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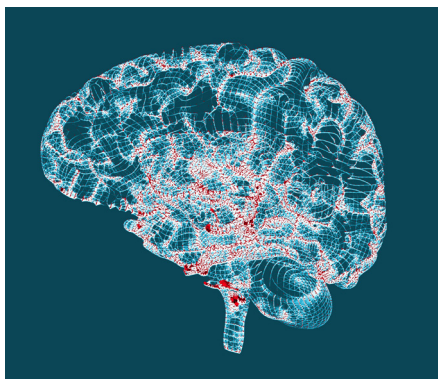
# Alzheimer's drug Leqembi expected to generate $12.9bn in sales by 2028

**Following its FDA approval, Leqembi is expected to make $12.9bn in sales**

**After receiving FDA approval in January 2023, Biogen/Eisai's new Alzheimer's disease Leqembi (lecanemab) is expected to become a blockbuster, with a predicted $12.9bn predicted to be made in sales between 2023 and 2028. The drug is still awaiting approval in the EU and Japan, with these approvals potentially making it the top-selling Alzheimer's drug.**



The monoclonal antibody targets amyloid beta A4 protein, selectively binding and eliminating amyloid beta plaques, which is thought to be significant for treating Alzheimer's disease. The FDA's approval of this drug followed data from the phase 2 Athena AD trial, which showed a significant reduction in the number of amyloid beta plaques in the brain as well as showing a statistically significant reduction in cognitive decline in patients treated with Leqembi compared to those on a placebo dose.

It is expected that the drug's biggest market will be in the US, with this region expected to contribute $7.7bn of the 2023-2028 forecasted sales. The anticipated further approvals are also expected to contribute to revenue growth.

In a press release published last week, Michael Irizarry MD, deputy chief clinical officer and senior vice president of clinical research at Eisai Inc, commented: "Our latest research examines the real-world outcomes based on lecanemab's impact on clinical results and safety, including its effect on health-related quality of life. Through our ongoing research, we hope to help simplify the patient journey and improve the lives of those living with Alzheimer's disease."

# European Commission delays release of major changes to pharma legislation

**The European Commission (EC) has again delayed the release of its new proposal for changes to Europe's pharma legislation. The decision was previously expected on 29 March 2023, but has been announced to be "slightly later".**

The EC is yet to provide an updated timeline for the proposal's release, but a spokesperson said that the agenda is "always indicative and adoption dates of Commission proposals may change any time, especially when these proposals concern reforms of complex legislations of major importance."

Approximately a year ago the EC released a 'road map' which outlined the issues it plans to address, such as unmet medical needs, market failures, antimicrobial resistance, drug shortages, and competition and unnecessary regulatory burdens, along with various other topics.

This roadmap states: 'The EU pharmaceuticals system needs to remain attractive in a competitive global environment, which demands regulatory attractiveness and agility while upholding the fundamental principles of safety, efficacy, quality and making sure that innovation reaches those who need it.' It was also noted in the roadmap that the Commission was considering 'a tailored system of incentives that links rewards with possible obligations,' for example launching products in all or most EU member states and increasing transparency around research and development funds.

Catherine Drew, a partner with the London-based law firm Pinsent Masons, who specialises in life sciences regulation, commented on the delay: "It's such an important project, and the suggestion of overhauling the entirety of the pharmaceutical regulatory regime, industry wants it to be right."

# Future Focus

# Bristol Myers Squibb works with SpaceX to study biomanufacturing in space

**It was announced last week that the SpaceX Dragon spacecraft will make its journey to the International Space Station (ISS) carrying important research in the areas of life sciences and technology. The spacecraft made its launch in April, and took some of Bristol Myers Squibb's (BMS) research with it.**

There are approximately 20 research projects on board, including BMS's project assessing the crystallisation of biotherapeutic compounds in microgravity. This research aims to investigate the crystallisation process and how it could improve biomanufacturing, as well as how it may eventually provide delivery of higher doses of proteins in the 'unique environment' that is space.

Other research on the spacecraft include two investigations using tissue chips to 'improve understanding of heart disease and develop new treatments' according to the ISS's press release; multiple projects evaluating 'technology in the harsh environment of space' that aim to use platforms outside the space station as 'the ultimate durability test'; and BMS's research into the crystallisation of biotherapeutic compounds in microgravity.


BMS's research aims to not only assess how compounds react to conditions in space, but also to understand which physical conditions result in large, high-quality crystals in microgravity. The press release explains that 'the team aims to determine how this knowledge could help improve biomanufacturing processes, elucidation of the structure of complex molecules and convenient delivery of higher doses of therapeutic proteins on Earth.'

Robert Garmise, the associate director of BMS's material science and engineering and the leader of the pharma's space station research project, commented: "In the future, we hope to continue to advance our knowledge of crystallisation of therapeutics in microgravity, and then taking our learnings and applying them to broader modalities."

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## Comment

**Considering contaminated medicines and their impact on public health**

Welcome to the May issue of *Pharmafocus*. The warmer weather brings with it a sense of change and growth as we move from the cold, wet winter to a slightly warmer and drier spring. Similarly, the pharma industry is always in a period of change with new developments and new treatment options in the works.

This month's issue covers exciting news ranging from AstraZeneca's positive trial results for its drug combination for the treatment of ovarian cancer (page 6), the first over-the-counter opioid overdose treatment receiving FDA approval (page 9) and positive data from aVaxziPen for its needle-free vaccines (page 11) to various partnerships and collaborations (page 12), including Bristol Myers Squibb's collaboration with SpaceX regarding biomanufacturing in space (page 2).

This issue also includes an insightful article by Michael Earl at Owen Mumford, who considers the benefits of connectivity while assessing how this can be utilised most efficiently by pharma companies (page 14).

Also in this month's issue, Betsy Goodfellow and James Spargo from *Pharmafocus* reflect on the contaminated cough syrup investigations, where products manufactured by Maiden Pharmaceuticals and Marion Biotech, among others, were connected to the deaths of children in the Gambia, Uzbekistan and Indonesia (page 16).

I hope you enjoy this issue.

*Betsy Goodfellow*

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# AstraZeneca's NMOSD treatment recommended marketing

**Pharma giant AstraZeneca has been given a recommendation by the EU's Committee for Medicinal Products (CHMP) for marketing authorisation for Ultomiris (ravulizumab), a treatment for adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 (AQP4) antibody positive (Ab+).**

Ultomiris is a C5 complement inhibitor that inhibits the C5 protein in the terminal complement cascade – part of the body's immune system. The complement cascade over-responds in NMOSD patients, which leads to the body to attack its own healthy cells.

The recommendation came after positive results from the CHAMPION-NMOSD phase 3 trial, which compared Ultomiris to an external placebo arm from the pivotal Soliris PREVENT clinical trial. 58 patients were enrolled, with participants having had a least one relapse in the 12 months prior to the study.

Data from the trial showed zero relapses were observed in Ultomiris patients with a median treatment duration of 73 weeks, and there were no new safety signals.

Orhan Aktas, MD, professor at the Department of Neurology, Medical Faculty at Heinrich-Heine-University, Düsseldorf, Germany, said: "Even one NMOSD relapse can lead to devastating long-term effects like vision loss, chronic pain and paralysis, which underscores the need for treatment innovations that help prevent relapses and optimise disease management. The sustained relapse risk reduction observed in the CHAMPION-NMOSD phase 3 trial supports the critical role this long-acting C5 complement inhibitor may have for the NMOSD community."

# Sanofi to cut insulin prices by 78% starting January 2024

**French pharmaceutical company Sanofi has announced that it will cut the list price of its Lantus (insulin glargine injection) 100 units/ml by 78%, beginning January 2024.**

This decision will mean a $35 cap on out-of-pocket costs for Lantus for patients without insurance, bringing it in line with the mandated amount for seniors funded by Medicare in the Inflation Reduction Act.

Sanofi has already taken measures to help patients afford their medication: in June 2022, it launched an unbranded Lantus biologic at -60% vs Lantus list price and cut the list price of its short-acting Apidra (insulin glulisine injection) 100 units/ml by 70%.

This announcement makes Sanofi the third major pharmaceutical company to cut insulin prices: both Eli Lilly and Novo Nordisk also announced price reductions.

Olivier Bogillot, head of US General Medicines at Sanofi, stated: "Sanofi believes that no one should struggle to pay for their insulin and we are proud of our continued actions to improve access and affordability for millions of patients for many years. We launched our unbranded biologic for Lantus at 60% less than the Lantus list price in June 2022 but, despite this pioneering low-price approach, the health system was unable to take advantage of it due to its inherent structural challenges. We are pleased to see others join our efforts to help patients as we now accelerate the transformation of the US insulin market. Our decision to cut the list price of our lead insulin needs to be coupled with broader change to the overall system to actually drive savings for patients at the pharmacy counter."


# Novo Nordisk to cut insulin prices by up to 75% in 2024


**Danish pharmaceutical company Novo Nordisk has announced that it will cut its prices for insulin products by up to 75%, beginning in January 2024.**

The price of Novolog and Novolog Mix 70/30 will be cut by 75%, with Novolin and Levemir seeing a 65% reduction in price.

Novo's cuts will take effect around the same time that the American Rescue Plan will be introduced. The timing means Novo will then be ineligible to pay rebates to the US Government, which would have had to have been paid under the Plan if it had kept its prices the same.

A Nova Nordisk spokesperson stated: "This [price cut plan] was designed to enhance Novo Nordisk's current offerings. The goal is for our collective programmes to help more and more people better afford their insulin. This is why, in addition to lowering our prices on certain insulins in January 2024, we will continue our other affordability offerings, including human and analogue insulins at Walmart and CVS, our My$99Insulin program, Immediate Supply program, Patient Assistance Program and our many co-pay savings cards."

Edwin Park, a research professor at the Georgetown University McCourt School of Public Policy, commented: "Lifting the cap was always intended to produce savings by either collecting those rebates in excess of the cap or discouraging manufacturers from further price increases, or encouraging them to lower their price increases to avoid this negative rebate liability."

# Molecular Templates announces hold for phase 1 study

**Molecular Templates has announced that the FDA has placed a partial hold on its phase 1 study for MT-0169 based on previously disclosed cardiac adverse events in two patients dosed at 50mcg/kg that triggered the dose reduction to 5mcg/kg last year. Since this reduction four patients have been dosed at 5mcg/kg and three at 10mcg/kg with no cardiac adverse events having been noted.**

Of the two patients who experienced cardiac adverse events, the first experienced asymptomatic grade 2 myocarditis, while the second experienced asymptomatic grade 3 cardiomyopathy.

Both patients had full recoveries after a few months and no grade 4 or 5 toxicities were observed at the higher dose level.

Under the FDA's current partial hold, current study participants may continue to receive treatment but no new patients can be enrolled until the hold is lifted.

The drug was intended to treat patients with relapsed multiple myeloma, and following the study resuming after protocol amendments in January 2022, patients were then treated with MT-0169 at lower dose levels of either 5mcg/kg or 10mcg/kg.

The FDA has asked the company to provide narratives on the two patients who experienced cardiotoxicity at the higher dose level, as well as justification for the revised dosage and data evaluating the clinical benefit-to-risk ratio for the lower doses.

Roger Waltzman, MD, chief medical officer at Molecular Templates, commented: "Patient safety is our highest priority. The 5 and 10mcg/kg cohorts have been completed and we have not observed any cardiac adverse events or other serious adverse events at these lower doses. One patient dosed at 5mcg/kg is in a stringent complete response and is in his seventh month of therapy. We look forward to sharing these data with the FDA and are confident in the benefit-risk profile of MT-0169 at these lower doses. We are excited to see early signs of clinical benefit in this difficult-to-treat patient population."

# Seamless Therapeutics launches with $12.5m in financing

**Seamless Therapeutics, a biotech focusing on the therapeutic potential of gene therapies, has announced it received $12.5m (€11.8m) in seed funding. The company will use the funding to accelerate research into its designer recombinases, a novel gene editing platform that will aid the treatment of severe diseases.**

Recombinases are a class of widely used enzymes that can precisely modify the genome of model organisms but, until now, they could not be applied therapeutically due to their limited programmability to act on new target sites. Seamless Therapeutics has changed this, with its pioneering platform having successfully reprogrammed site-specific recombinases to any given target sequence to make specific changes including inversion, excision, exchange and insertion from small to larger DNA fragments.

The seed round was led by both Wellington Partners and Forbion – representatives from both will now join Seamless' Board of Directors. The round also included non-dilutive financing from BMBF GO-Bio, a German Government initiative, which supports innovative start-ups in life sciences.

Anne-K Heninger PhD, co-founder and CEO of Seamless Therapeutics, commented: "Our goal is to apply our deep understanding of recombinases to leverage their inherent benefits to repair genetic alterations that cause disease. We believe our pioneering technology will allow us to shatter the boundaries that exist in gene editing methods today. Both Wellington and Forbion are visionaries and highly experienced biotech investors, and we look forward to working closely with them in our efforts to transform the gene editing landscape."

"Our modular platform has succeeded in reprogramming site-specific recombinases to any given target sequence effectively breaking the existing hurdles of leveraging this potential best-in-class gene editing system to treat human disease. I look forward to working with our founding investors and our highly skilled team to apply our deep knowledge of recombinases to develop a pipeline of novel treatments," said Felix Lansing, co-founder and CSO of Seamless Therapeutics.

# AstraZeneca reports positive results of drug combination in late-stage ovarian cancer trial

**AstraZeneca has announced positive high-level results from an interim analysis of the DUO-O phase 3 trial assessing a combination of Lynparza (olaparib) and Imfinzi (durvalumab) alongside chemotherapy and bevacizumab. This combination demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to chemotherapy plus bevacizumab.**

The drug combination was assessed for newly diagnosed patients with advanced high-grade epithelial ovarian cancer without tumour BRCA mutations.

At this interim analysis, data showing overall survival and other secondary endpoints was incomplete – however, the PFS showed a statistically significant and clinically meaningful improvement, and data on this is expected to be presented at forthcoming medical meetings.

The safety and tolerability of the drug combinations was as expected from previous trials and remained consistent with known profiles of the individual drugs.

Philipp Harter, director of the Department of Gynaecology and Gynaecologic Oncology, Evangelische Kliniken Essen-Mitte, Germany, and principal investigator for the trial, commented: "DUO-O showcases the power of academia and industry collaboration in advancing new treatment combinations for patients with ovarian cancer. I'm grateful for the academic cooperative study groups and patients around the world that made this trial possible and look forward to sharing the results with the clinical community."

Susan Galbraith, executive vice president of Oncology R&D at AstraZeneca, added: "While there has been significant progress for patients with advanced ovarian cancer, an unmet need still remains. These data from the DUO-O trial provide encouraging evidence for this Lynparza and Imfinzi combination in patients without tumour BRCA mutations and reinforce our continued commitment to finding new treatment approaches for these patients. It will be important to understand the key secondary endpoints as well as data for relevant subgroups."

# CANbridge Pharmaceuticals reports positive long-term data for glioblastoma multiforme drug

**Chinese biopharmaceutical company CANbridge Pharmaceuticals has announced positive long-term follow-up data from its clinical studies into a glioblastoma multiforme (GBM) drug.**

The phase 1/2 study of CAN008 (asunercept) plus temozolomide/ radiotherapy (TMZ/RT) involved nine newly diagnosed GBM patients. At the five-year study point, four were still alive – three years after the completion of the trial. All four were in the high-dose group, having received 400mg of CAN008 plus TMZ/RT.

The overall survival rate for the high-dose group was 83% at two years and 67% at three to five years. This raised the institutional database average, which at two years was 34.3%, 19.5% at three years, 16.1% at four years and 8.2% at five years. The high-dose cohort also saw a progression-free survival rate of 17.95 months, compared to a historic median of 6.9 months for GBM patients just receiving TMZ/RT.

CAN008 is currently in a phase 2 trial, with interim data analysis expected in mid-2023.

James Xue PhD, CANbridge founder, chairman and CEO stated: "While this is a small study, we are extremely encouraged by the high five-year survival rate of patients in our CAN008 Phase 1/2 trial, three years after its completion, in GBM, a cancer with typically poor outcomes. We look forward to the continued development of lead candidate, CAN008, currently in a phase 2 GBM trial in China, and to bringing this potentially new and promising treatment to brain cancer patients."

Gerry Cox MD PhD, chief medical officer and chief development strategist at CANbridge and a study author, commented: "We are pleased to see a median progression-free-survival of 17.95 months in CAN008 glioblastoma multiforme patients, more than double the historical median PFS for standard-of-care GBM patients, and that 67% of the CAN008 high-dose patients were alive after five years, in a cancer where patients typically progress very rapidly and survival rates are dismal. GBM is one of the deadliest cancers, with survival rates of less than 15 months, few treatment advances and a high unmet medical need."

# GSK shares promising clinical trial results for endometrial cancer therapy

**GSK has announced promising results from part 1 of the RUBY/ENGOT-EN6/GOG3031/ NSGO phase 3 trial for Jemperli (dostarlimab) alongside standard-of-care chemotherapy (carboplatin-paclitaxel) followed by dostarlimab, compared to chemotherapy and a placebo, in adult patients with primary advanced or recurrent endometrial cancer.**

The trial demonstrated a statistically significant and clinically meaningful improvement in progression-free survival (PFS) in the group that received Jemperli plus chemotherapy, compared to those who received a placebo plus chemotherapy. This first interim analysis also shows a clinically meaningful overall survival (OS) trend in patients treated with Jemperli compared to the placebo group. This analysis was done at 33% maturity, and statistical significance was not reached, however OS follow-up continues and further analysis is already planned.

The drug showed a consistent safety and tolerability profile, with the most common adverse events being nausea, alopecia, fatigue and anaemia.

Hesham Abdullah, senior vice president and global head of Oncology Development at GSK, commented: "These positive results from the RUBY trial bring us one step closer to addressing the significant unmet needs of endometrial cancer patients and add to the growing body of evidence on dostarlimab, strengthening our belief in its potential to transform cancer treatment as a backbone immuno-oncology therapy."

Dr Mansoor Raza Mirza, chief oncologist at Copenhagen University Hospital, Denmark and RUBY principal investigator, added: "Clinical practice has been waiting decades for a meaningful advancement in the standard of care for primary advanced or recurrent endometrial cancer. The results from the RUBY clinical trial, especially given the difficult-to-treat histologies included in the trial, demonstrate support for a new treatment standard with the addition of dostarlimab to current standard-of-care chemotherapy."

# InnoCare announced first subject dosed

**InnoCare has announced that the first subject has been dosed in its clinical trial of its novel targeted protein degrader ICP-490 in China. The company focuses on the treatment of cancer and autoimmune diseases, with this candidate aiming to treat multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL).**

The drug has been developed on InnoCare's molecular glue platform, and aims to overcome acquired resistance against earlier generation CRBN modulators. According to the company's press release: "Synergizing and enhancing efficacy of monoclonal antibodies (mAbs), ICP-490 provides strong rationale of synergistic combinations in the clinic, and demonstrates immense potential in the haematology field."

It is hoped that ICP-490 will demonstrate anti-tumour effects in various MM and diffuse large B-cell lymphoma (DLBCL). MM currently accounts for 10% of blood tumours, while NHL is the most common haematological malignancy in the world and is among the top ten most common malignant tumours in China, so new and effective treatments are always well-received.

Dr Jasmine Cui, the co-founder, chairwoman and chief executive officer of InnoCare, commented: "ICP-490 is a highly potent next generation CRBN Modulator. Developed for the treatment of multi-indications, it has the potential to become a blockbuster in our blood tumour pipeline. We will accelerate its clinical development and explore single or combined therapies, expecting to benefit the blood tumour patients early."

# Nanoscope Therapeutics announces positive results from phase 2b trial in retinitis

**US-based Nanoscope Therapeutics has announced topline results from its phase 2b RESTORE clinical trial. Currently, patients with vision loss due to advanced retinitis pigmentosa (RP) have no treatment options.**

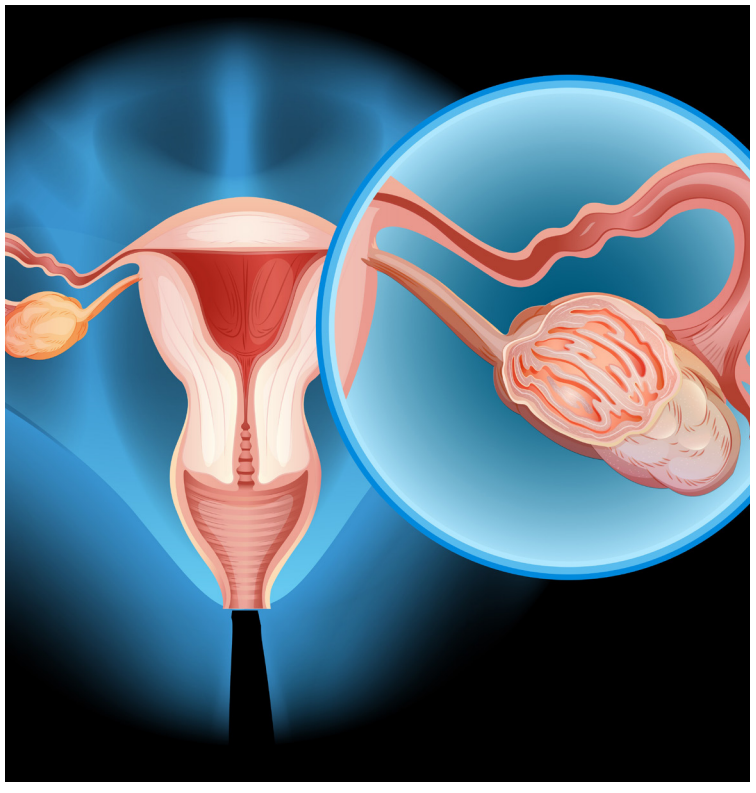
RESTORE was a multicentre, randomised, double-masked, sham-controlled phase 2b trial that studied the efficacy and safety of MCO-010, an ambient-light activatable Multi-Characteristic Opsin (MCO) optogenetic therapy for the treatment of RP, irrespective of gene mutation.

Within the trial, 18 patients with severe vision impairment due to RP were given a single intravitreal injection of MCO-010, while nine received a placebo. Results after a 12-month period showed vision function improvements after treatment with MCO-010, the data for which came from the Multi-Luminance Y-Mobility Test (MLYMT, vision-guided mobility). Other efficacy assessments included the Multi-Luminance Shape Discrimination test (MLSDT, near object recognition) and Best-Corrected Visual Acuity (BCVA).

In addition to the efficacy results, MCO-010 was well tolerated with no serious ocular or systemic adverse events.

Victor H Gonzalez MD, founder of Valley Retina Institute, McAllen, Texas and RESTORE investigator, stated: "I have had the privilege of observing substantial improvements in visual function in several patients who have enrolled in MCO-010 clinical trials over the past year. The fact that we see sustained and sometimes transformative gains in vision function, allowing them to walk in the clinic with more certainty, after a single treatment is remarkable and unprecedented. These participants who were living with severe vision impairment due to RP now have an improved quality of life, very different from before receiving MCO-010. In addition, MCO-010's favourable safety profile further strengthens my confidence in this groundbreaking treatment that I expect to become an important treatment option for people with advanced RP."

# Promising ovarian cancer drug enters phase 3 trial



**A new drug to treat ovarian cancer is set to enter the phase 3 UP-NEXT trial imminently. Upifitamab rilsodotin is an antibody-drug conjugate (ADC), designed to destroy ovarian cancer cells. The drug has also previously been used to treat other kinds of cancer.**

Ovarian cancer is largely incurable, as symptoms often don't appear until the disease has reached an advanced stage. It is also prone to recurrence, with around 70% of women diagnosed with the disease experiencing recurrences, according to the Ovarian Cancer Research Alliance.

The UP-NEXT trial aims to enrol 350 patients, specifically those whose ovarian cancer has returned following treatment with platinum-based chemotherapy drugs, such as cisplatin, carboplatin and oxaliplatin. Patients will be treated with either intravenous upifitamin rilsodotin or a placebo drug every four weeks following a round of chemotherapy treatment.

Dr Amanda Jackson, physician-researcher at the University of Cincinnati and principal investigator for the UP-NEXT trial, commented: "The drug is considered a maintenance medication. We're looking to see how well this drug works and is it going to change outcomes. Specifically, it's looking to see how long we can keep people's cancer at bay without it coming back. […] We usually start with the platinum-resistant group, and if you can prove that platinum-resistant patients can get benefit from this drug, then we keep moving it up further and further up the list to see if we can get a better impact. This is our only platinum-sensitive study open. When we get a drug at this level, we're really excited about it because there's a really good chance it could change how we treat patients in the future."

# Abbott gains FDA approval for Epic Max tissue valve for the treatment of aortic valve disease

**Abbott has announced that the FDA has approved its Epic Max stented tissue valve to treat patients with aortic regurgitation or stenosis. The device is the newest in Abbott's Epic surgical valve platform which the company has been developing for decades with positive results.**

Aortic regurgitation refers to when the aortic valve cannot close properly, while aortic stenosis refers to when it fails to open fully, both meaning the heart cannot pump blood effectively and blood flow to the body is reduced. This can lead to fatal heart failure, stroke and blood clots.

These diseased or damaged heart valves often cannot be repaired and so may be surgically replaced with either mechanical or bioprosthetic valves, such as Epic Max, which is recommended for patients who need valve replacement and aren't suitable for blood-thinning medication.

Joseph E Bavaria MD, cardiovascular surgery, University of Pennsylvania, commented: "The aortic valve is one of the heart valves most commonly impacted by cardiovascular disease, frequently requiring replacement. Abbott's Epic Max design optimises blood flow for patients and has a low profile that makes future cardiac interventions, if necessary, easier."

Michael Dale, senior vice president of Abbott's structural heart business, added: "With Epic Max, we're accomplishing two important things: first and foremost, we're improving heart valve haemodynamics, which is the purpose of the procedure. Secondly, we're preserving options and ability for patient lifetime disease management, an ever more critical point of consideration in device therapy selection."

# AstraZeneca's Lynparza approved by NHS England

**NHS England has approved the use of AstraZeneca's Lynparza (olaparib) for the treatment of patients with breast cancer and prostate cancer.**

This approval means men with advanced prostate cancer and women with HER2-negative early breast cancer who are at high risk of the disease returning will be offered olaparib through the NHS in England. The decision has already received praise from charities and clinicians.

The drug, taken as a tablet, is a type of targeted drug called a PARP inhibitor, which prevents cancer cells from repairing. It targets cancers with BRCA1 or BRCA2 mutations, stopping the cancerous cells from repairing their DNA therefore causing them to die.

Clinical trials have shown that prostate cancer patients treated with olaparib live for an additional "average of six months" according to NHS England. It has also been shown to reduce the risk of the BRCA-mutant, HER2-negative early breast cancer from returning within four years by almost a third.

It is expected that around 550 men with prostate cancer and 300 women with HER2-negative early breast cancer will be eligible for the drug each year in England.

NHS England chief executive, Amanda Pritchard commented: "Olaparib could have a huge impact on patients with a range of cancer types, giving many a better chance of survival while offering those with advanced forms of the disease precious extra months to live."

Johann De Bono, professor in Experimental Cancer Medicine at the Institute of Cancer Research (ICR), added: "Olaparib is an important example of how understanding the underlying genetics of patients, and their tumours' genomics, can be used to design highly targeted precision medicines. For patients with advanced prostate cancer and mutations in BRCA1 or BRCA2, these recommendations will be life-changing."

# FDA approves Novartis' Tafinlar and Mekinist combination

**The FDA has approved Novartis' combination therapy, Tafinlar (dabrafenib) and Mekinist (trametinib) for the treatment of BRAF V600E low-grade glioma (LGG) in paediatric patients over the age of one.**

Liquid formulations of the drugs have also been approved to make administration easier across various approved indications.

This is not only the first time a BRAF/MEK inhibitor has been developed in a formulation suitable for paediatric patients as young as one year, but it also makes Tafinlar and Mekinist the only approved combination therapy for BRAF V600E LGG in paediatric patients.

This is the sixth approval for the combination, which is also approved for several BRAF V600 solid tumours, such as lung cancer, melanoma and thyroid cancer.

Reshema Kemps-Polanco, Novartis Oncology US's executive vice-president, commented: "This new indication for Tafinlar and Mekinist is a potential new standard-of-care treatment option for young patients with this form of brain cancer with a BRAF V600E mutation, in formulations specifically designed for them. We are thankful for the families, including children and adolescents, that participated in the clinical trial that led to this approval and whose bravery has led to a new hope for children living with this serious brain cancer."

This approval follows positive results from the phase 2/3 TADPOLE clinical trial, which showed a significant improvement in overall response rate in patients treated with the combination therapy, when compared to a placebo group.

Dr Roger Packer, senior vice president of the Center for Neurosciences and Behavioral Medicine at Children's National Hospital, added: "It is more important than ever to test for genetic mutations in patients living with low-grade glioma. This FDA approval may offer new hope to paediatric patients living with BRAF V600E low-grade glioma. This has the potential to change the way healthcare providers treat these paediatric patients, offering a significant advancement compared to chemotherapy."

# First over-the-counter opioid overdose treatment approved by FDA

**The FDA has announced that it has approved Narcan, 4mg naloxone hydrochloride nasal spray for over-the-counter (OTC), non-prescription use. This is the first naloxone product to be approved for use without a prescription, and is the standard treatment for opioid overdose.**

This approval marks a big change in the treatment of overdoses, as the life-saving medication can now be sold directly to consumers in pharmacies, supermarkets, petrol stations and online.

Pricing and availability of the product is yet to be determined by the manufacturer, but according to the FDA's press release it is aiming to maintain the availability of the drug in the meantime.

FDA commissioner Robert M Califf MD, commented: "The FDA remains committed to addressing the evolving complexities of the overdose crisis. As part of this work, the agency has used its regulatory authority to facilitate greater access to naloxone by encouraging the development and approval of an over-the-counter naloxone product to address the dire public health need. Today's approval of OTC naloxone nasal spray will help improve access to naloxone, increase the number of locations where it's available and help reduce opioid overdose deaths throughout the country. We encourage the manufacturer to make accessibility to the product a priority by making it available as soon as possible at an affordable price."

Patrizia Cavazzoni, MD, director of the FDA's Center for Drug Evaluation and Research, added: "Naloxone is a critical tool in addressing opioid overdoses and today's approval underscores the extensive efforts the agency has undertaken to combat the overdose crisis. The FDA is working with our federal partners to help ensure continued access to all forms of naloxone during the transition of this product from prescription status to non-prescription/OTC status. Further, we will work with any sponsor seeking to market a non-prescription naloxone product, including through an Rx to OTC switch, and encourage manufacturers to contact the agency as early as possible to initiate discussions."

# Merck receives FDA approval for Keytruda in combination with Padcev to treat bladder cancer

**Merck (known as MSD globally) has announced that it has received FDA approval for Keytruda in combination with Padcev for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (la/mUC) who are not eligible for cisplatin-containing chemotherapy.**

This indication has been approved under the Accelerated Approval pathway based on the tumour response rate and durability of response (DOR), however continued approval for this indication may depend on the outcome of some confirmatory trials.

This approval marks the first of an anti-PD-1 therapy in combination with an antibody-drug conjugate in the US for this indication. This is based on data from the Keynote-869 trial, which assessed the dose escalation with three cohorts (the dose escalation cohort, cohort A and cohort K). The median follow-up time for the dose escalation cohort and cohort A was 44.7 months, whereas for cohort K it was 14.8 months. The median DOR for the dose escalation cohort and cohort A was 22.1 months, whereas for cohort K it was not reached.

Dr Eliav Barr, senior vice president, head of global clinical development and chief medical officer at Merck, commented: "This approval is a major milestone in the treatment of patients with locally advanced or metastatic urothelial carcinoma because it is the first approved combination of an immunotherapy and an antibody drug conjugate for these patients. This expands the use of Keytruda-based regimens to more patients with advanced urothelial carcinoma and demonstrates the value of collaboration in creating new combination approaches for patients in need of more options."

# NeuroRPM announces FDA clearance for AI monitoring app for Parkinson's disease on Apple Watch

**NeuroRPM has announced that it has received clearance from the FDA for its NeuroRPM device, which uses AI and existing Apple Watch technology to monitor symptoms of Parkinson's disease, offering continuous, day-to-day tracking of symptoms.**

The technology can continuously and passively track bradykinesia, tremor and dyskinesia, which are the predominant symptoms of Parkinson's disease. When integrated into an Apple Watch app, the technology can passively collect this data throughout a patient's daily life with little interruption. The app is now available to patients via a prescription.

Dr Alexander Ksendzovsky, director of functional neurosurgery at the University of Maryland, commented: "The clearance of NeuroRPM is a major milestone in the fight against Parkinson's disease. This technology will allow for unprecedented insights into the symptoms of Parkinson's disease including bradykinesia, tremor and dyskinesia, using critical health and wellness data from Apple Watch. NeuroRPM is able to assess even slight changes with accuracy comparable to that of a neurologist. This changes the game for the treatment of Parkinson's patients."

Atila Omer, NeuroRPM's president, added: "We are thrilled to be on the new frontier of digital health with NeuroRPM. By leveraging the power of Apple Watch, we are transforming the way individuals with Parkinson's disease understand their health, enabling care providers to make more informed clinical decisions which will lead to better health outcomes. We are honoured to help drive this revolution in healthcare."

# AbbVie shares results from study for new psoriasis therapy

**AbbVie has announced new 52-week data from a study assessing the efficacy of new IL-23 inhibitor, Skyrizi (risankizumab). Patients with moderate to severe psoriasis plaques had seem suboptimal responses to treatment with secukinumab or ixekizumab, both IL-17A inhibitor therapies, for over six months before switching to the new treatment.**

The data from this study was presented at a Late-Breaking Research session during the 2023 American Academy of Dermatology (AAD) Annual Meeting in New Orleans, US. The results showed that 56.3% of patients who received Skyrizi, without a washout period following their suboptimal response to other treatments, achieved the week 16 primary endpoint of reduced signs and symptoms of psoriasis.

Results from the 52-week analysis show that 63% of patients showed clear or almost clear skin at this endpoint; patients reported clear skin at both the 16 and 52-week endpoints; and patients reported no symptoms including pain, itching, redness or burning, at week 16 and week 52.

Nicole Selenko-Gebauer, vice president of global medical affairs at AbbVie, commented: "The evidence presented at the AAD meeting underscores the important role of SKYRIZI in helping patients in a difficult-to-treat population achieve skin clearance and a resolution of their burdensome psoriasis symptoms. Science is at the core of our work, and our continuing research represents our steady commitment to improving the standards of care, now and in the future, for patients with serious immune-mediated conditions like plaque psoriasis."

Professor Richard Warren from the University of Manchester and Norten Care Alliance, UK, added: "Advanced therapies represent an important option in the treatment of plaque psoriasis, but as a physician, it's critically important to continually assess if patients are having an optimal response to treatment, as residual psoriasis can still have a significant impact on a patient's life. This study showed that risankizumab was able to improve clinical signs and symptoms of patients who had a suboptimal response with the anti-IL-17 therapies secukinumab and ixekizumab, contributing to the whole of evidence supporting risankizumab use in moderate to severe plaque psoriasis."

# Kite's Yescarta CAR T-cell therapy shows statistically significant improvement in overall survival

**Kite has announced the primary overall survival (OS) analysis results of a phase 3 study into Yescarta for the treatment of adult patients with relapsed/refractory large B-cell lymphoma (R/R LBCL) within 12 months of completion of first-line therapy. The results showed a statistically significant improvement following treatment with Yescarta compared to the previous standard of care (SOC).**

Previously, patients have been treated with platinum-based salvage combination chemoimmunotherapy regimens, then high-dose therapy (HDT) and stem cell transplants for those who responded well to the salvage chemotherapy.

OS was chosen as a clinically important prespecified key secondary endpoint, and has been defined as the length of time from randomisation to death by any cause. The ZUMA-7 trial was part of a Special Protocol Assessment (SPA) with the FDA, meaning the agency agreed the trial design, clinical endpoints and statistical analysis prior to the beginning of the trial. This was also agreed upon by other health authorities.

The Zuma-7 trial has been called a 'landmark trial' as it is the first and largest phase 3 trial of any CAR T-cell therapy, 'with the longest follow-up, which has demonstrated event-free survival (EFS), the primary endpoint, that is superior to historical SOC treatment,' according to Kite's press release.

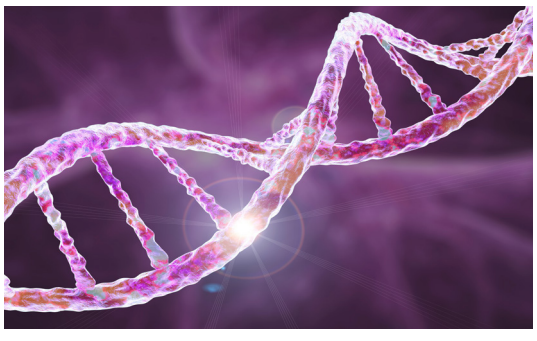
# Oxford Nanopore and 4bases collaborate on kit for BRCA1 and BRCA2 gene analysis

**Oxford Nanopore Technologies and Swiss company 4bases have announced a collaboration making 4bases kits with Oxford Nanopore's sequencing technology. These will be used to enable same day sample-to-answer results for BRCA1 and BRCA2 gene analysis.**

BRCA1 and BRCA2 gene mutations are linked to the increased risk of developing breast and ovarian cancers, so early identification can lead to life-saving early intervention. Identification can also get highly effective treatments, such as PARPi (Poly(ADP-ribose) polymerase inhibition), to certain cancer patients with BRCA1 and BRCA2 genetic mutations.

Current BRCA1 and BRCA2 testing can have a turnaround time of a few weeks to months, depending on the need to batch multiple samples. Because of this, clinical decisions such as treatment course or surgery sometimes have to be made without the results to help influence the decision.

To combat this, 4bases' kit targets the BRCA1



and BRCA2 genes through PCR-generating short amplicons compatible with Oxford Nanopore's built-in short fragment mode (SFM) sequencing. Following nanopore library prep and sequencing, the software identifies variants in the genes.

Gordon Sanghera, CEO, Oxford Nanopore Technologies, commented: "We are delighted to be working with 4bases on this important work to deliver distributed and accessible sequencing to scientists in Italy and Switzerland. In the first instance, we are excited to see how the combination of 4bases and nanopore sequencing will enable rapid characterisation of the BRCA1 and BRCA2 genes and significantly decrease the time to answer. As our collaboration develops we will see this expanded across the breadth of the 4bases portfolio and this will have a large impact on many research areas."

Fabio Grandi, CEO, 4bases, said, "With now over ten years of activity in the field of next generation sequencing, we at 4bases have witnessed every step of what we can call a revolution, leading to an always faster and more comprehensive acquisition of genomic data to the increasing benefit of clinicians involved with precision medicine. Our solutions are now used on a worldwide basis with the main sequencing systems and are now specifically adapted to the new Oxford Nanopore sequencing technology. After the development of 4eVAR, our new bioinformatics tool, completed last year, this strategic collaboration represents a new and exciting milestone in the 4bases development."

# Roche and Eli Lilly collaborate on Alzheimer's disease blood test

**Swiss biotech company Roche has announced a collaboration with US pharmaceutical company Eli Lilly to develop Roche's Elecsys Amyloid Plasma Panel (EAPP), which will be used to test for Alzheimer's disease before symptoms arise.**

EAPP measures phosphorylated Tau (pTau) 181 protein assay and apolipoprotein (APOE) E4 assay in human blood plasma; elevations in pTau 181 occur in the early stages of Alzheimer's, while presence of APOE4

constitutes the most common genetic risk factor. In July 2022, EAPP was awarded FDA Breakthrough Device Designation.

Currently, Alzheimer's detection relies on expensive and time-consuming PET brain scans and invasive spinal fluid analysis, together with cognitive testing. It is hoped this blood test will offer a faster and cheaper alternative, while still showing accurate results – a negative result means the patient is unlikely to be amyloid positive and therefore should be investigated for other causes of cognitive decline. The test can also be used as a way to more effectively recruit patients for Alzheimer's drug trials.

Matt Sause, CEO of Roche Diagnostics, stated: "We are excited to be collaborating with Lilly on such an important area of unmet medical need. Today, over 55 million people are living with dementia and this is projected to increase to nearly 140 million by 2050. Collaboration is essential to ensure these people receive a timely and accurate diagnosis. The Elecsys Amyloid Plasma Panel has the potential to streamline a person's journey to diagnosis and, therefore, access to future treatment options."

# Janssen reports new Rybrevant data for patients with advanced non-small cell lung cancer

**Janssen, part of Johnson & Johnson, has announced new long-term data from its CHRYSALIS study, which assessed Rybrevant (amivantamab) in patients with advanced non-small cell lung cancer (NSCLC) and epidermal growth factor receptor (EGFR) exon 20 insertion mutations whose disease continued to progress while receiving platinum-based chemotherapy.**

The data from this study demonstrated long-term response and safety profiles for this group, with the data being presented at the 2023 European Lung Cancer Congress (ELCC).

Study investigators assessed the safety and efficacy of the drug in this group of patients, who were treated with the recommended phase 2 dose of 1050mg (or 1400mg for patients weighing over 80kg). The primary endpoint was overall response rate (ORR) as per Response Evaluation Criteria in Solid Tumours Version 1.1. Further endpoints included duration of response (DOR), clinical benefit rate, progression free survival (PFS) and overall survival (OS).

After 19.2 months the median OS with Rybrevant was 23 months, with a two-year OS rate of 47%. The ORR was 37%, with a median DOR of 12.5 months, and a median PFS of 6.9 months.

Pilar Garrido, MD, associate professor of medical oncology at Universidad de Alcalá, head of Medical Oncology Department at the University Hospital Ramón y Cajal in Madrid, Spain, and principal investigator, commented: "With this new data, amivantamab showed long-term consistent efficacy regardless of prior therapies or response to prior platinum chemotherapy. Due to the aggressive nature of NSCLC with EGFR exon 20 insertion mutations, treatment with targeted therapies is an important consideration when identifying a treatment option for patients."

Martin Vogel, EMEA therapeutic area lead oncology at Janssen-Cilag GmbH, added: "Despite treatment advances, patients with advanced NSCLC with EGFR exon 20 insertion mutations continue to face poor clinical outcomes. These insights reinforce the potential of amivantamab as a targeted and effective option for these patients, and our commitment to lead the way in precision medicine approaches, whereby we are better able to identify the distinct patient populations most likely to benefit from specific treatments."

Kiran Patel, MD, vice president, Clinical Development, Solid Tumours, Janssen Research & Development, LLC, said: "The long-term CHRYSALIS data presented at ELCC support amivantamab as an important treatment option for patients with EGFR exon 20 insertion mutation-positive NSCLC, providing valuable clinical insights that may help inform treatment decisions. We're committed to transforming the treatment of lung cancer through continued research and the development of targeted therapies for genetic-mutated disease where high unmet needs continue to exist."

# aVaxziPen announces positive data for multiple diseases with novel needle-free vaccine

**aVaxziPen, a biotech company focusing on the development of a novel needle-free vaccine delivery platform, has announced that it will present data at the World Vaccine Congress (WVC) in Washington, US. The company plans to present a poster stating: "Needle-free, injectable solid dose vaccine delivery generates equivalent immune response with different antigens and animal models."**

The immunogenicity data from four in vivo models suggests that the company's needle-free solid-dose vaccine platform is an efficient way to deliver vaccines for various indications, including tetanus, anthrax, influenza and peanut allergies. The technology not only improves ease of administration and accessibility, but also has the potential to reduce vaccine hesitancy associated with needle-phobia.

The solid-dose formulation is also intended to improve thermal stability of standard-of-care vaccines, potentially reducing the need for cold-chain logistics during vaccine distribution.

The data presented at the WVC showed immunogenicity equivalence for aVaxziPen's needle-free solid-dose vaccines compared to traditional needle and syringe vaccines in four examples: a recombinant attenuated vaccinia virus expressing a peanut allergen, a tetanus toxoid vaccine with an alum adjuvant, a recombinant protective antigen anthrax vaccine and a recombinant influenza H7 vaccine.

Dr Keith Howard, aVaxziPen's chief scientific officer, commented: "With our needle-free technology we're on a mission to transform vaccine delivery for the benefit of communities around the world. Our novel solid-dose formulation technology coupled with our 'click-and-deliver' pen device has the potential to improve the accessibility and cost-effectiveness of every-day vaccines. The latest in vivo data, presented in Washington at the World Vaccine Congress, demonstrates how our technology generates comparable immune responses for several vaccines in a needle-free presentation."

# BioNTech and OncoC4 to partner for development and commercialisation of novel checkpoint antibody

**BioNTech and OncoC4 have entered a strategic collaboration for the co-development and commercialisation of a novel checkpoint antibody for multiple solid tumor indications. BioNTech will receive an exclusive worldwide license from OncoC4 for its anti-CTLA-4 monoclonal antibody candidate, ONC-392.**

The companies are expected to co-develop ONV-392 as either a monotherapy or in combination with anti-PD1 for the treatment of various solid tumour indications, with BioNTech also planning to combine ONC-392 with its other oncology candidates – allowing the company to assess complementary treatments to increase the therapeutic impact of the drug.

OncoC4 will receive an upfront payment of $200m as well as being eligible for development, regulatory and commercial milestone payments and tiered royalties. The drug has already received Fast Track designation from the FDA as a monotherapy for immunotherapy-resistant non-small cell lung cancer (NSCLC).

It is expected that a phase 3 trial assessing ONC-392 will begin this year, although it is currently also being evaluated in a phase 2 trial as a combination therapy alongside pembrolizumab to treat platinum-resistant ovarian cancer.

Professor Ugur Sahin, MD, co-founder and CEO of BioNTech, commented: "Despite being a prime target for more than a decade, we believe that targeting CTLA-4 has not reached its full potential in cancer immunotherapy. The data presented by OncoC4 on its ONC-392 antibody indicate a differentiated safety profile and encouraging clinical activity in various types of tumours. We believe that this antibody is a valuable addition to our immuno-oncology portfolio, whether used alone or in combination with our personalised immunotherapies."

Yang Liu, PhD, co-founder, CEO and CSO of OncoC4, added: "Because of its specific mechanism of action, we believe ONC-392 has the potential to broaden the reach of CTLA-4-targtting immunotherapy. We very much look forward to working hand-in-hand with BioNTech in developing ONC-392 for cancer indications with unmet medical needs."

# Pfizer signs $43bn deal to buy Seagen

**Pharma giant Pfizer has signed a definitive merger agreement valued at $43bn to buy biotech firm Seagen.**

US-based Seagen discovers, develops and commercialises cancer medicines through pioneering antibody-drug conjugates (ADCs) technology. It currently has four approved medicines in its portfolio, including three ADCs: Adcetris (brentuximab vedotin) for lymphoma; Padcev (enfortumab vedotin) for bladder cancers; and Tivdak (tisotumab vedotin) for cervical cancer.

The agreement will aim to develop Seagen's ADC technology with Pfizer's protein engineering and medicinal chemistry capabilities, leading to next-generation biologics and novel target combinations.

It will also grant Pfizer access to Seagen's developing technology, which can potentially generate several Investigational New Drug Applications (INDs), including next-generation ADC linker/payload technologies and other antibody platforms such as bi-specific antibodies that destroy tumours by using the immune system.

Pfizer chairman and CEO, Dr Albert Bourla stated: "Pfizer is deploying its financial resources to advance the battle against cancer, a leading cause of death worldwide with a significant impact on public health. Together, Pfizer and Seagen seek to accelerate the next generation of cancer breakthroughs and bring new solutions to patients by combining the power of Seagen's ADC technology with the scale and strength of Pfizer's capabilities and expertise. Oncology continues to be the largest growth driver in global medicine, and this acquisition will enhance Pfizer's position in this important space and contribute meaningfully to the achievement of Pfizer's near- and long-term financial goals."


# Théa Open Innovation and Galimedix announce partnership for development and commercialisation of GAL-101

**Théa Open Innovation (TOI) and Galimedix have announced that they have signed a licensing agreement granting TOI exclusive rights for the development and commercialisation of GAL-101, Galimedix's treatment for dry age-related macular degeneration (AMD), glaucoma and other ophthalmic indications with high unmet medical need, in Europe, the Americas, the Middle East and Africa.**

Galimedix is set to receive an upfront technology access fee and will receive further success-based milestone payments alongside royalties on net sales. TOI is expected to fund the remaining development of GAL-101 in dry AMD as well as taking charge of the registration and commercialisation of the drug, however Galimedix will continue to take responsibility for its mid-stage clinical trials. TOI also plans to invest in Galimedix, showing its interest in the company's pipeline, for example its Alzheimer's disease (AD) research.

Jean-Frédéric Chibret, president of the Théa Group, commented: "Through the partnership with Galimedix, Théa will be among the few companies globally that are working on an innovative drug for the treatment of dry AMD patients who are currently at risk of going blind. We are excited to be working with Galimedix, as this collaboration supports our continued commitment to building a strong, cutting-edge and diversified ophthalmological portfolio for eye care specialists around the world and their patients."

Alexander Gebauer MD, executive chairman of Galimedix Therapeutics, added: "We are excited to partner our front-runner programme, GAL-101, in ophthalmology with TOI, a company highly respected in and fully dedicated to the challenging field of ophthalmology already for several generations. This collaboration is an important milestone for Galimedix, as it further validates our technology and is critical to bringing GAL-101 through clinical development and approval to help patients who are currently at risk of gradually going blind. In addition, we are gratified by the strong support TOI has shown towards Galimedix by way of its equity investment in the company. This will enable us to move forward with our development plans for GAL-201, our next-generation oral compound for Alzheimer's disease."

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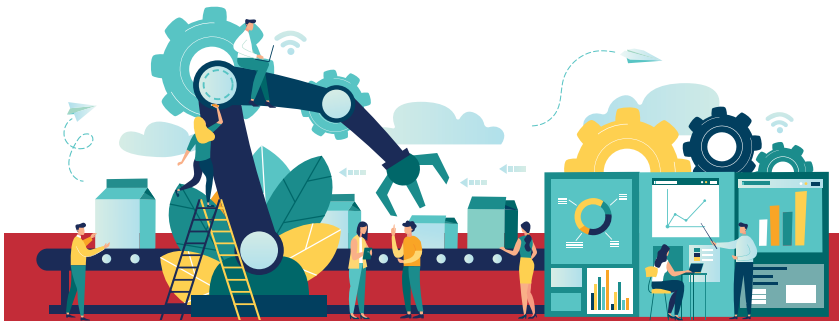

Industry Insight

# Connected drug delivery devices: considerations for developing digitised combination products

Michael Earl, director of Pharmaceutical Services at Owen Mumford, considers the benefits of connectivity and how this can be best utilised by pharma companies

**As part of a broader industry transformation towards 'Pharma 4.0', pharma businesses are looking to incorporate digital features in their drug delivery products, improving efficiency while gaining market advantage.[1] However, to get the most out of connectivity, companies need to take a considered and thoughtful approach.**

Many pharma companies may not have defined the best way to deploy connected devices, how to use the data most effectively or how to maximise the commercial model. In this piece, we will outline essential areas pharma companies should be considering during decision-making and when outlining product development strategies.

## Balancing cost with patient benefit

### *Reducing the burden on healthcare systems*

With pharma under increased pricing pressure, there may be concerns about the cost of introducing connectivity features to drug delivery devices.[2] However, there may be savings to be gained in the long term, for instance, through more effective medication delivery and reduced product wastage. For the wider healthcare system, there are also significant potential savings to be made through improved adherence – including fewer consultations, interventions or additional prescriptions.

One study found that each 10% increase in adherence among diabetes patients led to a reduction in annual healthcare costs by anywhere from 8.6-28.9%.[3] With environmental, social and governance (ESG) at the top of the pharmaceutical agenda, the associated sustainability benefits are also an attractive advantage.[4]

### *Remote support for injecting patients*

With remote monitoring increasingly common, connected devices can provide guidance and support for self-administering patients throughout the injection process, helping to reduce the level of device-handling errors and medication mismanagement.[5] Training and demo devices with enhanced sensors can provide specific feedback to patients who are using a device for the first time or who lack confidence when using a device. As more extended-release formulations are developed, feedback from connected devices may be especially valuable.[6] With patients undertaking injections less frequently, they are likely to benefit from extra support during each injection. Step-by-step guidance from connected drug delivery devices can help to ensure patients are still able to administer treatments correctly after a long period. However, pharma companies must balance the cost of device connectivity and the potential benefits for patients against the cost of injections that are infrequent or contain low-cost drugs.

### *Flexibility of choice in connected device selection*

In terms of connectivity solutions, add-ons may have the benefit of being far simpler from a

regulatory perspective than a new novel device. The flexibility to launch devices with or without connectivity depending on the market and patient group may make more sense commercially. However, creating novel devices incorporating connectivity should not be overlooked. Fully integrating connectivity into a device can ensure user needs are prioritised early in design development, whereas add-on solutions may have usability compromises. A further factor in the decision is environmental impact and how this compares with benefit and cost. To sum up, there is no 'one-size-fits-all' solution, as there are many factors at play.

Lastly, in terms of data capture, existing connected devices typically require a smartphone application, where data is entered manually, or which connects with the device through Bluetooth. With the advent of 5G technology, data on injection date, time, dosage and site can be instantly uploaded to the cloud without the need for patients to use a secondary device or application, providing benefits for less technically adept patients.



## Maximising the use of data from connected products

***Data generation for regulatory and reimbursement support***

Connected drug delivery devices may be an invaluable support for pharma companies developing novel drugs, to gather adherence data and any link to patient outcomes; this in turn may support regulatory submissions and the case for reimbursement. For rare diseases, in particular, where therapeutic targets are more specific and developing an effective therapy can be challenging and expensive, tracking adherence and effectiveness of treatments is even more critical.

***Assessing regulatory requirements in target markets***

Currently, patient and treatment electronic data from different sources tends to be collected separately and is not easily integrated effectively within healthcare systems to develop the holistic overview necessary to create a complete knowledge base and personalised treatment plans. New regulatory standards are necessary to streamline communication protocols and tackle the challenges of combining different data sets.[7]

One of the main challenges is the difference in health regulations between different countries, particularly in Europe where data privacy laws differ at national and regional levels – making it challenging to launch one product in multiple markets. To avoid the cost and complications of launching different products in separate regions, pharma companies will have to assess which regions are a top commercial priority, as well as regions where the regulatory environment and healthcare system are most appropriate for connected products.

However, there are positive changes on the horizon. The EU is looking to invest €220m from 2023 to 2027 in developing the European Health Data Space. This is a cross-border digital platform where people can control their own electronic health data, ensuring data privacy, while making data more interoperable and accessible. Similarly, the UK has a plan to centralise data storage and protection, and then make this repository available remotely to clinicians and researchers.[8]

***A new asset for clinical trials***

The collection of data from connected drug delivery devices could help transform clinical trials. Connected devices may facilitate some remote clinical trials, removing geographic constraints so a more diverse patient group can be involved. This ensures device suitability for a greater number of patient groups and helps reduce healthcare inequalities. Additionally, remote monitoring during clinical trials will allow data capture through the device itself, in a much more convenient way than the alternative paper or web-based forms. During clinical trials, real-time data from connected products allows researchers to make device design changes and treatment interventions where necessary. Post launch, device data may help to detect any user-related issues that occur across the device lifetime, helping manufacturing companies to perform root cause analysis and make appropriate changes to components or device design. We are likely to see increasing use of novel technologies and sensors to capture data about device performance to further companies' abilities to act on this data.

***Intelligent planning for a connected future***

The connected drug delivery devices market already measures $4.84bn and it is projected to continue expanding rapidly.[9] Digital features have the potential to offer greater benefits to patients, pharma companies and healthcare providers. However, pharma companies must ensure that they have reviewed the full scope of factors related to connectivity, taking the time to ensure their selected solutions are most suited to the needs of their patient groups and the regulatory context of their target markets.

*Author Bio*

*Michael Earl joined Owen Mumford as director of Pharmaceutical Services in November 2020. He was previously the commercial VP at Bespak, leading the commercial team to drive growth in its substantial medical devices business. Previously, he worked for a number of pharma, biotech and device companies. In a career spanning more than 35 years, he has been responsible for all aspects and stages of drug and device development and commercialisation. Michael has also completed a substantial number of commercial, licensing and M&A transactions.*

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# The cough syrup investigation: a timeline

Betsy Goodfellow and James Spargo from *Pharmafocus* explore the investigation around contaminated cough syrups following a timeline that includes products manufactured by Maiden Pharmaceuticals, Marion Biotech and other companies

**July 2022**
Children begin dying from acute kidney injuries in the Gambia.[1,2]

**August 2022**
One child is reported to have died in Indonesia after being treated with a paracetamol cough syrup from a health centre in south Jakarta, Indonesia; laboratory diagnosis showed that the child had excessive levels of urea and creatinine, both waste products that build up once the kidneys shut down.[3]

**Pre-September 2022**
Preliminary investigations find a connection between reports of children becoming unwell in the Gambia and cough syrup produced by Maiden Pharmaceuticals in India.[4]

**September 2022**
Four products with a possible connection to children becoming unwell are identified in the Gambia and reported to the World Health Organization (WHO): Promethazine Oral Solution, Kofexmalin Baby Cough Syrup, Makoff Baby Cough Syrup and Magrip N Cold Syrup, all manufactured by Maiden Pharmaceuticals.[5]

**October 2022**
BPOM (Indonesia's food and drug regulatory authority) reports that a number of children have died from kidney failure.[6]

**5 October –** WHO releases a Medical Product Alert for the four syrups manufactured by Maiden Pharmaceuticals, which have led to at least 66 deaths in the Gambia to date. Laboratory analysis found that the products contained 'unacceptable amounts of diethylene glycol and ethylene glycol as contaminants' according to WHO.[7]

**November 2022**

**6 November –** WHO releases a Medical Product Alert for various products identified in Indonesia. The products are: Termorex syrup (batch AUG22A06 only), Flurin DMP syrup, Unibebi Cough Syrup, Unibebi Demam Paracetamol Drops, Unibebi Demam Paracetamol Syrup, Paracetamol Drops (manufactured by PT Afi Farma), Paracetamol Syrup (mint) (manufactured by PT Afi Farma) and Vipcol Syrup.[8]

**December 2022**

**21 December** – A parliamentary committee in the Gambia recommended prosecution for Maiden Pharmaceuticals, however this is still pending.[9]

**January 2023**

**11 January –** WHO issues a Medical Product Alert for products manufactured by Marion Biotech sold in Uzbekistan. The products are Ambronol syrup and DOK-1 Max syrup; laboratory analysis suggests they have 'unacceptable amounts of diethylene glycol and/or ethylene glycol as contaminants', according to WHO.[10]

**23 January –** WHO issues a 'Call to Action' for all 194 member states with guidelines for governments and regulators, manufacturers and suppliers, and distributors.[11]

The guidance for governments and regulators suggests they:

- 'Detect and remove from circulation […] any substandard medical products that have been identified in the WHO medical alerts […] as potential causes of deaths and disease'[11]
- 'Ensure that all medical products […] are approved for sale by competent authorities and obtainable from authorised/licensed suppliers'[11]
- 'Assign appropriate resources to improve and increase risk-based inspections of manufacturing sites […] in accordance with international norms and standards'[11]
- 'Increase market surveillance including risk-based targeted testing for medical products released […]'[11]
- 'Enact and enforce, where relevant and as appropriate, laws and other relevant legal measures to help combat the manufacture, distribution and/or use of substandard and falsified medicines'.[11]

Manufacturers are asked to:

- 'Only purchase pharmaceutical grade excipients from qualified and bona fide suppliers'[11]
- 'Conduct comprehensive testing upon receipt of supplies and before use in manufacture of finished products'[11]
- 'Provide assurance of product quality including through certificates of analyses based on appropriate testing results'[11]
- 'Keep accurate, complete and proper records of purchase of materials, testing, manufacture and distribution to facilitate traceability during investigations in case of incidents'.[11]

**Maiden Pharmaceuticals**

Maiden Pharmaceuticals Ltd is a pharma company established in 1990, with a manufacturing plant based in Kundi-Haryana, India, and a corporate office in Delhi, India. The company focuses on manufacturing dosage forms such as tablets, hard gelatine capsules, liquid syrups and suspensions, liquid injections, powder for injections, ointments, creams and gels, among other forms and medications.

**Marion Biotech**

Marion Biotech is a biotech company established in 1999 and based in Noida, India. The company manufactures over 100 healthcare products including over-the-counter medications, herbal drugs and prescription medications. The company manufactures for the Indian market and also exports its products to other countries.

Suppliers and distributors are advised to:

- 'Only purchase pharmaceutical grade excipients from qualified and bona fide suppliers'[11]
- 'Conduct comprehensive testing upon receipt of supplies and before use in [the] manufacture of finished products'[11]
- 'Provide assurance of product quality including through certificates of analyses based on appropriate testing results'[11]
- 'Keep accurate, complete and proper records of purchase of materials, testing, manufacture and distribution to facilitate traceability during investigations in case of incidents'.[11]

**24 January** – WHO begins investigating cough syrup sold in Indonesia, manufactured by: PT Yarindo Farmatama; PT Universal Pharmaceutical; PT Konimex and PT AFI Farma.[12]

**March 2023**

**21 March** – Families in Indonesia are granted permission by the Indonesian Court to bring a class action lawsuit against the Indonesian government and eight pharmaceutical companies, as the investigation continues.[13]

**23 March –** Uttar Pradesh, a state in India, cancels Marion Biotech's manufacturing licence after products made at its Noida city facility were linked to the deaths of children in Uzbekistan. Three employees from this facility have been arrested.[14]

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## Move of the month

### Optibrium appoints Dr Hamed Tabatabaei Ghomi as head of research

**Optibrium has announced the appointment of Dr Hamed Tabatabaei Ghomi as head of research, this is the latest appointment in a series of senior level hires. Ghomi brings with him experience of strategic and industrial research in the bioinformatics space, as well as a positive academic record.**

In his new role Ghomi will lead Optibrium's Research Team in developing and implementing breakthrough methods, such as quantum mechanical and machine learning approaches, all intended to improve the productivity and efficiency of the drug discovery process. He will also work alongside the Software Development and Business Development teams, ensuring the translation of the company's in-house R&D into valuable drug discovery tools and services.

Previously, Ghomi worked at Illumina as bioinformatics manager, during which time he focused on computational protein engineering and small molecule design. He also holds various degrees, including a PhD in the Philosophy of Science from the University of Cambridge and a PhD in Computational Drug Design from Purdue University.

Commenting on his appointment, Ghomi stated: "I am delighted to be joining Optibrium at such a dynamic and exciting stage of growth. Its world-class team sits at the forefront of machine learning and quantum mechanical modelling, and I look forward to translating the Company's breakthrough R&D into impactful solutions for our customers' drug discovery programmes."

Dr Matthew Segall, chief executive officer at Optibrium, added: "We are pleased to welcome Hamed to the team. His impressive depth of industry and academic experience, centred around computational chemistry and bioinformatics, will drive cutting-edge advances in Optibrium's R&D, helping us to deliver the latest innovations in drug discovery to our users worldwide."

# Roz Bekker appointed managing director of Janssen UK and Ireland

**The Janssen Pharmaceutical Companies, part of Johnson & Johnson (J&J), has announced the appointment of Roz Bekker as the new managing director of Janssen UK and Ireland.**

In her new role Bekker will lead the UK and Ireland's commercial business strategy, aiming to deliver new solutions providing value to patients, healthcare professionals and healthcare systems.

Previously, Bekker worked for Janssen's EMEA Strategy Organisation as regional commercial strategy leader for Infectious Disease Vaccines (IDV) throughout this role she led the IDV Commercial Organisation and played an integral part in navigating the complexity of Janssen's COVID-19 vaccine pandemic response. Having joined Janssen in 2005, Bekker worked in various roles with increasing leadership responsibility, across both medical and commercial functions.

Prior to working at Janssen, Bekker worked as a clinician in South Africa, relocating to the UK in 2011.

Commenting on her appointment, Bekker said: "I am delighted to be leading the UK and Ireland team at such an important time for the life sciences sector. I believe that there is considerable opportunity to strengthen existing partnerships between Government, the health service and industry to improve care and ensure timely access to innovative treatments for patients. I am privileged to join this talented team to help build on the outstanding work that is already in progress, as we continue to make a real difference to the lives of people, health systems and society as a whole."

## Steve Jones appointed as Ingenza's chief financial officer

**Ingenza has announced the appointment of Steve Jones as chief financial officer (CFO). Jones has over 25 years of industry experience, and has previously held senior financial roles across a range of business sectors.**

Jones has experience as a chartered accountant and a fellow of the Institute of Chartered Accountants in England and Wales (ICAEW), as well as running a consultancy business that provides financial advice and resources to SMEs to help them to maximise their growth potential.

As well as his financial experience, Jones has extensive experience in the life sciences industry, for example he previously worked as finance director of a private pathology laboratory, a role in which he helped to quickly scale up business operations to respond to the COVID-19 pandemic.

In addition, Jones provides voluntary advice to the Soko Fund, which is a Scottish charity aiming to improve opportunities for women in Malawi by funding their university education.

Commenting on his appointment, Jones said: "I very much look forward to working closely with the Ingenza team to deliver on its strategic goals and build on the momentum of the company's already remarkable growth. I have contributed to the success and growth of several SMEs in the life sciences sector, and hope to bring the same positive outcomes to Ingenza in an exciting year of development."

## Syncona appoints Roel Bulthuis as managing partner

**Syncona Ltd has announced the appointment of Roel Bulthuis as managing partner and head of investments. Bulthuis has over 20 years of experience in life sciences venture capital, business development and investment banking, that he brings with him to his new role.**

Previously, Bulthuis worked at Amsterdam-based Inkef Capital as managing partner and head of healthcare. In this role he led the firm's growth into a leading European healthcare VC platform. Prior to this he worked as senior vice president and managing director of Merck Group's M-Ventures for almost ten years, playing an instrumental role in creating the business and growing it to a leading corporate venture capital fund. He has also held various senior positions in global business development at Merck Serono and was part of the investment banking team at Fortis Bank.

In his new role, it is expected that Bulthuis will manage and develop Syncona's growing investment team, while playing an important role on the leadership team.

Commenting on his new appointment, Roel Bulthuis stated: "Syncona has a unique approach to leveraging the best scientific innovation and creating globally leading life science businesses that have a real impact on patients. I am excited by the opportunity to embed myself into a team with such a breath of experience and expertise and look forward to contributing to the achievement of their important mission."

Chris Hollowood, chief executive officer of Syncona Investment Management Limited, added: "We are thrilled to welcome Roel to Syncona. He has an impressive track record of investing in great life science businesses through the cycle and taking a long-term view on generating value – both principles which are central to our approach. [...] I am looking forward to working alongside Roel and on behalf of the team welcome him to Syncona."

# Five health facts about The Gambia, Uzbekistan and Indonesia

Following the investigations into the substandard cough syrups sold in the Gambia, Uzbekistan and Indonesia, here are some key health facts and statistics about these countries.

1. As of 2019, the leading cause of death globally was ischaemic heart disease. Since then, this has remained the leading cause in lower-middle-, upper-middle- and high-income countries, however in low-income countries this drops to third with neonatal conditions being the leading cause of death.[1]
2. In 2019, the child mortality rate (probability of 5-14 year-olds dying per 1,000 children) was 10.33 in the Gambia, 3.76 in Uzbekistan and 5.14 in Indonesia, compared to 0.77 in the UK.[2]
3. In 2017 the leading causes of child deaths (from birth to the age of four) in the Gambia were acute lower respiratory infections (728.6 deaths) and prematurity (657.7 deaths); in Uzbekistan the leading causes were prematurity (2,793 deaths) and congenital anomalies (2,498 deaths); and in Indonesia they were prematurity (23,090 deaths) and acute lower respiratory infections (19,672 deaths).[3]
4. In 2020, the number of maternal deaths in the Gambia was 398.7; 7,826 in Uzbekistan; and 251.1 in Indonesia, compared to 66.83 in the UK.[4]
5. Finally, in 2019 the still birth rate per 1,000 births in the Gambia was 21.86, 6.55 in Uzbekistan and 9.46 in Indonesia, compared to 3.04 in the UK.[5]

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