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Industry Update October 2022

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Funder: This research received no external funding

Therapeutic Delivery

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Company news

Bend Bioscience invests in expansion of drug-delivery capabilities

Bend Bioscience (OR, USA) and NovaQuest Private Equity, have announced plans on 11 October 2022 to invest in a new facility in Bend, Oregon. The group will focus on developing new R&D partnerships, and early phase manufacturing and development activities based on proprietary particle engineering-based drug-delivery technologies. This new facility will consist of approximately 20,000 square feet of laboratory and processing areas and it is anticipated that manufacturing and analytical capabilities will operational by the end of Q2 2023. Announcing the investment decision, Dan Dobry, Bend Bioscience's co-founder said "*We feel Bend Bioscience will fill an unmet need, offering problem solving, formulation, and manufacturing for valuable but challenging therapies and collaborating to develop new technologies for the rapidly evolving problem statements in the in pharmaceutical industry*" [1].

Intravacc awarded US$14.6 million to develop intranasal gonorrhoea vaccine

Intravacc, a vaccine development company based in Bilthoven, The Netherlands, announced on October 2022 that it had been awarded a US$14.6 million contract by US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) to develop an intranasal vaccine for the prophylaxis of *Neisseria gonorrhoeae*, a sexually transmitted disease.

Intravacc intends to employ its proprietary outer membrane vesicles (OMV) platform deliver technology in the vaccine development. The new vaccine will be named, NGoXIM, and is based on gonococcal OMVs combined with sustained-release microspheres loaded with recombinant human IL-12. The company have reported that initial proof-of-concept studies with NGoXIM have indicated efficacy with a potent, lasting and cross-protective immune response in animal models. The sustained-release microparticles have been developed employing the proprietary technologies of Buffalo, New York-based company Therapyx. Therapx are also a partner in the NIH/NAID contract [2].

Eisai cuts the ribbon on $69M injectable drug-delivery facility

It was announced on 4 October 2022 that Eisai Co., Ltd (Tokyo, Japan) had completed construction of its new injection/research building 'Eisai Medicine Innovation Technology Solutions' ('EMITS') located at the Kawashima Industrial Park located in Gifu Prefecture, Japan. It is intended that this site will provide a global base for formulation-based research into injectable products facilitating therapeutic modalities including antibodies and antibody–drug conjugates. Additionally the company intends to further expand its research in liposomal and lipid nanoparticle formulations.

This announcement further strengthens Eisai's non-oral drug-delivery capabilities and builds on recent collaborative advances for the company including its partnership with Biogen on the Alzheimer's disease drug candidate lecanemab [3].

SURGE Therapeutics raises $26M series A financing

Cambridge Massachusetts-based developer of novel immunotherapeutics announced on 17 October 2022 that it had succeeded in raising $26 m of series a financing to help develop a novel injectable biodegradable hydrogel for the targeted, localized delivery of cancer immunotherapeutics at the site of surgical tumour resection. It is intended that this funding round will facilitate the initiation of clinical trials for the hydrogel delivery system. Discussing the

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results of this series of financing Dr Michael Goldberg, CEO and Founder of SURGE Therapeutics contextualised the possible benefits of this approach; "*Even after a tumor has been removed, it is common for a small number of cancer cells to remain behind, whether at the site of the primary tumor or elsewhere in the body. Indeed, 40% of cancer patients who undergo surgery relapse within five years, so this is a major unmet medical need. [. . . .] The Series A financing enables us to advance our proprietary intraoperative immunotherapies into clinical trials so that nobody has to grieve the loss of a loved one owing to cancer recurrence after surgery*". Robert Langer, the Chair of the Scientific Advisory Board, SURGE Therapeutics commented, "*SURGE seeks to radically redefine the process of care for cancer patients, creating a simple and effective treatment that could potentially be administered during any surgical oncology procedure. SURGE's novel approach has the potential to usher in a new pillar of cancer immunotherapy that could markedly enhance survival outcomes*" [4].

Acorda Therapeutics announce findings of In AMPYRA® arbitration case

On October 16 20022, Acorda Therapeutics, Inc. (NY, USA) announced that a final decision in a dispute with Alkermes PLC (Dublin, Ireland), regarding licensing royalties relating to AMPYRA (dalfampridine) had been issued. Under the terms of decision, Acorda was awarded $15 million plus prejudgment interest of $1.5 million from Alkermes. Additionally, Acorda is no longer obliged to pay any royalties to Alkermes on net sales for license and supply of AMPYRA. Acorda's AMPYRA® is an extended-release formulation of dalfampridine indicated to help improve walking in adults with multiple sclerosis.

Reacting to the findings Ron Cohen, MD, Acorda's President and CEO said, "*This award will allow Acorda to obtain more competitive market rates for the supply of AMPYRA, significantly reducing our cost of goods and meaningfully increasing the product's value to the company*" [5].

MedAlliance to be acquired by Cordis

It was announced on 19 October 2022 that the Geneva-based medical technology company MedAlliance is to be acquired by Cordis (Baar, Switzerland, and CA, USA). Under the terms of the agreement, the financial consideration is thought to be in the order of $1.135 Billion and include an initial investment of $35M with an upfront closing payment of $200M. Additionally provision has been made for regulatory achievement milestones of up to $125M and commercial milestones of up to $775M to 2029. Key to the acquisition is MedAlliance's proprietary sustained sirolimus drug-eluting balloon (DEB) program, SELUTION SLR™ (sustained limus release), which enables extended release of up to 90 days utilizing a technology that involves MicroReservoirs™ made from biodegradable polymer.

In 2020 SELUTION SLR was awarded CE Mark Approval both for the treatment of peripheral artery disease in and coronary artery disease. SELUTION SLR has also been awarded four breakthrough designations by the FDA [6].

Collaborations & agreements

Merck KGaA extends smart drug-delivery pact with BIOCORP

It was announced on 10 October 2022 that BIOCORP (Paris, France) Merck KGaA, (Darmstadt, Germany) have agreed to work on the development and supply of a version of BIOCORP's device, Mallya, as an accessory for one of Merck KGaA's drug-delivery pen injectors. Financial details on the agreement released indicate include payments from Merck KGaA of, up to €5 million for the development of the product within the first 3 years of the collaboration with additional revenues accruing of €8 million during the first 5 years after launch depending on achieving certain commercial milestones.

Mallya is developed by BIOCORP, is a Bluetooth enabled clip-on device for pen injectors. It is designed to collect specific information on the dose and time of each injection. It is then transfers information in real time to a companion software in an effort to support patients with self-injections and improve compliance. Mallya was the first in its category to receive the CE-mark and BIOCORP has already concluded development agreements with companies including Sanofi and Novo Nordisk to facilitate the delivery of therapeutics including insulin and human growth hormone.

Announcing the agreement Éric Dessertenne, CEO of BIOCORP said "*We are delighted with this new partnership with Merck KGaA, Darmstadt, Germany, extending our collaboration to additional therapeutic areas. We had already announced that there is a great opportunity for our connected device Mallya in various therapeutic areas. As in diabetes, Mallya aims to reduce patients' stress and improve compliance with their treatments to optimize and secure the results*" [7].

Approvals & regulatory updates

Supernus provides regulatory update on SPN-830

Supernus Pharmaceuticals, Inc. (MD, USA) announced on 10 October 2022, that it had received a Complete Response Letter (CRL) from the US FDA for its investigational apomorphine infusion device, SPN-830, New Drug Application (NDA). The device was designed to provide continuous treatment of motor fluctuations in Parkinson's disease.

The FDA's communication requires the company to supply additional information on device manufacturing, performance, quality and risk analysis. No additional efficacy and safety clinical studies were requested. The FDA has indicated that the resubmission by the company will be subject to a 6 month review timeline. Receipt of this CRL is the second time in 2 years that the FDA has refused approval of this device for continuous treatment of motor fluctuations [8,9].

Clinical trials

United Therapeutics announces top line data from the EXPEDITE study of remodulin induction prior to Orenitram therapy

United Therapeutics Corporation (MD, USA) announced preliminary analysis of the EXPEDITE study on 31 October 2022. Top line study results indicated that in patients suffering with pulmonary arterial hypertension (PAH), 79% of patients achieved the primary end point of study's primary end point of a 12 mg total daily dose of the company's proprietary Orenitram (treprostinil) extended-release tablet. The study was designed as a phase IV, multicenter, open-label 16-week study of Remodulin induction, which was followed by oral Orenitram optimization in patients with PAH. A total of 36 patients enrolled in the study with 29 completing it. Once enrolled the patients began in-patient or out-patient treatment on either intravenous or subcutaneous Remodulin followed by titration to a minimum dose of 20 ng/kg/min over the next 2 to 8 weeks. Following this patients were then transitioned to. The primary end point was to evaluate the percentage of patients who achieved an Orenitram dose of 4 mg three-times daily or higher at week 16. The company expect to release the full dataset for the EXPIDITE trial shortly. Orenitram (treprostinil) has been designed to release treprostinil at a near zero-order rate using an osmotic tablet technology [10].

Neurocrine Biosciences presents data from ONGENTYS® (opicapone) open-label study

Neurocrine Biosciences, Inc. (CA, USA) presented data detailing the baseline characteristics of patients with Parkinson's disease in the Opicapone Treatment Initiation Open-Label Study (OPTI-ON) on 24 October 2022 at the 2022 American Neurological Association Annual Meeting (ANA2022).

The study is an open-label, single-arm, multicenter, 6-month study of patients with Parkinson's disease experiencing 'OFF' episodes who were prescribed Neurocrine's once-daily ONGENTYS (opicapone) capsules as adjunctive treatment to the standard treatment of extended-release carbidopa/levodopa capsules.

Discussing the results Eiry W Roberts, MD, Chief Medical Officer at Neurocrine Biosciences stated "*The OPTI-ON study evaluated the use of ONGENTYS® as an adjunct treatment to carbidopa/levodopa in a real-world setting, beginning with consideration of the varied patient types and their existing treatment regimens. Full findings from the study will also examine treatment patterns, safety, and tolerability to complement results from the completed pivotal trials*" [11].

Trevi Therapeutics data from phase II trial of oral nalbuphine extended release

On 27 October 2022 Trevi Therapeutics (CT, USA) announced the data from the phase II trial in idiopathic pulmonary fibrosis (IPF) chronic cough of their investigational therapy Haduvio™ (oral nalbuphine ER). Top-line results from the CANAL (Cough And NALbuphine) trial for the treatment of chronic cough in IPF indicated a 76.1% reduction in 24 h cough frequency when compared with a 25.3% of placebo subjects. This reduction in the 24-h cough frequency was consistent also with the reduction in daytime cough frequency. The trials was a phase II, double-blind, randomized, placebo-controlled efficacy and safety study and it was designed with two-treatment, two-period crossover with 38 participants [12].

SiSaf seek Orphan Drug Designation status from the FDA

SiSaf Ltd, an RNA delivery and therapeutics company based in Guilford, England announced on 12 October 2022 that it had initiated a process to obtain an Orphan Drug Designation for SIS-101-ADO. SIS-101-ADO is a siRNA

therapeutic to be trialled with patients with a rare genetic skeletal disorder; Autosomal Dominant Osteopetrosis Type 2 (ADO2), and its therapeutic efficacy is mediated through an siRNA that suppress the expression of CLCN7. The therapeutic will be facilitated employing SiSaf's proprietary Bio-Courier® silicon stabilized hybrid lipid nanoparticles (sshLNP) technology. SiSAf's Bio-Courier® offers the ability to enhance siRNA delivery by modifying characteristics including particle size and surface charge and addition of targeting surface ligands.

Announcing this development SiSaf Founder and CEO Dr Suzanne Saffie-Siebert commented: "*In recent years, there has been an explosion of interest in RNA therapeutics for a wide range of medical concerns. Initiating the regulatory process to have our ADO2 therapeutic obtain Orphan Drug Designation will move this revolutionary treatment closer to the goal of alleviating the pain and suffering that this disease inflicts on people. Provided successful, SIS-101-ADO and other Bio-Courier® formulated drugs will not only be able to treat rare skeletal disorders but can clear the way for therapeutics for other rare diseases once thought impossible to treat*" [13].

atai Life Sciences announce phase I proof-of-concept clinical trial of intranasal INB-01

atai Life Sciences (NY, USA) announced the commencement of a proof-of-concept (phase 1) clinical trial for its intranasal INB-01. INB-01, a sol-gel based, drug-delivery technology and this proof-of-concept study is to look at its safety, tolerability and effective brain delivery. The trial will consist of either INB-01 or a placebo being administered to volunteers employing Aptar Nasal Drug Delivery Device (www.aptar.com/pharmaceutical/delivery-routes/nasal-device-drug-delivery-oindp/). The company has indicated that it expects top line results early in 2023.

The company claim that their proprietary INB-01 technology has been designed to deliver actives formulated as solutions that instantaneously transform to a gel in the nasal cavity. The novel technology has been successfully utilized with both water-soluble and insoluble compounds and extracts.

According to Florian Brand, Co-Founder, and CEO of atai Life Sciences: "*Exploring the mechanism of drug delivery is an opportunity for us to further enhance the treatment experience. INB-01 has the potential to provide superior drug uptake via the nose–brain barrier, reducing dose administered and dosing frequency. We are confident this will help patients and healthcare practitioners by easing administration, dosing, and providing faster relief to improve compliance*" [14].

Visiox Pharma submits NDA seeking approval for first once-daily brimonidine for glaucoma

It was announced on October 2022 that Visiox Pharma (NY, USA) had submitted a NDA to the FDA for its lead therapeutic candidate, PDP-716 (0.35% brimonidine tartrate). If successfully approved PDP-716 will be the first once-daily brimonidine to enter the market for the treatment of glaucoma. In submitting the application the company provided data on the drug candidate's ability to reduce inter-occular pressure (IOP) for ocular hypertension and open angle glaucoma.

Ryan Bleeks, Chief Executive Officer stated: "*This NDA submission marks a significant milestone for Visiox. We believe the patented TearAct™ delivery technology, which provides slow, consistent, and sustained release for IOP control throughout the day will address a significant unmet need for glaucoma patients.*"

Both PDP-716, and the TearAct™ delivery technology, a proprietary suspension formulation of resin microparticle-complexed drug, were licensed by Visiox from Sun Pharma Advanced Research [15].

Early stage development

Drug-delivery breakthrough to help gene editing technology

Mirkin *et al.* at Northwestern University (IL, USA) have reported, in a 6 October 2022 edition of *J. Am. Chem. Soc.*, the development of nanostructures, spherical nucleic acids (SNAs), which can enhance the delivery of CRISPR/Cas9 systems. The team have developed a methodology to transform the Cas-9 protein into the SNA and load it with the components required for gene editing.

Discussing the findings of the paper Mirkin stated: "*These novel nanostructures provide a path for researchers to broaden the scope of CRISPR utility by dramatically expanding the types of cells and tissues that the CRISPR machinery can be delivered to. We already know SNAs provide privileged access to the skin, the brain, the eyes, the immune system, the GI track, heart and lungs. When this type of access is coupled to one of the most important innovations in biomedical science in the last quarter-century, good things will follow*" [16,17].

Mercury Bio develops advanced highly targeted drug-delivery system

Mercury Bio (NM, USA) announced on 26 October 2022 that it has developed proprietary drug delivery technology focussed on the improved RNA therapeutics to targeted diseased cells. Mercury Bio's biomolecular, advanced drug delivery system (ADDS™) has been designed by engineer naturally occurring vesicles to encapsulate the RNA therapeutics. The vesicles are modified to display a cell-specific targeting mechanism with a view to improving site-specific delivery. The company claim that this low cost technology will enhance speed to market and with enhanced targeting improve patient outcomes.

Bruce McCormick, CEO of Mercury Bio commenting on the announcement; "*Curing many diseases now does not require new drugs; it needs new drug delivery systems. The ability to deliver RNA and small-molecule drugs directly to target cells is a reality that will change the way we approach disease*" [18].

Efficient nanovaccine delivery system boosts cellular immunity

A paper in 31 October 2022 *Journal of Controlled Release* by Harada *et al.* (Osaka Metropolitan University, Japan) describes how the research group have synthesized an antigen carrier, using liposomes with pH-responsive polysaccharides on their surface that preferentially transports cancer antigens to dendritic cells. In the paper the authors claim that by incorporating positively charged cationic lipids into the liposomes, this system allows for the activation of cellular immunity, using a fraction of the amount of antigen that was previously required. Although the authors conclude that additional work is still required to elucidate the mechanisms of highly adjuvant effects by combination of polysaccharide derivatives and cationic lipids on the liposome, nonetheless this initial study indicates that it may have usefulness for the design of lipid-based nano-vaccines [19,20].

Summary

October 2022 saw the acquisition of the Swiss company MedAlliance by US-based Cordis. Also this month Merck KGaA announced an extension of its drug-delivery agreement with BIOCORP. Meanwhile both Eisai and Bend Bioscience have invested heavily in facilities to expand their drug-delivery capabilities. Supernus provided an update on the issues they are still encountering with the NDA for investigational their apomorphine infusion device, SPN-830.

Financial & competing interests disclosure

The author has no 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. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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