MEDIUS DEAL WATCH January 2018

One key question for 2018 is whether the recent US tax changes will have an effect on M&A in our industry - time will tell. The year opened with a small batch of >$1bn M&As although these are not particularly mega deals. However pharma companies on the prowl for acquisitions still have to consider the high valuations of biopharma companies resulting from the surge in stock market prices.

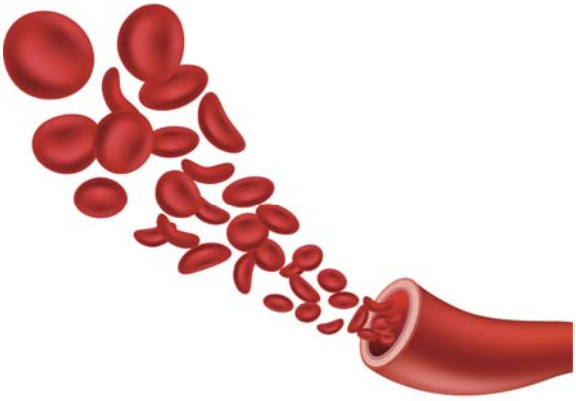
Our top 20 deals for January amounted to almost $40bn in aggregate headline value. In comparison, this time last year January's top 20 deals represented $52bn in aggregate headline value (buoyed by J&J's $30bn acquisition of Actelion). The aggregate value of the top 20 deals in January 2016 was only just over $10bn, so perhaps 2018 is starting to show some green shoots of recovery for the deal making environment - again time will tell.

Three companies have been particularly active in deal making this month: Sanofi, Celgene and Takeda - more on this below.

Spin outs don't always last long as independent companies

In our recent annual deal review for 2017 we highlighted how the spin out business model is alive and kicking and how spin outs, especially from large biopharma companies, have turned out to be a rich source of new products for licensees and acquirers alike. Biogen's spin out, Bioverativ, had not even got past its first anniversary as a Nasdaq-listed company before being snapped up by Sanofi for $11.6bn (although this is not quite as fast as Shire's move to take over Baxalta when it was spun out of Baxter in July 2015). Paying $105 per share in cash (~64% premium over Bioverativ's closing price on 19 January), Sanofi gains the marketed products, Eloctate (haemophilia A therapy) and Alprolix (haemophilia B therapy), as well as a pipeline of candidates focused on rare blood disorders. During 2016 Eloctate and Alprolix generated $847m in sales. Based on a share price around launch in the region of $44, this must be a pleasing result for Bioverativ's original investors. However, in the meantime the US Securities and Exchange Commission (SEC) has issued a lawsuit against some traders for insider trading based on a series of suspicious transactions that made about $4.9m.

Rare blood disease products in vogue - Sanofi part 2



In the early part of January it was made public that Novo Nordisk had made an unsolicited $3.1bn (€28 per share) bid for Ablynx in December, which the Ablynx Board rejected. Novo Nordisk's particular interest was in lead asset caplacizumab, a Nanobody therapeutic which inhibits von Willebrand factor (vWF) for the treatment of acquired thrombotic thrombocytopenic purpura (TTP), a rare, life threatening blood clotting disorder. Ablynx submitted its MAA to the EMA for approval of caplacizumab in February last year and, according to Reuters, Ablynx has forecast peak caplacizumab sales of €1.2bn. Strategically caplacizumab represented a good fit for Novo Nordisk as it complements the company's portfolio of products focused on haemophilia. By the end of January, however, Sanofi had swept in and offered €45 per share valuing the deal at $4.8bn. Sanofi was also interested in caplacizumab, which fits not only with its rare disease focus but also enhances its portfolio of products for rare blood diseases coming from its acquisition of Bioverativ a week earlier.

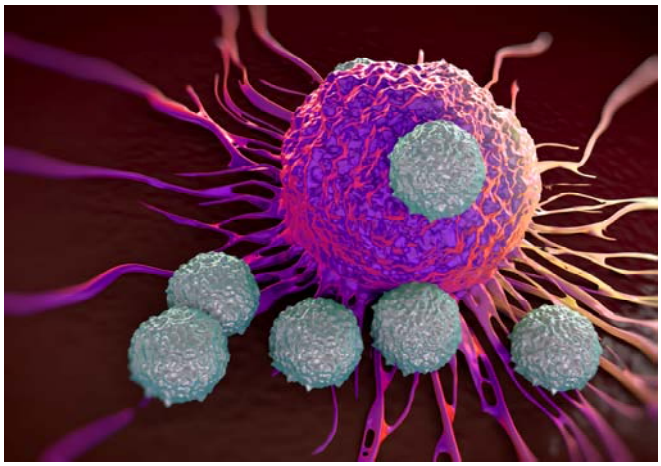
Celgene back in acquisition mode

While Sanofi led the way with a committed spend of $16.4bn in January, Celgene also had a bumper spending spree this month by first acquiring Impact Biomedicines for a potential $7bn in early January and then it scooped up the remaining 90% of its CAR-T and TCR technology partner Juno Therapeutics for $9bn.

Whether Celgene will pay $7bn in the long run for Impact remains to be seen. The headline value contains significant sales milestones linked to performance of Impact's lead phase 3 stage asset fedratinib, an oral JAK2 kinase inhibitor in development for the treatment of myelofibrosis and polycythemia vera, both rare bone marrow cancers. Celgene will pay approximately $1.1bn upfront for Impact and further contingent payments based on regulatory approval for fedratinib in myelofibrosis and other indications could amount to $1.4bn.

In the event fedratinib achieves global annual net sales of over $5bn, aggregate tiered sales-based milestone payments could total a maximum of $4.5bn, representing nearly two thirds of the Impact deal value. This is a high percentage. Interestingly Impact was originally formed in 2016 after the acquisition of the rights to fedratinib from Sanofi.

Back in June 2015 Celgene and Juno announced a ten year collaboration to combine their respective immunology expertise to develop new immunotherapies for cancer and autoimmune diseases based on T cell technologies. Built around a series of reciprocal co-development and co-promotion options, Celgene made an initial payment of approximately $1bn to secure the deal, which included the purchase of ~9.1m Juno shares at $93 per share. Celgene is now paying $87 per share to buy Juno which represents ~29% share price premium over Juno's closing price on the previous Friday.



Having terminated the development of its lead CAR-T therapy, JCAR015, early last year after several patient deaths in a phase 2 clinical trial in relapsed/refractory B -cell acute lymphoblastic leukaemia (ALL), Juno's share price had been in the low $20s for several months. The company switched focus to its JCAR017 programme and recently reported promising data in a pivotal trial for relapsed and/or refractory diffuse large B-cell lymphoma (DLBCL). According to Celgene's press release, regulatory approval for JCAR017 in the US is anticipated in 2019 with potential global peak sales of approximately $3bn.

Takeda moves in neurodegenerative diseases and stem cell therapy

Meanwhile Takeda, ranked 4th in the top deal makers of 2017, had a busy first week of the New Year entering into an option and collaboration agreement with Denali Therapeutics paying $155m on agreement closure (including an upfront of $40m, a preclinical milestone of $5m and a payment of $110m to purchase approximately 4.21m Denali shares at $26.10 per share). Denali had also been busy having completed a $250m IPO in early December. The company has a focus in neurodegenerative diseases and a technology, Antibody Transport Vehicle (ATV) technology, which can enhance blood-brain barrier (BBB) penetration of antibody molecules via the transferrin receptor. Under this transaction Takeda gains options to three Denali programmes for neurodegenerative disorders: the ATV: BACE1/ Tau and ATV: TREM2 programmes, which are both at preclinical stage for Alzheimer's disease, and a third undisclosed discovery stage programme. More details on the financials for the deal are summarised in Box 1.

A few days later Takeda announced it was paying $628m (~82% share price premium) to buy Belgian company TiGenix NV and its lead asset Cx601 (darvadstrocel), an allogeneic stem cell therapy for local administration for the treatment of complex perianal fistulas in patients with Crohn's disease. The companies were already partners having signed a $432m licensing deal in July 2016 for ex-US rights to Cx601 with double digit royalties due on net sales (DW Issue 73). In December 2017, the CHMP of the EMA gave a positive opinion recommending a marketing authorisation for Cx601, so it was probably a good time for Takeda to make a move.

Licensor Acquired/ Licensee Acquirer	Product / Technology	Deal Type	Headline ($m)
Bioverativ/ Sanofi	Portfolio/ pipeline in haemophilia and other rare blood disorders	Acquisition company	11,600
Juno Therapeutics/ Celgene	CAR-T and TCR therapeutics portfolio incl JCAR017 (liso-cel), CD19-directed CAR-T in pivotal trials for DLBCL	Acquisition company - remaining 90%	9,000
Impact Biomedicines/ Celgene	Fedratinib, highly selective JAK2 kinase inhibitor for myelofibrosis (p3) and polycythemia vera	Acquisition company	7,000
Ablynx/ Sanofi	Nanobody platform + product pipeline; lead product caplacizumab for acquired thrombotic thrombocytopenic purpura (pre-reg)	Acquisition company	4,800
Denali Therapeutics/ Takeda Pharmaceutical	Up to 3 candidates for neurodegenerative diseases based on Denali's ATV platform: ATV:BACE1/Tau (pc), ATV:TREM2 (pc), undisclosed discovery programme	Option, collaboration	1,063
Syros Pharmaceuticals/ Incyte	Gene control platform to identify up to 7 therapeutic targets with a focus in myeloproliferative neoplasms	Collaboration, option	879
Arvinas/ Pfizer	Drug candidates using PROTAC (PROteolysis TArgeting Chimeras) Platform to create small molecules aimed at degrading disease-causing cellular proteins	Collaboration, licence	830
Molecular Partners/ Allergan	Option exercise for 2 DARPins from Allergan's ophthalmology alliance signed in 2012	Option exercise (2 options)	640
TiGenix/ Takeda	Cx601, lead asset, allogeneic expanded adipose-derived stem cells (eASC) locally administered for treatment of perianal fistulas in Crohn's disease (pre reg)	Acquisition company	628
Cascadian Therapeutics/ Seattle Genetics	Lead programme tucatinib, oral, small molecule TKI highly selective for HER2 (p2)	Acquisition company	614
MacroGenics/ Roche	Discover/ develop lead candidate bispecific molecules based on DART platform with Roche's CrossMAb and DutaFab technologies	Collaboration, licence	380
Jiangsu Hengrui Medicine/ TG Therapeutics	BTK inhibitor programme, incl lead candidate TG-1701 (p1) and another BTK inhibitor (pc)	*Licence	350
Addex Therapeutics/ Indivior	ADX71441, selective positive allosteric modulator (PAM) for addiction (pc)	Licence	339
TeneoBio/ TESARO	Multi-specific antibodies for up to 6 undisclosed oncology targets using UniRat® platform and discovery engine TeneoSeek	Collaboration, licence	310
Immunomedics/ Royalty Pharma	Royalty rights to sacituzumab govitecan (IMMU- 132) across all indications	Royalty monetisation, share purchase	250
Agenus/ HealthCare Royalty Partners	Royalties on sales of GSK's QS-21 containing vaccines	Royalty monetisation	230
Jiangsu Hengrui Medicine/ Arcutis	SHR0302, selective JAK inhibitor, for dermatology disorders (currently p2 for RA in China)	**Option, licence	223
Karyopharm Therapeutics/ Biogen	Oral SINE compound KPT-350 (IND ready) + other assets for neurological and neurodegenerative conditions	Licence	217
Teva Pharmaceuticals/ Alder Biopharmaceuticals	Patents covering anti-calcitonin gene-related peptide (CGRP) antibodies and methods - eptinezumab (p3)	† Patent settlement, non-exclusive licence	200
Mallinckrodt/ Baxter International	RECOTHROM® Thrombin topical and PREVELEAK® Surgical Sealant to control bleeding in surgery	Acquisition assets	185

All deals are for worldwide rights unless stated otherwise:
** ex Asia but includes JP*
*** US, EU, JP*
† ex JP, KR

DLBCL = diffuse large B-cell lymphoma
BTK = Bruton's Tyrosine Kinase

Box 1: Summary of Denali/ Takeda key deal terms

- On Effective Date: Takeda pays $155m (upfront cash $40m, preclinical milestone $5m, $110m to purchase ~4.21m Denali shares at $26.10 per share)
- Denali covers costs for pre-IND product development for the 3 targets during option period
- Option period for each target lasts until a product is IND-ready, or ~5 years after target selection, whichever is earlier
- Up to $25m per programme in preclinical milestones ($5m of this paid on the Effective Date)
- $5m for each target for option exercise
- Up to $707.5m in clinical/ regulatory milestones in total
- Up to $75m per product in sales milestones
- On option exercise Denali and Takeda will share 50:50 development/ commercialisation costs and share profits
- In the event of opt out/ termination of cost sharing provisions, Denali to receive royalties in the low-mid teens (or low-high teens if Denali has met a co-funding threshold at opt out)

Teva/ Alder Biopharmaceuticals patent settlement

We have featured Teva in Deal Watch over the last few months but more focused on the company's divestment activities to tackle its debt crisis. In order to resolve a patent dispute relating to a European patent owned by Teva, which was granted in 2013, Alder and Teva entered into a European patent settlement and global licence agreement in January with respect to calcitonin gene-related peptide (CGRP) antibodies. Under the terms of the agreement Alder receives a non-exclusive global licence (excluding Japan and Korea) to Teva's CGRP patent portfolio to develop, manufacture and commercialise eptinezumab, its phase 3 CGRP antibody for the treatment of migraine. In exchange for the licence, Alder will withdraw its appeal at the European Patent Office and pay $25m upfront to Teva. A further payment of $25m is due on first regulatory approval of eptinezumab and there are sales milestones of $75m each at annual sales of $1bn and $2bn. Teva will also receive royalty payments of 5-7% on net sales.

Selling royalties

Royalty monetisation models in which a company sells future royalties in return for non-dilutive capital have been around for quite some time. During January two such deals were announced.

Agenus brought in $230m ($190m cash upfront and up to $40m in milestones) from HealthCare Royalty Partners (HCR) in return for its royalties on sales of GSK's vaccines which contain the adjuvant QS-21 Stimulon. In October 2017 GSK's QS-21 Stimulon herpes zoster vaccine, Shingrix, was approved by the FDA. GSK's malarial vaccine, Mosquirix which also contains Agenus' QS-21 Stimulon, was approved for use by the EMA in 2015.

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.

Agenus will use the income from the HCR deal to redeem a royalty bond it entered into with Oberland Capital in 2015 for a $100m loan; the remaining funds will be used to progress the clinical development of the company's immuno-oncology antibody therapeutics against the checkpoint targets CTLA-4 and PD-1 .

Also in January Immunomedics sold tiered royalty rights on global net sales of its antibody drug conjugate, sacituzumab govitecan, to Royalty Pharma for $175m. In parallel Royalty Pharma also purchased $75m of Immunomedics shares at $17.15 per share (~15% premium). In this transaction the royalty rate ranges from 4.15% on net annual sales of up to $2bn down to 1.75% on net annual sales >$6bn. The incoming cash will be used by Immunomedics to fund its operations into 2020 including to progress development of sacituzumab govitecan in metastatic triple-negative breast cancer (TNBC), advanced urothelial cancer and other cancers.

Winding back to last February (DW Issue 80), Immunomedics announced a licensing agreement with Seattle Genetics for sacituzumab govitecan with a potential headline value of just over $2bn and $250m upfront plus a $57m equity investment, but an activist investor scuppered the deal claiming it undervalued the asset (DW issues 81 and 83). The whole episode resulted in the resignation of the Immunomedics CEO and CSO.

Undeterred Seattle Genetics went on to buy Cascadian Therapeutics at the very end of January for $614m ($10 per share, 69% premium). This acquisition brings tucatinib, an oral tyrosine kinase inhibitor that is highly selective for HER2. Tucatinib is currently being evaluated in a phase 2 pivotal trial in patients with HER2-positive metastatic breast cancer, including patients with or without brain metastases. The acquisition helps to bolster Seattle's late stage pipeline and comes at a lower price tag than last year's aborted licence with Immunomedics.

DEAL WATCH

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