



MEDIUS DEAL WATCH

November 2015

Strategic business expansion or financial engineering?

This month, at long last Pfizer has found a willing acquisition target that may provide the tax inversion it has been desperate to achieve since its first bid for AstraZeneca made in January last year.

The \$160bn takeover of Allergan will create the largest pharmaceutical company in the world with sales of \$64bn compared to the second ranked pharmaceutical company, Novartis, with \$47bn. Pfizer shareholders will receive 1 share of the combined company (with the option to receive cash in lieu of combined company shares) and the Allergan shareholders will receive 11.3 shares for each Allergan share. Pfizer shareholders will own around 56% of the combined company. The deal represents a 30% premium on the Allergan share price in October. The combined company will have a tax domicile in Ireland and as a result Pfizer will reduce its tax rate from around 25% to 17-18%. In addition Pfizer expects to make \$2bn of synergy savings.



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Fundamentally, this deal is about the financial gain from financial engineering and not the expansion and development of a pharmaceutical business. Allergan is a company that has been built on a series of acquisitions of mature products and companies and has a low R&D spend at \$1bn in 2014 (8% of sales) and a CEO who, according to a Reuters report, believes that drug discovery is not required to play in the big league. In contrast Pfizer spent \$8bn on R&D in 2014. The merger is expected to close in the second half of 2016 and both companies have the right to terminate under specified circumstances with termination fees of up to \$3.5bn. The termination fee may become a reality if the US politicians succeed in changing the rules on tax inversions soon.

Double dealing

Looking at the other deals announced in November, for once, the top half of the table is not simply all acquisitions, with four licensing deals reporting headline values of >\$900m of which two were with the same company, Hanmi Pharmaceutical, a Korean public company.

Firstly on 5th November Hanmi and Sanofi signed a worldwide licence to develop a portfolio of long acting diabetes products. Needing to build up its pipeline, Sanofi paid €400m (approx. \$437m) upfront in a deal which has the potential to deliver €3.5bn (approx. \$3.8bn) in R&D and sales milestones with double digit royalties on sales. Included in the package are three products: a weekly insulin, a fixed weekly dose combination of GLP-1-RA/insulin and epeglenatide, a long acting glucagon like peptide-1 receptor agonist. Hanmi has retained an exclusive option to co-commercialise the products in South Korea and China. Only a matter of days later, Hanmi was back in the headlines with another announcement, this time for a deal with Janssen Pharmaceuticals. Again this was a global deal (excluding South Korea and China), and also in the diabetes space, for oxyntomodulin based therapies which include HM12525A (LAPSGLP/GCG), a GLP-1/glucagon receptor dual agonist. It is planned to take HM12525A into phase 2 studies during 2016. The upfront payment is \$105m with a further possible \$810m in milestones and, as for the Sanofi deal, double digit royalties on a tiered basis.

Overall 2015 has been a very busy year for Hanmi which in March closed a \$690m deal with Lilly for a phase 1 BTK-inhibitor in autoimmune indications and also in July finalised a \$730m exclusive deal with Boehringer Ingelheim for HM61713, an orally active third generation EGFR agent in small cell lung cancer (SCLC).



Licensor Acquired / Licensee Acquirer	Deal type	Product /technology	Headline \$m
Allergan / Pfizer	Acquisition - company	Creates a new no 1 pharma company with sales of \$64bn (tax inversion)	160,000
Dyax Corporation / Shire	Acquisition - company	Includes KALBITOR marketed for acute attacks of HAE + lead programme, DX-2930, p3-ready mAb targeting plasma kallikrein	6,546
Hanmi Pharmaceutical / Sanofi	Licence	3 diabetes products 1) efpeglenatide, long-acting GLP-1 agonist 2) weekly insulin 3) fixed-dosed weekly GLP-1-RA/ insulin combo. Option to co-commercialise in Korea, China	4,259
Mindray Medical / Excelsior Union Solid Union	Acquisition - company	Portfolio of marketed medical device products	3,300
ZS Pharma / AstraZeneca	Acquisition - company	Lead product ZS-9, potassium-binding compounds for hyperkalaemia in pre-registration	2,700
Cardioxyl Pharmaceuticals / Bristol-Myers Squibb	Acquisition - company	Lead asset: p2 CXL-1427, nitroxyl (HNO) donor (prodrug) - iv treatment for acute decompensated heart failure (ADHF)	2,075
Lexicon Pharmaceuticals / Sanofi	Collaboration, licence	Sotagliflozin, p3 oral dual inhibitor of sodium-glucose cotransporters 1 and 2 (SGLT-1 and SGLT-2). Option to US co-promote	1,700
BioNTech / Sanofi	Collaboration, licence - multi yr	Discover/ develop up to 5 cancer immunotherapies, each a synthetic mRNA mixture. Option to co-develop/co-commercialise EU/US	1,560
Hanmi Pharmaceutical / Janssen Pharmaceuticals	Licence	Oxyntomodulin-based therapies including HM12525A * in p2	915
Astellas Pharma / LEO Pharma	Acquisition – assets	Marketed global dermatology portfolio	724
Array BioPharma / Pierre Fabre	Licence collaboration	Binimetinib, a MEK inhibitor, and encorafenib, a p3 BRAF inhibitor **	455
Heptares / Teva	Licence drug-discovery agreement	Small molecule calcitonin gene-related peptide (CGRP) antagonists for migraine	410
Ablynx / Novo Nordisk	Discovery collaboration, licence	Multi specific Nanobody® drug candidates in undisclosed TA with option to expand to second Nanobody programme. Option to expand to 2nd programme	399.5
Poli Group / Almirall	Acquisition – company	Dermatology focused R&D company with formulation technology and 3 clinical stage projects	386
AstraZeneca / Perrigo	Acquisition – asset	Entocort® (budesonide) marketed for mild to moderate Crohn's disease ***	380
Ocata Therapeutics / Astellas Pharma Laurel	Acquisition – company	Regenerative medicine pipeline focus on ophthalmology, inc products for Stargardt's macular degeneration, dry AMD, and myopic macular degeneration, p2	379
Collectis / Servier	Option exercise	UCART19, CAR-T allogeneic immunotherapy being tested for chronic lymphocytic leukaemia and acute lymphoblastic leukaemia. P1 ready, option to license	338.2
SurgiQuest / Conmed Corporation	Majority acquisition	AirSeal® System, integrated access management technology for use in laparoscopic and robotic procedures	265
DenTek Oral Care / Prestige Brands Holdings	Acquisition – company	Marketed oral care products	225
Heptares / Pfizer	Strategic discovery collaboration	New therapeutics against up to 10 GPCR targets across multiple therapeutic areas	222+
Interprotein / Ipsen	Research collaboration, option	Therapeutic peptide discovery using Ipsen's peptide expertise and Interprotein's Protein-Protein Interaction (PPI) and helix-loop-helix-peptide (HLHP) technology. Option to license	175
Idera Pharmaceuticals / GlaxoSmithKline	Licence, collaboration	Antisense platform for selected targets in renal disease	100

All deals global unless otherwise stated: *excluding Korea China **excluding US, Canada, Japan, Korea and Israel ***US

Abbreviations: HAE, Hereditary angioedema

Partnering



Strategy

Valuation



Due Diligence

Negotiation



Benchmarking

“...deal covering up to five cancer immunotherapies..”

Sanofi triple deals

As well as Hanmi holding the headlines, Sanofi was busy closing multiple deals; another in diabetes and one in oncology and an open R&D deal with AstraZeneca. Staying with diabetes, so strategically important, Sanofi put in place a collaboration with Lexicon Pharmaceuticals for sotagliflozin (LX4211), an oral treatment for type 1 and type 2 diabetes. Sotagliflozin is an oral dual inhibitor of sodium-glucose cotransporters type 1 and 2 (SGLT1 & SGLT2) which are responsible for glucose reabsorption by the GI tract and kidney respectively. Enrolment has started for phase 3 studies in type 1 diabetes.

Under the agreement Lexicon receives an upfront payment of \$300m with a further \$1.4bn in development, regulatory and sales milestones. Almost becoming the norm, the royalties were reported as being rising double-digit on net sales. Lexicon will continue to lead the development programme and has retained commercial rights to type 1 diabetes in the USA.

Sanofi's other major investment in November and in the top tier of licensing deals this month was its collaboration with BioNTech. A package deal covering up to five cancer immunotherapies, the headline value was \$1.56bn with an upfront fee of \$60m; the subsequent milestone terms per product could reach in excess of \$300m. Sanofi will gain access to BioNTech's mRNA formulation technology to generate new cancer immunotherapies. A more innovative deal with no money attached, was the open innovation deal between Sanofi and AstraZeneca who have agreed to a direct exchange of 210,000 compounds from their respective proprietary compound libraries. Both companies benefit from an increased range of compounds “as the starting point in the search for new small-molecule medicines”.

It is not surprising that Sanofi has accelerated its deal making activity because its third quarter 2015 sales growth was only 3.4% and business operating income declined slightly. The low growth was driven by a 6.6% decline in diabetes sales. A few days after the results were published the company set out a ‘strategic road map’ that showed sales growth of 3 - 4% over the next 5 years and a number of actions to improve results such as increased spend on R&D, cost savings and a review of strategic options (in other words ‘divestment’) for its animal health and European generics businesses.



The trend for doing double deals in quick succession was not limited to the major players such as Hanmi, Sanofi and AstraZeneca as Heptares and Astellas also delivered on the double. Heptares reported two collaborations, firstly with Teva and also with Pfizer, the deals being announced just a few days apart. Paying \$10m upfront with a possible further \$400m in milestones, Teva has secured exclusive global rights to small molecule calcitonin gene related peptide agonists for the treatment of migraine. Next up for Heptares was the drug discovery deal with Pfizer where Heptares is using its GPCR structure guided platform to discover novel agents to selected GPCR targets. The upfront was not disclosed but the subsequent payments are for up to \$189m per target with tiered royalties on commercial sales. In addition, Pfizer is making an equity investment through its Japanese subsidiary purchasing \$33m of new shares at a 25% premium representing approx. 3% of the extended share capital.



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.

Pharma streamlining - sell and buy

Astellas was busy, both buying and selling, acquiring Ocata Therapeutics and divesting a global portfolio of derma products to Leo. Valued at €675m (approx. \$724m with an estimated sales multiple of 3) Astellas' divestment is the biggest transaction in Leo Pharma's history and brings with it stronger access to markets such as Russia and China. The deal includes Protopic (tacrolimus) for severe eczema treatment, skin creams Locoid and Locobase and acne therapy Zineryt (erythromycin/zinc acetate). Japanese Protopic rights are excluded from the deal; Protopic is one of Astellas mid-tier products with sales of ¥21.7bn (\$176m) last year, down from ¥25bn in the prior year following US patent expiry. The deal does not include any manufacturing facilities and brings in the cash for other opportunities such as the Ocata acquisition. Ocata operates in the field of regenerative medicine and is being acquired through Laurel Acquisition (a subsidiary of Astellas). The offer is \$8.50 cash per share where Laurel is merged into Ocata giving a headline value of \$379m. The acquisition brings an ophthalmology focus with products for Stargardt's macular degeneration, dry AMD, and myopic macular degeneration.

Also doing the double and buying and selling AstraZeneca continued its busy deal profile with the acquisition of ZS Pharma and the divestment in the US of Entocort. Paying \$90 per share (headline value \$2.7bn) in acquiring ZS Pharma, AstraZeneca gains access to ZS-9, a possible best in class product for hyperkalaemia which is under FDA review. Estimated global peak sales for ZS-9 are in excess of \$1bn. So selling off the US rights for Entocort (budesonide), in the non-strategic field of mild to moderate Crohn's disease seems like small beer but the \$380m paid by Perrigo will help balance the books! Perrigo may have got a better deal from AstraZeneca than Tillotts (subsidiary of Zeria) who bought non-US rights to Entocort in July. Perrigo paid a multiple of 3.2x sales for the US rights whereas Tillotts paid 4.1x sales.

Being talked about still in relation to Baxalta has not deterred Shire from pressing ahead to consolidate its rare disease portfolio with the acquisition of Dyax for a headline value of \$6.5bn, paying \$37.30 cash per share (approx \$5.9bn) with additional value through CVRs of \$4 per share, which represents a further \$646m on approval of DX-2930 in hereditary angioedema (HAE). DX-2930 is expected to enter phase 3 studies by the end of the year and has received Fast Track, Breakthrough Therapy and Orphan Drug designations. Given that Shire's Cinryze is already approved in HAE, It will be interesting to see what the regulators say on the anti-competition front.

So as we approach the year end for 2015 the fantastic deal flow that kicked off in 2014 shows no sign of abating and we can look forward to the last minute rush in December as everyone tries to close before the year end.

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