MEDIUS DEAL WATCH

July & August 2018

This issue of Deal Watch focuses on deal activities during the months of July and August. Despite the holiday season the number of transactions was reasonably buoyant with the usual mix of acquisitions of companies and assets, and licensing partnerships, with and without options.

We have included 24 transactions in our table of top deals by headline value for the period which covers deals over $100m. Of these 24, the majority (17 deals) focused on the "newer" therapeutic entities such as antibodies and antibody-based molecules, proteins, oligonucleotide-based therapeutics and gene therapies.

In terms of therapeutic areas, immuno-oncology and oncology predominate in keeping with typical trends, but there were also several deals in dermatology and other therapeutic areas which do not always feature so frequently, such as haematology, ophthalmology and diabetes.

Top of the Deal Watch table are five >$1bn licensing deals. Apart from the MorphoSys/ Galapagos licence with Novartis which is for a single asset, an antibody for atopic dermatitis at phase 2 stage (and see below), the other four deals cover multiple discovery / early stage programmes. The table later illustrates the relative differences in the timing of the potential payments associated with these deals. The $111m upfront paid by Novartis for a phase 2 asset is 10% of the headline value compared to approximately 2-3% for the early stage discovery deals. Roche's early stage payments to PureTech Health amounting to $36m include research funding and some preclinical milestones.

Dissecting the billion dollar deals

Partners	Comments	Headline $m	Upfront $m	Upfront as % H'line	Milestones $m	R&D funding	Royalties
Affimed/ Genentech	Multi-programme discovery for cancer immunotherapies	5,096	96	1.9%	5,000	Genentech near-term funding	Y, nd
Immatics/ Genmab	Cancer immunotherapies discovery - 3 programmes + option to 2 programmes; Immatics has co-pro option in selected EU countries	2,804*	54	1.9%	550/prog	Genmab	Tiered
MorphoSys | Galapagos/ Novartis	MOR106 antibody for atopic dermatitis in phase 2 (income split 50:50 MorphoSys:Galapagos)	1,111	111	10%	1,000	Novartis	Low teens to low twenties
Anima Biotech/ Lilly	Multi-programme discovery in undisclosed indications	1,050	30	2.9%		14 from Lilly	Low to mid single digit
PureTech Health/ Roche	Multi-programme discovery in undisclosed indications	1,036	36 inc research support, early pc milestones	3.5%	1,000	Roche	Y, nd

** assumes $550 per programme for all 5 programmes*

Gene therapies are Go

What seems quite striking in the table of top value transactions is that there were three gene therapy deals. Having faltered for decades, enthusiasm for gene therapy and related technologies seems to be a recurring theme this year and includes large pharma.

Presumably spurred on by Spark Therapeutics' FDA approval for Luxturna, a gene therapy to restore vision in patients with biallelic mutations of the RPE65 (retinal pigment epithelial 65 kDa protein) gene, Novartis paid $105m upfront and up to $65m in milestones for ex-US rights in January this year (DW issue 91).

Building its gene therapy expertise, in April Novartis went on to acquire AveXis and its portfolio of gene treatments, including late stage, lead product AVXS-101 for spinal muscular atrophy (SMA), for $8.7bn in cash (DW issue 94).

Other large pharma partaking in the gene therapy uptick earlier this year included AbbVie with its $1.1bn licence with Voyager Therapeutics for treatments for Alzheimer's and other neurodegenerative diseases (DW issue 92) and Pfizer's licence with Sangamo Therapeutics for neurodegenerative disorders (DW issue 91).

Not to be left out in August Astellas announced it was acquiring ophthalmic gene therapy company Quethera and its lead preclinical programme for glaucoma for $110m in upfront and contingent payments.

Meanwhile amongst the smaller players PTC Therapeutics is acquiring Agilis Biotherapeutics and its rare CNS gene therapy portfolio for $945m. The headline comprises $200m upfront ($50m in cash and ~$150m in common stock), $60m in development milestones, up to $535m in regulatory milestones, tiered commercial milestones of $150m, and 2-6% of annual net sales for products in Friedreich's ataxia and Angelman syndrome.

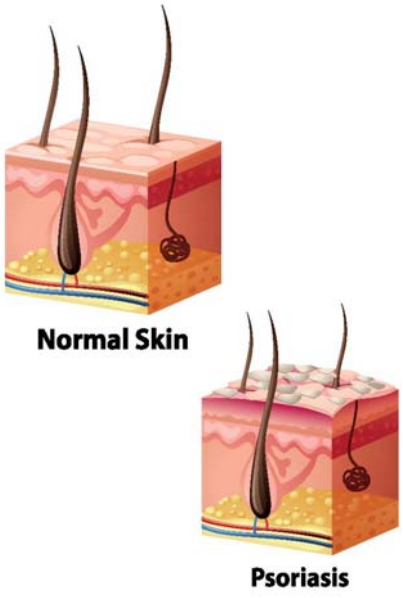
Also active in this area is Axovant Sciences which licensed the exclusive worldwide rights to Oxford BioMedica's phase 1/2 stage OXB-102, a gene therapy for Parkinson's disease in June (DW issue 96) and then in July licensed from Benitec Biopharma the global rights to a gene therapy treatment (BB-301) for oculopharyngeal muscular dystrophy (OPMD). In addition Axovant and Benitec have entered into a research collaboration for five other gene therapy programmes in neurological disorders. Overall potential payments to Benitec if all programmes are successful could be up to $665m and Benitec retains 30% of the net profits on worldwide sales of the OPMD product.

These are just a few examples of gene therapy technology partnerships and as development programmes progress it looks increasingly as if this approach can offer a real alternative therapeutic armamentarium for treating a range of disorders.

All things skin

In our annual Deal Watch analysis for 2017, there were seven deals in dermatology representing just over 2% of all the deals we reviewed. There were four dermatology deals in our top 24 during July and August for assets at various stages of development.

In the largest of these Novartis is paying up to $1.1bn with $111m upfront for a phase 2 antibody targeting IL-17C (MOR106) as a treatment of atopic dermatitis and potentially other indications. IL-17C is a cytokine which has been related to dermal inflammation; it is up-regulated in inflammatory skin disorders such as psoriasis and atopic dermatitis.



Licensor Acquired/ Licensee Acquirer	Product / Technology	Deal Type	Headline ($m)
Affimed/ Genentech	Multiple programmes to discover NK cell engager-based immunotherapeutics to treat multiple cancers	licence, collaboration	5,096
Immatics Biotechnologies/ Genmab	T-cell-engaging bispecific immunotherapies - 3 programmes + option to 2 programmes (discovery)	licence, collaboration, options	2,804
MorphoSys | Galapagos/ Novartis	MOR106, mAb vs IL-17C for atopic dermatitis (p2)	licence	1,111
Anima Biotech/ Lilly	Translation inhibitors for Lilly target proteins using Translation Control Therapeutics platform; multiple programmes (discovery)	licence, collaboration	1,050
PureTech Health/ Roche	Milk-derived exosome platform (Brain-Immune-Gut (BIG) Axis) for oral administration of Roche's antisense oligonucleotide platform; multiple programmes (discovery)	licence, collaboration	1,036
Agilis Biotherapeutics/ PTC Therapeutics	Gene therapy platform for rare monogenic diseases affecting CNS inc GT-AADC in Aromatic L-Amino Acid Decarboxylase (AADC) Deficiency (p2b)	acquisition - company	945
Ziylo/ Novo Nordisk	Early-stage synthetic glucose binding molecule platform for glucose-responsive insulins	acquisition - company	800
Benitec Biopharma/ Axovant Sciences	BB-301 + 5 additional gene therapy products in neurological disorders (pc)	licence, collaboration	665
Allergan/ Almirall	US dermatology portfolio - marketed acne and dermatosis products: Aczone, Azelex, Tazorac, Cordran tape, and Seysara (pre-reg)	*acquisition - assets	650
Adapt Pharma/ Emergent BioSolutions	Portfolio of opioid overdose and addiction treatments; lead product NARCAN® (naloxone HCl) Nasal Spray (marketed)	acquisition - company	635
argenx/ AbbVie	ARGX-115, mAb vs immuno-oncology target glycoprotein A repetitions predominant (GARP) (pc)	option exercise	625
AliveGen/ Biogen	ALG-801 (p1a) and ALG-802 (pc) proteins that act as ActRIIB ligand traps to inhibit myostatin pathway signaling for neuromuscular indications	acquisition - assets	562.5
ABL Bio/ TRIGR Therapeutics	5 antibody programmes vs undisclosed targets for oncology indications	** licence	554.3
Revolution Medicines/ Sanofi	Joint development of SHP2 inhibitors in NSCLC, other cancers with certain mutations (pc)	licence, collaboration, option	550
Visterra/ Otsuka	Hierotope antibody platform + product portfolio in kidney diseases, cancer, chronic pain and infectious diseases; lead product in p2	acquisition - company	430
BioNTech/ Pfizer	mRNA-based influenza vaccines	licence	425
JW Pharmaceutical/ Leo Pharma	JW1601 for atopic dermatitis (pc)	** licence	402
Sichuan Kelun-Biotech/ Harbour BioMed	Anti-PD-L1 mAb A167 for various cancers (p2) + A167 combination therapies	† licence	350
GlaxoSmithKline/ Dermavant Sciences	Tapinarof, aryl hydrocarbon receptor modulating agent (TAMA) (p2) and back-up programmes for psoriasis, atopic dermatitis	†† licence	331
PaxVax/ Emergent BioSolutions	Oral vaccine portfolio: Vivotif for typhoid fever, Vaxchora for cholera (marketed)	acquisition - company	270
Roche/ Global Blood Therapeutics	Inclacumab, mAb vs P-selectin, for vaso-occlusive crises in sickle cell disease (p2 for cv indication)	licence	127
Glenmark/ Harbour BioMed	Bispecific antibody targeting HER2 and CD3 for HER2-positive cancers (p1)	‡ licence	120
Quethera/ Astellas	Undisclosed gene therapy for patients with glaucoma (pc)	acquisition - company	110.3
I-Mab Biopharma/ ABL Bio	Bispecific antibody + 3 more antibody programmes vs undisclosed targets	† licence, collaboration	102.5

All deals are for worldwide rights unless stated otherwise:

* US ** ex South Korea †ex Greater China ††ex China ‡Greater China

The licensors, Galapagos and MorphoSys, developed MOR106 through a strategic discovery and co-development alliance initiated in 2008; they will split the licensing revenue on a 50:50 basis. In addition to regulatory, commercial and sales-based milestones of up to $1bn, Novartis will also be responsible for all future research, development, manufacturing and commercialisation costs for MOR106.

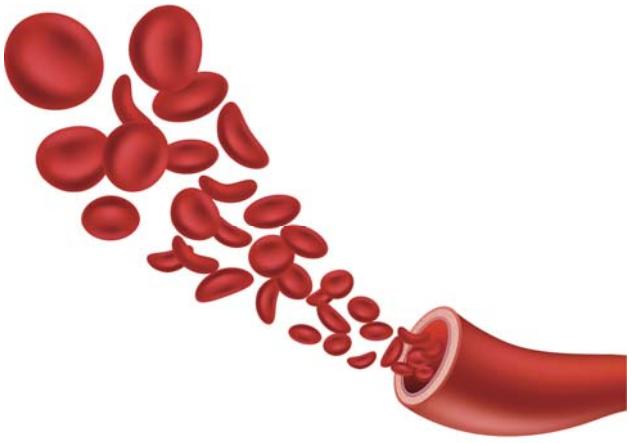
Three other dermatology deals in the top 24 for the two-month period were for what can be regarded as the classical approach to treating skin conditions, i.e. topical or oral small molecule therapeutics. Early in August Almirall announced that it was acquiring a US portfolio of five products from Allergan's Dermatology unit for $550m in cash upfront with $100m in potential earn-outs payable in 2022 based on portfolio performance. The portfolio comprises three marketed topical products for acne: Aczone® (dapsone), Tazorac® (tazarotene), Azelex® (azelaic acid), and Cordran® Tape (fludroxycortide), a topical corticosteroid-tape marketed for the treatment of dermatoses. These four products generated sales of $70m in H1 2018. The fifth product acquired by Almirall is Seysara™ (sarecycline), an oral tetracycline-based antibiotic for moderate to severe acne vulgaris, which is awaiting FDA approval. Peak sales for Seysara are estimated in the $150-200m range.

Through its $402m deal ($17m upfront) with JW Pharmaceutical, skin specialist Leo Pharma brings in exclusive global rights (excluding Korea) to JW1601, an orally available histamine H4 receptor inverse agonist with anti-pruritic and anti-inflammatory dual effect for the treatment of atopic dermatitis.

And in the fourth dermatology deal of the period, GSK has granted to Dermavant Sciences the rights to tapinarof, a topical aryl hydrocarbon receptor modulating agent (TAMA) in phase 2 trials for the treatment of psoriasis and atopic dermatitis. Paying nearly $200m upfront and a further ~$132m in milestones Dermavant gets rights to tapinarof outside China as well as preclinical back-up programmes.

Tackling complications in sickle cell disease

GSK is not the only large pharma to be divesting assets recently. In the second half of August Roche licensed global rights to inclacumab, a monoclonal antibody against P-selectin, to Global Blood Therapeutics (GBT) as a treatment for vaso-occlusive crises (VOC) in patients with sickle cell disease (SCD). P-selectin is an adhesion molecule found on endothelial cells and platelets that contributes to the cell-cell interactions that are involved in the pathogenesis of VOC. Its inhibition is a validated target in SCD which reduces the incidence of VOCs. Under the terms of the agreement Roche receives $2m upfront and up to approximately $125m in development and commercialisation milestones for the SCD indication plus tiered royalties on net revenues. Roche was previously developing inclacumab for patients with coronary artery disease but discontinued the inclacumab programme following phase 2 trials. GBT plans to submit an IND for inclacumab in 2021.



Novo Nordisk's sweet spot

One of Novo Nordisk's key core focus areas is the treatment and management of diabetes. In a research and strategy update last November among the company's stated aims were plans to maximise its insulin franchise by focusing on value and volume share and to strengthen its leadership in developing drugs to treat obesity. According to the WHO the global obesity problem has nearly tripled since 1975; in 2016 there were more than 650m obese adults worldwide and 41 million children under the age of 5 were overweight or obese (obesity = BMI of ≥30; overweight = BMI of ≥25). However only a small fraction, about 2%, are taking obesity medication.

Novo Nordisk's acquisition of UK biotech Ziylo, a spin out from the University of Bristol, announced in August is right on strategy. The deal is worth a potential $800m should all development, regulatory and sales milestones be met. Ziylo's technology focuses on its glucose binding molecule platform and brings to Novo the potential to develop glucose responsive insulins. Insulins that can be engineered to respond to glucose in complex environments such as blood, could enable better metabolic control for example by eliminating the risk of hypoglycaemia.

Meanwhile Novo Nordisk has also signed up with Evotec to use the latter's drug discovery platform to identify and develop small molecule therapeutics for the treatment of diabetes and obesity as well as co-morbidities such as nonalcoholic steatohepatitis (NASH), cardiovascular diseases, and diabetic kidney disease. No financial information for the strategic alliance has been disclosed.

Other activities of note

While big deal headlines are always eye catching, it is interesting to monitor other activities even if they don't necessarily have huge BioDollar tags. In July GSK and 23andMe announced a four year collaboration to discover new drug targets, identify patient subgroups of disease and enable rapid identification and recruitment of patients for clinical studies. Apparently 23andMe now has over 5m customers who want to learn about their personal genetic profile. 23andMe customers can also choose to participate in research and contribute their information to the company's genetic and phenotypic database.

GSK has made a $300m equity investment in 23andMe and will become 23andMe's exclusive collaborator for drug target discovery programmes. The initial four year period for the collaboration can be extended for a fifth year and the parties will share the funding on a 50:50 basis. Both GSK and 23andMe will share in the proceeds from new therapies arising from the collaboration.

Jill Ogden has over 30 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.

Christi Mitchell

In closing this issue the Medius team are deeply saddened to have lost our dear friend and colleague Christi, who passed away on 31 August. Christi brought many years of experience in IP portfolio management and strategy. Her expertise included the acquisition and licensing of products and technologies, as well as the valuation of companies, products and inventions.

With an academic background in Genetics, Molecular Biology and Business Management, Christi was based in the US for a while and then returned to the UK where she worked for a number of companies including BTG plc.

Christi then founded the IP management and commercialisation company, Highbury Ltd and was also a Medius team member. She was the former President for the Licensing Executive Society (LES) in Great Britain and Ireland and held various positions in the LES over many years.

Christi had extensive international licensing and commercialisation experience with academia, the NHS, and companies ranging from start-up to international and individual inventors. She loved to travel and her IP and technology transfer experience extended across the US, EU, Australia, New Zealand, India, Japan, Singapore and South Korea.

Our thoughts go out to Christi's children Naomi and Laurence and her extended family.

DEAL WATCH
medius associates

Tel: +44 (0) 20 8654 6040
dealwatch@medius-associates.com

Deal Watch data are available to support your benchmarking and valuations.
Please contact us for details about our Client specific services.