MEDIUS DEAL WATCH

June 2015

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The month of June saw a mixture of deals covering a wide range of therapeutic areas, including aesthetic medicine, CNS, diabetes, respiratory, vaccines and anti-infectives, oncology and autoimmune diseases. Of our top 20 transactions for the month, seven were acquisitions of companies, business units or assets and the remainder were partnership deals including the collaboration between Anokion and Astellas to form a new company, Kanyos Bio, to exploit Anokion's technology for the development of therapeutics for certain autoimmune indications. Five of the partnerships have various option arrangements built into their structures.

The business of aesthetics

The largest deal of the month was Allergan's acquisition of Kythera Biopharmaceuticals for $2.1bn, payable as 80% in cash and 20% in new Allergan shares issued to the Kythera shareholders. The price at $75 per share represents an approximate 24% premium over the Kythera share price the day before the announcement. Kythera has a portfolio of novel prescription products for the aesthetic medicine market which complement Allergan's facial aesthetics portfolio, including Botox.

Kythera's lead asset is KYBELLA, previously known as ATX-101, which is an FDA approved, proprietary injectable formulation of a synthetic version of deoxycholic acid for the reduction of submental fat (double chin). Deoxycholic acid is a naturally occurring molecule in the body that aids in the breakdown and absorption of dietary fat.

When KYBELLA is injected into subcutaneous fat, it causes the destruction of fat cells and, once destroyed, these cells cannot store or accumulate fat. The product was approved by the FDA in April 2015 and regulatory submissions have been made in Switzerland, Canada and Australia with other markets to follow.

In addition to KYBELLA, Allergan also gains access to setipiprant (KYTH-105), which is a selective oral antagonist of the prostaglandin D2 (PGD2) receptor under investigation for male hair loss. Kythera in-licensed the IP covering setipiprant from Actelion and the University of Pennsylvania in March 2015. The setipiprant hair loss programme is essentially drug repurposing. The molecule has been tested in multiple clinical trials as a potential treatment for allergic inflammation, including a phase 3 study in seasonal allergic rhinitis patients, and overall has a safety database of over 1,000 subjects. Setipiprant is progressing towards an IND with plans to initiate a proof of concept study to establish its efficacy in male subjects with androgenic alopecia.

Immune modulators in cancer and beyond

Both Juno Therapeutics and Celgene have had a busy month in forming alliances in the immunotherapy area. Early in the month Juno acquired X-BODY for $44m comprising $21m in cash and 439,265 shares of Juno stock, with certain research, clinical, regulatory and commercialisation milestones downstream. The X-BODY acquisition gives Juno access to an antibody discovery platform that allows rapid selection of fully human antibodies, even against difficult targets.

Near the close of the month, Juno and Celgene announced a $1bn, 10-year collaboration to develop novel immunotherapies for the treatment of cancer and autoimmune diseases focused on T cell therapeutic strategies, and initially on Chimeric Antigen Receptor Technology (CAR-T) and T Cell Receptor (TCR) technologies. Celgene paid Juno $150m upfront and will pay $846m to purchase 9.1 million shares of Juno's common stock (about 10% of the company) at $93 per share (a share price premium of 100% compared to the prior closing price). During the period of the collaboration and under certain conditions Celgene can increase its stake in Juno so it could own up to 30% of Juno's common stock.

As we have seen previously for Celgene alliances, the deal structure contains a complex set of multiple elements and programmes, with deployment of options in both directions. In summary:

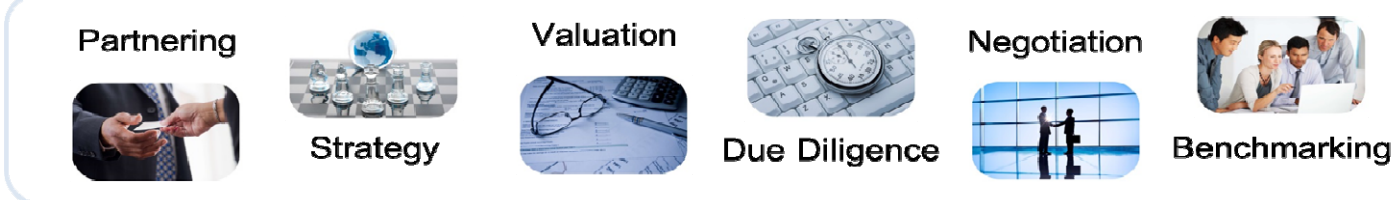
- Celgene has the option to be commercialisation partner for Juno's existing oncology and cell therapy autoimmune candidates, including Juno's CD19 and CD22 CAR-T product candidates.
- For Juno-originated programmes co-developed under the collaboration, Juno will be responsible for R&D and will retain commercialisation rights in North America, whilst Celgene will be responsible for development and commercialisation in the rest of the world, and will pay Juno a royalty on sales in those territories.
- Celgene has an option to co-promote two selected Juno-originated programmes, excluding CD19 and CD22, except in China, and may select a third programme.
- Juno will have the option to enter into a co-development/ co-commercialisation agreement for certain Celgene-originated candidates that target T cells and, if executed, the partners will share global costs and profits, 70% Celgene:30% Juno; Celgene will lead global development and commercialisation with Juno having a co-promotion option for the US and certain EU territories.

Licensor Acquired / Licensee Acquiror	Product / Technology	Deal Type	H'line ($m)
Kythera Biopharmaceuticals/ Allergan	Rx aesthetic medicine products - incl KYBELLA for double chin (FDA approved)	Acquisition - company	2,100
Welch Allyn/ Hill-Rom Holdings	Medical diagnostic equipment manufacturer	Acquisition - company	2,050
Bio-Reference Laboratories/ OPKO Health	US-based full service clinical laboratory incl genomics and genetic sequencing	Acquisition - company	1,470
Halozyme Therapeutics/ AbbVie	ENHANZE platform technology to improve sc delivery (up to 9 targets)	Collaboration, licence	1,193
Parion Sciences/ Vertex Therapeutics	Epithelial sodium channel (ENaC) inhibitors, incl P -1037 (p2) and P-1055 in CF and other pulmonary diseases	Collaboration, licence	1,170
Bayer Diabetes Care/ Panasonic Healthcare	Diabetes Care business - blood glucose monitoring product portfolio	Acquisition - business	1,153
Juno Therapeutics/ Celgene Corporation	10-yr immunotherapy collaboration - CAR-T and T Cell Receptor (TCR) technologies; incl Juno's CD19 and CD22 directed CAR-T candidates	Collaboration	1,000
Anokion/ Astellas Pharma	Formation of Kanyos Bio based on Anokion's technology for induction of antigen-specific immune tolerance	NewCo formation, collaboration	760
Unum Therapeutics/ Seattle Genetics	Antibody-coupled T-cell receptor technology for 2 antibodies (platform)	Licence, collaboration - co-dev/ co-comm	615
Almac Discovery/ Genentech	Small molecule inhibitors of a ubiquitin specific protease (USP) target (discovery)	Licence, collaboration	364
Spinifex Pharmaceuticals/ Novartis	Lead candidate EMA401 - oral treatment for chronic pain, particularly neuropathic pain (p2)	Acquisition - company	200
Eolas Therapeutics/ AstraZeneca	Orexin-1 Receptor Antagonist (EORA) programme for smoking cessation and other indications (preclinical)	Licence, collaboration	145
*Taiho Pharmaceutical/ Servier	TAS-102, oral combination of anticancer drugs (trifluridine + tipiracil hydrochloride) (approved JP, pre-reg US, EU)	Licence	130
GlaxoSmithKline/ Pfizer	Meningitis vaccines Nimenrix and Mencevax (marketed)	Acquisition - assets	130
Lycera Corporation/ Celgene Corporation	Orally bioavailable RORgamma agonists for ex vivo use + lead programme, LYC-30937 (oral gut-directed ATPase modulator for IBD, p1)	Collaboration, options to acquire and license	105
Boston Children's Hospital/ Proteus/ Grünenthal	Neosaxitoxin, novel anaesthetic for local anaesthesia and post-op pain management	Collaboration, licence	85
**BioCryst Pharmaceuticals/ CSL	RAPIVAB (peramivir injection) for the treatment of influenza (marketed)	Licence	46
X-Body/ Juno Therapeutics	Antibody discovery technology	Acquisition - company	44
Microchips Biotech/ Teva	Implantable electronic drug delivery device for Teva drugs	Collaboration	35
Kode Biotech/ Agalimmune	Function-Spacer-Lipid (FSL) cell surface membrane modification technology	Licence	31

All deals are worldwide unless otherwise noted – see below:

* EU and other countries (ex North America, Mexico, JP/Asia)

** excluding Japan, South Korea, Taiwan, Israel



Celgene's second deal of the month was with US-based Lycera, a company developing small molecule immunomodulatory therapeutics for the treatment of autoimmune diseases and cancer. In return for $82.5m upfront, Celgene gains an option to license Lycera's portfolio of ex vivo RORgamma agonist compounds. RORgamma is a master control switch of immune system activation and ex vivo treatment with RORgamma agonists has been shown to enhance the therapeutic benefit of adoptive T-cell therapy by improving both immune cell persistence and activation. In addition to the upfront payment, Lycera could receive payments of $22.5m in the near term associated with the ex vivo licence option rights.

As part of the collaboration the companies will also progress clinical development of Lycera's LYC-30937, a phase 1 stage, oral gut-directed ATPase modulator, which is in development for the treatment of inflammatory bowel disease (IBD). As referenced above Celgene has become notable for its creative deal structuring and options to acquire its partners have been a common feature in recent transactions. The Lycera deal follows this pattern with Celgene obtaining the exclusive right to acquire it partner at the end of the option period or on achievement by Lycera of pre-specified clinical milestones. Financial terms for exercising the option to acquire have not been disclosed.

Platform technologies

Usually deals for drug delivery and formulation technologies are of lower value than transactions involving novel molecules or platforms for new molecule discovery at a comparable stage. The Halozyme/ AbbVie deal for Halozyme's ENHANZE technology certainly has an impressive headline at nearly $1.2bn, with an initial $23m upfront. This deal covers up to nine AbbVie targets with milestones of around $130m per target payable based on development, regulatory and sales-based events plus tiered royalties.

The ENHANZE technology is based on a proprietary recombinant human hyaluronidase enzyme (rHuPH20) that temporarily degrades hyaluronan, a chain of natural sugars in the body, to aid in the dispersion and absorption of injected therapeutic drugs. The technology allows the volume of biologics that can be administered by subcutaneous (sc) injection to be increased. This means that some biologics, that could only previously be administered by intravenous (iv) infusion, can be delivered by sc injection. Furthermore biologics already delivered by sc injection may require fewer injections.

Halozyme has several case studies to validate its technology and these illustrate the greater convenience and associated reduction in overall healthcare costs that are possible. Roche has two products approved in Europe, Herceptin SC and MabThera SC, and Baxter has HyQvia approved in the US and EU, which utilise the Halozyme approach. Herceptin SC and MabThera SC can be administered in approximately 5 minutes by sc injection compared to 0.5-1.5 hours and 2.5 hours, respectively, that was required for the iv infusion for the original formulations.

In a rather different approach to drug delivery, Teva has entered into a partnership with Microchips Biotech to access the latter's implantable drug delivery device for chronic drug therapy, initially in one selected disease area. Teva is paying $35m upfront as an equity investment and technology access fee. Further financial terms were not disclosed. The Microchips Biotech electronic device contains microchip arrays that can store hundreds of drug doses for periods ranging from months to years. The device, which has been tested in the clinic for the delivery of parathyroid hormone in osteoporosis patients, can be programmed to release drug at precise times and on a pre-determined schedule and will have wireless control features.

Jill Ogden has over 27 years of commercial and R&D experience in the bio-pharmaceuticals and healthcare industries from roles in biotechs and mid-caps. Her main areas of focus have included product and technology deals covering biologics, drug delivery and other platforms. She has led and been involved in a wide range of transactions including licensing, divestment deals and corporate M&A.

Non-pharma deals of note

This month saw a number of large diagnostic and device-based transactions. Whilst we usually focus on pharmaceutical-focused deals in our Deal Watch articles, we have included two diagnostic and device-based deals with price tags of over $1bn in this month's table to illustrate that consolidation is not just happening in the pharmaceutical/ biotechnology sector. Hill-Rom's acquisition of Welch Allyn for $2.05bn (approximately 3 x sales) follows a series of acquisitions over the last few years to build its portfolio of patient care solutions, which includes hospital beds, wound treatment systems, respiratory care and surgical equipment. The Welch Allyn business brings point-of-care diagnostics products and capabilities, including physical examination instruments and accessories and vital signs and cardiac monitoring solutions.

Opko's strategy in its $1.47bn acquisition of Bio-Reference Laboratories at $52.58 per share (approximately 60% premium) is to gain access to a range of diagnostic capabilities including a leading focus in molecular diagnostics. Through subsidiary companies, Bio-Reference Laboratories has accumulated genetic and genomics data that can be exploited for Opko's internal drug programmes and also made available to industrial partners and academic scientists to enhance drug discovery and clinical development. Opko will also use Bio-Reference Laboratories' services and distribution channels to boost sales of its own diagnostics products such as 4Kscore test, a blood test that provides a patient's specific personalised risk score for aggressive prostate cancer.

The consequences of acquisitions

One of the consequences of M&A is the need to assess a newly combined portfolio for potential anti-competitive issues. This was the case following the $20bn asset swap deal announced in April 2014 in which Novartis and GSK swapped vaccine and oncology assets. When GSK acquired two additional rival meningitis vaccines from Novartis, namely Menveo and Bexsero, the European Commission and other antitrust regulators were concerned that this gave GSK too much power in the market. As a result GSK has sold two of its own meningitis vaccines, Nimenrix and Mencevax, to Pfizer for $130m. Combined sales of Nimenrix and Mencevax were around $53m in 2014. This acquisition by Pfizer will help to boost its vaccine business and follows on from the purchase of Baxter's portfolio of marketed vaccines in July 2014.

Meanwhile Pfizer still appears to have a large appetite for a grand scale acquisition and rumours continue to abound around who might be the next target.

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