An industry update: the latest developments in therapeutic delivery covering July 2019

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The present industry update covers the period 1–31 July 2019, with information sourced from company press releases, regulatory and patent agencies as well as scientific literature.

Business development

Financing

Ocular TherapeutixTM

Ocular TherapeutixTM, Inc. (MA, USA) is a biopharmaceutical company focused on the formulation, development and commercialization of eye-disease therapies, which applies a bioresorbable hydrogel-based formulation technology. It was announced on 11 July 2019 that the company entered into an employment agreement, with the purchase of up to 60,000 shares in its common stock outside of the 2014 Stock Incentive Plan. The company also announced in the same month the commercial launch of DEXTENZA[®] (dexamethasone intracanalicular insert), which is US FDA approved for the treatment of ocular inflammation and pain following ophthalmic surgery. This product received a specific J-Code (J1096) by the Centers for Medicare and Medicaid Services (MD, USA) and Ocular Therapeutix announced the assignments of C White as Senior Vice President and P Kitchen as Chief Operations Officer [1].

Orum Therapeutics

Orum Therapeutics (Daejeon, South Korea) announced on 17 July 2019 a Series B financing round of over \$30 million. This involves new investors, IMM Investment (Seoul, South Korea), Smilegate Investment (Seongnam, South Korea), KTB Network (Seongnam, South Korea) and Stasets Investment (Seoul, South Korea) as well as the previous ones InterVest (Antwerp, Belgium) and KB Investment/Solidus Investment (Seoul, South Korea). The capital raised through this funding round are intended to be used for the expansion of its proprietary, cell-specific and cell-penetrating antibody platform technology, termed OromabTM, which targets ‘undruggable’ proteins. Oromab delivers therapeutic payloads by binding to cell-specific receptors, internalizing through receptor-mediated endocytosis and escapes through the early endosome into the cytosol, where it is released and the antibodies engage with the target and are therapeutically active. Therapeutic applications include inhibition of Ras and tumor-specific intracellular oncogenes, delivery of oligonucleotides or enzymes for cancer and rare diseases and targeted degradation of disease-related proteins. The new capital raise is also meant to expand the company’s laboratories in Korea and Boston [2].

ArunA Bio

ArunA Bio, Inc. (GA, USA), with a recent presence established in Research Triangle Park (NC, USA), is utilizing neural exosomes for the treatment of neurodegenerative diseases. The company completed on 24 July 2019 a \$13 million common stock financing, with existing and new private investors along with participation by several institutional investors, including Eshelman Ventures (NC, USA). Proceeds from financing are intended to advance the development of its exosome delivery platform and further to build a product pipeline of novel, neural, exosome-based therapies addressing neurodegenerative diseases (such as amyotrophic lateral sclerosis, Huntington’s Disease,

stroke). The objectives of these studies are to validate the current neural exosomes and to investigate their anti-inflammatory, neuroprotective and neurodegenerative therapeutic benefits by their properties. Further, the company intends to test the feasibility of delivery of novel therapeutic compounds, such as siRNAs and antibodies across the blood–brain barrier. The data from these investigations will support the Pre-Investigational New Drug application to the FDA, and will further the intention to expand the manufacturing capacity. The company is also exploring partnerships with other pharmaceutical and biotech companies working in the same clinical indications to advance the neural exosome platform [3].

Licensing

Orexo

Orexo AB (Uppsala, Sweden) is working on opioid addiction and pain based on innovative drug-delivery technologies. The company announced on 10 July 2019 a licensing agreement with Mundipharma Pty Limited (Sydney, Australia) to exclusively commercialize Orexo's lead product, Zubsolv[®], for the treatment of opioid dependence as part of a comprehensive treatment plan. This treatment plan includes counseling and psychosocial support in Australia and New Zealand. The products are currently commercialized in the main market of USA by the company or via other partners worldwide. Orexo will receive royalties on future net sales and the launch is expected to take place in the first half of 2020. Zubsolv is also approved in Europe where partnering discussions are underway [4].

Glaukos

Glaukos Corporation (CA, USA) works on medical technology and pharmaceuticals for the treatment of glaucoma, corneal disorders and retinal diseases. The company announced on 22 July 2019 a licensing agreement with Intratus, Inc. (CA, USA), which granted a global exclusive license to research, develop, manufacture and commercialize its patented, noninvasive drug delivery technology. The platform targets the treatment of dry eye disease, glaucoma and other corneal disorders such as allergy, blepharitis and conjunctivitis. The drug formulations are cream based and are administered to the outer surface of the eyelid, resulting in transdermal delivery of the drug substance. Recent clinical studies have demonstrated efficacy and adverse effects, the latter often associated with topical eye drop administration. No financial terms of the licensing agreement were disclosed [5].

Development & manufacturing agreements

Biocorp

Biocorp (Paris, France) develops and manufactures device-drug delivery combinations and announced on 3 July 2019 to have completed an exclusive license with Sanofi (Paris, France) to connect its Mallya[®] diabetes management device to Sanofi's integrated diabetes care products. The device is a sensor cap that attaches onto an injection pen to automatically record and transmit wireless dosage information. This device meets the requirements for a CE Class IIb medical device designation. Under the terms of these exclusive negotiations, Biocorp will receive an initial payment of €4 million from Sanofi to support related development activities [6].

Regulatory news & approvals

Clinical trials

Takeda

Takeda Pharmaceutical Company Limited (Osaka, Japan) announced on 22 July 2019 the first outcomes of the VISIBLE 2 clinical trial, which evaluated the efficacy and safety of Vedolizumab, an investigational, subcutaneous formulation of the biologic to treat Crohn's disease. This Phase III randomized, double-blind, placebo-controlled study evaluates the efficacy and safety of the drug with the primary end point of the trial to have a statistically significant ratio of patients achieving clinical remission by week 52, compared with a placebo [7].

Oyster Point Pharma

Oyster Point Pharma, Inc. (NJ, USA) focuses on the discovery, development and commercialization of treatments for ocular surface diseases. The company announced on 24 July 2019 that its C-01 nasal spray to treat dry eye disease entered the Phase III ONSET-2 clinical trial. The Phase III ONSET-2 clinical trial is a multicenter, randomized, double-masked, placebo-controlled clinical trial to evaluate the safety and efficacy, with the first patients enrolled. The primary end point is tear production of the secondary patient-reported symptom assessment of dry eye disease, measured by the Eye Dryness Scale [8].

Publications

University of Santiago de Compostela

The Nano-Oncology Unit at the Health Research Institute of University of Santiago de Compostela (Santiago, Spain) published on 18 July 2019 their work on exosomes. As commonly known, the lack of effective tumor-specific drug-delivery formulations is an unmet clinical need, especially for innovative drug formats such as therapeutic oligonucleotides. Exosomes have been previously reported to be favorable drug-delivery systems that are applicable to a wide range of malignancies, with organotrophic properties. Tumor-derived exosomes, which thereby have tumor-targeting properties, can efficiently reach metastasis lesions. Because of their complex composition and unknown biological functions, safety is still to be addressed for translation into the clinic. The authors describe in the article the recent work on exosome-mimetic nanosystems that have been shown to induce natural tumor-derived exosomes mimicking their structure and functionality. However, it provides a well-controlled composition to target microRNA-145 mimics to lung adenocarcinoma tissue. The liposome technology of exosome-mimetic nanosystems is well described and can be tailored with therapeutic compounds and specific proteins (in this study, integrin $\alpha\beta4$) to enable defined organ targeting. The research group has extensively worked on this nanoparticle platform that mimics exosomes and demonstrated considerable production, methods of composition and regulatory advantages [9].

Nanotechnology drug delivery review

Also, a few good oversight reviews have been published this month. Navya *et al.* described literature results on next-generation nanotechnology cancer treatment platforms. They create an inventory of nanomaterials currently utilized for anticancer therapies and the importance of physicochemical properties on their use in cancer management. State-of-the-art strategies for drug targeting, local release and toxicology management are discussed as well [10].

Conclusion

Reports on new financing (Ocular Therapeutix, Orum Therapeutics, ArunA Bio) and licensing (Orexo and Glaukos [CA, USA]) demonstrated that the investment environment into innovative therapy and drug-delivery technologies is still friendly. Connected drug–device combinations are increasingly emerging, such as Biocorp's Mallya Biocorp sensor cap, which is utilized for Sanofi's diabetes management platform. Interesting and relatively novel is the use of an engineered, endogenous delivery mechanism, known as an exosome. ArunA Bio and University of Santiago de Compostela report on the use of exosomes as delivery platforms for various therapeutics payloads now going into clinical studies. Finally, therapeutic areas that appear mature in drug delivery and ocular diseases see further innovation in topical formulations (Ocular Therapeutix, Glaukos and Oyster Point Pharma).

Financial & competing interests disclosure

OC Steinbach is an employee of TransCode Therapeutics Inc. 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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