An industry update: the latest developments in therapeutic delivery

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The present industry update covers the period 1 October–31 October 2017, with information sourced from company press releases, regulatory and patent agencies as well as scientific literature. While the corporate news in October was traditionally dominated by the announcement of the third quarter results, with most of them showing market and revenue growth but also an increasing number of initial public offerings after years of slower financial development, we also saw trends continuing toward an increasing number of convergences of drugs with nanotechnology, devices and 21st century information technology. Whether it is using E Ink's 'Smart Patch', AstraZeneca's autoinjector, Elektrofi's Elektroject suspensions or NanoOlogy's NanoPac, there is an ever increasing number of combinations of devices, drugs and applications reaching, more and more the clinic and the market. Controlled release is another feature increasingly addressed by many of the above innovations. For example, the drug-loaded x-ray imageable microscopic beads that have been developed by researchers at UCL Cancer Institute (London, UK) take this one step further in order to pursue local, controlled and *in situ* validated local delivery.

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Business development

Market reports

A number of reports in the subject field were published in October, most notably the 'Global Topical Drug Delivery Analysis, Companies Profiles, Size, Share, Growth, Trends and Forecast to 2024' [1] and 'Drug Delivery Infusion Systems – Medical Devices Pipeline Assessment, 2017' [2]. Respectively, these reports provide an overview of Drug Delivery Infusion Systems in the development and transdermal drug-delivery devices and topical drug-delivery formulations further segmented into solid, semi solid and liquid, clinical indications and users.

The 7th Annual Partnership Opportunities in Drug Delivery (PODD) event took place on 19th & 20th October in Boston (MA, USA), presenting an overview aimed at pharma and biotech scientists and business developers on the latest drug-delivery technologies available, along with an update on deals and opportunities to extend the life cycle of a drug and improve therapies [3].

Financing

BioTime, Inc.

BioTime, Inc. (CA, USA) develops and commercializes products that address degenerative diseases, such as age-related macular degeneration. On 13th October, it was announced that the pricing of its public offering of common stock has an expected gross proceedings take-in of \$25 million. The company plans to use the net proceeds from this offering to fund clinical trials, research and to develop programs, as well as for general working capital [4].

Licensing & collaboration agreements

E Ink

E Ink Holdings (MA, USA) (a leading innovator in electronic ink technology) and LTS Lohmann Therapie-Systeme (a transdermal therapeutic systems manufacturing company – Andernach, Germany) announced on 23rd October

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that they are to collaborate on a 'Smart Patch' prototype. This is a transdermal therapeutic system delivering medication in a convenient, controllable and comfortable way, and can also convey patch-related information using an E Ink display. This may improve medication adherence, therefore affecting therapeutic outcomes [5].

LEO Science

LEO Pharma (MA, USA) (a pharmaceutical company that addresses dermatological and thrombotic conditions) announced on 11th October a collaboration agreement with Elektrofi (MA, USA), who are a Cambridge-based biotechnology company focused on drug-delivery innovations, in order to explore advanced formulation technology for dermatological drug delivery based on the Elektroject™ process technology for the subcutaneous delivery of antibodies. Elektrofi utilizes a novel therapeutic microparticle suspension system (Elektroject) to generate high-concentration, low-viscosity antibody-carrier combinations. Many antibody formulations become unusable at high concentrations due to their high viscosity. However, Elektroject suspensions result in >15-fold antibody concentrations compared with typically administered ones without exceeding viscosity limits. This enables health-care professionals to subcutaneously administer high doses of antibody-based therapies in relatively small volumes within seconds [6].

Development & manufacturing agreements

Vetter Pharma

Vetter Pharma (Ravensburg, Germany) specializes in complex packaging for autoinjector and pen systems for prefilled drug-delivery systems. On 19th October, it announced a major expansion of its secondary packaging capacities in order to meet the rising market demands. This is consistent with the company's continuous extension of new filling lines that consequently needs increased downstream packaging capacity [7].

Alnylam Pharmaceuticals

On 18th October, an exclusive licensing agreement was announced between Alnylam Pharmaceuticals, Inc. (MA, USA) (an RNAi therapeutics company) and Vir Biotechnology (a company that aims to address serious infectious diseases) for the development and commercialization of RNAi therapeutics for infectious diseases, such as chronic hepatitis B virus (HBV). The companies will collaborate on HBV and up to four additional RNAi therapeutic infectious disease indications. Alnylam initiated a Phase I/II trial in July 2016 for chronic HBV infection and now, using the Enhanced Stabilization Chemistry-Plus (ESC+) GalNAc conjugate technology, plans to advance a new candidate, ALN-HBV02 in order to enhance therapeutic index and target specificity. An upfront payment will be given to Alnylam, which will comprise of money and shares of Vir common stock and more than \$1 billion in potential milestone payments related to the successful advancement of this new candidate (ALN-HBV02) and other infectious disease programs. Tiered royalties will also be received for products that will be ultimately commercialized by Vir under this collaboration, depending on whether Alnylam, on a per product basis, chooses to decline its co-development and profit share option [8].

Regulatory news & approvals

Product approval

AstraZeneca

On 23rd October, an announcement was made by AstraZeneca (DE, USA) saying that the US FDA had approved its BYDUREON® BCise™ (exenatide extended-release) injectable suspension. This injectable suspension is an improved once weekly, single-dose autoinjector device for adults with Type-2 diabetes, who have uncontrollable blood sugar levels despite being on one or more oral medicines (in addition to diet and exercise) with hopes to achieve glycemic control. Unlike other glucagon-like peptide-1 receptor agonists, it uses a continuous-release microsphere delivery system that is designed to provide consistent therapeutic levels of the active ingredient in order to maintain a steady state. It has been shown in clinical trials that, on average, HbA1c was reduced by up to 1.4% and that weight loss was achieved when the injectable suspension was used as a monotherapy or in combination with metformin or other antidiabetic combinations [9].

Tandem Diabetes Care

On 24th October, Tandem Diabetes Care®, Inc., (CA, USA) (the manufacturer of the only touchscreen insulin pumps available in the USA), made an announcement that it will make any new features that have been approved

by the FDA for the t:slim X2™ Insulin Pump available at no charge to all in-warranty users. As it currently stands, Tandem is the only company to provide remote software updates (as the new features are approved by the FDA) for its insulin pumps [10].

Kala Pharmaceuticals

On 25th October, Kala Pharmaceuticals, Inc., (MA, USA) announced that it has submitted an NDA to the FDA for INVELTYS™ (KPI-121 1%). Should the application be approved, the company expects INVELTYS, which is a topical product, to be the first twice-daily ocular corticosteroid indicated for the treatment of ocular inflammation and pain in patients that have undergone ocular surgery. In this treatment, Kala's proprietary Mucus-Penetrating Particle technology is used. Mucus Penetrating Particles are selectively sized nanoparticles with proprietary coatings that can significantly increase drug distribution and penetration in the ocular tissues. By facilitating penetration through the tear film mucus, Mucus-Penetrating Particles increased delivery into the ocular tissues by more than threefold in preclinical studies [11].

Clinical trials

UCL Cancer Institute

On 9th October, researchers from the UCL Cancer Institute (London, UK), and the specialist healthcare company BTG plc (London, UK) began the first clinical trial of an experimental treatment for liver cancer. This experimental treatment uses targeted anticancer drug-loaded x-ray imageable microscopic beads that are placed directly in the liver. The trial will evaluate delivering a precisely controlled dose of vandetanib (which is an inhibitor of various tumor growth pathways), directly to the arteries that supply a liver tumor by preloading the drug on a radiopaque bead, which researchers can then image through CT scans. The aim of this is to improve upon the current treatments that are used for patients with metastatic colorectal cancer and primary liver cancer. Current treatments include trans arterial chemoembolization, which involves injecting beads through an artery using a catheter to block the tumor-feeding blood vessels, which subsequently interrupts the tumor's supply of nutrients and oxygen. These beads are further loaded with chemotherapy drugs that are released over time directly *in situ*. In order to improve the treatment of patients with metastatic colorectal cancer and primary liver cancer, the beads used in the VEROOnA (vandetanib-eluting radiopaque beads in patients with respectable liver malignancies) study are preloaded with the vandetanib, which is a multikinase inhibitor. This can potentially inhibit the formation of new tumor blood and lymph vessel growth, which may also prevent the blocking of the immune response and metastasis [12].

NanOlogy

On 16th October, NanOlogy LLC (TX, USA) announced the enrollment of the first patient for their NanoPac® (nanoparticle paclitaxel) trial, for which the treatment is a suspension administered locally for the treatment of prostate cancer. NanoPac as a nanoparticle technology platform will be evaluated for preliminary efficacy and safety in a Phase II study using intratumoral injection with transrectal ultrasound guidance in patients 4 weeks prior to radical prostatectomy. Results were presented at BIO Investor Forum on 17th October in San Francisco (CA, USA).

An extensive clinical development program is now being carried out for the NanoPac sterile suspension, which includes clinical trials in pancreatic cancer, prostate cancer, ovarian cancer (with orphan drug designation) and pancreatic mucinous cysts [13].

Patents

Eos Biosciences

Eos Biosciences, Inc. (CA, USA) (who are developing a novel nanobiologic particle drug-delivery platform technology [Eosomes], and who have a pipeline of proprietary oncology-specific products) announced on 17th October that a second patent has now been issued to Eos Biosciences (US Patent No. 9,789,201) by the US Patent and Trademark Office, for Eos-001, which is the company's HER3-targeted Eosome with doxorubicin payload. Eos also intends a strategic product pipeline expansion into the application of Eosomes to other disease areas of high impact (such as diseases of the CNS), and also into immuno-oncology [14].

Publications

Wenzhou Medical University

A plethora of nanoparticle formulations has been applied to target-specific drug-delivery systems, showing advantages in cancer treatments. On 30th October, a study by Ye *et al.* from Wenzhou Medical University (Zhejiang, China) was published, which used chitosan-coated doxorubicin nanoparticles to inhibit liver cancer cell growth by inducing cell-cycle arrest and apoptosis [15].

Lanzhou University

In another research study published in October, via host–guest interactions between ferrocene-terminated acetylated-maltoheptaose (Fc-AcMH) and β -cyclodextrin-terminated four-arm star maltoheptaose (MH4- β -CD), Shi *et al.* from the Lanzhou University (Lanzhou, China) generated solely oligosaccharide-based supramolecular amphiphiles. By self assembling to form spherical supramolecular nanoparticles, these constructs serve as potential drug-delivery platforms that respond to the intracellular microenvironment [16].

Financial & competing interests disclosure

O Steinbach is an employee of Royal Philips Electronics North America Corporation. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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