.

Stericool specialises in hydrogen peroxide based solution low temperature sterilisers for emerging markets. Founded in 2008, Stericool has its headquarters and manufacturing site in Ankara, Turkey. The acquisition will be included under Getinge's new business category unit Surgical Workflows and will increase potential for growth in East/South Europe and the rest of the world.

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Anti-Microbial Resistance

Secondly, clinical trial regulations have been a hindrance. Since, for ethical reasons, it is not practicable to give patients with an infection a placebo, large non-inferiority trials have to be performed, which are large, time consuming, and expensive. The FDA's regulations with regards clinical trials are restrictive; using FDA draft guidance it is predicted that a Ventilator-Acquired Pneumonia (VAP) indication trial would require 2400 patients and more than 10 years to complete. It should be noted that the EU has a more flexible and pragmatic approach than the FDA.[4] Thus there is a need for global regulatory alignment and innovative approaches for antibiotic registration.

Finally, it is hard to discover new antibiotics. GSK screened over a million compounds from its chemical library in 67 HTS campaigns on different bacterial targets and pathogens. They got 5 leads with only 1 compound getting to development.[5]

As a result of these factors several companies have left the field over the last few years leaving a few major players such as GSK, Sanofi, Roche and Merck & Co. It is not all doom and gloom however. What has become clear is that the way forward is collaboration between all stakeholders, from large pharmaceutical companies and public entities, through to biotechnology/emerging pharmaceutical companies and academic laboratories.

The Way Forward

Over the last few years the regulatory authorities such as the European Medicines Agency (EMA) and the FDA have already done much to align and streamline their approval procedures for antimicrobials to make it easier for drug companies. A lot of work has also been done by regulators to streamline the design of clinical trials for antibiotics so that they are not unnecessarily burdensome, addressing significant problems (many particular to trial design for anti-infectives) which once undermined the development process.

The European Union (EU) included the New Drugs For Bad Bugs Programme (ND4BB) as part of its IMI venture in 2012. The IMI venture was devised to provide a platform for collaborative pre-competitive research between EFPIA member pharmaceutical companies, academic institutions and small biotechnology companies across many therapeutic areas.

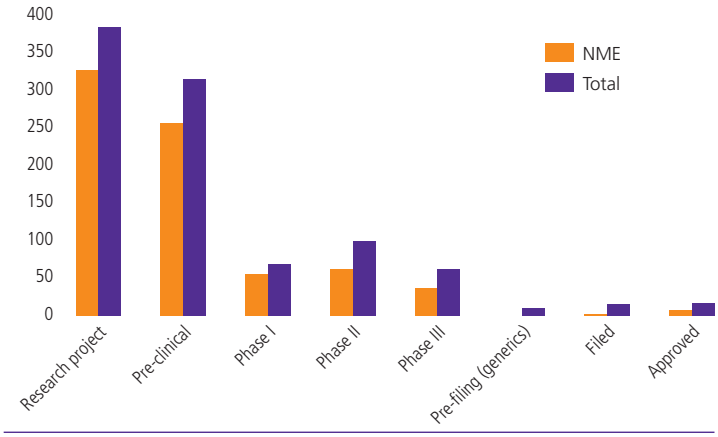
In 2014, the IMI launched ENABLE, which is a ground-breaking drug discovery project in that it is the first "competitive" consortium in the area leading to the generation of patentable new drugs.

Other projects launched, or to be launched, in the programme include: DRIVE-AB focussing on the development of a new business model for antibiotic development to reinvigorate investments and promote the responsible use of antibiotics, as well as a project to explore ways of promoting the host response to bacterial infections.

In the United States, President Obama issued in 2014 Executive Order (EO) 13676: Combating Antibiotic-Resistant Bacteria which outlines steps for implementing the National Strategy on Combating Antibiotic-Resistant Bacteria and addressing the the policy recommendations of the President's Council of Advisors on Science and Technology (PCAST)'s report on Combating Antibiotic resistance.

Moreover, the FYs 2016 budget proposes nearly doubling the amount of Federal funding for combating and preventing antibiotic resistance to more than $1.2 billion.

Global Anti-Bacterial R&D Pipeline Figure 1



Antibiotic Deal Making

Despite the fact that new approvals had dropped markedly during the beginning of the century, the early stage R&D pipeline is looking healthier than may perhaps be expected, as is shown in Figure 1.

This pipeline reflects the many biotechnology companies working on anti-bacterial agents ranging from small molecules to antibodies, as well as the host response to infection and virulence factors. Furthermore, following the exit of many of the large multi-national companies in the 1990's, several are re-entering the space or strengthening their positions. Whilst the majority of published deals for early stage antibiotics involve grant funding from academic, governmental institutions and not-for-profit organisations rather than traditional licensing agreements, sizeable deals are possible for companies with promising agents in the pipeline, particularly those in later stages of development.

Earlier this year, Merck & Co. acquired Cubist Pharmaceuticals, which had developed and launched Cubicin (Daptomycin). Daptomycin is a natural product derivative whose development was stopped by Lilly in 1991 due to side effects observed in clinical trials. Cubist acquired the rights, and through the use of longer dosing intervals and dose adjustment, were able to reduce the side effects and the drug now earns roughly $1 billion per year. Merck & Co also inherited Zerbaxa, for complicated urinary tract and intra-abdominal infections caused by Gram-negative bacteria, and Cubist's oxazolidone, Sivextro, resulting from the latter's acquisition of Trius Therapeutics. Roche has grown its antibiotics pipeline through licensing and collaboration agreements with several companies, including Polyphor, Discuva, Spero Therapeutics and Meiji Seika Pharma and discovery stage collaborations with Phylogica, RQx and AMRI via its Genentech subsidiary. Actavis acquired Durata Therapeutics in 2014 for $675 million to help build out its stable of treatments for infectious disease. GSK and Sanofi entered a collaboration in 2013 for lead optimization against Gram-negative pathogens as part of its in-kind contribution to the IMI ENABLE project. However, AstraZeneca announced earlier this year that it is exiting early stage research by spinning off its early stage small molecule anti-infectives unit into a stand-alone company, Entasis. The new firm received $40 million funding and a bundle of early-stage assets. However, Basilea Pharmaceuticals, similarly spun out of Roche in 2000, demonstrates the potential for success for such dedicated small companies.

To read the full white paper:
www.pharmaventures.com/consult/white/1

1 Cooper & Schlaes, *Nature* 472, 32, 2011
2 http://www.medicalprogresstoday.com/2013/05/sex-superbugs-and-antibiotics.php
3 Hamad, B. *Nature Reviews Drug Discovery* 9, 675-676 (September 2010)
4 Schlaes, http://antibiotics-theperfectstorm.blogspot.fr/2012/07/europe-leads-way.html
5 Payne *et al, Nature Reviews Drug Discovery*, 6, 29, 2007

Eye Catching Opportunities

The Fast Growing Ophthalmic Drug Market

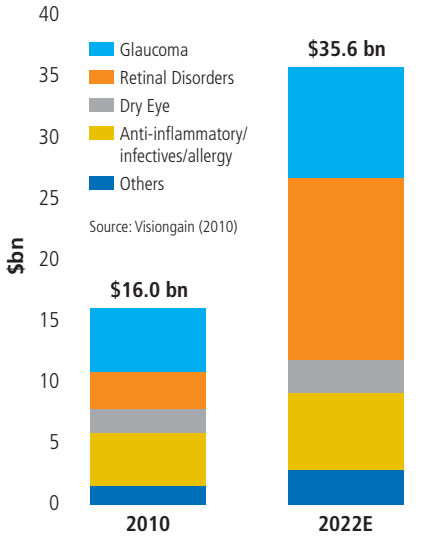
Issac Jacob | Senior Director, PharmaVentures Limited

The ophthalmology drug segment continues to shine brightly with a number of deals announced in November such as Genentech's partnering with Novartis to split ex-US rights to Ophthotech's eye drug, which could be worth more than $1 billion. Allergan, another of the major players in the market, recently acquired rights to Mimetogen's tavilermide for $50 million upfront and more payments down the line.

Biopharma's interest in the segment is buoyed by the strong growth in ophthalmology drug sales which are benefiting directly from substantial increases in the number of people suffering from age related ophthalmologic conditions in Western markets and Japan. The developing world is adding to this momentum as increasing affluence drives increased expenditures in all areas of healthcare including vision impairment and eye diseases. The headwinds created by positive demographics for the sector are being exploited by the emergence of new technologies for treating ophthalmic diseases.

The global ophthalmic drug market is estimated to grow at a CAGR of 7% from $16.0 billion in 2010 and to reach $35.6 billion by 2022 with retinal disorders being a clear standout and the segment's expected growth of 14.2% fast outpacing the sector. Much of the growth is being driven by retinal disorders which are expected to jump dramatically from $3.0 billion in 2010 to $14.8 billion in 2022. This growth in retinal disorders is being driven by new innovative drugs that have been developed for the treatment of disorders such as AMD, diabetic macular oedema (DME) and retinal vein occlusion (RVO). The foundations for growth are already established with the successfully marketed drugs Lucentis and Eylea expected to continue growing strongly, and capturing over $9 billion in revenue by 2020 (compared to $7 billion in 2014).[1]

Global Transaction Activity



New Technologies Bolster the Pipeline

The ophthalmology drug development pipeline is looking healthy with over 600 ophthalmology drug R&D products being developed for almost 1,000 ophthalmic indications. Almost 55% of the current drug candidates are either at the research project or pre-clinical stage, and another 40% in the clinic for development. The large amount of drug candidates in earlier stages of the drug development continuum points to healthy innovation, and is indicative of the strong corporate and investor interest in ophthalmology drug market.

Given the growth in the ophthalmology market, the R&D effort is being carried out by large global ophthalmology players as well as many new start-up companies, and should provide a healthy environment for collaborations and partnerships. Data from EvaluatePharma indicates that there are currently 340 drug candidates which are unpartnered, with the majority of them in the earlier phases of clinical development.

Ophthalmic Deal Making is Accelerating

Deal making in ophthalmology seems to be accelerating from a low of just 21 deals in 2012 to 35 deals already in the

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1 Cowen & Co. (2015). Therapeutic Categories Outlook.

Charles Macfarlane
Board Member

Mr. Macfarlane spent 40 years in the Procter & Gamble Company, primarily in the International Divisions, starting in consumer products marketing and later in general management. He transferred to join the group that took P&G into the Pharmaceutical industry in 1978 and led the international start-up. In 1985 Mr. Macfarlane led the successful acquisition of the French pharmaceutical group, Nativelle, and went on to serve as its President and Director General for six years in Paris. From this position Mr. Macfarlane also served as P&G's pharmaceutical executive responsible for Southern Europe (86-91). In 1991 he established the pharmaceutical Business Development role in Europe and relocated to London. In 1996 Mr. Macfarlane assumed responsibility for all Alliance, Licensing and Acquisition activity of P&G in the expanded Health Care Global Business Unit (incorporating Pharmaceuticals, OTC medicines, Oral Care, Iams Pet Care, and Pur Water Treatment). Mr. Macfarlane retired from P&G in September 2006.

Since 2002 Mr. Macfarlane been a member of the Board of Directors of British American Business and was a member of the Executive Committee until 2014. He is a member of the Institute of Directors and the Pilgrims Society. He served on the Board of Healthcare Brands International, an OTC healthcare company successfully sold in 2011.

industry insight

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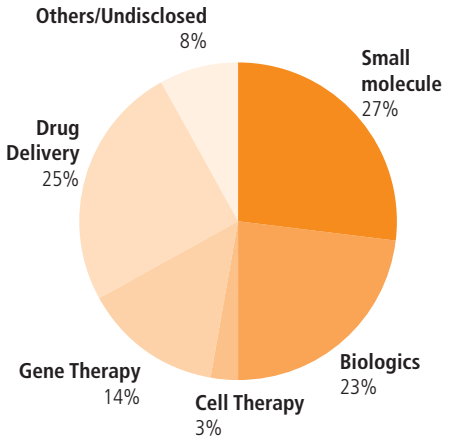
first three quarters in 2015. There were 176 licensing and M&A transactions associated with ophthalmology drugs for the period between 2010 – Q3 2015. Of the 72 M&A transactions, close to 60% were for pure ophthalmology targets, while the remainder involved target companies which were focused on multiple therapeutic areas including ophthalmology. M&A transaction activity has been especially robust in 2013 and 2014. Deal sizes have varied but there have been a number of large notable transactions that have commanded strong valuations, including Actavis' acquisition of Allergan ($66 billion at 25.4x LTM EBITDA) and Merck's acquisition of Inspire Pharmaceuticals ($430 million at 3.6x LTM Revenue).

Licensing activity has been just as robust with 104 deals in the last 5 years and 26 deals completed in just the first three quarters of 2015, with the level of licensing deal making in 2015 set to eclipse recent performance.

The majority of the licensing transactions involved assets that were in pre-clinical or at Phase II. The concentration of licensing transactions at the pre-clinical stage follows the classic pattern of entrepreneurial biopharma companies developing drugs themselves until outside capital is required for clinical studies. The other peak in licensing activity is with companies at Phase II and this is likely due to this stage being a large value inflection point, as well as a point at which substantial additional capital is required for further organic development At Phase II, large corporates are more willing to acquire a de-risked asset and the selling shareholders may see strategic benefit from gaining the large corporate's technical and regulatory know-how, distribution capability and deeper pocket book to fund more expensive late stage clinical studies.

Unsurprisingly given the focus on retinal R&D, most of the licensing transactions occurred in retinal diseases. The trend towards novel technologies was also evidence by the increasing numbers of deals involving biologics, cell therapy and gene therapy. It is very likely that the industry will be seeing the high activity levels in the new technologies sustained as smaller and nimbler start-ups continue to create exciting novel treatments for diseases.

Licensing Transactions by Technology Classification (2010 – Q3 2015)



To read the full white paper:
www.pharmaventures.com/consult/white/1

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Heads of Terms
Are Asset Swaps better than Mega Mergers?

AG and Novartis announced that it will divest its influenza vaccines business to CSL Limited for $275 million.

The question is whether asset swaps are a better alternative to mergers? Rather than returning the often questionable value to shareholders through huge mergers, asset swaps appear to make more sense strategically in that they are more precision based. The strategic decision to seriously remain in one sector by building it or disposing of it is much more calculatable than estimating the outcome of a large merger. The real test, of course, is time itself as we observe the performance of the companies mentioned above.

Dr Fintan Walton
Chief Executive,
PharmaVentures Ltd.

conference update

2ND ANNUAL
biotechandmoney LONDON

ETC Venues, 155 Bishopsgate, London, UK

2-3 February 2016

The 2nd Annual Biotech and Money London 2016 event is a two-day congress providing the education, strategies and solutions you need to enable more effective funding, investment, business planning and partnering.

Biotech and Money targets an executive-level only audience and will help find solutions to the challenges of modern deal making, funding financing and investment. The second day will focus on showcasing pharma and medtech opportunities for partnership and investment.

Keynote speakers to include:

- Sir Chris Evans OBE, Chairman, Excalibur Group
- Shaun Grady, Vice President, Business Development Operations, AstraZeneca
- Luigi dela Corte, Head of WWBD, GlaxoSmithKline
- Peter George, CEO, Clinigen
- Darrin Disley, CEO, Horizon Discovery
- Jim Mellon, Serial Entrepreneur and Founder, Mann Bioinvest

Event Website: http://biotechandmoney.com

To arrange a meeting with one of the PharmaVentures Team at Biotech and Money, please contact Maria Seal, maria@pharmaventures.com

Forthcoming Conferences

2nd Annual Biotech & Money London
2-3 February, London

SACHS Associates: 9th Annual European Life Sciences CEO Forum & Exhibition
15-16 March, Zurich

Bio-Europe Spring 2016
4-6 April, Stockholm

BioTrinity 2016
25-27 April, London

Anglonordic Life Science Conference XIII
19 May, London

BIO 2016 international Convention
6-9 June, San Francisco

To meet with PharmaVentures experts at any of these conferences contact:
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Or

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