



MEDIUS DEAL WATCH

October 2015

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This month saw a bumper crop of deals. Our top featured deals by headline value include seven transactions of \$1bn or more, of which four were multi-target R&D collaborations. Many of this month's deals were focused on oncology and immuno-oncology to continue the trend from previous months, but we also saw transactions in areas including rare diseases, CNS, autoimmune and inflammatory diseases and allergy.

Retail pharmacy consolidation

Near the end of the month there was the announcement of Walgreens Boots Alliance's proposed acquisition of rival Rite Aid Corporation in a cash transaction for a total enterprise value of approximately \$17.2bn, including debt. This deal will combine the second and third largest drug store operators in the US and as a result it will no doubt be scrutinised by the US antitrust authorities. At \$9 per share this is a 48% premium above Rite Aid's value at the close of trading the day before the announcement. Walgreens forecasts that the acquisition will provide more than \$1bn in savings from cost overlaps and speculation is already rife that it will be the Rite Aid stores, of which there are nearly 4,600 across the US, that will take the brunt of the cuts.

Echoing some of the hefty termination provisions we saw last year in big pharma deals, if antitrust clearance is not obtained, Walgreens must pay a termination fee of \$325m.



Vertex buys into "molecular scissors"

The lead R&D collaboration of the month in October's table was that between CRISPR Therapeutics and Vertex with Vertex paying \$105m upfront (\$75m in cash and \$30m equity) to gain access to CRISPR Therapeutics' technology for gene editing.

CRISPR Therapeutics is a relatively new company having raised \$25m in Series A Financing in April last year. It was founded on IP covering the CRISPR/Cas-9 gene editing technology which is one of the hottest technologies around at the moment. This technology can be likened to "molecular scissors"; essentially it can be used for gene editing, i.e. adding, disrupting or changing the sequence of specific genes. As such CRISPR/Cas-9 offers an enabling approach to correct defective genes with the potential for curative therapies.

The collaboration between CRISPR Therapeutics and Vertex will evaluate the use of CRISPR/Cas9 in a number of diseases with defined genetic targets, including cystic fibrosis and sickle cell disease. Typical of the structure of multi-target research alliances, Vertex has the option to an exclusive licence for up to six gene-based treatments that emerge from the 4-year collaboration. In the event each programme is successful, Vertex will pay development, regulatory and sales milestones of up to \$420m per programme plus royalties. The \$2.6bn headline in the table assumes that all six programmes are successful.

Given the potential of the CRISPR/Cas9 technology it is not surprisingly that this is a hugely competitive area with IP owned by a number of institutions and associated spin-out companies. Other biotechs exploiting the CRISPR/Cas-9 technology for the development of therapeutics include Editas Medicine, Intellia Therapeutics and Caribou Biosciences; both Novartis and AstraZeneca have already developed collaborations in the area.

Continuing the theme of nucleic acid-based therapeutics

Whilst on the subject of developing therapies using technologies focused at the nucleic acid level, it is interesting to see three other deals in the top 20 this month involving nucleic acid-based approaches to therapeutic development.

The research collaboration between Arcturus Therapeutics and Ultragenyx Pharmaceutical covers the discovery and development of mRNA therapeutics to certain rare disease targets using the Arcturus UNA Oligomer chemistry and LUNAR nanoparticle delivery platforms. Whilst the headline value is over \$1bn, the upfront is \$10m (or 0.8% of the headline value) and the financials cover ten rare disease targets. Initially the companies will focus on two targets. Arcturus is eligible to receive R&D and sales milestones of up to \$156m per target, R&D funding plus royalties in the mid-single to low double-digit range.

Janssen's partnership with Canadian biotech enGene, facilitated through J&J Innovation, brings gene therapies for inflammatory bowel disease (IBD) and includes an undisclosed upfront payment and equity investment, R&D funding and potentially \$339m in R&D and commercial milestones plus tiered royalties. Under the agreement Janssen has an option to license enGene's lead candidate, EG-12, for the gut-localised expression of the anti-inflammatory cytokine IL-10 in indications such as IBD.



Licensor Acquired / Licensee Acquirer	Product / Technology	Deal Type	Headline (\$m)
Rite Aid Corporation/ Walgreens Boots Alliance	US retail pharmacy chain	Acquisition - company	17,200
CRISPR Therapeutics/ Vertex Pharmaceuticals	CRISPR-Cas9 gene editing technology for discovery of new treatments for genetic diseases incl sickle cell disease, CF	4yr research collaboration, options (up to 6 programmes)	2,625 ‡ (420/prog)
PharMEDium Services/ AmerisourceBergen Corp	US provider of compounded sterile preparations (CSPs) to acute care hospitals	Acquisition - company	2,575
RIMSA/ Teva Pharmaceutical	Mexican pharma/ distributor	Acquisition - company	2,300
Five Prime Therapeutics/ Bristol-Myers Squibb	CSF1R antibody programme, incl FPA008 (p1) in immunology/ oncology in combination with Opdivo/ other therapies	Licence, collaboration	1,740
Arcturus Therapeutics/ Ultragenyx Pharma	mRNA therapeutics for rare diseases using Arcturus chemistry and nanoparticle platforms - up to 10 targets (discovery)	Research collaboration, licence, options	1,570 ‡ (156/prog)
Innovent Biologics/ Lilly	Up to 3 anti-PD-1 based bispecific antibodies for oncology	Expansion of existing collaboration	1,000 ‡
Adheron Therapeutics/ Roche	Lead asset SDP051 mAb against Cadherin-11 in RA, fibrotic diseases (p1 complete)	Acquisition - company	580
** Merck Serono/ BioMarin	Kuvan and pegvaliase (Kuvan marketed; pegvaliase p3)	Regaining of rights	564
Alpine Immune Sciences/ Kite Pharma	2 transmembrane immunomodulatory protein (TIP™) programmes (discovery)	Research collaboration, licence	535
XOMA Corporation/ Novartis	Anti-transforming growth factor-beta (TGFβ) antibody programme incl XOMA089 plus other TGFβ1 inhibitors (pc)	Licence	517
Novera therapeutics with OICR/ Janssen Biotech	Novel small compounds for haematological malignancies (discovery)	Research collaboration, option, licence	345
enGene/ Janssen Biotech	"Gene Pill"/ enema non-viral gene delivery; lead candidate, EG-12, for gut-localised cytokine IL-10 expression in IBD (pc)	Collaboration, option to licence	339
*** Regeneron Pharma/ Mitsubishi Tanabe Pharma	Fasimumab (REGN475), nerve growth factor mAb for musculoskeletal pain (p2b)	Collaboration, licence	325
Immunomic Therapeutics/ Astellas Pharma	LAMP-vax products for allergic diseases incl ARA-LAMP-vax for peanut allergy (pc) + other research programmes	Licence	300
Arvinas/ Genentech	PROTAC technology - bifunctional small molecules targeting proteins for degradation/ removal (discovery)	Licence, options	300
Emisphere Technologies/ Novo Nordisk	Oral formulations of 4 classes of molecules targeting metabolic disorders, incl diabetes and obesity using Eligen Technology	Licence, development agreement	222 ‡ (62.5/excl prog)
† Telesta Therapeutics/ Ipsen	MCNA for non-muscle invasive bladder cancer (BLA filed)	Licence	137
Proteros biostructures/ Merck & Co	Proteros' epigenetics technology and structure guided discovery platform for oncology targets (discovery)	Collaboration - R&D	126
†† Genexine/ Tasgen Bio-Tech	3 clinical and 2 preclinical therapeutic protein/ peptide candidates	2 licences	125

All deals are worldwide unless otherwise noted – see below:

- * ex China, Lilly has opt-in rights for co-development/ commercialisation in China
- ** BioMarin already had exclusive rights to Kuvan in US, Canada and to pegvaliase in the US, JP; BioMarin will now have exclusive global rights to Kuvan and pegvaliase with the exception of Kuvan in JP
- *** JP, South Korea + 9 other Asian countries, excl China
- † ex US, Canada, South Africa, Mexico, South Korea and JP
- †† China
- ‡ Multiple programmes - headline value assumes all are successful

Abbreviations:

- RIMSA = Representaciones e Investigaciones Medicas S.A de C.V.
- CSF1R = colony stimulating factor 1 receptor
- OICR = The Ontario Institute for Cancer Research
- PROTAC technology = Proteolysis-Targeting Chimera
- MCNA = Mycobacterium phlei cell wall-nucleic acid complex

a considerable amount of restructuring within large pharma “

The collaboration focuses on enGene's non-viral vector platform based on biocompatible polymers for gene delivery to cells lining the intestine and allows the nucleic acid constructs to be administered via the oral or enema route. As part of the transaction Janssen can explore the therapeutic potential of enGene's platform to deliver one additional undisclosed target.

The third nucleic acid-based deal in our table of this month is between Immunomic Therapeutics and Astellas Pharma for LAMP-vax DNA vaccine products for the treatment or prevention of allergic diseases in humans. The transaction includes ARA-LAMP-vax at the preclinical stage for peanut allergy, as well as a number of other research programmes for food or environmental allergies. In an atypical financial structure for an early stage R&D collaboration / licence, Immunomic Therapeutics will receive an upfront payment of \$300m and be entitled to royalties of 10% based on net sales of potential products for allergic diseases. This is unusual as most early stage deals have relatively small upfronts with most of the consideration being back-loaded. Immunomic Therapeutics will retain the rights to its LAMP-vax platform for other applications, including cancer immunotherapy.

Whilst considering nucleic acid-based approaches, it was interesting to see that mRNA company Moderna Therapeutics, which has a number of deals under its belt with AstraZeneca, Alexion and Merck & Co, has launched a wholly-owned venture called Caperna to focus exclusively on the development of personalised cancer vaccines. This is Moderna's fourth venture in what it calls the Moderna Ecosystem. The other ventures are: Onkaido to develop mRNA drugs in oncology; Valera to develop vaccines and therapeutics for the prevention and treatment of viral and bacterial infectious diseases; and Elpidera focused exclusively on mRNA-based treatments for rare diseases.

Shifting focus and business alignment

There has been a considerable amount of restructuring within large pharma companies over the last few years with strategic decisions made to exit specific therapeutic areas to allow a focus on other areas. This was exemplified by the major asset swapping amongst pharma companies of last year. Another approach to realignment where products are developed through licensing partnerships is to investigate whether the original licensor has the capabilities to take back rights to the product of interest. This month's deal between Merck Serono (Merck KGaA) and BioMarin is a good example of this approach.



Over the past few years, Merck KGaA has been realigning its healthcare business to focus on oncology, immuno-oncology, immunology and neurology and so its partnership with BioMarin for treatments for phenylketonuria (PKU) was no longer a good strategic fit.



Jill Ogden has over 28 years of commercial and R&D experience in the biopharmaceuticals and healthcare industries and provides our biologics, early stage deals and platform technologies expertise. She has worked for a number of mid-caps and biotech companies, both public and private. Jill has led and been involved in a wide range of product and technology deals, including corporate M&A.

In the original PKU-focused deal dating back to 2005, Merck signed an exclusive licence with BioMarin for the oral drug Kuvan (sapropterin dihydrochloride), which is now marketed, and an option to develop pegvaliase (PEGylated recombinant phenylalanine ammonia lyase), which is currently in phase 3 trials. Under the terms of the 2005 agreement, Merck Serono paid \$25m upfront and BioMarin was eligible for downstream milestones of up to \$232m covering both products in multiple indications.

Under this original agreement Merck Serono had received exclusive rights to market Kuvan in all territories outside the US, Canada and Japan and the option to develop pegvaliase for markets outside the US and Japan. The new agreement brings back to BioMarin worldwide rights to Kuvan and pegvaliase, with the exception of Kuvan in Japan where BioMarin's partner is Daiichi Sankyo.

Kuvan was approved in the US in 2007 and is also approved in another 50 countries, including EU countries. Sales of the product will fit well into BioMarin's commercial infrastructure for its enzyme replacement therapies Naglazyme (galsulfase), for the treatment of Mucopolysaccharidosis VI, and Vimizim (elosulfase alfa) for Morquio A, a rare inherited lysosomal storage disorder. Global sales of Kuvan by Merck Serono were \$56m in 2014.

BioMarin is paying approximately \$564m to Merck Serono to reacquire the rights, with an upfront payment of approximately \$365m plus an additional \$65m if combined sales of Kuvan and pegvaliase reach undisclosed cumulative sales thresholds. The deal also includes regulatory milestone payments for pegvaliase of approximately \$134m.

More big pharma acquisitions on the horizon?

We cannot close this month's Deal Watch without mentioning the reports filtering out near the end of October that Pfizer is back on its acquisition hunt. This time it seems that Allergan is the target. It was not that long ago that we were commenting on Actavis' \$70bn acquisition of Allergan (the combined company then rebranded itself Allergan). With a current market cap in the region of \$119bn, Allergan is an Irish company and so this transaction would provide Pfizer with the tax advantages it has been seeking. Quite how the US tax legislators and government authorities will view Pfizer's latest foray into the field of tax inversion if the bid goes ahead remains to be seen, but they will no doubt be making a lot of noise.