MEDIUS DEAL WATCH

March 2018

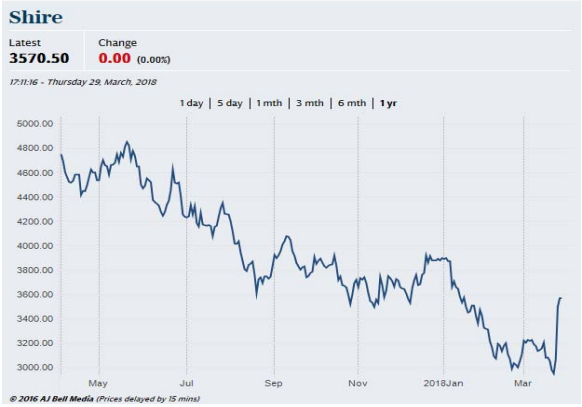
Are we on trend this Spring?

Just when Medius's predictions for 2018 indicating a low level of major M&A deal activity seemed to be coming true, a couple of major deals have been announced. But the situation remains that, in comparison with previous years, the number of M&A deals in the March Deal Watch table remains low, with a commensurate increase in the number of licence deals. Also, interestingly, so far none of the M&A seems to be driven by the tax changes in the US. In addition, it proved difficult to find a top 20 deals with fully disclosed headline values therefore for this month our table includes some deals with no defined headline value.

Of course the big headline at the top of the table was the announcement by GSK on 28th March for acquisition for $13bn of the remaining 36.5% held by Novartis in the companies' OTC joint venture. Originally formed back in 2014 as part of a corporate realignment, which included changes to its vaccine [acquiring] and oncology [divesting] businesses, GSK had held the majority share of 63.5% of the equity so this was a logical step.

The buyout had been heralded by the announcement made on 26th March reporting that GSK was pulling out of the running for acquiring Pfizer's consumer healthcare unit. The decision to withdraw had come close on the heels of Reckitt Benckiser's election not to go further in discussions with Pfizer. This news was well received by shareholders reflecting the concern that debt would have been required to fund the acquisition. With two major potential purchasers declining, it will be interesting to see if Pfizer continues with the trade sale or opts to spin out the assets into a separate company.

Also, at the time of going to press, rumours are abounding about the potential purchase of Shire by Takeda which has led to a 20% increase in Shire's share price. Shire has had a challenging time since its $32bn acquisition of Baxalta which completed in June 2016. Shire has not apparently welcomed the takeover however it may appeal to its shareholders as the stock has not performed well post Baxalta. Watch this space!



Second in our monthly Deal Watch table was the deal announced between Eisai and Merck & Co with a headline value of $5,760m. Eisai's tyrosine kinase inhibitor Lenvima (lenvatinib mesylate) for the treatment of multiple types of cancer is currently approved as monotherapy in thyroid cancer, as well as in combination with everolimus for second line treatment of renal cell carcinoma. There are a further 11 indications under consideration. This deal included a $300m upfront payment with up to $650m for option rights to Lenvima, $450m for R&D expenses plus $385m in clinical and regulatory milestones. A further maximum of $4bn in sales milestones completes the package with a share of gross profits.

Celgene's relentless deal activity

Celgene was, as ever, very busy in the headlines and secured three spots in the March Deal Watch table with deals with Prothena, Vividion and bluebird bio. The Prothena deal has a headline value of $2,093m and is focused on antibodies that target tau and TDP-43, the latter of which is linked to amyotrophic lateral sclerosis. The deal terms include a $100m upfront payment and with $50m equity investment.

The grant of rights includes exclusive access to clinical assets in the USA on filing INDs with the right to extend the territories available to it on completion of phase 1. The balance of the headline consists of up to $80m per programme on exercise of the US rights and $55m per programme on exercise of global rights plus an additional $565.5m per programme in regulatory and commercial milestones.

Celgene's deal with Vividion covers a 4 year alliance [extendable for a further 2 years] for the discovery of small molecules that interact with the ubiquitin proteasome system. Celgene is making a payment of $101m upfront including the purchase of equity; in return it has rights to opt in to exclusive worldwide rights on IND acceptance.

Licensor/ Acquired	Licensee/ Acquirer	Deal type	Product/ Technology	Headline $m
Novartis	GSK	Equity acquisition	Purchase of Novartis share in the OTC JV	13,000
Eisai	Merck & Co	Joint development & commercialisation	Lenvima, a tyrosine kinase inhibitor for multiple cancers	5,760
Prothena	Celgene	R&D collaboration	TDP 43 in neurological diseases	2,093
Ionis	Akcea	Exclusive global licence	inotersen and AKCEA-TTR-L_R for hereditary transthyretin amyloidosis	1,700
Prexton Therapeutics	Lundbeck	Corporate acquisition	Brings access to foliglurax for Parkinson's	905
Pfizer	Biogen	Asset acquisition	PF 04958242 in P2 development for cognitive impairment in schizophrenia	590
Ligand Pharmaceuticals	Roivant Sciences	Exclusive global licence	LGD 6972 glucagon receptor antagonist	549
NXThera	Boston Scientific Corporation	Corporate acquisition	Brings access to the Rezum system for symptoms of BPH	406
Heidelberg Pharma	Magenta Therapeutics	Research agreement & collaboration	Use of Magenta's stem cell platform with proprietary antibodies to specific targets	334
C4X Discovery	Indivior	Exclusive global licence	Includes C4X3256 oral orexin-1 receptor antagonist programme	294
Aptose Biosciences	Ohm Oncology	Global licence	APL 581 a dual BET/kinase inhibitor in PC for haematological cancers	125
Spinal Kinetics	Orthofix International	Corporate acquisition	Manufacture of artificial cervical and lumbar discs	105
Carna Biosciences	Sumitomo Dainippon	Joint development & commercialisation	Novel kinase inhibitors for psychiatric and neurological disorders	102
Vividion	Celgene	Discovery collaboration	Focused on ubiquitin proteasome system to break proteins	101 upfront
Nabriva Therapeutics	Roivant Sciences	Exclusive licence*	Lefamulin, a pleuromutilin antibiotic for the treatment of pneumonia	101
Sanofi	Evotec	Licence	10 assets in early stage infectious disease portfolio excluding vaccines	75 upfront
bluebird bio	Celgene	Co-development, co-promotion	Bb2121 in the USA for multiple myeloma	70
			Financial terms not disclosed	
Five Prime	UCB	Licence	Undisclosed target for inflammatory diseases from protein discover platform	
Shire	Caladrius Biosciences	Global licence	CD34+ stem cell therapy for refractory angina	
Regeneron	Alnylam	Collaboration	Identification of RNAi treatment in non-alcoholic steatohepatitis [NASH]	

* People's Republic of China, Hong Kong, Macau and Taiwan.

The last deal this month for Celgene was that with bluebird bio for co-development and co-promotion of bb2121, an anti B cell maturation antigen CAR-T cell therapy for relapsed multiple myeloma in the USA. This builds on the original [2013] collaboration between the parties.

Not surprisingly, it was noted by Evaluate that Celgene has invested more on in-licensing assets over the last decade than any other biopharma business. Many of the deals are for early stage assets at which point it is difficult to be precise on the exact value. Time will tell if these deals represent good value. The company is undertaking a share buyback programme, $4bn in shares were repurchased in 2017.

Evaluate data on Celgene's deal activity over the past few years:

	Number of deals	Upfront	Total deal value
M&A	26	23.46	30.54
Licensing	45	3.99	19.67
Total	71	27.45	50.21

No longer required in the wardrobe: out licensing pre-loved / non-core assets

The big pharma companies are busy stream lining their pipelines with Pfizer divesting PF-04958242, an AMPA receptor potentiator for cognitive impairment in schizophrenia, to Biogen. [PF-04958242 also has potential for use in Alzheimer's disease]. The deal has a potential value of $590m of which the upfront accounts for $75m, with $515m in milestones and royalties in low to mid-teens.

In the same vein, Sanofi is out-licensing its anti-infective portfolio to Evotec which consists of ~10 early-stage anti-infective projects [excluding vaccines] plus staff. Interestingly, Sanofi is funding the project with an upfront fee of $74m being paid to Evotec, but certain option rights are being retained by Sanofi. So, in effect, this outsourcing of non-core development allows Sanofi to concentrate on other fields such as cancer and blood disorders.

Shire was also in on the out-licensing act granting worldwide rights to its late stage CD34+ stem cell therapy to Caladrius Biosciences; no financial terms were disclosed for this deal.

Diabetes deals make a comeback in fashion

Another company with a very busy BD department is Roivant which closed deals with both Ligand Pharmaceuticals and also Nabriva Therapeutics. These announcements came hot on the heels of Roivant's deal last month with Poxel for its anti-diabetic agent Imeglimin which has completed phase 2 development. Roivant's business focus is to identify and secure access to "overlooked" drug candidates.

Roivant picked up rights to Ligand's LGD-6972, a glucagon receptor antagonist, which builds on its diabetes portfolio. Roivant paid $20m upfront with a potential $514m in milestones. Now, with two late stage assets in diabetes, the $1.1bn financing secured from SoftBank last year will certainly be needed to support the costly late stage clinical trials. To secure Nabriva Therapeutics' lefamulin in greater China, Roivant paid a lower price tag: $5m upfront with a further $90m in development and commercial milestones. Lefamulin is a pleuromutilin antibiotic for the treatment of pneumonia and has completed one phase 3 study in moderate to severe community-acquired bacterial pneumonia.

Beware the Ides of March

But it was not all good news this month, with Orexigen filing for Chapter 11 bankruptcy protection and the withdrawal of Zinbryta from the multiple sclerosis market by AbbVie/Biogen in the USA. With a black box warning over concerns for liver safety requiring risk-management and strict liver monitoring, this decision was not so surprising. Biogen has, of course, a major presence in the MS market with four drugs for MS so acquiring PF-04958242 from Pfizer makes perfect sense.

Proving that the path of science does not always run smoothly, there was a high number of projects being reported as either discontinued or on a clinical hold, as per the table below:

Company	Project	Indication
Solid Biosciences	SGT 001	Duchenne muscular dystrophy P1/2
Anthera	Sollpura [liprotamase]	Exocrine pancreatic insufficiency P3
VBL Therapeutics	VB-111	Missed end point in glioblastoma P3
Demira	olumacostat	Missed end point in moderate to severe acne P3
Protagonist	PTG 100 integrin antagonist peptide	Moderate to severe ulcerative colitis P2b
Ablynx	vobarilizumab	Missed end point in systemic lupus erythematosus P2

Teva announced that it was terminating the Sosei | Heptares 2015 deal for small molecule CGRP antagonists for the treatment of migraine. Sosei will regain all rights to the programme including HTL 0022562, the molecule lead which is due to go into phase 1 later this year.

On a more positive note, spin outs seem to be *a la mode*, with AstraZeneca's Medimmune spinning out six early stage molecules from auto-immune/inflammation programmes into a new company Viela Bio. This spin out includes the anti-CD19 monoclonal antibody inebilizumab, which is currently in mid-stage development for the treatment of neuromyelitis optica. Funding of up to $250m is coming from a consortium which includes AstraZeneca as the largest minority shareholder.

Sharon Finch, the founder of Medius, has extensive business development experience working both in industry and for over 20 years with Medius. Sharon works primarily on partner searches and transactions.

She is the Editor of the Business Development and Licensing Journal and is the Course Director for the PLG MSc in Pharmaceutical Business Development & Licensing run by the University of Manchester.

Creative deals

It is always a challenge to know how to move forward when your partner, in this case GSK, elects not to take up its options which is where Ionis was in August last year. Inotersen was in development for patients with TTR amyloidosis [ATTR] a rare disease. This month Ionis announced that a new partner is in place in the shape of Akcea, noting that Akcea is an affiliate of Ionis [Ionis held 68% of Akcea's shares].

Akcea will hold worldwide rights to inotersen and IONIS TTR LRx in exchange for an upfront payment of $150m payable in shares of common stock. In return Ionis is purchasing more shares in Akcea raisings its level of ownership to 75%. There will be milestones due of $90m on approval in the US and EU with further milestones due on other territorial regulatory events. In full these milestones may reach $1.3bn. The companies are operating a profit share of 60:40 with Ionis retaining 60% until the launch of IONIS TTR LRx when the ratio switches to 50:50.

Finally to note RNAi still remains very much on trend and Regeneron and Alnylam closed a collaboration to identify RNAi treatment for NASH. It is a 50:50 arrangement for research, co-development and commercialisation.

So all in all a very interesting, eclectic Spring collection.

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