



MEDIUS DEAL WATCH

February 2018

February may be the shortest month, but companies have managed to pack plenty of activity into its 28 days. On top of all the activity, which includes an all-time-high licensing deal, there has also been plenty of rhetoric and rumour, the consequences of which we will no doubt be writing about throughout 2018 and beyond.

Tax Reform: the winners and losers

The US tax reforms announced at the end of 2017 have produced winners and losers among the major pharmaceutical companies, and it looks as though the majority of the majors will get a significant boost to their cash flow from the new tax regime. In particular, Regeneron, AbbVie, Roche and Amgen may find themselves with greater opportunities to invest as a result, whereas AstraZeneca, Teva, Novartis and Allergan may find themselves constrained for investment. Of course, every constraint has a flip side – the strategic as well as commercial value of tactical divestments may offer opportunities for companies to acquire or license assets from these companies, as they seek to balance their cash flow.



So, what will companies be doing with (or for) their additional cash flow? In January (DW Issue 91) we noted a bumper month for acquisitions. Of the Top 10 deals, 6 were acquisitions, representing 91% by headline value. A survey by Biotech and Money published in February 2018 found that investors expect the activity in mergers and acquisitions in biotechnology to increase, driven by tax breaks, repatriation of offshore cash and the continuing appetite for larger companies to gain access to innovative technologies through acquisition of early-stage companies. In February's Top 10 deals however, this trend has not been borne out. Not only has the overall value of the Top 10 declined, by 57% from \$37bn to \$16bn, but only 3 of the Top 10 are acquisitions, and these represent only 19% of the total, by headline value.

Table 1: Leading Pharma Companies' Projected Change in Tax Rates

Company	Projected Change in Tax Rate	Projected 2018 Tax Rate
AstraZeneca	+2-6%	16-20%
Teva	+1.7 – 3.7%	17-19%
Novartis	+1.9%	16%
Allergan	+1.4%	14%
Sanofi	-1.5%	22%
GSK	-1 – 2%	19-20%
Eli Lilly	-2.5%	18%
Pfizer	-3%	17%
Gilead	-1.5 – 3.5%	21-23%
Amgen	-3 – 4%	14-15%
Roche	-3 – 6.6%	“the low 20s”
AbbVie	-9.9%	9%
Regeneron	-8 – 12%	15-19%

Source: Fierce Pharma

Top Dollar

Much of the change in value is due to some eye-watering amounts paid for collaboration and licences, notably the deal between BMS and Nektar. In contrast to the usual “biodollar” inflation of deal values, BMS paid over half of the deal’s value in upfront money.

Table 2: Upfront payments in Top 20 Licensing Deals; February 2018

Licensor	Licensee	Product Stage	Upfront (\$) / assured payments	Headline (\$m)	Upfront as % of Headline
Nektar Therapeutics	BMS	Phase 1/2	\$1bn cash \$850m equity	\$3.63bn	51%
Wave Life Sciences	Takeda	Phase 1b/2a	\$110m cash \$60m equity \$60m over next 4 years	\$2.06bn	11%
Sangamo Therapeutics	Kite Pharma	Platform	\$150m	\$3.16bn	5%
Theravance Biopharma	Janssen Biotech	Phase 1	\$100m	\$1bn	10%
Voyager Therapeutics	AbbVie	Platform	\$69m	\$1.05bn	7%
Pieris	Seattle Genetics	Platform	\$30m	\$1.23bn	2%
Poxel	Roivant Sciences	Phase 2 completed	\$35m cash \$15m equity	\$660m	8%
Polyphor	Santhera	Phase 1	\$7m (in Santhera shares)	\$136m	5%
Mologen	Oncologie	Phase 3	\$3.7m in cash \$2.45m in equity	\$129m	5%

Sources: Press releases



BMS – Nektar Deal: The Details

Given the extraordinarily high value of Nektar's agreement with BMS it is worth looking at it in some detail.

The product is NKTR-214, a CD122-biased agonist, which stimulates endogenous tumour-infiltrating lymphocytes (TILs) by targeting the CD122 specific receptors on the surface of the T cells and natural killer (NK) cells.

Preclinical studies indicated concentrations of the product in tumour cells that enable an antibody-like dosing regimen. The single agent Phase 1 trial demonstrated that the product increases PD-1 expression on CD4+ and CD8+ T cells in the blood and tumour and, in September 2016 BMS initiated a clinical collaboration with Nektar for a Phase 1/2 trial of NKTR-214 with BMS's checkpoint inhibitor the anti-PD-1 antibody Opdivo (nivolumab). Citing promising early data from this study (PIVOT) BMS has now invested \$1.85bn upfront for the global development and commercialisation collaboration. Key aspects of the deal include:

- ◇ Payment of \$1bn in cash and purchase of 8.28m shares in Nektar at \$102.60 per share (\$850m)
- ◇ Global profits on NKTR-214 to be shared between Nektar and BMS at 65:35 respectively
- ◇ Joint clinical development plan for combinations of NKTR-214 with Opdivo® and Opdivo® / Yervoy® combinations in 20 indications for 9 tumours
- ◇ Exclusive rights for BMS in 20 indications for 9 tumours
- ◇ Nektar to book worldwide revenue for NKTR-214
- ◇ Nektar retains rights to develop NKTR-214 with other anti-cancer agents

Focusing on the last point, Nektar has already entered a separate research collaboration, with Takeda in May 2017, to explore the combination of NKTR-214 with 5 of Takeda's oncology compounds, and it is in a Phase 1/2 study in combination with Roche's Tecentriq® and Merck & Co's Keytruda® indicating that the compound is likely to be the gift that keeps on giving. Not surprisingly Nektar's share price has more than quadrupled over the last four months, from \$23.37 at the start of November 2017 to \$100.29 at the start of March.

US Drug Prices – When will actions speak louder than words?

Product forecasts are the key element in negotiating and agreeing the financial terms of a deal. Having a forecast based on clear assumptions is the basis for two companies harmonising their expectations for the product and this underpins the common understandings which are essential for effective alliance management after the deal is signed. Forecasts are, of course, developed using assumptions on several factors; broadly

- ◇ Patient numbers
- ◇ Competitive environment / market share
- ◇ Timing
- ◇ Probability of success
- ◇ Price

All of these are subject to unknowns and uncertainties and forecasts must, by their nature, take into account these variables. Of these five, the one that pharmaceutical companies have the most flexibility and control over is the final one: price. It also feeds directly into the bottom line, which is why the recent threats to US drug pricing have made companies, and their investors, nervous.

Throughout his election campaign Trump repeatedly promised to bring down pharmaceutical prices. Nothing happened in 2017 – perhaps unsurprisingly – except more anti-drug company rhetoric, including characterising the drug companies in mid-October as “getting away with murder”, a comment which caused a temporary wobble in drug company share prices. On 31st January, in his “State of the Union” address, Trump returned to the topic, announcing that he will “make the fixing the injustice of high drug prices one of our top priorities”. Again, the leading companies’ share prices wobbled. However, the confirmation of the appointment of an industry insider, Alex Azar as Secretary of Health and Human Services, together with his announcement that dealing with the opioid crisis is a priority, has stabilised the issue, for the moment.



The activity more likely to have an impact on drug prices is the announcement by three of the US’s most high-profile companies: Amazon, JPMorgan Chase and Berkshire Hathaway that they are setting up their own insurance programmes for employees. Although few details have been released, the expectations are that such an organisation, and any others that follow their lead, will have significant purchasing power and that drug prices will be in their sights. And it’s not just rhetoric and bluster, but a genuine initiative by three of the most powerful and respected CEOs in the US. So, in the already complex field of forecasting pharmaceutical sales one of the key variables just added more uncertainty, to add to all the others.

The US government may get in one blow to the industry when the Senate’s budget deal brings forward the increased drug companies’ contributions to the Part D “donut hole” from 50% to 70% from 2020 to 2019. The donut hole is the mechanism whereby consumers foot the bill for their prescription costs under Medicare when annual costs go above what their insurers will pay but are still below the “catastrophic coverage” threshold. The budget deal will shift the burden from the insurers to the drug companies, without benefit to the patient, and companies with products for chronic diseases in the elderly, such as diabetes, are likely to be hardest hit.

“The FAANGs are out”

Or, rather, they are in. The FAANGs: Facebook, Amazon, Apple, Netflix & Google, not content with occupying our lives in their chosen segments, are also targeting our health, and several announcements this month show that the growing importance of electronics and digital management is increasingly being appreciated, and purchased, by the medical industry.



Roche has announced that it will acquire Flatiron Health, a company backed by Alphabet, the parent company of Google. Flatiron has an electronic medical record system that analyses the records of patients having treatment for cancer and makes recommendations for better treatments. Roche led the \$175m fundraising in Flatiron in 2016, and has now purchased the remaining shares for \$1.9bn.

Deal Watch Table - February 2018

Licensor Acquired/ Licensee Acquirer	Product / Technology	Deal Type	Headline (\$m)
Nektar / BMS	NKTR-214 (CD122-biased agonist) in combination with Opdivo and Yervoy in 9 tumours and 20 indications	Collaboration, licence	3,630
Sangamo / Kite Pharma	ZFN (zinc finger nuclease) platform gene modifying technology for ex vivo cell therapies	Collaboration, licence	3,160
Wave Life Sciences / Takeda	WVE-120101, -120102, -397201; nucleic acid therapies for multiple neuromuscular disorders	Collaboration, licence	2,060
Flatiron Health / Roche	Electronic medical records for optimising cancer treatments	Acquisition	1,900
Pieris / Seattle Genetics	Agonistic costimulatory Anticalin® proteins for antibody-drug conjugates	Collaboration, licence	1,230
Voyager Therapeutics / AbbVie Biotechnology	AAV gene therapy for delivery of tau-directed MAbs to the brain to treat dementia, including Alzheimer's	Collaboration, option	1,050
Theravance Biopharma / Janssen Biotech	TD-1473, oral pan-Janus (JAK) inhibitor in inflammatory intestinal diseases	Collaboration, licence	1,000
MPI Research / Charles River Laboratories	Non-clinical CRO; testing services to biopharmaceutical and medical device companies	Acquisition	800
Poxel / Roivant Sciences	Imeglimin (tetrahydrotriazine-containing oral anti-diabetic / glimin) for type 2 diabetes	*Collaboration, licence	660
Viralytics / Merck & Co	Cavatak®; CVA-21, oncolytic Coxsackievirus type A21 for oncolytic immunotherapy, including Keytruda® combinations	Acquisition	397
TetraGenetics / Undisclosed	Five additional programmes to use TetraExpress™ platform for recombinant protein production	Collaboration, licence	300
TandemLife / LivaNova	ExtraCorporeal Life Support and percutaneous Mechanical Circulatory Support	Acquisition	250
ImmunoQure / Servier	Human interferon-α autoantibody for APS-1, systemic lupus erythematosus and Sjögren's syndrome	Collaboration, licence	204
Strategic Science Tech. / Daré Bioscience	SST-6007; 5% topical sildenafil for female sexual arousal disorder	Collaboration, licence	160
Polyphor / Santhera	POL6014; selective inhibitor of human neutrophil elastase for cystic fibrosis and other neutrophilic pulmonary disorders	Licence: development & commercialisation	136
Mologen / Oncologie	Leflotolimod, TLR9 agonist for development in solid tumours	** Collaboration, licence	129
Oraxion Therapeutics / Undisclosed	ORX-301 for Niemann-Pick Type C disorder and Focal Segmental Glomerulosclerosis	Option	125
Oxford Biomedica / Bioverativ	LentiVector Enabled technology for haemophilia	Collaboration, licence	105
Avid Bioservices / Oncologie	Phosphatidylserine (PS)-targeting programme, including bavituxumab, an anti-cancer immunomodulatory MAb	Licence	103
Shanghai Tech University / Jing Medicine Technology	Novel small molecule anti-cancer drugs	Collaboration, licence	100

All deals are for worldwide rights unless stated otherwise:

* US, Europe, certain East & Southeast Asia countries

** Global co-development; licence for China, Hong Kong, Macao, Taiwan, Singapore



Anticipated benefits of the acquisition include using the data collected from cancer patients to improve the personalised treatments for patients, to improve Roche's research and trials and potentially to provide real-world evidence in support of product prices.

The importance of electronic medical records is also of note in Apple's announcement in late January that it is working with 12 US hospitals to aggregate health records with patient-generated records in a feature called Health Records. This feature will enable patients to access information, such as test results, on their iPhones. In August 2016 Apple acquired Glimpse, the health data company with artificial intelligence technology to read, code and standardise medical records and this launch (at the beta stage) is the next important step.

If companies or countries seek a model on how to optimise electronic health records, the system introduced by Estonia, which covers the entire population, might be worth a look. Estonia (population 1.3m) has the most advanced digital society system in the world with a "once only" policy; data entered into one silo in the system is accessible across the entire system, underpinned by a secure data platform, X-Road.

Amazon, in addition to the insurance initiative mentioned above, has already entered the health care field with its Basic Care range, launched in August 2017 using products from Perrigo, the Michigan-based manufacturer of OTC and generic pharmaceuticals.

This month there has been one major announcement from a non-FAANG company of an initiative in e-health. AstraZeneca has increased its activities in China through strategic partnerships with Alibaba and Tencent. The agreement with Alibaba, the Chinese e-commerce company, aims to harness Alibaba's artificial intelligence and data collection to improve disease management. And the arrangement with Tencent is aimed at addressing the problem of sales of counterfeit medicine.



Rumours Abound

Rumour is, according to Shakespeare, "a blunt monster with uncounted heads". And this month the monster is busy. According to the Wall Street Journal, Acorda is exploring a potential sale, with Biogen and UCB mentioned as likely purchasers. Now that the FDA has accepted the filing of the NDA for Inbrija (levodopa for inhalation) for Parkinson's Disease, rumour is now suggesting several other potential purchasers, including Roche and AbbVie, who are already active in this condition. CNBC reported that Walgreens had ended takeover talks with the wholesaler AmerisourceBergen (in which it holds a 26% stake) which resulted in a fall in AmerisourceBergen's share price of 6% - from \$101 to \$95.

In September 2017 Merck KGaA announced that it was considering strategic options for its consumer health business, including its sale. Nestlé was reported to be the leading contender, but in early February Reuters reported that Nestlé had jibbed at the valuation and was no longer in the running.

Meanwhile, it was noted by Bloomberg that Pfizer's consumer health division, also under consideration for a transaction, has only two companies which have expressed interest: GSK and Reckitt Benckiser. The Financial Times noted that Sanofi's generic division, which has been on the block for a year, appears to be approaching a sale to a private equity fund. Finally, the planned acquisition of the specialty generics company, Akorn, by Fresenius, announced in April 2017 (DW Issue 82) may be at risk of not going ahead because of alleged breaches of FDA data integrity requirements. All these rumours suggest that the interest from pharmaceutical companies for "non-core" assets is reducing, which may be good news for companies seeking funds for "classical" patented novel pharmaceutical assets.

It's been a bad month for Novartis, which has been accused of bribing politicians in Greece. The Greek parliament has voted to investigate allegations that 10 senior politicians, including the former health minister and two former prime ministers, illegally accepted €50m over the 10 years to 2015.

The purchase by Teva of Allergan's generics division in 2015 for \$40bn is approaching closure with an agreement achieved over the dispute about the working capital that was part of the deal; this has finally been settled for a payment by Allergan to Teva of \$700m (\$387.4m net of tax). Allergan is continuing to sell the shares it acquired in Teva as part of the deal and announced that it plans to sell its remaining position in 2018.



Catharine Staughton

Catharine supports Medius clients in various aspects of business development, particularly in product forecasting, the financial structuring of licensing deals and all aspects of finance. Catharine gained her financial experience at Robert Fleming (now part of JP Morgan), and her business development experience at Medeva and Antisoma.

Deal Watch data are available to support your benchmarking and valuations.

Please contact us for details about our Client specific services. www.medius-associates.com



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