Drug Development & Delivery

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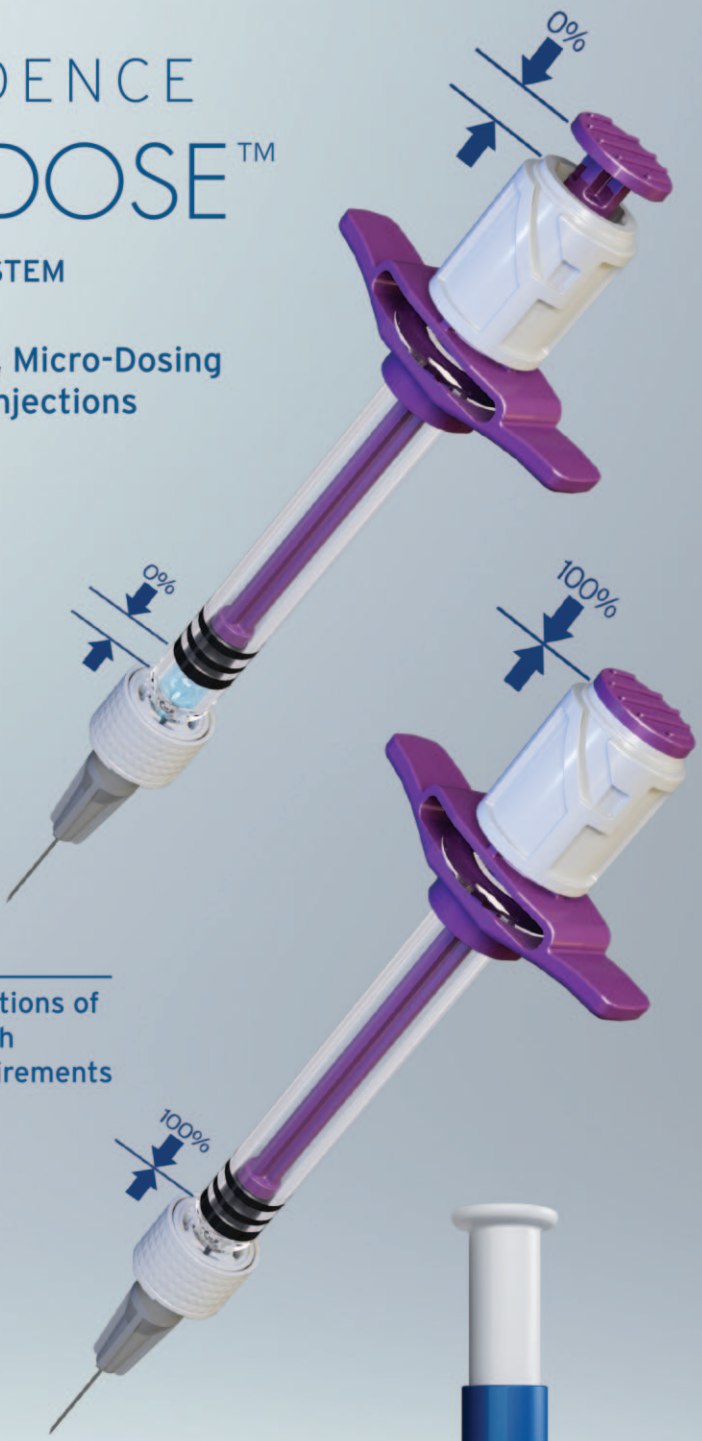

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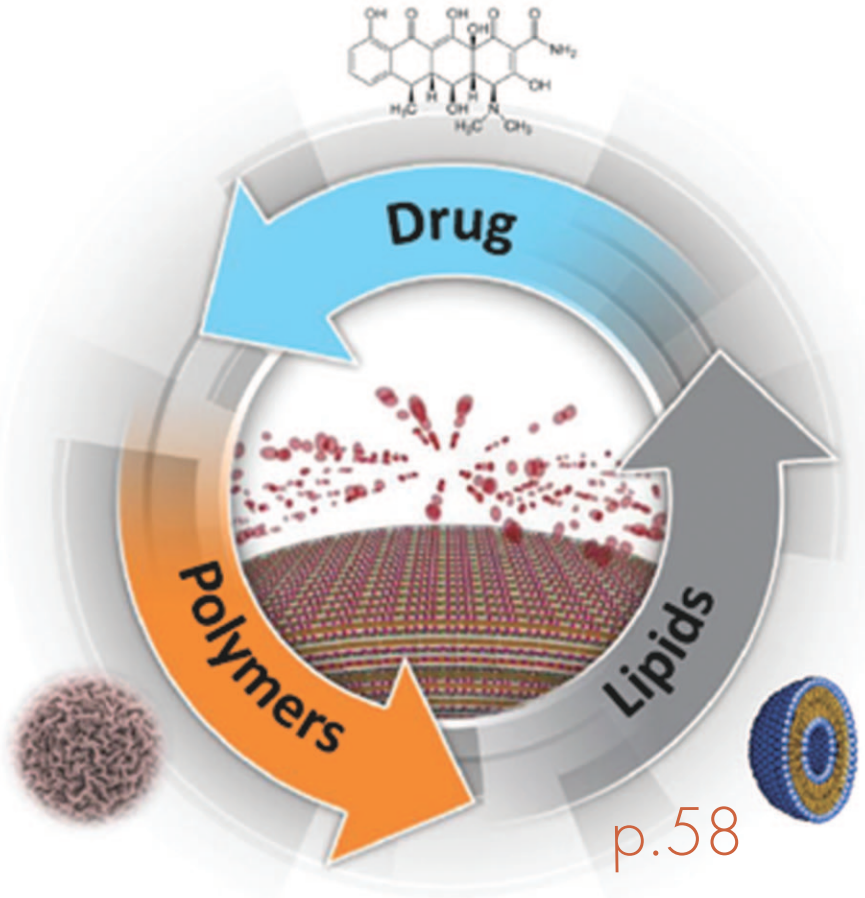

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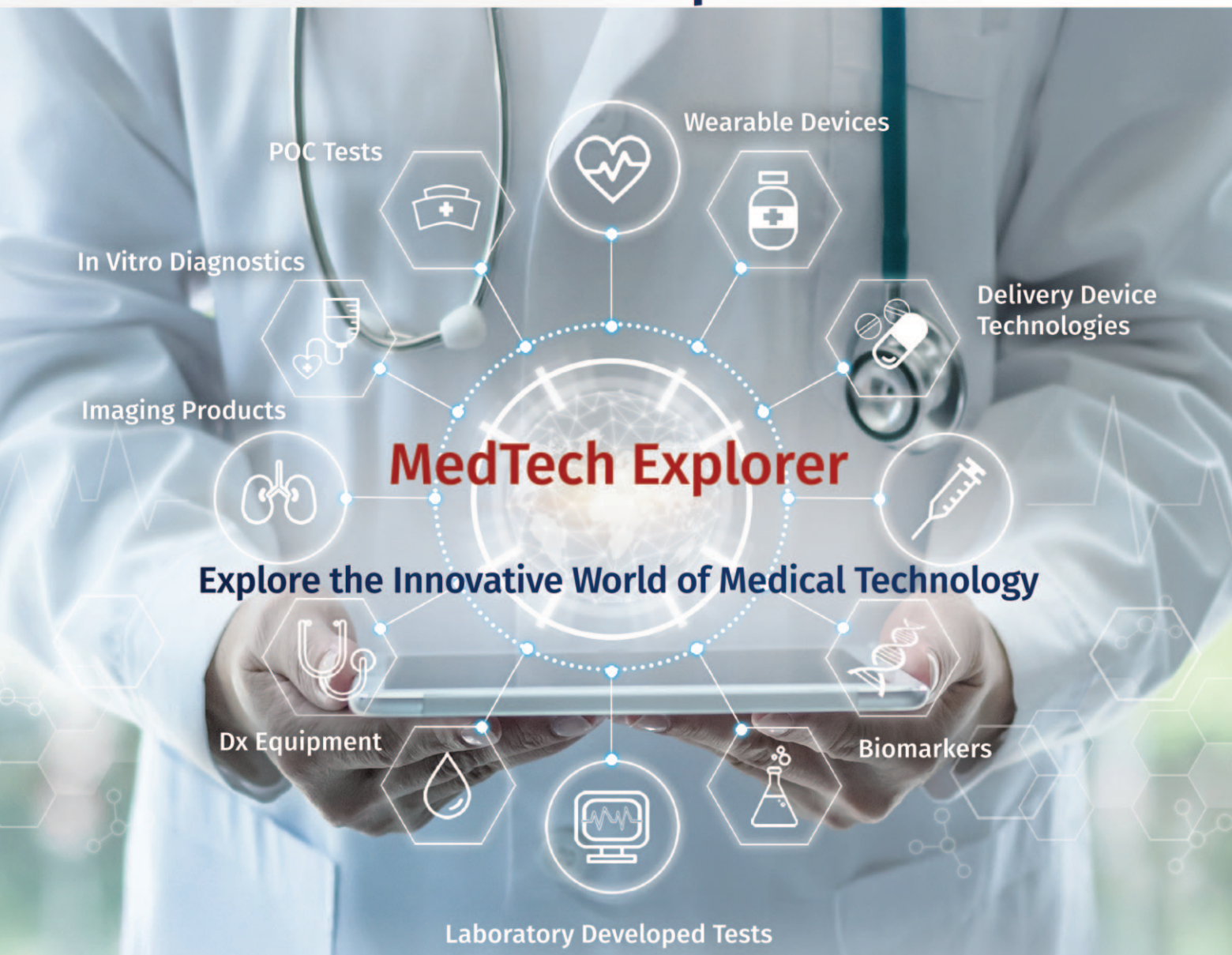

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Ardena Completes Divestment of its Södertälje Drug Substance Site in Sweden to Nanologica

Ardena recently announced it has completed the divestment of its drug substance (API) site in Södertälje, Sweden, to Nanologica AB. The business will operate as a wholly owned subsidiary within the Nanologica Group and will revert to its original name, Syntagon AB.

The Södertälje facility is a well-established drug substance (API) CDMO with more than 45 employees and a strong track record in small molecule active pharmaceutical ingredients. The facility supports programs from early development through clinical supply all the way to commercial manufacturing and has benefited from significant investments in chromatographic purification and falling film distillation capabilities in recent years.

As part of the agreement, Ardena will become a shareholder in Nanologica, and Jeremie Trochu, CEO of Ardena, will join Nanologica's Board of Directors.

The companies have a long-standing relationship, and Ardena is confident Nanologica is the right owner to support the Södertälje site and its team moving forward. Ardena will remain a customer through an ongoing services agreement, ensuring continuity for existing customer programs, and both companies will collaborate on new customer projects where relevant.

Jeremie Trochu, CEO of Ardena, commented: "This transaction supports Ardena's strategy to focus investment and growth on specialized capabilities that enable precision medicines and deliver meaningful patient impact across drug product, nanomedicine, drug conjugates, biomarkers and bioanalysis.

"At the same time, it reflects our commitment to ensuring the best long-term future for the Södertälje site and its talented team. Nanologica is a partner we know well and is ideally positioned to build on the strong foundation in Södertälje and offer an exciting future for the site. I'm pleased to partner with Andreas and the entire Nanologica team, and I look forward to joining their Board of Directors."

Ardena will continue to support customers with an integrated approach to development and manufacturing, enabling efficient progress from early development through clinical and commercial stages for complex therapies. The transaction has been completed following satisfaction of customary closing conditions.

Ardena is a specialist pharmaceutical Contract Development and Manufacturing Organization (CDMO) and bioanalytical Contract Research Organization (CRO) enabling precision medicines and other complex therapies. Its integrated solutions enable innovative and complex molecules through services in nanomedicine and drug conjugates, advanced drug product development and manufacturing, solid-state chemistry, bioanalytical services, and CMC regulatory support. Ardena's nanomedicine capabilities cover the formulation, process development, and GMP manufacturing of advanced delivery systems including lipid, polymeric, and metal nanoparticles.

Nanologica is a Swedish life science tools company that develops, manufactures, and sells advanced consumables to pharmaceutical companies. Nanologica's silica-based products are developed for the purification of peptide drugs, such as insulin and GLP-1 analogues, and are designed to support efficient and long-lasting purification processes. Nanologica is headquartered in Södertälje, Sweden, and its share (NICA) is listed on Nasdaq Stockholm Main Market.

Vetter Pharma to Build New Manufacturing Site in Germany

Vetter Pharma has confirmed its plans to build a state-of-the-art production facility in the Saarland region of southwest Germany. This strategic investment marks a significant milestone in the company's long-term global growth strategy. Construction is scheduled to begin in the second quarter of 2026. Initially, approximately €480 million have been allocated for the first construction phase of the new commercial production plant. Operations are expected to commence in 2031.

The Contract Development and Manufacturing Organization (CDMO) acquired the approximately 95-acre industrial property in the city of Saarlouis at the end of 2024. This location was chosen following careful strategic investment considerations and supported by significant regional advantages. Vetter sees the potential to create up to 2,000 jobs in the long term. The European Commission has approved up to €47 million of state aid for this extensive project.

"With the construction of our new production facility in Germany, we continue on our path to sustainable growth. Long-term success derives from striking the right balance between stability and expansion," emphasizes Senator h.c. Udo J. Vetter, Chairman of the Advisory Board and member of the owner family. "With our investments in the state of Saarland, only a five hour drive away from our headquarters in Ravensburg, we are strengthening our commitment to Germany's economic landscape while reaffirming our engagement as a strategic partner to the global pharmaceutical market."

In parallel, the company recently began construction on a new clinical production site in Des Plaines, Illinois, USA. This new aseptic manufacturing facility emphasizes Vetter's commitment to providing high-quality services and drug products during early clinical development.

For over 75 years, Vetter has been committed to quality, innovation, and responsibility in the production of sterile pharmaceuticals, improving the lives of patients worldwide. To meet growing customer demand and increasing market requirements, the company is investing in its existing sites in Germany, Austria, and the United States. With its newly planned commercial site, Vetter will significantly expand its production capacity.

Vetter is a leading Contract Development and Manufacturing Organization (CDMO) with headquarters in Ravensburg, Germany, and production facilities in Germany, Austria, and the US. As a global player, the independent pharmaceutical service provider is also present in the Asia-Pacific markets of Japan, China, South Korea and Singapore with sales locations. Around the world, renowned pharma and biotech companies benefit from decades of experience, high quality, modern technologies, reliability, and commitment of its more than 7,700 employees. In close collaboration with its customers, the Vetter team helps enable the supply to patients all over the world with medicines, many of which are vital. The CDMO provides support from drug product development through clinical and commercial filling to a wide range of assembly and packaging services for vials, syringes, and cartridges. With innovative approaches, Vetter develops prefilled drug-delivery systems together with its customers to continuously improve patient safety, comfort, and compliance. Vetter takes responsibility for sustainable practices and operates as a socially and ethically responsible corporate citizen.

PhaseV Launches AI-Powered Enrollment Lab: Eliminating Guesswork & Grounding Study Design in Clinical Reality

PhaseV recently announced the launch of its new Enrollment Lab solution at the 17th Annual SCOPE Summit. A high-impact addition to the PhaseV ClinOps platform, this AI-powered solution enables sponsors to quantify a study's true enrollment potential and model the impact of protocol trade-offs prior to protocol lock.

"With the AI Enrollment Lab, we are replacing theoretical planning with evidence-based certainty much earlier in the development lifecycle," said Raviv Pryluk, PhD, CEO and Co-founder of PhaseV. "By uncovering enrollment constraints and trade-offs, we enable sponsors to 'stress-test' their designs and ensure that every study is grounded in a verified, accessible patient population before site identification even begins."

PhaseV's population-first approach accelerates traditional site-level surveys with real-world EHR data to model enrollment dynamics in real-time. By analyzing the intersection of patient eligibility and trial competition, the Enrollment Lab allows study teams to explore alternatives and evaluate how specific inclusion/exclusion criteria impact patient volume. This enables sponsors to optimize design, identify untapped geographic regions, and pinpoint high-opportunity, lightly contested patient segments.

"The Enrollment Lab is an additional layer to our ClinOps platform," said Elad Berkman, CTO and co-founder of PhaseV. "The ability to translate protocol design choices and competitive pressure into a clear view of real patient access is a significant technical step forward. Our precision-guided approach enables teams to execute clinical trials with greater accuracy, accelerating the delivery of new therapies to market."

Strategically positioned early in the study planning workflow, the Enrollment Lab establishes what is realistically achievable before moving to the side identification phase. By revealing where eligible patients exist after accounting for both eligibility constraints and competitive access, the tool informs protocol design and geographic focus. This creates a foundation for PhaseV's site identification tools to then identify and prioritize investigators based on their ability to deliver against a realistic enrollment plan.

Boston-based PhaseV is leading the next era of clinical development through its integrated, multi-modal AI/ML platform that optimizes every phase of the clinical trial lifecycle. The company's core solutions – including the ClinOps, Trial, Portfolio, and Response Optimizers – enable biopharma sponsors and CROs to select the best assets, indications, and patient populations and then rapidly design, plan, and execute optimized fixed, Bayesian, and adaptive trials. With intelligent, data-driven solutions, PhaseV has delivered significant ROI for over 40 leading pharma and biotech sponsors across multiple therapeutic areas, reducing trial costs by up to 50% and increasing the probability of success by over 30%. Learn more at www.PhaseVTrials.com.

Boehringer Ingelheim's Investigational Asset Delivers Proteinuria Reduction in Phase II Kidney Trial

Boehringer Ingelheim announced results from a 12-week Phase II clinical trial evaluating apecotrep (BI 764198), an oral, potential first-in-class, non-immunosuppressive TRPC6 inhibitor for people with primary focal segmental glomerulosclerosis (FSGS). Apecotrep reduced proteinuria, a key indicator associated with kidney damage, by 40% in the 20 mg dose group compared to placebo.

The Phase III trial (NCT07220083) is open for recruiting adults and adolescents with primary FSGS. An additional Phase II trial (NCT07355296) evaluating the safety and efficacy of apecotrep in other proteinuric kidney diseases will start in the first quarter of this year.

Apecotrep demonstrates Boehringer's commitment to addressing high unmet medical needs across a broad spectrum of kidney diseases. This includes primary kidney conditions where no approved disease-modifying therapies currently exist.

Primary FSGS is a rare, progressive kidney disease which can end in kidney failure. Despite its severity and burden for patients, there are currently no approved targeted therapies. There remains a significant unmet need for a targeted therapy that addresses the root cause of the disease.

In primary FSGS, the protein Transient Receptor Potential Channel 6 (TRPC6) is hypothesized to be overactivated on podocytes, cells responsible for the kidney's filtration system. This allows excessive calcium to enter the cells, causing progressive podocyte injury and loss, and ultimately, proteinuria and kidney disease progression. Apecotrep intends to protect podocytes and slow down disease progression by decreasing proteinuria.

Highlighting its potential as a new treatment option for primary FSGS, apecotrep was granted Breakthrough Therapy Designation by the Center for Drug Evaluation (CDE) of the National Medical Products Administration of China and Orphan Drug Designations by the European Medicines Agency (EMA) and the Japanese Ministry for Health, Labour and Welfare (MHLW).

Apecotrep is an investigational, potential first-in-class, oral, once daily, non-immunosuppressive TRPC6 inhibitor that is being developed as a potential treatment for people living with primary FSGS. Its mechanism of action intends to counter the overactivation of TRPC6, a protein channel essential for the structure and function of podocytes, which are specialized cells responsible for the kidney's filtration system. The compound was discovered and developed by Boehringer Ingelheim, and is part of its Cardiovascular-Renal-Metabolic portfolio.

In the Phase II trial, a response to treatment defined as greater than or equal to 25% reduction in urine protein-creatinine ratio (UPCR) was observed in 35% of participants receiving apecotrep across all dose groups after 12 weeks, compared to 1 out of 14 (7.1%) in the placebo arm. The greatest proportion of patients responding to apecotrep were in the 20mg dose (44.4%). Furthermore, a 40% ($p=0.0024$) reduction in UPCR compared to placebo was observed with 20 mg dose. Finally, apecotrep was generally well-tolerated.

Focal segmental glomerulosclerosis (FSGS) is a type of podocytopathy in which podocyte injury and loss result in excess protein in the urine (proteinuria). Approximately, 50% of people with primary FSGS progress to end-stage kidney disease (ESKD) within 5-10 years.

Halo Pharma to Become a Stand-Alone Drug Product Contract Development & Manufacturing Organization

Halo Pharma, a leading CDMO specializing in drug product pharmaceutical development and manufacturing services, will become a stand-alone business as a result of the sale of the Noramco API and associated businesses to Siegfried.

Halo Pharma was purchased by the Noramco Group from Cambrex in 2023. With the sale of the API related assets of the Noramco Group, Halo will serve as a dedicated platform for drug product CDMO services. Halo's sterile CDMO business is expected to be online in the second half of 2026 with a state-of-the-art Groninger UFVN FlexFill filling line and Skan isolator. The line, with change parts, can fill vials (2-30 mL), syringes (0.5-10 mL) and cartridges of various sizes in ready-to-use formats. Halo will continue to offer oral solids, liquids and semi-solids from both Halo sites. To support sterile investment, Halo has recently launched the capability to perform sterile product development including analytical testing and formulation services.

"Anytime you can focus on doing one thing really well, success is inevitable," said Lee Karras Normaco Group CEO. "I look forward to working with the Halo teams more directly at both sites. We already have significant interest from established pharma companies looking to sign up in advance for sterile CDMO services," he went on to say.

Halo Pharma is a rapidly growing contract development and manufacturing organization (CDMO) that provides scientific and development expertise, as well as a wide spectrum of manufacturing services, from its locations in Whippany, New Jersey, USA, and Montreal, Quebec, Canada, to its international client base. Halo Pharma offers fully integrated capabilities across a variety of dosage forms, including solid, semi-solid, and oral liquid, and is expanding to include sterile vial, prefilled syringe, and cartridge formats. The company is registered to work with any of these dosages in the CI–CV DEA designations. Halo Pharma's capabilities in tech transfer, process and product development, production, scale-up/validation, and analytical method development allow it to partner with clients from development through commercialization — or at any point along the way. For more information, please contact services@halopharma.com.

Nanexa Announces Breakthrough Preclinical Data Demonstrating Exceptional Pharmacokinetic Profile for Monthly Semaglutide Formulation

Nanexa AB recently announced exceptional preclinical results for its long-acting semaglutide formulation developed using the company's proprietary PharmaShell drug delivery platform. PharmaShell encases active pharmaceutical ingredients at the atomic level in a highly protective, extremely thin film coating (approximately 30 nm thick) of slow-dissolving non-toxic inorganic oxides.

Recent preclinical studies demonstrate an extraordinary pharmacokinetic (PK) profile, indicating a very low ratio between the maximum and minimum plasma concentration over the dosing interval following once-monthly subcutaneous administration. The plasma concentration is significantly more stable than that typically achieved with weekly administration of the marketed product Wegovy (semaglutide).

A key hallmark of the new formulation is its low initial peak – a feature considered critical in reducing gastrointestinal (GI) adverse events commonly associated with GLP-1 therapies. By avoiding the sharp plasma concentration spikes often linked to nausea and other GI symptoms, Nanexa's formulation may offer a more tolerable initiation and maintenance profile for patients. The preclinical results show clear dose-linearity, and significantly improved bioavailability compared with Nanexa's earlier liraglutide formulations. Improved tolerability is strongly linked to improved adherence, which is a key issue associated with GLP-1 therapies.

With these highly encouraging preclinical findings, Nanexa is shifting its development focus from liraglutide to semaglutide, reflecting the substantial therapeutic and commercial opportunity for long-acting GLP-1 treatments.

The advancement of this semaglutide program builds directly on the clinical Phase 1 data from Nanexa's liraglutide program, presented in 2025, which provided key insights into PharmaShell performance in humans. Those findings enabled refined modelling, improved formulation strategies, and faster advancement for Nanexa toward clinical readiness for semaglutide.

"These latest results represent a major milestone for Nanexa," said David Westberg, CEO of Nanexa. "Demonstrating such a long release profile and low ratio between the maximum and minimum plasma concentration for monthly administration is exceptional and highlights how powerful the PharmaShell® technology can be for complex molecules like semaglutide. We are excited about this data which will strengthen our position to secure commercial partnerships."

Nanexa is bringing the control, precision and versatility of Atomic Layer Deposition (ALD) technology to drug formulation. The company's proprietary PharmaShell platform is a unique drug delivery system that enables a high drug load, thus low injection volume, creating a new generation of 'super generic' formulations that will provide greater convenience and reduce costs in the treatment of conditions such as metabolic diseases like type 2 diabetes and obesity, hematology/oncology, cardiovascular disorders, psychiatry, and many others.

Nanexa develops its own products and also has collaboration agreements with several pharma companies, including the latest license and option agreement with Moderna. Nanexa's share is listed on Nasdaq First North Growth Market in Stockholm (NANEXA).

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Vortex Biotech Opens New State-of-the-Art Laboratory at Manchester Science Park

Vortex Biotech Holdings Limited has announced the opening of its advanced laboratory facilities at Manchester Science Park. The new site significantly enhances the company's R&D and commercial delivery capacity and strengthens its position as a leader in liquid biopsy technologies for precision oncology.

The laboratories are designed to GLP-ready specifications, allowing future expansion into clinical trial support and commercial product and services development. The site also serves as the company's European hub for research partnerships, with planned collaborations in single-cell analysis, molecular profiling, and AI-driven data integration.

Backed by EMV Capital, Vortex' proprietary liquid biopsy platform isolates and enriches circulating tumour cells (CTCs) and other rare biomarkers from blood samples, enabling high-sensitivity cancer detection, monitoring, and translational research. The Manchester facility will accelerate the company's ongoing programmes in clinical validation, biomarker discovery, and commercial services development.

Nigel Brooksby, Non-Executive Chairman at Vortex, said: "The establishment of our laboratory at Manchester Science Park is a strategic step in expanding collaborations with leading academic and clinical institutions and positions the company for growth.

"The Park's proximity to the University of Manchester, NHS Manchester Foundation Trust, and a thriving life sciences ecosystem provides direct access to world-class expertise, clinical samples, and translational infrastructure essential for advancing liquid biopsy into clinical practice."

To mark the opening, Vortex hosted a formal launch event on 26 January 2026 at its new Manchester facilities, bringing together regional stakeholders, investors, and members of the Greater Manchester innovation ecosystem. The event included presentations from the Vortex management team and from EMV Capital, the deep tech and life sciences investment group and Vortex's lead investor, as well as remarks from Andy Burnham, Mayor of Greater Manchester. This was followed by tours of the new laboratories, technology demonstrations, and a celebratory reception.

Joe Manning, Managing Director at MIDAS, Manchester's Inward Investment Agency, added: "Vortex Biotech's decision to relocate from London to Manchester Science Park shows what Greater Manchester can offer life sciences companies looking to scale. The technology developed will enable earlier cancer detection through blood samples, strengthening Greater Manchester's position in cancer diagnostics. The company chose our city region because we offer direct access to the University of Manchester's research capabilities, partnerships through the NHS Manchester Foundation Trust, and a talented workforce. The expansion will create new skilled jobs in diagnostics, science, data and operations, with a commitment to developing local talent through apprenticeships and early-career pathways."

With this expansion, Vortex is positioned to accelerate its commercialisation pathway and deliver non-invasive diagnostic solutions that improve outcomes for cancer patients worldwide.

Vortex Biotech Holdings Limited develops advanced liquid biopsy platforms for the capture, enrichment, and analysis of circulating tumour cells (CTCs) and other blood-borne biomarkers. Its proprietary microfluidic technology enables sensitive, label-free, and viable cell isolation for downstream molecular and cellular analysis. For more information, visit https://vortexbiosciences.com/.

Argo Biopharma Announces First Patient Dosed in Phase 2b Trial of siRNA Therapeutic in Patients with Elevated Lp(a)

Argo Biopharmaceutical Co., Ltd. recently announced the first patient has been dosed in a global Phase 2b clinical trial sponsored by Novartis evaluating DII235, also known as BW-20829, in adults with elevated Lipoprotein (a) (Lp(a)) and Atherosclerotic Cardiovascular Disease (ASCVD). In connection with the molecule's advancement into Phase 2b under its exclusive license and collaboration agreement with Novartis, Argo Biopharma will receive milestone payments that will support ongoing research and development efforts across its hepatic and extra-hepatic siRNA portfolio. BW-20829 is the sixth asset in Argo's pipeline to enter mid-stage global clinical development.

"We are pleased that Novartis has advanced BW-20829 into Phase 2b clinical development," said Dr. Dongxu Shu, Co-Founder, Chairman of the Board, and Chief Executive Officer of Argo Biopharma. "This milestone underscores the strength of Argo's discovery and early clinical development capabilities, together with Novartis' scientific rigor and speed of execution to bring forward therapeutic options for patients' unmet cardiovascular needs. Cardiovascular disease remains the leading cause of morbidity and mortality worldwide, and the progression of BW-20829 into Phase 2b represents a meaningful step toward the potential development of additional therapeutic options for patients with elevated cardiovascular risk."

BW-20829 is an siRNA therapeutic developed from Argo's proprietary RADS platform, and is designed to enable potent, durable gene silencing with differentiated safety and delivery characteristics through hepatic delivery. Argo Biopharma continues to advance a cardiovascular and specialty disease pipeline via hepatic siRNA, and maintains an earlier-stage portfolio of extra-hepatic siRNAs targeting multiple tissue types and therapeutic areas. Information regarding the Phase 2b clinical study can be found on ClinicalTrials.gov. Study Details | NCT07235046 | A Study of DII235 in Adults With Elevated Lipoprotein(a) | ClinicalTrials.gov

Argo Biopharma is a clinical-stage biotechnology company committed to developing next-generation RNAi therapeutics to provide better treatment options for patients worldwide. The company has established a robust and diverse pipeline of RNAi molecule candidates targeting a wide range of indications, including cardiovascular diseases, viral infections, metabolic conditions, and specialty/rare diseases. Currently, Argo Biopharma has six RNAi candidates in clinical development. For more information, visit www.argobiopharma.com.

iXCells Biotechnologies & Rosebud Biosciences Partner to Advance Organoid-Based Models for Rare Diseases

iXCells Biotechnologies and Rosebud Biosciences recently announced a partnership to develop a personalized, human-based approach for predicting drug safety and informing translational decision-making in rare diseases. As iXCells enters its next phase of growth, the collaboration expands the Company's custom integrated platform and strengthens the suite of modeling technologies available to customers seeking advanced predictive and physiologically relevant systems.

Through this partnership, iXCells will integrate Rosebud's organoid generation and characterization expertise into its existing iPSC solutions, enabling access to complex 3D human systems that better represent tissue-level biology and simulate therapeutic response. The combined workflow brings together iXCells' scalable, modular iPSC platform, iPSCore, with Rosebud's AI-driven organoid platform, designed to generate scalable, reproducible human tissue data for drug discovery and safety assessment. Together, the technologies offer researchers more complete and biologically representative model systems for understanding disease mechanisms and drug safety.

The expansion of organoid capabilities reflects iXCells' continued investment in next-generation modeling technologies that meet growing customer demand for human-relevant and predictive systems. Organoids are an essential component of translational research strategies, particularly for evaluating drug toxicity and tissue-specific responses. This integrated offering delivers the consistency, scalability, and reproducibility required for screening, engineering, multi-omics profiling, and mechanism-of-action studies within a unified, end-to-end solution.

Steve Smith, Chief Executive Officer of iXCells Biotechnologies, commented: "Our focus has always been on anticipating what our partners will need next, and Rosebud brings impressive depth in organoid science that aligns perfectly with that vision. This collaboration enhances our end-to-end platform and expands our ability to deliver next-generation models that reflect human biology with greater depth and accuracy. In areas such as rare diseases, where predicting human-specific safety and response earlier can significantly impact development timelines and patient outcomes, these integrated systems provide critical insight. This partnership reflects the strategic direction we are taking as iXCells scales its platform to support more complex, translationally focused programs for our partners."

Kitch Wilson, Chief Executive Officer and Co-Founder, Rosebud Biosciences, added: "Our partnership with iXCells allows us to make advanced organoid systems more accessible to researchers who need models that better represent human biology. By combining our complementary strengths, we can support deeper exploration of disease biology and help drive the next generation of therapeutic discovery."

iXCells Biotechnologies is a leading San Diego, CA-based cell technology company focused on generating a wide variety of predictive human disease models. In addition, iXCells is pursuing custom and patient-specific services leveraging its expertise in the preparation, handling, engineering and differentiation of induced pluripotent stem cells (iPSCs) and in the isolation of primary cells along with associated services for descriptive and functional cell characterization, compound screening and toxicology testing.

Rosebud Biosciences builds industrialized, AI-powered human organoid platforms for drug discovery, toxicology, and precision medicine. The company integrates automated organoid differentiation, scalable robotics-driven workflows, and advanced machine learning analysis to generate large volumes of standardized, clinically meaningful human data.

Sharp Services Makes Significant Investment to Expand Injectables Packaging Capacity at its European Facilities

Sharp Services recently announced it has invested over €20 million in its European packaging facilities in response to strong market demand in the injectables market. The investment is focused on adding capacity and capabilities for the assembly, labelling, packaging and cold storage of a variety of injectable formats – including autoinjectors, pen devices, pre-filled syringes and vials – at Sharp's facilities in Hamont-Achel, Belgium and Heerenveen, The Netherlands.

The expansion at the Belgian facility will quadruple the existing cold-chain warehouse capacity and double ambient storage space, as well as add a new syringe assembly and blister packaging suite. Additional device assembly and packaging capacity are also planned. In addition, Cobot' (collaborative robot) technology has been introduced to enhance production efficiency for adjacent pre-filled syringe and autoinjector packaging lines.

The facility in Hamont-Achel has been extensively upgraded to also include a carport solar system which will deliver clean, renewable energy in alignment with Sharp's sustainability goals. The system is expected to supply 50% of the site's electricity demand in clean, renewable electricity once fully commissioned in mid-2026.

Sharp's Netherlands facility will expand its GMP production capacity – including the addition of two Grade D packaging suites – to accommodate new syringe assembly and packaging programs and vial packaging capacity, which is due to be operational at the end of 2026.

Robert O'Beirn, Managing Director, Sharp Clinical & Sharp Europe commented: "Our European facilities have a long-established reputation for successfully delivering the complex packaging services required for injectable drug formats. This investment represents a significant increase in our capacity to support our pharma clients, as sustainably as possible, with their injectable drug launches in the EU market."

This investment in Sharp's Belgium and Netherlands facilities is part of the company's larger $100 million expansion of capacity and capabilities in support of the evolving needs of its clients, announced in November 2025.

Sharp is a leader in pharmaceutical packaging, clinical trial services & sterile manufacturing, with a heritage spanning more than 70 years. We partner with pharmaceutical and biotechnology clients, offering solutions and support from phase I trials all the way through commercial launch and lifecycle management. Together, our 2,500+ strong team leverage the capabilities in state-of-the-art GMP facilities in the US, UK, Belgium, and the Netherlands. For more information on Sharp and its solutions, visit www.sharpservices.com.

Formulation Forum

Solid Oral Dosages: Controlled Release of Drugs

By: Shaukat Ali, PhD, Sr. Director, Scientific Affairs & Technical Marketing, and Jim Huang, PhD, Founder & CEO, Ascendia Pharmaceutical Solutions

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KEYWORDS: controlled release, sustained release, extended release, matrix tablets, direct compression, co-processed excipients, coating polymers

INTRODUCTION

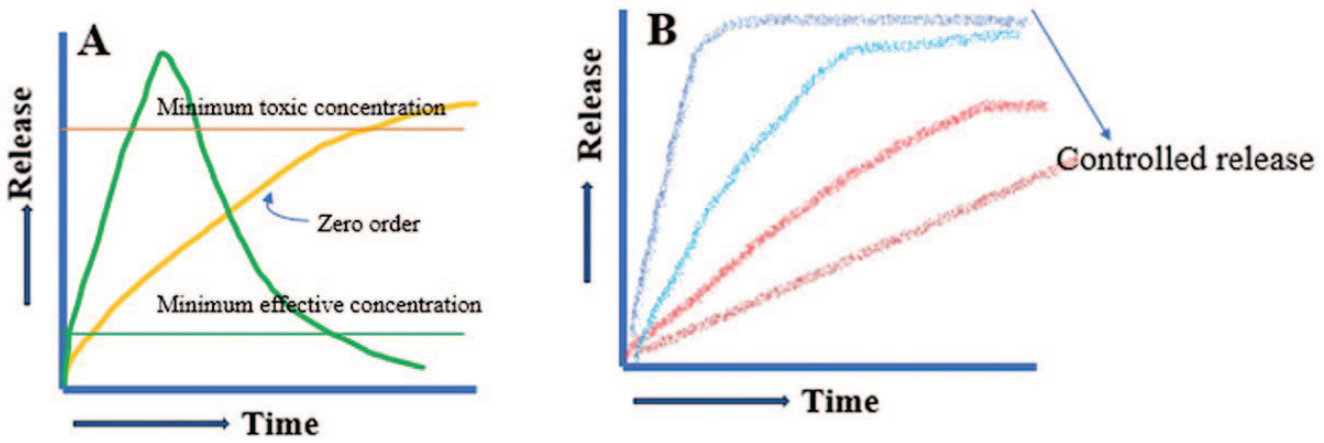
There is a continued interest in controlled release of drugs across all modalities. It is due, in part, to increase the safety risk associated with immature release or dose dumping to prevent drug overdose. As more molecules discovered are poorly soluble and less orally bioavailable, developing a solid oral dose form (SODF) poses further challenges associated with complex mechanisms for controlling the release of drug from a particular dosage.[1] In spite of these challenges, drug manufactures and excipient manufactures alike are taking aim at different technologies for better understanding of mechanisms allowing the controlled release of drug to maintain the optimal concentration in systemic circulation.[2]

CONTROLLED DRUG DELIVERY SYSTEMS

Figure 1 illustrates the immediate release and controlled release of single dose curves typically demonstrated by matrix tablets (A) and variations in release profiles of a drug preferably controlled by coating thickness of the coating polymer (B).

Controlled drug delivery systems based on the dissolution can be divided into matrix and reservoir or encapsulated dissolution systems. Zero

FIGURE 1



Illustrations of controlled release drugs as function of time.

FIGURE 2

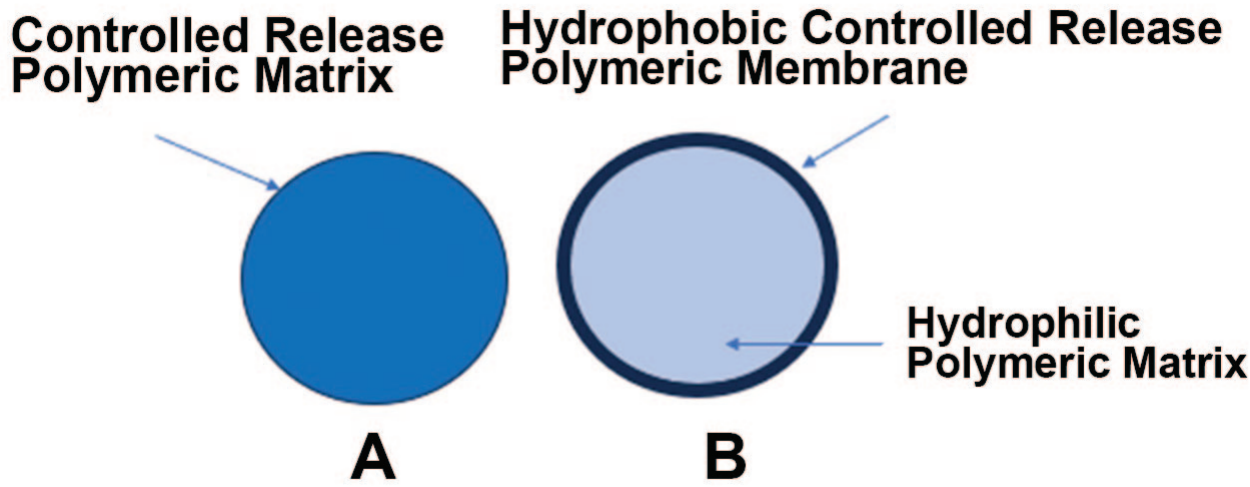


Illustration of water soluble matric with controlled release coating layer and insoluble matrix without coating layer from monolithic tablets.

order release, for example, allows the release independent of concentration of drug; whereas first order release is directly dependent on the concentration of drug by achieving the desired minimum effective concentration (MEC) and minimum toxic concentration (MTC) (Figure 1A).[2] Therapeutic Index (TI) is the safe amount of drug far below its toxic level. Therapeutic window is the concentration range of drug between efficacy and toxicity.

Figure 2 illustrates monolithic tablets derived from insoluble or hydrophobic polymeric excipients in the matrix and by membrane coating of hydrophilic water-soluble polymeric matrix with uniformly distributed drug molecules.[3] In a diffusion-controlled release matrix, for example, the drug is trapped inside and released via diffusion through polymeric matrices (Figure 2A) or through inert water-insoluble polymeric membrane (Figure 2B) in which the rate limiting step is the diffusion of drug.[4]

Spansul® is a controlled/sustained release system that was used for Dexedrine® (dextroamphetamine) in which the core beads are coated with varying thickness of beeswax or glyceryl mono stearate for 12-hour release to treat narcolepsy. Contac® also used this platform technology for controlled release via a polymer coating.[5] Over the years, controlled-release drug delivery remains the most widely used technology for a number of drugs with the goal to extended the release and to reduce dosing frequencies, making it patient centric. A few examples of earlier developed coated drugs include Compazine®, Dexedrine®, Ornade®, Thorazien®, Cardizem®, Diamox®, Plendil®, Procanbid®, among others.

Matrix dissolution systems are controlled by polymeric excipients homogeneously distributed within a tablet or pellet. Dissolution or release of drugs through these dosages depends upon the nature of excipients and drugs, including their hydrophilic and/or hydrophobic characteristics. In a polymeric system, as the drug dissolves, it migrates to surface (Cs) from the core matrix to bulk solution (C), and is controlled by diffusion layer as shown in Figure 3, and by Noyes-Whiney equation below:

$$dm/dt = D*A*(C_s - C)/h$$

Where, D is the diffusion coefficient, A is the surface area of the matrix, and m is the total amount of drug dissolved from the surface. The aqueous layer essentially acts as a barrier through which the drug molecules are diffused. Thus, the drug concentration in the diffusion layer is always higher than the bulk solution, and DC is the difference between Cs and C (shown in the equation and illustrated in Figure 3).[5]

Examples of commercially available controlled release drugs include Anpec® SR; Cordilox® SR; Imdur Durules, Isoptin® SR; Monodur Durules®; Nuelin® SR; Sinemet® CR; Theo-Dur®; Adalat® OROS; Adalat® tablets, Agon SR; Ceclor® CD; Felodur ER; Keflor® CD; Kinidin Durules®; MS Contin®; Naprosyn® SR; Plendil® ER; Tenuate Dospan®.[6] Others include Tempule® as capsulea and Dospan®, Chronotab®, Repetab®, Extentab® Adalat®, among others. Adalat®, for example, an extended release nifedipine tablet coated with a water-soluble polymer, involves coating by a sustained release polymeric excipient.

EXCIPIENTS FOR CONTROLLED RELEASE FORMULATIONS

Excipients for controlled release applications are shown in Table 1. These excipients play an important role in deciding the dose selection for a particular drug, either insoluble or soluble, depending upon the delivery mechanisms, delivery period, or

FIGURE 3

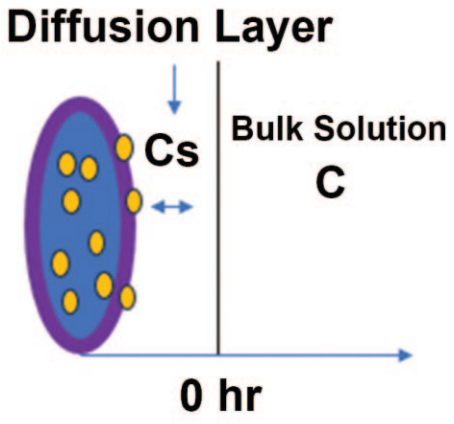


Illustration of drug dissolution through a matrix tablet.

delivery route.

Many of these excipients are used in several technologies, including direct compression, wet granulation, roller compaction, melt extrusion, and spray drying among others. The key attributes required are quality, drug compatibility, particle size, flowability and thermal stability, and porosity. In addition, their compatibility with downstream processing could contribute to greater stability and shelf-life of the drug products on storage and packaging.

Majority of controlled released drugs are monolithic tablets or pellets, wherein the drugs are homogeneously distributed within the matrices, which are typically composed of water-insoluble and non-porous excipients. Matrix tablets, due to lack of coating, often require higher percentage of polymers depending upon the nature of drugs. For instance, if the drug is hydrophilic, higher percentages of polymers per dose are required to achieve the desired release characteristics or vice versa. Thus, there is a lesser chance of dose dumping from the matrix tablets. In contrast, coating polymers, if not applied in the appropriate amounts, the monolithic tablets can lead to dose dumping or uncontrolled release. In several cases, the polymers are highly compressible and prepared either by co-processing of multiple excipients "in one" to yield higher compatibility in direct compression at lower compression force or produced synthetically as co-polymer or mixture of copolymers or other ingredients with enhanced compactability and performances to minimize the premature drug release.

The following will cite a few examples of controlled release excipients and their attributes from monolithic matrix tablets and polymeric coated tablets.

POLYVINYL ACETATE-BASED EXCIPIENTS

Polyvinyl acetate-based controlled released polymer (Kollidon® SR, MW 450,000 D) is a spray dried powder composed of water-insoluble polyvinyl acetate and water-soluble PVP K-30 as a pore former. It's highly compatible with many processing technologies, such as direct compaction, roller compaction, wet granulation, melt granulation, melt extrusion, and others. With its excellent flowability, <30° angle of repose, average particle size of 80-100 microns, and higher compressibility, low Tg (35°C-40°C), less hygroscopicity, Kollidon SR can be an excellent choice for directly compressible matrix tablets.[7] For its unique composition, the controlled release of drugs depends upon their unique composition containing polyvinyl acetate (PVAc), a hydrophobic polymer and its PVP-K30, a pore former through diffusion mechanism. Because it's pH independent, it is highly compatible to most drugs (either acidic or weekly basic).

In a highly water-soluble propranolol formulation with Kollidon SR, it showed an extended release over 16 hours at pH 2 (0-2 h) and PBS 6.8 (2-16 h) buffer from monolithic compressed tablets, each weighing 330 mg, 10 mm in diameter and composed of API: Kollidon SR (1:1) and compressed at 10 kN, 18 kN, 25 kN compression forces.[8] The release data also suggests the release profiles were independent of compression forces. For insoluble drugs, the concentration of Kollidon SR could vary from

TABLE 1

Natural Excipient	Synthetic Excipient
Polysaccharides	Polyacrylic acid
Alginates sodium	Polyethylene glycol (high MW)
Chitosan	Polyvinyl alcohol
Carboxymethyl cellulose sodium	Polyvinylpyrrolidone
Hydroxypropylcellulose	Polyvinyl acetate
Hydroxy propylmethylcellulose	Poloxamers
Methylcellulose	Carbopol
Starch	Polycaprolactone
Xanthan gum	Polyglycolic lactic acid copolymer
Locust bean and guar gum	Polylactic acid
TimeRx®	Hydrogenated castor oil
Beeswax	

Excipients for CR Formulations

low to medium range. Thus, typical recommendation for a water- insoluble drug, polymer concentration could range 15%-25%, while for water-soluble drugs, Kollidon SR counts could be 40%-50%. Because it is approved in several drugs and listed in the IID, the maximum amount of Kollidon SR could be a 564 mg maximum daily dosage.[9]

CELLULOSIC EXCIPIENTS - DIRECTLY COMPRESSIBLE GRADES

Ashland offers a range of excipients for controlled release tablets, including Benecel™ DC HPMC that offers good flowability and compressibility at lower compression force. Those DC grades include Benecel K4M PH DC, K15M PH DC and K100M PH DC with the nominal viscosity of 80-120 mPas, 200-300 mPas, and 562-1050 mPas, respectively, and typically used at 2% polymer concentration of each. Other controlled release HMPC grades include Benecel L100 V PH, K250 PH, K750 PH, K1500 PH, with the viscosity of 80-120 mPas, 200-300 mPas, 562-1059 mPas, and 1125-2100, mPas, respectively, and used at 2% polymer concentration of each.

Schwing et al. investigated Benecel K100M XRF in monolithic metformin HCl tablets, prepared by extra-granulation with HPMC K100M in direct compression, each weighing 600 mg, 11 mm in diameter, and compressed at 25 kN. The dissolution profiles of metformin tablet showed over 16 hours release and was independent of rotary speed either at 20 rpm or 40 rpm.[10] In comparison with HPMC CR grade, the dissolution profile was consistent and showed over 16 h release.

IFF (Roquette) offers Methocel™, a cellulose-based excipient for controlled release. It is a water-soluble polymer composed of methylcellulose and hydroxypropyl methylcellulose (hypromellose) in different amounts. Depending upon the ratios of the two, one of the grades of Methocel™ K100M Premium, an HPMC, high molecular weight grade, is a preferred excipient for controlled release application.[11]

Kumar et al. used Kollidon SR and HPMC based Methocel K100M in combination for ondansetron matrix tablets (drug/polymer, 1:1) at pH 2 and pH 6.8. Both showed >90% zero order release over 24 hours, but the Kollidon SR showed the distinct shape and characteristic of tablets by the insoluble PVAc, while PVP acts as a pore former.[12] Methocel K100M, when used as matrix without Kollidon SR, showed an immediate release as pH 1.2 but slower release at pH 6.8, suggesting that drug was soluble in acidic pH, but was less soluble at higher pH, with an extended 40% release over 12 hour period.

The matrix tablets composed of five individual controlled release excipients, such as Compritol® 888ATO, Eudragit® RS, Methocel® K100M, Polyox® WSR301, and Precirol® ATO5, were evaluated as placebos and with varied combinations of acrivastine and pseudoephedrine. *In vitro* dissolution data suggests that due to water-soluble API, none of the excipients used alone gave the desired sustained release over 8 hours, but the lipid–based Compritol combined with hydrophilic Methocel produced the optimal drug release showing an extended release over 8 hours for acrivastine and pseudoephedrine.[13] In another study, Knarr and Rogers evaluated HPMC with different substitutions of hydroxypropyl (HP) moieties and found that gliclazide matrix tablets containing HPMC with higher HP substitutions could lead to desired controlled release over 10 hours.[14]

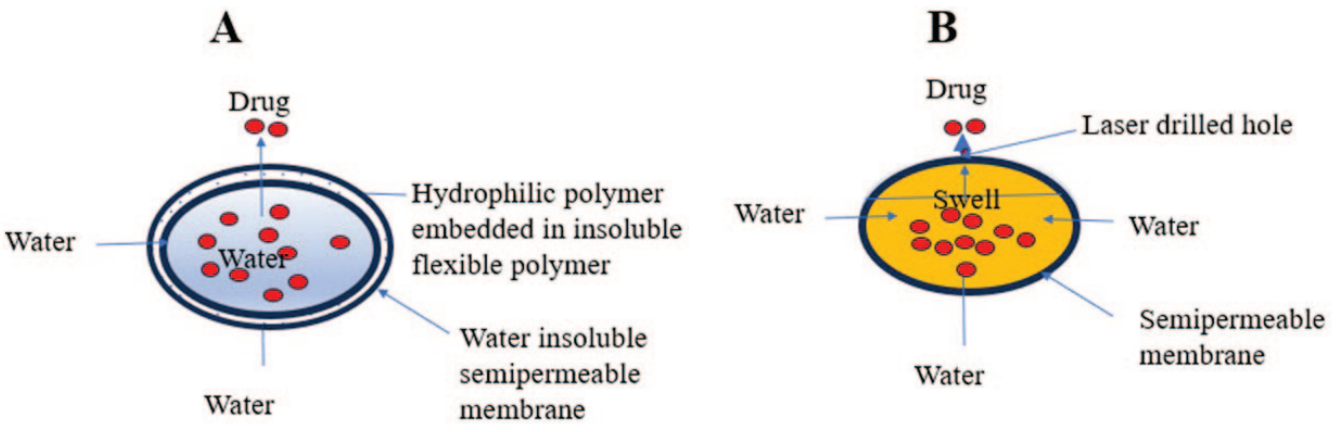
For monolithic matrix tablets, osmotically controlled polymers are also used. The mechanism by which the drug released requires the diffusion of water from high concentration from outside to lower concentration within the matrix, thus allowing the matrix to swell and push the drug to diffuse either through a pore in semipermeable membranes.[5] Semipermeable membranes like resin membrane allows water to permeate inside from outside, which helps diffuse the drug by building the internal pressure within the matrix tablet. The porosity of the semipermeable membrane is critical and might be controlled by pore formers, such as hydrophilic polymers and solubilizers. Table 2 below lists a range of semipermeable polymers used in controlled release applications. Their water vapor transmission (WVTR) values are also listed.[5]

Kollicoat SR 30D, composed of polyvinyl acetate, acts as a semipermeable membrane and allows the controlled release of solute through diffusion.[15] In a study, Ambroxol HCl pellets coated with Kollicoat SR 30D at 10% and 20% weight gains. The resulting pellets were compressed into tablets, each weighing 400 mg, 100N in hardness, and 10 mm in

TABLE 2

Polymer	WVTR (g/100 in2/24 h/ 1 mm thickness)
Polyvinyl acetate	n/a
Polyvinyl alcohol	100
Cellulose acetate	40-75
Ethyl cellulose	75
Cellulose acetate butyrate	50
Polycarbonate	8
Ethylene vinyl acetate	1-3
Polyethylene	0.5-1.2

FIGURE 4



Semipermeable membrane in controlled release technologies.

diameter. The drug release from pellets, compressed in tablets composed of 50% MCC and 1% magnesium stearate as lubricant in tablets, was relatively slower with 20% coating vs 10% polymer, and showed over 24 hours release in both cases.[16] The controlled release of drug is a result of water permeation through polyvinyl acetate semipermeable membrane, which has tendency for greater elasticity and self-repairing mechanism, so that the release rate is maintained over an extended period without being ruptured (Figure 4A).

In an osmotic controlled release oral delivery system (OROS), however, the core tablet is composed of a matrix with two layers, an active layer with drug and a physiological inert push layer (Figure 4B).[17] As the tablet absorbs water through the semipermeable membrane, the polyethylene oxide swells and pushes the active and exerts pressure against the active layer and releases the drug through laser drilled holes. If it was not drilled through with a laser, the semipermeable membrane can still allow water to permeate through osmosis, but the solute or drug can't diffuse through. In OROS technology, the water-insoluble cellulose acetate membrane is most frequently used to control the release through a laser drilled hole as indicated in Figure 4B. The controlled release in the GI tract is independent of pH. Drug delivery through OROS follows zero order kinetics. The release of drug through a laser drilled orifice depends on the rate at which the water enters in the core matrix, thus, the release is independent on the pH outside in GI tract.

Thapa et al. evaluated ethyl cellulose-based Surelease®, a coating system composed of ethyl cellulose 20 cps, medium chain triglycerides, and oleic acid, for efficient coating of a model water-soluble and half-life of 2-6 h drug methimazole with a short processing time.[18] The coating suspension was easily diluted with water and sprayed onto a pellet with the desired weight gain. The higher coating thickness resulted in slower and controlled release.

In an example, a carbamazepine coated tablet with and without 5% fine grade crospovidone, each composed of 200 mg drug, weighing 407 mg with 11 mm diameter and 136 N hardness and <0.1% friability, and with 12.5% weight gain, showed an extended release over 16 hours vs 20% release without crospovidone (Kollidon CL-M), suggesting this fine grade crospovidone helps as a pore former in the tablet.[19]

Mechanical stress on the polyvinyl acetate-based coated tablet was also assessed. For example, metoprolol tablet, each composed of 200 mg drug, 5 mg PVP K30 as pore former with dicalcium phosphate as soluble matrix, coated with Kollicoat SR 30D at 4.6-10 mg/cm^2 weight gains, was subjected to stress test by friability and by puncturing a hole in the tablet. The dissolution data of all tablets with and without defects, was identical to freshly coated tablets, and showed an extended release over 16 hours. Taken collectively, the data suggests that polyvinyl acetate-based film around the tablet is highly flexible due to low Tg, and also possesses a self-healing mechanism that prevents dose dumping.

In another study, Ahmad et al. evaluated Kollicoat SR 30D for controlled release of diltiazem HCl from sugar pellets prepared by coating drug with a hydrophilic polymer, Kollicoat IR (PEG-PVA (1:3) graft copolymer) used as binder and pore former in different ratios with Kollicoat SR 30D (5:1 and 5:2). The authors demonstrated that using active layering and coating, the release was independent on drug/IR ratios over an extended period, but was dependent upon the concentration of SR30, as it showed slower release with higher coating weight gain and vice versa.[20]

EUDRAGIT® NE 30D

Polyacrylate based neutral co-polymers have been used in controlled release applications for coating of tablets and pellets.[21] Eudragit® NM 30D, for example, is also

available as an aqueous 30% dispersion for controlled release applications. It is highly flexible like Kollicoat SR 30D and may not require plasticizers for film coating of matrix tablets and multi-particulates.[22] Eudragit NE 30D has a molecular weight of 750,000 D; whereas NM 30D has a molecular weight of 600,000 D. The glass transition temperatures (Tg) of NE 30D and NM30D, are 8°C and 11°C, respectively. Because both are neutral polymers, the release of drug is independent of the gastrointestinal pH. While there are no examples of NM 30D available, NE 30D has been used in controlled release coating of multi-particulate pellets and tablets and buccal films. In another study, Arno et al. evaluated Eudragit NE 30D in wet granulation of extended release of metformin and gliclazide tablets. The authors demonstrated that increasing the amount of polymer controlled the release over 6-8 hours.[23] In a typical granulation, 1000 mg of metformin HCl and 160 mg of gliclazide were wet granulated with 348 g of NE30 D dispersion (104.4 mg of polymer content), with 100 mg of dibasic calcium phosphate, 17.4 mg of PVP K30, and 11.6 mg of colloidal silica. *In vitro* data from combo tablet showed 30%-40% release in the first hour and the complete release slowly over 8 hours.

In a study, Cuppock et al. evaluated a blend of highly flexible and hydrophilic Eudragit NE30 and hydrophobic Kollicoat SR30D. The authors concluded that release of drug involved diffusion through intact polymeric film coatings rather by diffusion followed by convection through water-filled cracks.[24]

SUMMARY & FUTURE PERSPECTIVES

With continued interest in drug delivery for challenging molecules, we find that controlled release remains at the fore front of innovators. With the need to reduce dosing frequencies and alleviate adverse effects, finding the appropriate excipients compatible to drugs and hence, the desired technologies, could be highly complex. As more new drug candidates are being discovered, drug manufacturers are open to adapting new technologies to expedite the development. As it is relevant to other dosages, the solid oral dosage form (SODF) continues to gain momentum for small and large molecules both for immediate and controlled release. The latter offers a significant advantage over former applications, due in part to better controlling abilities, reducing pill burden, and more so for affordability and meeting patient compliance. Ascendia offers a range of options for oral formulations. AmorSol®, for example, applicable to amorphous solid dispersions (ASDs), and EmulSol® for liquid microemulsion and nano-emulsions, can be widely used for a wide spectrum of small and large molecules across all modalities for immediate and controlled release. If extended release is required, these technologies can be further optimized to tailor formulations to achieve the desired extended release profiles. For example, SEDDS formulations requiring fluid bed coating of pellets with insoluble drugs in solid SEDDS can be extended to a range of water insoluble drugs and to further improve the stability of drugs like ramipril.[25] ◆

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Leadership Panel

5 Trends to Watch for in 2026

By: Cindy H. Dubin, Contributor

In this fourth annual exclusive Leadership Panel discussion, *Drug Development & Delivery* life science leaders discuss the role of AI in drug repurposing, the future of personalized medicine, the importance of sustainability, and how to keep pace with innovation amid real-time FDA reviews. This year's roundtable leaders are: Paul O'Shea, CSO, Exemplifyy BioPharma (a Symeres company); Dr. David Butler, Chief Technology Officer, Hongene; and Rick Seibert, CIO, SVP, Corporate Technical Services, Sharp.

Paul O'Shea
CSO
Exemplifyy BioPharma
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Hongene

Rick Seibert
CIO, SVP
Corporate Technical Services
Sharp

1. AI & DATA ANALYTICS INTEGRATION WILL BE PERVASIVE IN DRUG DISCOVERY & INNOVATION

Mr. O'Shea: AI and data analytics are becoming foundational to modern R&D, particularly as drug discovery programs are increasingly divided into smaller, faster-moving stages. Quality data is more important than ever, and organizations are relying on digital tools to generate insights from limited early-stage experiments and to interpret those outputs in ways that guide funding decisions and downstream development. The growing value of AI lies in its ability to uncover patterns that human assessment alone might miss. Whether in complex solid-state screening datasets, process optimization studies or early risk-assessment exercises, AI-guided processes can help shape an investigational new drug (IND)-enabling strategy.

The industry is also recognizing that digitalization must be paired with scientific context. Although AI can accelerate decision-making, scientists are still required to interpret what the data means for regulatory expectations, impurity control or next-step technical design. With the development of innovative modalities, including lipids, radioligands, and polymer-based delivery systems, the volume and complexity of datasets will continue to expand. This makes secure, compliant data management and AI-enabled insight generation integral to faster and more flexible drug discovery and development.

Dr. Butler: AI and data analytics are increasingly being embedded in early drug discovery workflows. This is particularly prevalent in modalities such as RNA therapeutics, where sequence space, delivery optimization, and manufacturability each present multidimensional challenges. We expect AI integration to become increasingly prevalent across early discovery, candidate optimization, and manufacturability prediction. For RNA modalities, AI models are already accelerating sequence design, secondary structure prediction, and predictive modeling of innate immune activation or off-target motifs. They are also beginning to support LNP formulation optimization, helping teams reduce experimental complexity and focus on the most promising candidates.

Equally important is AI's role in developing and innovating CMC with the implementation of digital systems that continuously capture process data across manufacturing operations. These datasets create opportunities for AI-assisted yield prediction, impurity tracking, and automated process optimization, which may shorten development cycles and improve batch-to-batch consistency.

As the industry moves toward higher-volume oligonucleotide and mRNA products, AI will allow companies to make data-driven decisions about scalability, cost of goods and sustainability. Rather than being a specialized tool, AI is likely to become increasingly integrated across the pipeline, from discovery to commercial manufacturing, where it can support faster innovation and improved patient outcomes.

Mr. Seibert: AI is rapidly reshaping how drug discovery and innovation occur, and that shift will ripple across the entire pharmaceutical supply chain – including CDMOs. As pharma companies adopt AI to accelerate early-stage discovery, they will increasingly expect their downstream partners to operate with a similar level of intelligence—delivering faster insights, higher-quality outputs, and more connected operations across the value chain.

In the CDMO environment, AI is already providing high-value predictive insights. By evaluating historical performance and real-time operational data, AI can forecast demand, optimize inventory, and recommend the most efficient production schedules. This enables both CDMOs and their clients to respond faster, use resources more effectively, and drive higher overall throughput and reliability.

Given the pace of advancement, AI's role within CDMOs is expected to grow exponentially – moving from operational support into increasingly sophisticated applications that enhance quality, efficiency, and innovation across the full development lifecycle.

However, as industry moves toward increased automation and intelligence, maintaining strong human oversight will be essential. The pharmaceutical industry operates in a highly regulated environment, where quality, data integrity, and patient safety cannot be compromised. AI-driven insights must be validated, interpreted, and governed by experienced professionals who understand regulatory expectations and can ensure systems are used compliantly. Human review of AI recommendations – par-

ticularly those affecting product quality, batch disposition, and regulatory submissions – will remain critical in this transition. CDMOs that strike the right balance between leveraging AI and preserving expert human judgment will be best positioned to adopt these technologies responsibly and effectively.

2. AI WILL BE ESSENTIAL IN DRUG REPURPOSING

Mr. O'Shea: By rapidly interpreting preclinical observations, solid-state behavior, analytical trends, impurity profiles, and historical performance across related chemistries, AI can help significantly accelerate drug repurposing. These tools help teams recognize when a molecule with setbacks in one program may hold promise elsewhere, enabling the swift pivots that are increasingly essential in early development. Data interpretation supported by AI gives sponsors faster clarity on feasibility, regulatory implications and the most efficient path toward new IND submissions.

Drug repurposing itself is gaining traction because the economic and geopolitical climate is pushing organizations toward lower-risk discovery and development models. Developers are dividing programs into smaller and more achievable milestones. When a candidate falters, the ability to rapidly slot in a new molecule or redirect an existing one protects budgets and timelines. Strategic partners with deep scientific breadth can help translate AI-generated insights into practical next steps, ensuring teams understand what the data means for manufacturing, formulation and clinical-trial readiness. As reshoring pressures, cost constraints, and diverse modality pipelines grow, repurposing offers a path to resilience in drug discovery and development.

Dr. Butler: AI is transforming drug repurposing by enabling rapid, large-scale interrogation of large biological and clinical datasets to identify new therapeutic hypotheses for repurposing existing molecules. Machine Learning models can help detect disease-target associations, mechanistic overlaps, transcriptomic signatures, and real-world evidence patterns that would be difficult to identify at scale. As these tools mature, they are poised to accelerate the repurposing cycle while reducing uncertainty and cost.

Repurposing continues to attract interest because it aligns with the industry's need for speed, reduced development risk, and capital efficiency. Existing molecules carry known safety profiles, allowing developers to bypass years of toxicology studies and move directly into proof-of-concept trials. As development timelines shorten, payers become more demanding and clinical expectations rise, the ability to move forward with fewer unknowns makes repurposing a pragmatic path to both clinical and commercial impact.

AI amplifies this value across multiple points in the development process, from identifying unexpected therapeutic opportunities to supporting work on optimizing dosing and patient stratification. For nucleic acid therapeutics, AI-driven transcriptomic and pathway analyses are beginning to surface new genetic targets that pair well with established delivery platforms, opening up opportunities for both novel indications and repurposed mechanisms.

3. PERSONALIZED MEDICINE WILL ADVANCE AS CELL AND GENE THERAPIES SCALE FROM NICHE TREATMENTS TO BROADER PLATFORMS

Dr. Butler: As cell and gene therapies (C&GTs) mature into scalable platforms, we believe that personalized medicine is evolving from bespoke interventions into modular, accessible therapeutic systems. Standardized manufacturing solutions and compositional and delivery innovations will enable developers to move beyond one-patient-at-a-time manufacturing toward indication- and genotype-specific product architectures.

For nucleic acid technologies (NAT), this shift is especially powerful. Oligonucleotides and mRNA already permit sequence-level customization, allowing rapid redesign for individual specific mutations or defined patient subgroups without reinventing the entire manufacturing process. As process technologies advance, a larger number of "n-of-1" therapies may become feasible in defined contexts, with far greater consistency, lower cost, faster turnaround times, and greater consistency than today's bespoke approaches.

At Hongene, we are investing directly in this future. In collaboration

with leading innovators, we are building a dedicated oligonucleotide synthesis suite to support personalized and ultra-rare genetic disease programs. In parallel we are advancing our HiXCap™ cap analog technology to the clinic to enable more potent and durable mRNA personalized cancer vaccines (PCVs). Together, these capabilities position us to help partners deliver personalized medicines at a scale and speed that were previously unattainable.

Ongoing advances in bioinformatics, patient stratification, and targeted delivery are helping to further strengthen this trajectory. Simultaneously, emerging tools, such as tissue-specific LNPs, antibody-oligonucleotide conjugates, and next-generation cap analogs and nucleotides, enable drugs to be tuned to both the disease and relevant organ system.

As C&GT platforms become more scalable, these developments are making personalized medicine more accessible by reducing cost of goods sold (COGS), improving manufacturing resilience and facilitating regulatory harmonization, turning what were once niche therapies into viable global interventions.

4. A CONTINUED FOCUS ON SUSTAINABILITY INITIATIVES

Mr. Seibert: Regarding corporate initiatives, sustainability has become one of the pillars of our strategy over the last several years. We see it as a positive force for innovation and collaboration. Sharp recognizes that there is an immediate need for action to address the threat of climate change and that action must be embedded in a data-driven, science-based methodology. Establishing SBTi targets for our organization became a key objective of our sustainability strategy in 2025. Our targets were validated in July, marking a significant step in our journey to reducing our environmental impact and contributing to a more sustainable future.

As a CDMO, Sharp operates in a highly interdependent way with clients and our own supplier network, and we recognize that the scale of carbon reductions required will not progress fast enough without broad and significant cooperation across that network.

While we need to ensure our Scope 1 & 2 emission reductions remain on track, Scope 3 is the predominant challenge for most organizations and collaboration is the cornerstone to progressing Scope 3 in the pharma supply chain.

As part of our clients' Scope 3 emissions, it's clear that we need to focus on our carbon reduction planning to enable them to achieve their own SBTi goals. Once we achieved validation of our SBTi targets in July, our focus immediately moved to establishing measurable, year-on-year actions that will drive overall progress towards reaching our SBTs. The roadmap to deliver this progress is a Climate Change Transition Plan for our operations that outlines the pathway to achieving our Near- and Long-Term targets.

We are making progress on the energy-efficiency initiatives already underway and have assessed energy consumption at our facilities with the aim of improving current sustainability performance. We are considering the impact of, for example, moving to more energy-saving measures, such as LED lighting, more efficient HVAC selection, optimized heating and cooling settings, motion sensor lighting, etc. We are making plans to improve our waste management processes at our facilities to maximize reuse and recycling of waste materials, while avoiding landfill and decreasing incineration where possible. These immediate actions will support both our interim milestones and our long-term net-zero ambition.

As with many companies in the supply chain, we need to deepen our sustainability reporting processes by collaborating more closely with our own suppliers to capture their carbon emissions data, to increase transparency, and identify opportunities for shared reductions. This visibility is essential, not only for achieving our own SBTi pathway but also for contributing positively to our clients' climate goals. No entity or organization will be able to transition independently at the required speed or scale to successfully reach their climate goals.

As a CDMO, and experts in the assembly, labeling, and packaging of pharma products, we also recognize the important role we play in accelerating the identification and qualification of lower-carbon materials and processes. In 2023, we established our Sustainable Materials Innovation Group (SMIG) whose role is to deepen innovation efforts by identifying and validating new materials and designs

for more sustainable pharma packaging. This multi-disciplinary group at Sharp recently published our Eco-Design Principles, which attempt to educate and influence packaging design at the earliest stages of a drug launch, so together with our clients we can try to design as much waste and carbon as possible out of the drug packaging process.

Sharp is one of eight co-founders of the Alliance to Zero, whose main ambition is to facilitate the transition of pharma to net zero injectable devices. Each member company in the Alliance is committed to demonstrating measured carbon reductions within its own operations as part of its sustainability goals. The Alliance offers a collaborative forum for sharing best practices, research, and innovation through pragmatic solutions that can be applied directly to improving each company's GHG emissions.

Dr. Butler: At Hongene, sustainability is a design principle shaping our facilities, processes, and partnerships. We are committed to achieving carbon neutrality by 2030 while expanding the capacity required to meet global demand for RNA therapeutics. To support this ambition, we have incorporated renewable-energy infrastructure, including 100% solar-powered exterior lighting and electric vehicles for on-site logistics and invested in solvent-recycling systems that reduce organic-waste generation.

Hongene's foundation in biocatalysis underpins our commitment to sustainable innovation, and our chemoenzymatic ligation platform exemplifies how advanced technology can enhance both efficiency and environmental responsibility. By delivering higher yields and reducing solvent consumption, this approach enables a greener and more scalable route to siRNA, sgRNA and other oligonucleotides. Additionally, as a vertically integrated one-stop CDMO, we further minimize environmental impact by consolidating raw material production and RNA manufacturing under one roof, cutting transportation needs and reliance on third-party suppliers.

We measure environmental progress through third-party ESG assessments, including our recent EcoVadis Bronze Rating, and continue to partner with organizations such as the ACS Green Chemistry Institute to advance industry-wide best practices. These efforts ensure sustainability remains embedded in both Hongene's operations and the broader NAT manufacturing ecosystem.

5. REAL-TIME FDA REVIEWS AND PLATFORM-LEVEL DESIGNATIONS WILL INFLUENCE HOW COMPANIES KEEP PACE WITH INNOVATION

Dr. Butler: Real-time FDA review pathways and platform-level designations, such as Advanced Manufacturing Technology (AMT), represent a shift toward regulatory models designed to support innovation, quality and digital readiness. For NAT, these frameworks might support earlier adoption of optimized manufacturing platforms, such as enzymatic oligonucleotide synthesis or high-efficiency mRNA production, into clinical and commercial use.

For companies like Hongene, these developments further encourage investment in scalable, well-characterized, digitally monitored manufacturing systems. Building on this foundation, the implementation of continuous data capture, advanced analytics, and automated process controls can help support customers seeking platform-level regulatory strategies.

These FDA initiatives will also elevate expectations for process transparency and change-management discipline. Manufacturers that can demonstrate statistical control, digital traceability, and sustainability advantages are more likely to move faster through regulatory pathways.

Real-time review and platform designations can help compress development timelines and allow innovative technologies to reach patients sooner. They signal a future in which regulatory speed is directly linked to technological maturity, encouraging companies to modernize proactively rather than reactively. ◆

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PREFILLABLE SYRINGE SYSTEM

Beyond Components: Designing Prefillable Syringe Systems to Streamline Success

By: Katie Falcone

INTRODUCTION

The self-administered biologic market is expected to reach $146.0685 billion by 2034.[1] Delivery devices, such as prefilled syringes, autoinjectors, and pen injectors, have been significant catalysts for the expected growth in subcutaneous, self-administered biologics. Notably, prefilled syringes have emerged as a cornerstone technology, with industry reports estimating that more than 60% of biologics are delivered via these devices.[2] Additionally, prefilled syringes for vaccine administration will undoubtedly play a vital role in the efficiency and scalability of future immunization campaigns.

And yet, development teams are still taking component-based approaches to building their prefillable syringe (PFS) systems that frankly will not meet the needs of a fast-paced and ever-evolving market. What's needed is a shake up that can address PFS performance, regulatory, and supply challenges that plague pharmaceutical manufacturers in early phases of development.

YOU CAN'T BUILD A PFS SYSTEM OUT OF COMPONENTS

Typically, pharmaceutical manufacturers must source primary PFS components (syringe barrel, needle shield or tip cap, and syringe plunger) from multiple suppliers. This can result in downstream issues that may not be visible from the component level at the outset, but can show up later as delays, rework, and regulatory inquiries.

Often, companies must spend sacred time and money compiling component-level data sets to generate system-level performance data for their selected device. With multiple component suppliers, procurement teams are left to combat mismatched order quantities and massive lead times to optimize supply for clinical trials and commercial inventory.

When it's time for regulatory submission, and regulators or notified bodies inevitably come back with questions on how the assembled PFS performs, 3-way CDAs and finger pointing ensues in a fruitless quest for answers.

Sound familiar? You can stop building your PFS from components and instead opt for an integrated, verified prefillable syringe system.

West Synchrony™ S1 PFS system provides a broad product portfolio including 1 ml long and 2.25 ml staked needle options for biologics and 1 ml standard staked needle and Luer lock options for vaccines.

UNLOCK SYSTEM-LEVEL PERFORMANCE DATA

True transparency means having access to consolidated performance data for the entire PFS system, not just individual components from various suppliers. Fragmented data increases complexity, regulatory uncertainty, and risk. West has transformed this landscape with its pre-generated verification data package — uniquely available with the West Synchrony™ S1 prefillable syringe (PFS) system.

Robust, system-level data ensures all necessary testing has been completed for the platform, independent of the molecule. Thus, pharmaceutical companies remain shielded from the pitfalls of fragmented component-level data, which traditionally requires extensive effort to synthesize into a holistic approach.

STREAMLINE REGULATORY SUBMISSIONS WITH ONE ACCOUNTABLE SOURCE

Combination products face intricate regulatory landscapes, especially when navigating global compliance. All too often, companies are underprepared with fragmented data when it comes time for their regulatory submission. They ask multiple component suppliers for documentation, and what they get back is in various formats and different levels of visibility.

When your PFS system is designed and owned by the same supplier, you can refer to a single Design & Development File. This approach simplifies the regulatory process, improves submission efficiency, and accelerates global market access.

Staked needle system options come with either a rigid or soft needle shield and Luer lock system options will have an integrated tip cap.

As the sole developer and owner of the West Synchrony S1 PFS system, West has created one DMF with the US FDA, Health Canada, and China that encompasses the entire syringe system. Additionally, all necessary data needed for your technical file to be submitted to notified bodies in Europe is readily available in one regulatory package included in the system offering.

SIMPLIFY PFS PROCUREMENT & SUPPLY

Development timelines often suffer due to supplier coordination and variable component availability. Relying on a single, verified PFS system streamlines procurement and supply chain management. With one accountable supplier, you can reduce lead time variability, minimize delays, and enable quicker responses to change, helping you meet critical milestones.

Every lot of the West Synchrony S1 PFS system produced undergoes rigorous system-level batch testing, ensuring that device constituent part integrity and performance are verified before incoming inspections.

BEST PRACTICES FOR PFS SYSTEM STRATEGY

West has been helping pharmaceutical manufacturers bring life-saving therapies to patients for more than 100 years. Best practices have accumulated along the way that have informed the design and development of the West Synchrony S1 PFS system. When scouting PFS options, companies need to consider:

Starting Early: Most R&D groups begin drug trials in vials, understandably, because vials are variable when it comes to injection volume. However, when that drug candidate has proven itself and it's time to transition into a prefillable syringe, the submission timeline gets tight. Developing a device can take many months up to a

The system also includes high performance West NovaPure® and FluroTec™ barrier film plungers.

few years and should not be started too late in your process. Otherwise, you risk missing important tests and/or not creating the necessary scientific depth of data as required by regulatory agencies.

Having a Proactive Approach to Supply: Tie technical configuration to realistic, phase-appropriate supply frameworks. PFS supply elements, such as lead times, order quantities, and scalability, should align with clinical and commercial plans to ensure cost-efficient, reliable supply.

Embedding the Regulatory Strategy: Treat regulatory documentation as an integral part of the system design, not an afterthought. With system-level regulatory documentation at the ready, you can support timely submissions.

FROM COMPONENTS TO SYSTEMS: A PARADIGM SHIFT

Prefillable syringes for biologics and vaccines can no longer be assembled as a set of parts; they must be treated as engineered systems with data, supply, and regulatory strategies built in from the start.

The West Synchrony S1 PFS system embodies this system-level approach. By choosing an integrated, verified system, emerging biotechnology and pharma teams can align with the best practices outlined in this article and be on their way to their clinical fill faster equipped with system-level performance data for their device constituent part, an embedded regulatory strategy, and simplified supply.◆

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BIOGRAPHY

Katie Falcone is the Director, Technical Services, at West Pharmaceutical Services. She is a seasoned professional with more than a decade of experience in the pharma/biotech industry, specializing in parenteral packaging. In her role, she leads technical collaboration by leveraging her expertise to drive customer success, enable data-driven decision making, and deliver innovative drug delivery solutions.

CONTROLLED RELEASE

Challenges in Consistent & Predictable Delivery of Drugs Using Oral Controlled Release Technologies

By: True Rogers, RPh, PhD, Matthias Knarr, PhD, and Mark Dreibelbis, PhD

INTRODUCTION

Quality by Design (QbD) is a systematic approach to pharmaceutical development that emphasizes the integration of quality into the design, development, and manufacturing processes. This approach is grounded in the principles of sound science and quality risk management, aiming to ensure consistent product quality by understanding and controlling variability throughout the product lifecycle.[1-3] The concept of QbD has gained significant attention in the pharmaceutical industry as it is a proactive approach for identifying and mitigating potential quality issues early in the development process. However, implementation of QbD principles has been challenging as it can be difficult to interpret and apply guidance set out by regulatory bodies like the US FDA and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH).[4] That said, understanding how variability impacts drug products is a common theme among the guidance.

Variability in delivery of pharmaceutical drug products can arise from numerous sources, including the properties of the formulation ingredients [i.e., the active pharmaceutical ingredient (API) and the excipients], manufacturing processes, patient differences, and the interactions of the four factors.

- **API Properties:** The solubility, stability, and bioavailability of the API can significantly impact the final product's performance.
- **Excipient Selection:** Excipients play a critical role in drug formulation, affecting the drug's stability, quality, release performance, and overall efficacy.
- **Manufacturing Processes:** The techniques, equipment, and conditions used during manufacturing can introduce variability, including drift, consequently affecting product quality.
- **Patient Differences:** Physiological and genetic differences among patients can influence how a medication works, adding another layer of complexity to ensuring consistent drug delivery.

Patient-to-patient (or population-to-population) differences can be difficult to control and are of interest in patient-focused drug development but are not explored in this article.[5] The sources of ingredient, process, and final drug product variability can be broadly categorized into intra-batch variability (variations within a single batch) and inter-batch variability (variations between different batches).[4,6]

Excipient selection is a key consideration within the QbD framework, particularly for controlled release (CR) technologies. Excipients must be chosen carefully to ensure they deliver the needed processability, quality, stability, and performance during and following the manufacture of dosage forms. Understanding the impact of these factors is essential for developing robust and consistent drug products.

CONTROLLED RELEASE TECHNOLOGIES

Controlled release (CR) technologies deliver drugs at a predetermined rate, maintaining therapeutic levels over an extended period. Common CR technologies include:

- **Matrices:** These systems comprise a monolithic matrix, typically using a polymeric material to control drug release

through diffusion and/or erosion mechanics. The type of matrix and its properties can significantly impact release performance.

- **Osmotic Pump Tablets:** These tablets use osmotic pressure difference between the inside of the dosage and the external environment to deliver the drug at a controlled rate. Careful selection of the design and function of these systems is needed to attain targeted performance.
- **Barrier Membranes:** These membranes control drug release by acting as a barrier between the API and the external environment, limiting the diffusion pathways by which an API can migrate out of the system. Tailoring the properties and applications of barrier membranes achieves the desired release performance.

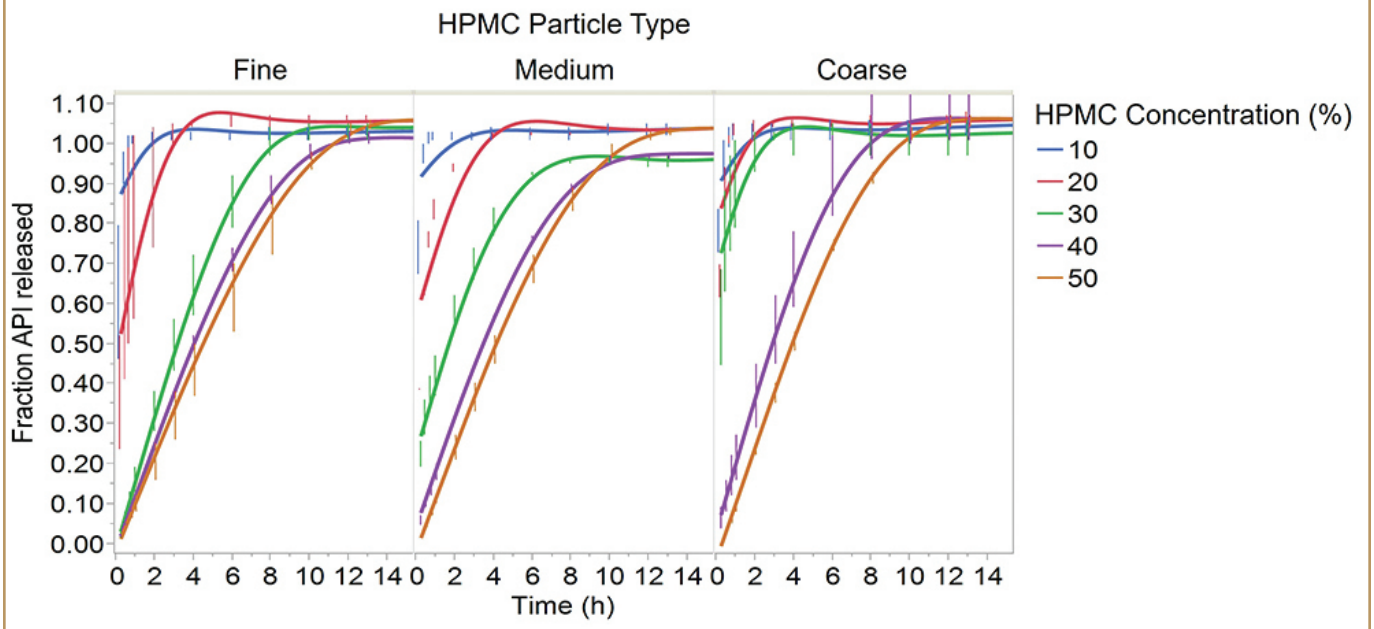
Each CR technology has unique key attributes that are important for consistent product performance. Excipients, API and manufacturing variables (and often their interactions) all contribute to both performance robustness and consistency of the drug product. The critical to quality (CTQ) properties of a given drug product must be evaluated on a case-by-case basis. However, there are many examples of how excipient attributes, API properties, and manufacturing process parameters impact drug product performance and consistency. Presented below are examples of how excipients and their interactions with either API or manufacturing process can lead to inconsistent performance and key elements to reduce variability.

IMPORTANCE OF THE PERCOLATION THRESHOLD IN CR MATRICES

Controlled release properties of matrices often rely on the interconnection of polymeric particles to form a continuous phase. The minimum concentration to form the continuous phase is known as the percolation threshold (PT). Once at or above the PT, the drug release becomes more consistent and predictable.

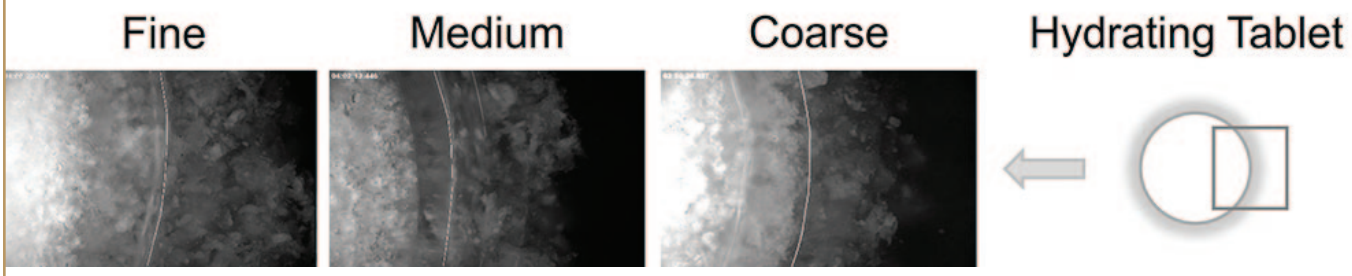
The particle size of the rate controlling polymer influences the percolation threshold and the consistency of drug release from CR matrices.[7] For example, Figure 1 illustrates the combined influence of hydroxypropyl methylcellulose (HPMC) particle sizes (fine, medium, coarse particles made from sieve cuts of the commercial material) and polymer concentration in the tablet (10%-50%) on controlled release from matrix tablets (7.5 wt% Gliclazide, 0.5% talc, 0.5% magnesium stearate, HPMC at specified concentration and remaining composition made of lactose and microcrystalline cellulose in 1:1 ratio).[8] The data clearly demonstrates that increasing the HPMC concentrations (>30%, depending on the particle size) reduces drug release variability. In addition, finer HPMC particles result in slower and more consistent drug release at lower HPMC concentrations, compared to coarser particles. Finer particles hydrate rapidly and uniformly, facilitating the coalescence of polymer chains and the formation of a continuous swollen gel layer barrier - a

FIGURE 1



Impact of fine, medium, and coarse HPMC particles and the HPMC content on CR performance.

FIGURE 2



Images of the formation of a swollen layer around the HPMC tablet with coarse, medium, and fine particle sizes of HPMC at 30% concentration.

prerequisite for controlled release. This observation is consistent with the findings of Mason et al., who emphasized the importance of early swollen (gel) layer formation in achieving robust controlled release.[9] A study by Kulinowski et al. also highlighted the importance of particle size distribution in achieving consistent gel formation and drug release.[7]

In contrast, coarser HPMC particles exhibit delayed hydration and less uniform swelling, which can hinder the formation of a percolating polymer network, especially near or below the percolation threshold (PT). The PT is approximately 30% for fine HPMC particles and increases for coarser particles to approximately 40%. Formulating below the PT can lead to incomplete swollen (gel) layer formation, increased water ingress, and dose dumping or higher performance variability (Figure 1).

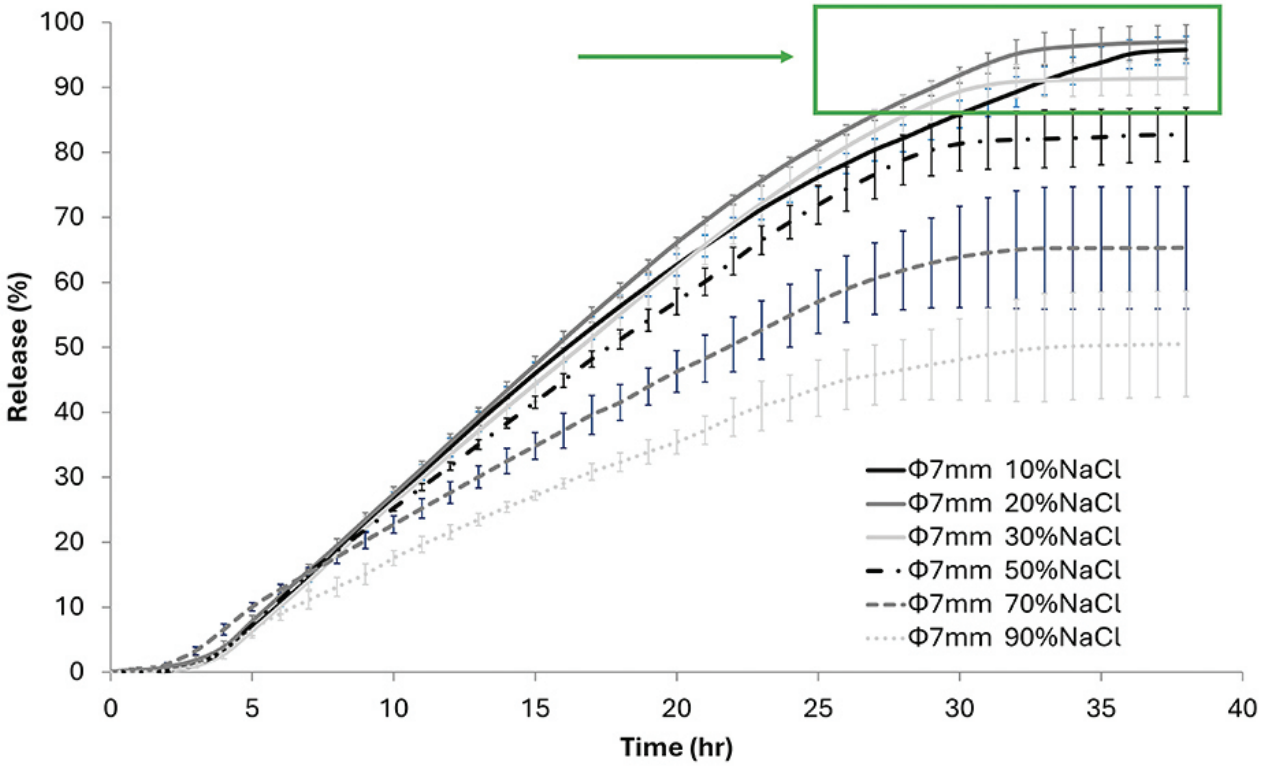
The images in Figure 2 provide visual confirmation of the hydration/swelling behavior of HPMC matrices with different particle sizes at 30% HPMC concentration. The images show the formation of a swollen gel layer around the tablet surface for coarse, medium, and fine HPMC grades. Notably, the fine particle size results in a more uniform and contiguous swollen layer, even at early hydration stages, compared to the coarse particle size. This observation supports the mechanistic insights proposed by Mason et al., who used confocal laser scanning microscopy (CLSM) to demonstrate that early stage gel layer morphology is a key determinant of controlled release performance.[9] The coarse particle size, by contrast, shows a more heterogeneous and delayed swollen (gel) layer formation, with visible gaps and irregularities in the network. The inter-particle distances are too large to allow effective coalescence, preventing the formation of a robust swollen gel layer. Such behavior aligns with the percolation theory framework, where a minimum polymer content and spatial proximity are required to form a continuous network in the design of robust controlled release systems.

REDUCING VARIABILITY IN OSMOTIC PUMP TABLETS

Osmotic pump tablets offer opportunity to achieve zero-order release if the formulation and manufacturing factors are properly selected.[10-13] The dissolution profiles in Figure 3 demonstrate that the right balance of osmogen, like sodium chloride, and swelling polymer, like polyethylene oxide (PEO), in the push layer reduces drug dissolution variability and allows for more complete release of the dose. When the salt level is too high, the low polymer content not only leads to incomplete API release but also high variability in release.[14] When the salt level is too low, the osmotic pressure is insufficient to achieve complete drug release. At 20% sodium chloride content in the high viscosity PEO push layer, the proportion of osmogen and push polymer in the example formulation are balanced and leads to complete release with low variability. It has also been reported that the amount of drug loading can influence the extent to which that drug is released.[10,15] Increasing the drug loading, without significant alternations to the formulation, can result in incomplete drug release.

The water solubility of an API can impact the release rate from an osmotic pump tablet, as shown in Figure 4. A moderately water-soluble API, like acetaminophen (left), is not significantly impacted by variability and changes in polymer viscosity or in the ratio of the drug layer to push layer.[14] However, release of poorly water-soluble API, such as nifedipine (right), can be impacted by changes in tablet properties, like the drug to push layer ratio. A drug to push layer ratio of 4 to 1 resulted in incomplete drug release (70%-80%); an issue that was corrected by increasing the push layer amount (2 to 1 drug to push layer ratio). In both API examples, the viscosity grade of the swelling polymer had little to no impact on drug release. It should be noted that the three grades used

FIGURE 3



The nifedipine release from osmotic pump tablets formulated with different amounts of sodium chloride in the push layer ranging from 10% to 90%. Choosing the right amount of salt will reduce variability in drug release and result in more complete drug release.

in this example were all very high viscosity grades of PEO: 2wt% solution viscosities of approximately 2,000 cP (POLYOX™ WSR 301), 6,000 cP (POLYOX™ WSR Coagulant) and 9,000 cP (POLYOX™ WSR 303). A similar study also found negligible impact to dissolution when the viscosity of the PEO in the push layer was modulated between high viscosity grades.[10] In contrast, too low of PEO viscosity will lead to incomplete release.[16] In fact, the right combination of low viscosity PEO in the drug layer with high viscosity PEO in the push layer leads to zero-order release.[16]

PROCESS IMPACTS ON BARRIER MEMBRANE COATINGS

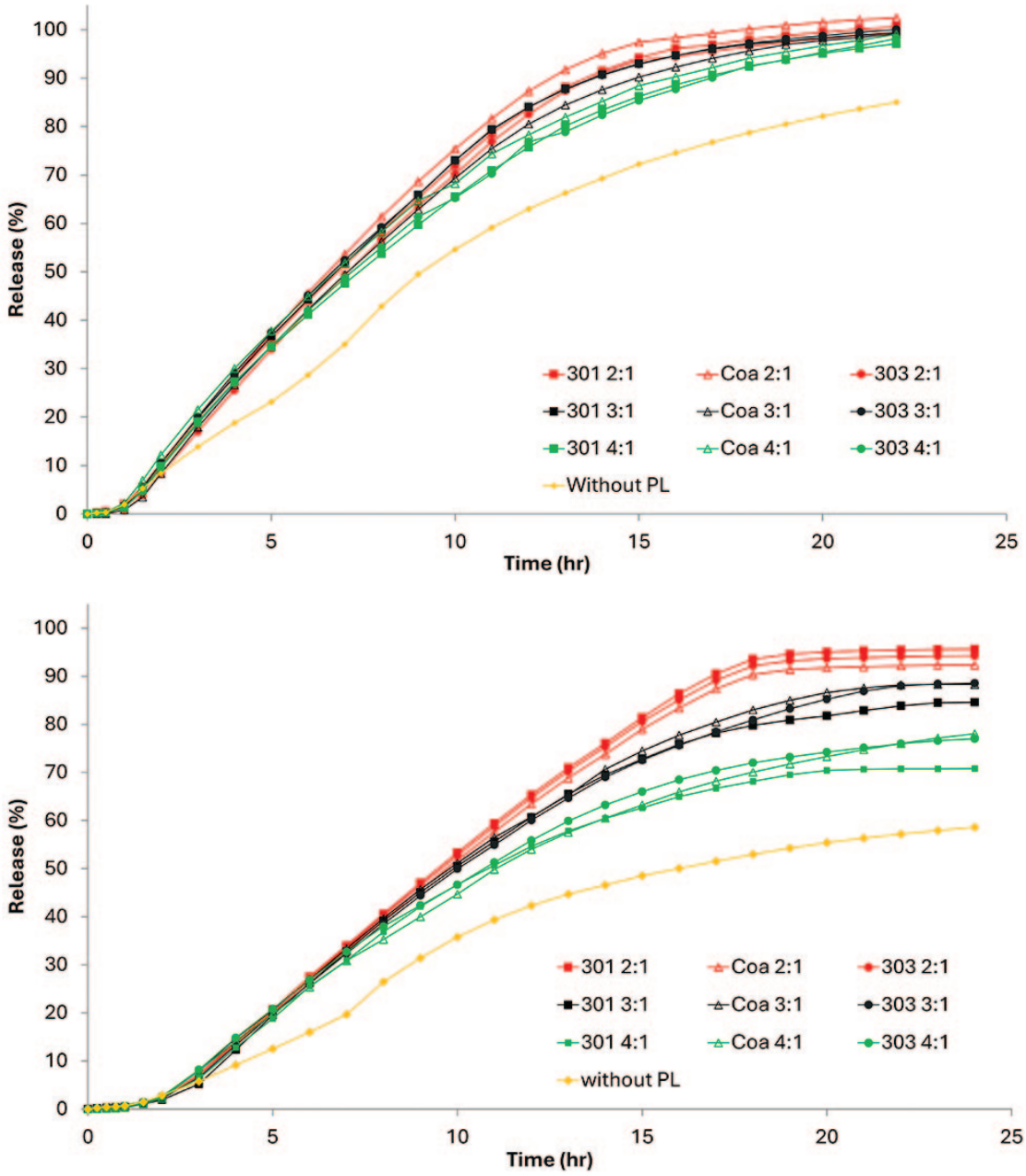
Several aspects could impact consistency of controlled release performance through barrier membranes, such as the substrate the barrier membrane is coated onto, the active and inactive ingredients making up the substrate, the rate-controlling polymer and its properties, whether the rate controlling polymer is being applied from suspension or solution, presence of plasticizer(s) and other ingredients in the coating formulation, and processing and post-processing conditions during and after coating. All aspects cannot be covered in this article, but the following examples will highlight the need for understanding critical to quality attributes that could impact performance.

The substrate can range in size and geometry from a small spheroidal bead or pellet up to a tablet or large caplet. Surface area to volume ratio and geometric shape could impact barrier membrane consistency. An irregularly shaped granule with rough surface might require more barrier membrane to be applied to attain complete envelopment than either a smooth round bead or a large tablet or caplet. The figures below depict an ideal substrate scenario in terms of a smooth, round shape with minimal surface irregularity and absence of edges.

The applied barrier membrane should be of uniform thickness, at least 50 μm thick as a general rule. There are exceptions, such as push-pull osmotic pump (PPOP) tablets, where the barrier membrane can be 150-200 μm thick. The applied barrier membrane should ideally be defect-free, and the barrier membrane should leave no substrate beneath uncoated.

A polymer applied from solution ideally delivers a more robust and defect-free barrier membrane than a suspended polymer applied from latex or pseudolatex dispersion. That stated, there are concerns associated with environmental or residual

FIGURE 4



Release profile impact of drug:push layer ratio and polymer viscosity grade in the push layer of osmotic pump tablets formulated with acetaminophen (left) and nifedipine (right). Release is [relatively] push layer-independent for acetaminophen, but nifedipine release is highly dependent on drug:push layer ratio. Both drugs experience incomplete release when a push layer is excluded.

solvent impacts from organic solution systems, so aqueous latexes and pseudolatexes are commonly used. Plasticizer is required in aqueous dispersion coatings as it facilitates coalescence of polymer droplets into a film during casting and curing. The figure below shows beads coated with Aquacoat® ethylcellulose dispersion (ECD) with either 24% or 16% dibutyl sebacate (DBS) as plasticizer. At 16% DBS, there are still defects in the applied barrier membrane in the form of cracks. These cracks can lead to faster and inconsistent drug dissolution. Increasing plasticizer level to 24% removes visual evidence of those defects.

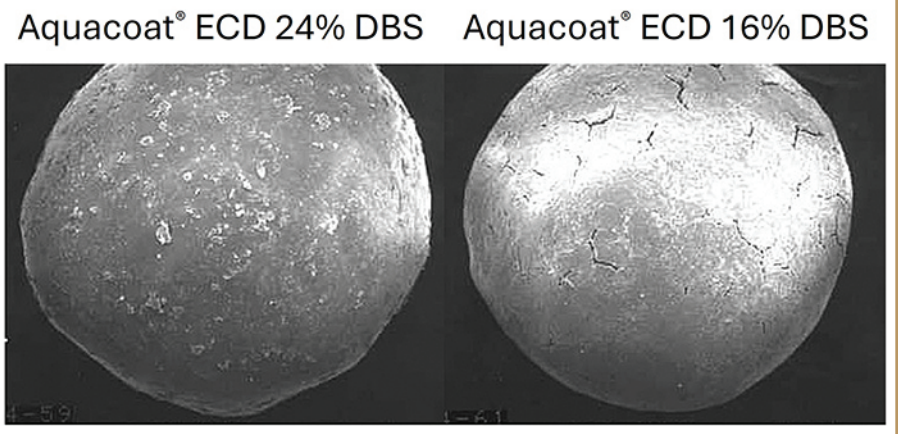
Film curing (curing method, temperature, or duration) can significantly impact controlled release performance. A case study using a tolterodine tartrate formulation with ECD coating demonstrates how each of these factors influence the controlled release properties of the barrier membranes.[17] First, curing via fluid bed dryer (FBD) is preferred to tray drying for several reasons, but for brevity, fluid bed processing more uniformly cures the bar-

rier membranes on each of the coated substrates and keeps them moving during curing, so that there is less opportunity for substrate agglomeration. Film defects can form during separation of agglomerated substrates, resulting in variability in drug release or dose-dumping. The tolterodine tartrate release in this example is faster for the tray cured samples compared to the fluidized bed cured samples (cured for 2 hours at 55°C), an indication that the films from the tray dried samples were either not fully cured or had defects due to agglomeration of coated particles during curing, followed by introduction of film defects when the particles were deagglomerated. Care still needs to be taken with fluidized bed curing, as the coating might attrit during fluidization before sufficient coalescence has occurred.

Curing temperature also impacts film formation. When uncured (left at room temperature) or cured at low temperatures (35°C using FBD in this case), tolterodine tartrate release is rapid and complete within less than 2 h. Curing at higher temperatures (greater than 45°C in this case study) extended tolterodine tartrate release to about 8 h. Curing at higher than necessary temperatures could have deleterious effects, which should be confirmed on a case-by-case basis.

The case study shows that curing at 55°C for 0.5 and 1 h is insufficient duration to allow complete film coalescence to occur. Release kinetics did however change and become consistent after curing 2 to 3 h. The recommendation from this case study would be to cure using FBP dryer at 45 to 55°C for 2 h to allow for sufficient film coalescence to attain desired controlled release performance.

FIGURE 5



Scanning electron micrographs of ethylcellulose coated spheres, where the ethylcellulose dispersion contained either 24% plasticizer (a) or 16% plasticizer (b). Less plasticizer resulted in incomplete film formation and cracking.

KEEPING QBD IN THE FOREFRONT

Ensuring consistent delivery of active pharmaceutical ingredients through oral controlled release (CR) technologies is a multifaceted challenge. Variability can stem from the intrinsic properties of the API, the selection and behavior of excipients, and the nuances of manufacturing processes. These sources of variability – both within and between batches – can significantly impact the performance and efficacy of CR drug products.

The application of Quality by Design (QbD) principles offers a structured approach to understanding and controlling these variables. By systematically identifying critical material attributes and process parameters, QbD enables the development of more robust and reliable drug delivery systems. However, the complexity of CR technologies means that not all interactions can be predicted or managed through QbD alone.

Continued research is essential to deepen understanding of the mechanisms driving variability in CR formulations. Advancements in material science, process analytics, and modeling tools will be key to refining CR technologies and enhancing their consistency. A combination of rigorous scientific inquiry, thoughtful formulation design, and adaptive manufacturing strategies will be required to meet the evolving expectations for quality and performance of controlled release drug products. ◆

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Special Feature

Artificial Intelligence in Drug Discovery, Development & Delivery

CRDMOs, device manufacturers & drug makers debunk common AI myths

By: Cindy H. Dubin, Contributor

In the pharma industry, the Artificial Intelligence (AI) market is projected to grow from more than $4 billion this year to a whopping $25.7 billion by 2030. However, McKinsey & Company claims that medicine makers have yet to see substantially shorter development timelines or improvements in preclinical or clinical success rates.[1]

But several industry gurus believe this new year holds a lot of promise for AI. John Chinnici, CEO of Ledger Run, a next-generation software suite developer, says: "Next year will be a turning point where AI's promise in life sciences finally meets pragmatic execution."

"In 2026, expect the transformation of drug development from a predominantly human-driven, sequential process into a continuously learning, agentic AI-supported pipeline," agrees Andrew Mackinnon, Global Executive General Manager, Medable, whose AI-powered clinical trials platform has been deployed in nearly 400 trials in 70 countries. "Instead of researchers and clinicians manually generating hypotheses, designing studies, reviewing data, and coordinating decisions across long cycle times, agentic AI systems will autonomously propose targets, run virtual experiments, optimize protocols, monitor safety signals, and surface decision-ready recommendations."

Despite the potential of AI, all industry insiders agree that humans will not be removed from the equation. Instead, they will move into higher-value oversight roles, validating AI-generated options and steering strategy while AI handles the labor-intensive, multi-step analytical and coordination work. "The result will be a funnel that's faster, more adaptive, less linear, and increasingly self-optimizing, marking the first true structural redesign of the R&D model in decades," says Mr. Mackinnon.

In this inaugural, exclusive Artificial Intelligence *Drug Development & Delivery* special feature, leading drug makers, device manufacturers, and contract organizations dispel the myths around AI and Machine Learning (ML) in the pharma industry and share how they are using AI to streamline clinical trials, automate lab tests, optimize resource allocation, enhance development timelines, and improve patient-friendly dosage forms.

At the Phillips Medisize Chippenham site, where inhalation formulation capabilities are located, AI can enable scientists and engineers to devote more time to analyzing data, uncovering insights, and focusing on innovations that directly benefit patients and customers.

Adare Pharma Solutions: AI Is Only As Good As The Support It Receives

"One of the biggest myths in the industry is that AI will instantly transform drug development on its own," says Tom Sellig, CEO of Adare Pharma Solutions. "In reality, AI is a tool, and just like all tools, it's only as effective as the systems, people, and practices that support it."

Successful CDMOs already know that bringing a therapy to market depends on structured processes, rigorous oversight, and clear communication. Those same fundamentals are what AI integration requires to be truly effective.

"AI can certainly accelerate insights, but it must operate within the same disciplined framework CDMOs rely on to deliver therapies," he says. "AI will never be a replacement for a team of experienced experts, but AI can enhance those teams' capabilities and help them make better informed decisions, identify risks earlier, and move programs forward with greater confidence."

Mr. Sellig says that AI's greatest potential value will be in reducing friction across the development and manufacturing lifecycle. As programs become more complex and timelines shrink, sponsors will depend ever more on integrated, end-to-end partners, like Adare, that can keep projects moving.

"AI's strength lies in how it can help connect data across development, manufacturing, and packaging operations, helping teams spot risks, uncover opportunities for cost and time savings, and make more informed decisions," he says. "With AI-driven predictive intelligence, teams can transition from reactive problem-solving to proactively steering operations."

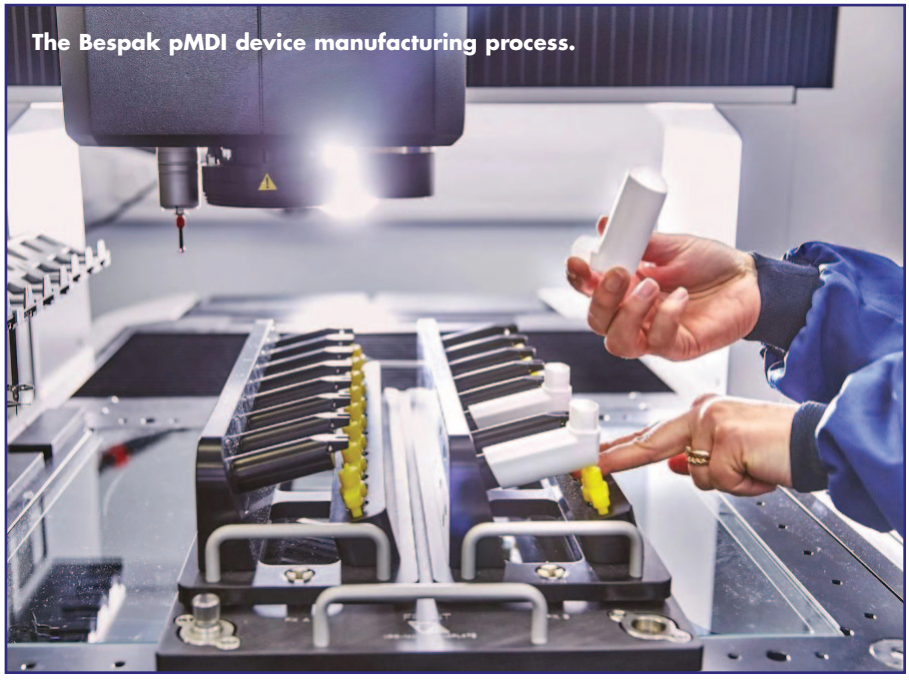
AI will also provide value by enhancing how patient-friendly dosage forms are designed and optimized. As technologies like 3D screen printing enable more personalized and multi-layered therapies, AI can help predict performance, refine tailored formulations, and streamline scale-up, he says.

Bespak: Facilitating Performance Simulations Without Costly Experiments

There is a myth that regulators, such as the FDA and EMA, won't accept AI models. However, the FDA and the Centre for Research on Complex Generics (CRCG) recently partnered in a workshop on "Modeling and Artificial Intelligence (AI) in Generic Drug Development and Product Lifecycle Management: Regulatory Insights and Future Trends." During the workshop, the FDA and EMA explained their guidance with regard to AI and their desire to work with generic product developers from the start and bring in novel AI methodologies, explains Alan Harris, Chief Technology Officer of Bespak. The workshop identified many concrete examples of AI being deployed in drug substance and drug product development, including in complex drug-device combination products for simulations of lung deposition and pharmacokinetic performance. The use of AI is also being considered by regulatory authorities like FDA to support submissions reviews and data analysis.

There is also a belief that AI can offer solutions to everything. "The myth of AI providing a silver bullet has been debunked," Mr. Harris says. "While many areas may benefit from AI, scientists remain indispensable to manage how AI is used in development and to share relevant approaches in regulatory discussions."

For its part, Bespak is seeing more novel active pharmaceutical ingredients (APIs) coming through the clinic with its drug development partners, but the role of AI in their development is still in its infancy. "Historically, APIs in respiratory medicine – Bespak's focus area – are small and many variants on the market are modest molecular "redesigns" performed in traditional ways by chemists," he explains. "As biologics become more popular in respiratory medicine, the role of modelling and AI will increase in early development to fa-



The Bespak pMDI device manufacturing process.

cilitate simulations of biological, physical, and chemical performance without costly experiments."

Bespak is already exploring AI for modeling and simulation tools. In collaboration with the Centre of Excellence in In Silico Regulatory Science and Innovation (CEiRSI) network, Bespak is investigating innovative uses of AI and modelling to support the UK's ambition to be a powerhouse in drug development innovation.

Bespak is also developing a Digital Engineering Platform to deploy modeling, simulation, and AI across all modalities of its R&D and scale-up services, from formulation and process development to device design and inhaler *in vivo* performance. Mr. Harris explains: "While some of these areas are in early stages, we have several years' experience in deploying AI and simulation tools for respiratory device and pMDI valve finite element analysis and computational fluid dynamics to de-risk, speed up, and reduce the cost of device development. We can even simulate the filling process of pMDI cans, which has never been done before. By offering these services to customers from a menu of options, we can support their development and regulatory plans and work alongside their own R&D teams."

The use of AI simulation tools for device design and optimization has generated designs and simulated different use conditions, materials, and other factors without needing to produce pilot tools and parts. This facilitates cost savings and speeds up the development process, which can ultimately benefit patients, he says.

Going forward, Mr. Harris says AI will likely support every aspect of product development from start to finish, including target APIs, formulation, device development, clinical study design, and process development through to ex-device performance, and PBPK models. Beyond this, AI will have more operational but equally beneficial uses in process control, defect/rejects analysis, real-time monitoring of product quality, and data analysis.

Enzene: Distill Complex Data Into Actionable Insights

Today, Enzene's Fully Connected Continuous Manufacturing™ technology is evolving rapidly to include real-time feedback that can improve bioprocessing efficiency and reduce waste through intelligent, 'self-adaptive' systems.

"Today's large language models demonstrate how AI can distill vast, complex information into actionable insights," says Russell Miller, Vice President, Global Sales and Marketing, Enzene. "Applied to bioprocessing, enormous datasets from sensors, batch records, and quality systems will be processed without the fear of data interpretation overwhelming human operators."

He adds that AI can not only summarize and suggest responses, but can also predict process outcomes, optimize parameters dynamically, and support real-time decision-making.

"In the near future, these capabilities will evolve into autonomous bioprocessing environments powered by digital twins—virtual models that continuously learn and adapt from live data," he says. "This means faster development cycles, reduced variability, and proactive compliance, ultimately accelerating innovation and improving patient access to life-saving therapies."

Mr. Miller sees a transition from AI being viewed as an assistant to one in which AI is the backbone of truly intelligent biomanufacturing ecosystems.

Gerresheimer: Refining Patient Interaction

Artificial intelligence is transforming connected health devices by enabling intelligent, personalized, and intuitive support. AI has the potential to transform therapy support by shifting from reactive to anticipatory models and by providing access to reliable medical information. According to Giacomo Bruno, PhD, Digital Health Platform Lead at Gerresheimer, AI systems can identify risks, such as adherence decline or technique errors, before they escalate by analyzing behavioral patterns, routines, environmental data, and population trends. These systems deliver timely interventions for maximum impact.

Gerresheimer is integrating AI directly into devices, packaging, digital platforms, and patient services to create seamless,

Enzene's FCCM™ platform seamlessly connects every manufacturing step to deliver true end-to-end continuous biologics production.

adaptive experiences that fit naturally into daily routines, explains Dr. Bruno. "Instead of requiring additional apps, Gerresheimer's smart, connected approach activates AI through simple interactions, such as scanning a QR code or tapping an NFC tag on devices like the Gx Inbeneo® autoinjector," he says. "This provides immediate access to AI-driven support via familiar messaging apps, such as WhatsApp, iMessage, Facebook Messenger, and Google Messages, without the need for new downloads or learning curves. Patients receive tailored reminders, electronic Instructions for Use (eIFU) with visuals, and direct answers to questions, resulting in effortless engagement and higher adherence."

Dr. Bruno says that this integrated AI approach benefits all stakeholders. Patients receive proactive, personalized guidance, while healthcare providers access real-time insights. Caregivers stay informed, and payers see improved outcomes through better compliance.

"This approach optimizes therapy effectiveness and usability," he says. "Gerresheimer aims to redefine patient interaction by combining AI-driven guidance with connected devices and low-friction communication channels."

Patients also benefit from instant, validated guidance in plain language through reliable channels, bypassing unreliable sources. AI extends the reach of healthcare professionals with continuous, context-aware reinforcement, reducing their workload while maintaining clinical oversight.

"Gerresheimer views AI as essential for safer and more adherent patient experiences, where reliable support is consistently accessible through common tools such as chat apps," says Dr. Bruno. "This ultimately improves outcomes and efficiency throughout the pharmaceutical ecosystem."

Smart NFC-enabled Gx Inbeneo® autoinjector providing instant access to AI-driven patient support via everyday mobile devices (Gerresheimer).

ICON Clinical Research: Predictive Analytics Forecasts Post-Marketing Requirements

One of the biggest myths surrounding AI in drug development is that it will completely replace human decision-making and expertise. AI is not a standalone solution but a strategic enabler. While AI-driven tools offer remarkable capabilities, such as screening millions of compounds rapidly, optimizing clinical trials, and improving operational efficiency, they work best when combined with human expertise. "Rather than replacing scientists, clinicians, and decision-makers, AI allows them to focus on higher-value, more complex tasks by automating repetitive and data-intensive processes," says Robert Ellison, Vice President of Data & Applied Analytics at ICON Clinical Research.

In reality, he says AI is transforming drug delivery by enabling precision and personalization. Machine Learning (ML) models can stratify patient populations using biomarkers and real-world evidence, helping to tailor therapies to individual biological profiles. This ensures that the therapies being developed are both more targeted and effective, he says.

"AI-designed drugs progressing quickly to Phase II trials represents a shift towards therapies that are not only faster to develop, but are also more likely to succeed due to their alignment with specific patient needs," says Mr. Ellison. "Additionally, deep learning in medical imaging improves endpoint evaluations, contributing to better data quality for regulatory submissions and enhancing targeted drug delivery mechanisms."

ICON has several proprietary tools that embed AI across the clinical development continuum to deliver measurable efficiencies and cost savings. The CRO uses platforms to leverage decades of trial performance data, real-world evidence, and Machine Learning algorithms, accelerating site identification, reducing start-up time-

lines and improving enrolment rates. For example, predictive analytics tool forecasts post-marketing requirements early in the development cycle, enabling sponsors to mitigate regulatory risks and avoid costly delays.

Operationally, ICON has a pair of review tools that streamline documentation-heavy processes, from site contracts to trial master file management, reducing manual effort and improving compliance. "AI technology helps us to identify key opinion leaders in rare disease areas by analyzing millions of publications at speed, cutting timelines from months to days," he explains. In medical imaging, deep learning algorithms automate segmentation and annotation tasks, reducing processing time from hours to minutes while maintaining accuracy through expert validation.

ICON also deploys AI tools for resource forecasting and operational metrics, ensuring optimal resource allocation and faster decision-making. "Together, these solutions have shortened trial timelines, improved data quality, and reduced operational risk – helping sponsors bring therapies to patients sooner while maximizing return on investment," he says.

Mr. Ellison says that the future of AI in the pharmaceutical industry lies in generative AI and large language models (LLMs), which are already demonstrating potential in summarizing complex datasets, drafting documents, and analyzing vast data lakes. "These tools offer not only efficiency gains but also a significant advantage in knowledge management, decision-making, and operational workflows," he says. "When responsibly integrated, AI will help the pharmaceutical industry accelerate innovation, reduce risk, and deliver life-changing therapies to patients at a faster pace."

Lifecore recognizes the potential for AI to help automate laboratory testing.

Lifecore: AI Tools Must Fit Within Regulatory Frameworks

Like many in the industry, Lifecore Injectables CDMO is investigating the manner in which AI tools may fit into and benefit a highly regulated manufacturing environment. While the buzz around AI has been steadily building for quite some time, regulatory bodies like FDA have only just recently drafted industry guidance on AI. With this guidance now in hand, Lifecore's teams are working to ensure that any AI tools it considers will fit within regulatory and risk-based frameworks prior to testing and adoption. At the same time, Lifecore is working to ensure that its use of these tools does not open the company up to risk regarding the exposure of intellectual property or privacy concerns.

At present, Lifecore has taken initial steps to investigate and utilize AI tools aimed at reducing administrative workload and improving clarity of communications, explains Matt Augustson, Senior Vice President of Information Technology at Lifecore. For example, AI tools are used to help draft quality investigation summaries to ensure that all details are clearly and effectively captured and collated. "The reduction in hours spent on these tasks has been dramatic, allowing investigators to spend more time working through active investigations, reviewing drafts for accuracy, and finalizing reports for release," he says.

For Lifecore, another area of interest for future AI considerations is the automation of laboratory testing. At times, this may involve collaboration with robotic systems, leading to a further reduction in the need for human involvement. "For example, we've seen systems that are designed to help automatically identify and flag agar plate growth," he says. "Again, these types of systems seem to offer promise, but need to be investigated within our specific environment to ensure that they can reliably perform operations over time."

Lonza: AI-Enabled Toolkit De-risks Development at Every Stage

As drug developers and manufacturers face intense pressure to bring more and more complex compounds to market faster, they increasingly rely upon advanced technologies powered by AI and ML to expedite innovative solutions. In that context, AI can be misconstrued as an all-knowing oracle that provides a single correct answer. The reality is that AI provides a ranked list of possibilities with their associated confidence scores. Essentially, AI is a data-driven partner that helps lab chemists explore a wider range of possi-

bilities and focus their own expertise where it can be most impactful, says Aaron Johnson, Manager of Cheminformatics and Data Science, Lonza Advanced Synthesis.

To harness the power of technological innovation, Lonza has developed an AI-enabled toolkit to de-risk development at every stage, ensuring phase-appropriate optimization and improving the chances of clinical success. The toolkit is a connected ecosystem of predictive tools designed to facilitate better decision-making earlier in the development cycle. At its core is Lonza's AI-enabled Route Scouting Service, which incorporates computer-aided synthesis planning technologies to compute the shortest and most viable retrosynthetic paths to intermediates or active pharmaceutical ingredients (APIs), leveraging proprietary informatics, supply chain information, and the expertise and decision-making of experienced chemists.

Another toolkit offering, Solid Form Services (SFS), incorporates Lonza's predictive co-crystal model, which uses ML algorithms to screen thousands of molecules in minutes, enabling rapid identification of the optimal solid form for the drug product.

"Together, these tools act as powerful 'copilots' for our expert chemists, augmenting their skill and intuition while allowing them to innovate more robust and scalable workflows," says Mr. Johnson. "The synergy directly boosts efficiency and sustainability in production, facilitating the delivery of high-quality products with limited environmental impact (due to reduced chemical and material waste), a reliable supply chain, and the fewest number of synthetic steps."

Internal validation studies demonstrate that Lonza's AI-enabled models achieve predictive accuracy exceeding 86%, allowing the company to accelerate discovery with a high degree of scientific reliability. The toolkit also enables confirmation of the effectiveness and performance of top-rated candidates while minimizing development time, reducing costs, strengthening intellectual property, and ultimately accelerating the clinical readiness of customers' compounds. "By integrating these validated AI tools into our daily work, we unlock new levels of innovation and operational excellence, creating a distinct competitive edge in drug development and manufacturing," he says.

Lonza deploys technologies to compute the shortest and most viable retrosynthetic paths to intermediates or active pharmaceutical ingredients (APIs).

Looking to the future, Mr. Johnson envisions potentially valuable applications of AI in areas such as formulation development, where the technology can be used to predict excipient compatibility, and in process chemistry, in which AI can optimize reaction conditions for yield and purity. Additionally, as demand grows for highly potent APIs, he expects increased use of AI-driven simulations to predict reaction outcomes, optimize process parameters, and minimize waste, leading to more efficient and sustainable production. On the manufacturing side, AI can aid in optimizing facility design and containment strategies, which can minimize worker exposure to hazardous materials and the environmental impact of such materials. Johnson also expects increasing use of AI-powered tools to streamline supply chain management, improving the predictability and security of raw material sourcing.

"All these possibilities inform Lonza's long-term vision, which is to create a connected ecosystem of AI tools that bridge the entire development cycle, allowing insights from one stage to accelerate the next," he summarizes.

MedPharm: Support Predictions of Drug/Excipient Interactions

"Artificial Intelligence is a hot topic across all industries now, and drug product development is no exception," says Charles Evans, PhD, Senior Vice President of Pharmaceutical Development at MedPharm. "However, depending on who you speak with, there is often a gap between what people believe it can do, what it can do now, and what it can do in the future."

He says a common misconception or myth is of AI replacing scientists, practical experiments, and independently predicting clinical outcomes. In reality, the use of AI in guiding direction and planning, accelerating insight and context, and supporting decisions when paired with strong scientific judgment is where it brings most value. AI systems can learn patterns, simulate find-

ings from data, generate new options, and predict outcomes, but they still require human interpretation and validation.

For example, *in-silico* modelling AI can be extremely useful for narrowing down large molecular libraries, exploring theoretical mechanisms, or predicting how a drug might behave in different excipients, but it cannot replace empirical science, Dr. Evans stresses.

"A study by Lenn *et al.* (2018) on RNA aptamer delivery through intact human skin found that, although modelling would likely have suggested the molecule was too large to penetrate the skin, laboratory testing demonstrated that it could cross the skin barrier," he explains. "Likewise, while AI may be able to predict certain formulation behaviors, it is unlikely to capture every chemical or physical interaction within a complex formulation that is composed of not only the drug(s) but numerous excipients with differing functionalities, which may have never been looked at before. As such, robust preformulation, formulation development, and *in-vitro/in-vivo* testing is still required to check and validate any AI predictions, though of course, such data may prove useful in any further work. It is also important to note that any AI model is limited by the data it has been trained on, and for new chemical or biological entities there may be little-to-no prior data available."

A major benefit of AI is cost and time saving, which is multi-faceted, both in supportive functions and in core R&D activities. AI provides decision support by highlighting potential risks, predicting likely outcomes, and helping teams focus resources on experiments most likely to succeed. Such an approach, he says, reduces wasted effort and material costs. "In formulation development, AI has the potential to support prediction of drug/excipient interactions, stability trends, and likely drug-release profiles, which although currently need to be checked, would still truncate the process itself and help inform the next development steps," he continues.

Even without fully implemented predictive models, AI is already useful for analyzing experimental data, highlighting patterns, and identifying areas where additional testing may be most impactful. For Dr. Evans, the future for AI lies in supporting faster and more informed decision making while helping to improve the probability of success across the development pipeline. "We have already seen this in AlphaFold, an AI system developed by Google DeepMind, which predicts the 3D structure of proteins with high accuracy and significantly accelerates biological research."

In addition, large language models (LLMs) have been shown to speed up the approval of clinical trials; and clinical study reports, which typically take 9-10 weeks to summarize clinical results, can be reduced to around a week, he says. "As more systems are developed and the current systems mature, their ability to further reduce, de-risk, and importantly support scientific decisions should offer significant value to the pharmaceutical industry."

Phillips Medisize: Delivering Predictive Insights & Streamlining Workflows

In the discovery and development stages at Phillips Medisize, AI helps eliminate low-value administrative tasks by automating data management and processing. This shift allows scientists and engineers to devote more time to analyzing data, uncovering insights, and focusing on innovations that directly benefit patients and customers, explains Dave Thoreson, Vice President, Global Operations, Phillips Medisize.

"Strategically deploying AI — especially Machine Learning (ML) — in our manufacturing processes has further driven significant cost and time savings," he says. "AI delivers predictive insights and consolidates complex datasets that were previously inaccessible, empowering our teams to make faster, more informed decisions."

ML accelerates data analysis by efficiently identifying hidden patterns and potential risks that traditional methods might miss. By augmenting human expertise, AI enables Phillips Medisize's workforce to concentrate on higher-value activities and reduce manual, repetitive tasks. Additionally, AI helps mitigate unconscious human biases through objective, data-driven insights. This improves the accuracy of decision-making, leading to more effective project prioritization and better allocation of resources, he says. "Collectively, these advantages streamline workflows, cut down trial-and-error cycles, and reduce costs — enabling us to help our customers bring therapies to market faster and with greater efficiency."

Looking ahead, Mr. Thoreson believes that AI holds transformative potential across many facets of the industry, with the greatest value in enhancing data-driven decision-making and operational efficiency. "Ultimately, the benefit to the patient or healthcare provider will be delivering solutions faster," he says. "With data insights from ML enabling better, faster decision making, innovation can happen faster."

Predictive AI, while promising, remains challenging to fully validate and can sometimes underperform due to the complexity and variability of real-world conditions. However, ML applications focused on sorting, categorizing, and analyzing large datasets tend to deliver more

consistent and actionable results.

In manufacturing specifically, ML can accelerate operational efficiency and optimize cycle times by automating routine tasks, improving predictive maintenance, and enabling smarter resource allocation. "These gains hold promise to not only improve internal efficiency but also have downstream impacts — speeding up time to market for new products and ultimately benefiting patients by providing faster access to innovative medicines," he says. "In summary, AI's most valuable contribution will be its ability to augment human expertise with faster, more precise data analysis and decision support, driving both operational excellence and improved customer outcomes."

Portal Instruments, Inc.: Broaden What Science Can Create & Enable What Patients Can Receive

The myth is that AI will instantly discover new drugs. The reality is that it does not replace biology, clinical validation or manufacturability constraints, etc. What AI truly does is collapse cycle times by eliminating thousands of dead ends early. "The winners will be those who integrate AI tightly with experimental data, device engineering, and real-world constraints, not those who expect AI to "solve" drug delivery development in isolation," says Patrick Anquetil, CEO, Portal Instruments, Inc.

As AI platforms expand the universe of new biologics (e.g. higher concentrations, higher viscosities), they will create therapies that will be increasingly difficult to deliver through traditional devices. For Portal, this accelerating trend aligns directly with what PRIME NEXUS (a closed-loop, computer-controlled drug delivery system) is built to solve:

- Higher-viscosity formulations: AI-designed molecules frequently optimize potency at the expense of injectability; NEXUS is engineered specifically to deliver viscous or large-volume drugs that spring-based pens cannot handle.
- More precise PK/PD requirements: As AI optimizes molecular behavior, dosing precision, and delivery rate control become far more important; Portal's closed-loop, software-defined delivery architecture meets that need.
- Rapid iteration: When drug designs change quickly, pharma partners cannot wait 9 to 18 months for new hardware. A software-configurable platform like NEXUS allows device parameters to be tuned in minutes rather than through hardware redesigns.

"Today we use AI to design our adaptive delivery algorithms: AI helps us optimize motor control and flow rate in real time," he says. "In short, AI is broadening what science can create and Portal is enabling what patients can actually receive." In the future, Mr. Anquetil believes that AI will assist in:

- Predictive maintenance: Forecast device or cassette issues before they occur.
- Adherence intelligence: As patients struggle with chronic injections, NEXUS will help analyze use patterns, predict drop-off risk, and prompt targeted interventions.
- Clinical insight generation: Aggregated, de-identified data supports payers, providers, and pharma with evidence on real-world use and persistence.

"The real opportunity is seamless drug-device integration powered by AI," he says. "Instead of treating the molecule and the delivery system as separate problems, AI could match a biologic's physical properties with the optimal delivery parameters in-silico at the moment the molecule is designed. This would allow pharma to anticipate viscosity, volume, and delivery constraints upfront, thus enabling faster development, smoother launches, and ultimately more personalized dosing for patients."

Quotient Sciences: 50% Reduction In Formulation Development Time

Artificial Intelligence has firmly established itself as a transformative force in drug discovery. Over the past decade, AI-driven platforms have demonstrated clear

AI will soon unify molecule design with advanced delivery systems like NEXUS, ensuring every new therapy is engineered to be deliverable from day one (Portal Instruments).

benefits in target identification, lead optimization, and molecule design. By leveraging vast biological and chemical datasets, AI can predict drug-target interactions, assess toxicity, and even generate novel molecular structures through generative algorithms. These capabilities have significantly reduced timelines and costs compared to traditional trial-and-error approaches, enabling pharmaceutical companies to accelerate the journey from concept to candidate, explains John McDermott, Vice President, Scientific Consulting, Quotient Sciences.

While discovery remains the most mature application of AI, new use cases are emerging across other stages of drug development, particularly in formulation design and optimization. Historically, formulation development has relied on human experience and labor-intensive experimentation to address drug delivery challenges relative to a target product profile.

AI and Machine Learning are now being deployed to streamline these processes. "Techniques such as Bayesian optimization and active learning allow iterative refinement of models using minimal initial data, guiding scientists toward the most informative experiments," he says. "This 'decision-support' tool also helps improve the quality and robustness of the formulation development process."

Quotient Sciences' own experiences in evaluating such approaches show reduced formulation development time by up to 50%, while simultaneously providing greater understanding of the relationships between composition and laboratory endpoints. If the model is developed further to enable predictions of clinical product performance, it will give clients a streamlined pathway to their next milestone with greater confidence of clinical success, says Mr. McDermott.

"However, despite these advances, AI will never replace human expertise. These models are only as good as the data they are trained on and the prompts they receive," he says. "In pharmaceutical development — where regulatory compliance, patient safety, and nuanced scientific judgment are paramount — human-in-the-loop approaches remain essential. Scientists guide AI systems by framing the right questions, validating outputs, and interpreting predictions. This ensures that AI augments rather than overrides human decision-making."

Mr. McDermott points to one industry perspective (ValenceAI), which notes that explainable AI and interactive workflows are critical to building trust and ensuring ethical, accurate outcomes in high-stakes environments like drug development.

In December, Quotient Sciences forged a partnership with Intrepid Labs to advance the use of AI in early drug development. Under the terms of the agreement, Quotient Sciences will have access to Intrepid's Machine Learning model, Andromeda, an AI platform for development and optimizing clinical performance of drug products. Andromeda supports rapid exploration of formulation options, reducing experimental burden, minimizing drug substance demands, and enhancing data-driven decision making. The partnership builds on the companies' existing collaboration where Intrepid's AI model was incorporated into Quotient's Translational Pharmaceutics® platform to accelerate the identification of optimal formulation compositions and reduce time to transition new drug products into clinical development.

"In summary, AI has moved beyond its early promise in discovery to become a versatile enabler across the drug development continuum," he says. "Its integration into formulation development represents a paradigm shift — one that accelerates timelines, reduces costs, and improves product quality. Through careful experimental design and human-in-loop oversight, AI will help us deliver better medicines, faster."

Sapio Sciences: Multiplies Scientific Throughput & De-risks Decisions

The greatest myth is that AI will autonomously replace the scientist. That view understates the challenges that drug development must overcome to yield positive results.

"The reality is partnership: scientists lead the work and remain in control, and AI amplifies and accelerates its impact," says Mike Hampton, Chief Commercial Officer, Sapio Sciences. Furthermore, wet lab verification remains essential because models can predict, but only experimentation can confirm. "Used well, AI multiplies scientific throughput and de-risks decisions by collaborating with accountable human experts, helping the industry to deliver treatments faster," he says.

The biggest near-term opportunity in the field of AI is finding ways to democratize its access for the scientific community. "Most labs now run multiple specialized tools for modeling, screening, and analysis, but without integration they create more friction than progress," he explains. "Scientists spend more time figuring out where trustworthy AI models are, who can access them, and how to utilize them rather than interpreting the results."

The breakthroughs, Mr. Hampton explains, will come from orchestrating deep, science-centric AI tools, creating a single, governed environment where models con-

nect, data flows cleanly, and every action is traceable. "AI only delivers value when it is built into an integrated workflow with clear ownership and high-quality data, and these workflows are accessible to scientists," he says. "The teams that focus on unifying the AI environment in the lab will move faster and gain a lasting edge."

Simtra BioPharma Solutions: Laying The Foundation For Meaningful AI Integration

Artificial intelligence is transforming drug development, but misconceptions persist. One of the greatest myths is that AI can already deliver a fully automated, end-to-end drug program. In reality, AI's strengths are still within early phases of the development process, namely in the discovery phase where it is used in the screening and identification of the right molecular entity to provide the desired therapeutic benefit within an acceptable toxicity level. "Once programs advance into clinical development and large-scale manufacturing, AI's role becomes limited as data complexity rises and process records remain less digitized," says Luis Mustafa Perez, Vice President of Operational Execution at Simtra BioPharma Solutions. "While AI is revolutionizing discovery and adding value in isolated use cases, the notion of end-to-end autonomous drug development is far from today's reality."

Generative AI, however, is pushing boundaries. Acting as a full-stack molecular design engine, it accelerates hit identification and early-stage development, enabling AI-designed drugs to reach Phase II trials faster. This progress sharpens the focus on precision and targeted delivery. "Yet, as early-stage acceleration shifts bottlenecks downstream, the industry must modernize and digitize delivery models," he says. "Creating a 'digital space' for rapid experimentation and hypothesis-driven candidate selection is critical. CDMOs are beginning to implement AI-driven systems for process development, leveraging proprietary data to enhance learning and adaptability."

Simtra BioPharma Solutions is laying the foundation for meaningful AI integration. While AI has supported process development through simulation models and clinical experiment design, the gains have primarily been in productivity and cost avoidance rather than direct reductions in R&D timelines or manufacturing expenses, Mr. Perez explains. "True transformation will come as data systems and operational workflows become fully digitalized, enabling AI to influence decision-making at scale," he says.

Looking ahead, AI's greatest potential lies in unlocking insights into previously inaccessible processes, he says. By connecting disparate systems, datasets, and models, AI can surface trends and risks earlier, guide optimization, and empower smarter, faster decisions. For CDMOs, this means not only improving speed, cost, and reliability but also helping clients design better products that achieve their intended therapeutic purpose. Mr. Perez concludes: "The future of AI in drug development is about amplifying human expertise through connected intelligence."

Stevanato Group: Improve Defect Detection Accuracy Up To 99.9%

Stevanato Group has realized significant cost and time savings by integrating Artificial Intelligence into automatic visual inspection lines used in one of its client's production processes. The AI platform uses deep learning models to improve defect detection accuracy up to 99.9% for cosmetic and particle inspection, while reducing false rejects by a factor of ten. "This means fewer good products are discarded and less time spent on costly re-inspection," says Federico Scattolin, System Owner AI, Stevanato Group.

AI also eliminates the need for frequent machine reprogramming and optimization, which traditionally requires manual intervention and long setup times. By learning from real production data, the system is robust to variations, speeding up changeovers and reducing downtime, he

Leveraging AI-driving insights during process development: digital tools are helping teams optimize workflows and accelerate decision-making in drug manufacturing (Simtra BioPharma Solutions).

explains.

"Using Stevanato Group cloud-based SG Vision AI platform — a secure solution featuring deep learning models — customers work in a GMP-compliant environment," Mr. Scattolin continues. "SG Vision AI helps deliver enhanced inspection performance by increasing detection rates and minimizing false rejection rates, while reducing costly re-inspection. Customers can upload, label, and manage data easily through a user-friendly interface, while benefiting from continuous expert support for model development and qualification."

Overall, he says these improvements translate into faster production cycles, lower operational costs, and more efficient resource use — helping Stevanato Group and its partners deliver reliable quality control while saving time and money.

Thermo Fisher Scientific: AI Model For Vial Particle Inspection Reduces Rejection Rates By 84%

There is a myth that Artificial Intelligence (AI) will eliminate the need for scientists, but the reality is that AI will only enhance – not replace – human expertise. Throughout drug discovery and development, scientists are already leveraging AI/Machine Learning (ML) models as part of a digital toolkit to help them process and analyze vast datasets, as well as predict outcomes. This means that they can spend more time on smart, targeted experimentation to get to the heart of complex challenges, says Sanjay Konagurthu, Senior Director, Science and Innovation, Pharma Services, Thermo Fisher Scientific. "As a CDMO and CRO, Thermo Fisher sees AI as a powerful enabler that helps teams make faster, more informed decisions that translate into better patient outcomes," he says.

AI/ML technologies can help drug developers address common formulation challenges that impact efficacy with greater speed and precision than previously possible via traditional trial-and-error experimentation. Whether drug developers are tackling solubility, permeability or bioavailability, modeling First-in-Human (FIH) dosing, identifying the right packaging to ensure stability, gathering data for an Investigational New Drug (IND) application or preparing to scale up for production, data-driven insights will improve outcomes and accelerate progress, he says.

"In this way, AI/ML-enabled platforms help drug developers to better understand molecule behavior, save valuable active pharmaceutical ingredients, shorten timelines, and mitigate risks," says Mr. Konagurthu. "Furthermore, by predicting formulation behavior, scientists can leverage AI-enabled insights to address challenges in real time before they derail programs."

From using predictive modeling to helping its customers design experiments more efficiently to optimizing manufacturing processes that minimize batch failures, Thermo Fisher's deployment of AI has resulted in measurable cost savings at numerous stages of drug development. To date, Thermo Fisher has used AI/ML and predictive modelling to support early development, formulation development, and process development, as well as stability predictions for more than 400 compounds.

"In some of our manufacturing processes, we have leveraged the combination of human expertise with an AI model for vial particle inspection to reduce rejection rates by 84%," he says. "We also rolled out a manufacturing operating system that enables intelligent alarm analysis and performance modeling beyond standard analytics. Most recently, we began work to integrate OpenAI's advanced interface and Application Programming Interface (API) technology across operations, particularly in our clinical research business to reduce clinical trial cycle times to help identify therapies less likely to succeed, enabling customers to reallocate investments toward more promising drug candidates. The impact is tangible – we've supported the development and commercialization of small molecule blockbusters,

A Thermo Fisher Scientific researcher runs digital data analysis.

solved hundreds of solubility issues, and been involved in the development of numerous innovative therapies."

As the pharmaceutical and biotech industries continue to prioritize bringing safe and effective therapies to market, many are exploring how to make treatments even more accessible, especially delivering novel therapies (often large molecules) in formats such as oral solid dose drugs. Once deemed suitable for injectable delivery only, large molecules face new possibilities as AI-enabled technologies enable drug developers to experiment with formulations to deliver them orally. GLP-1 medications are a great example, with several candidates showing promising results in clinical trials.

"AI/ML technologies bring an extraordinary amount of value to the biopharma industry, and that value will only continue to grow," says Mr. Konagurthu. "These technologies can transform how data informs key decisions throughout the drug development journey, which, in turn, accelerates the process that gets life-changing therapies to patients."

Veridix: Reshaping Clinical Research

The greatest myth is that AI is a magic button that will completely replace people or fully automate trials end-to-end. The reality is that AI's impact is maximized when embedded into structured processes, unified data models, and multidisciplinary teams, says Fareed Melhem, President of Veridix, an Emmes Group company. Clinical trials involve thousands of context-specific judgments. AI augments human expertise — orchestrating data, documents, and analysis. This accelerates cycle time and removes operational drag so teams can focus on science and patient outcomes.

The acceleration of AI-designed molecules changes the entire downstream operational model. Veridix's approach to embedding AI has been to connect the entire clinical workflow rather than introduce isolated tools. "When assets reach Phase I/II with less historical data and more uncertainty, we need a trial engine that can learn and adapt in real time," says Mr. Melhem. "With our Document Authoring Agent, we can generate protocol drafts, SAPs, and downstream study documents in days instead of weeks. More importantly, the protocol becomes machine-readable, enabling our downstream data, biostats, and monitoring agents to orchestrate workflows automatically."

On the analytics side, Veridix's biostats and analytics agents ingest the SAP directly, generate TFL shells, configure listings, and produce analysis-ready TFLs with real-time validation. "This doesn't just make the work easier, but it allows us to run analysis as often as needed to constantly re-evaluate dose exploration, recruitment patterns, safety signals, and operational risks with a speed that matches the pace of AI-driven drug development," he says. "The shift isn't just speed — it's tighter integration between documents, data, and analytics, enabling trials that truly adapt as evidence accumulates – and analytics feed instantly into Clinical Study Reports."

Across the Veridix–Emmes ecosystem, the impact of AI has beyond cost savings; it has fundamentally reshaped cycle times. The Document Authoring Agent has reduced protocol, SAP, and medical-writing timelines by 60% or more, routinely delivering protocol drafts in three days instead of six weeks and automatically generating downstream documents that used to require multiple teams and handoffs, he explains.

The Data Management Agent also automates study builds directly from the protocol to drive cleaner, standardized data throughout a trial, which enables faster mid-study changes, significantly reducing queries and accelerating downstream analysis. Mr. Melhem says: "As a result, we are eliminating weeks to months of latency across the study timeline. The result for sponsors is a dramatic reduction in cycle time and higher predictability; for investigators, fewer manual queries and administrative burdens; and for patients, cleaner data, and faster recognition of safety and efficacy signals."

Mr. Melhem says AI's greatest potential going forward lies in creating a more connected and anticipatory clinical ecosystem. As agents continue to mature, they will enable trials where design, data capture, and analysis are inherently aligned — reducing friction and allowing insights to surface far earlier than they do today.

"The next frontier is real-time adaptability: trials that can forecast operational risks, adjust based on emerging data, and integrate multimodal evidence without manual intervention," he envisions. "Rather than automating isolated tasks, AI will increasingly function as the fabric that links decisions, systems, and stakeholders across the study lifecycle. That shift — toward intelligent orchestration and continuous learning — is where we see the most profound potential to reshape clinical research."

Vetter: Navigate Disruption, Build Resilience & Enhance Competitiveness

"Artificial Intelligence is undoubtedly one of the most transformative technolo-

gies of our time," says Titus Ottinger, Managing Director, Vetter. "However, for a CDMO like Vetter, AI creates real value only when it is applied in a concrete, transparent, and secure way."

In an enterprise context, AI's applications can broadly be categorized into three areas:

- AI for Everyday Efficiency – Tools that simplify daily tasks such as writing, planning, or summarizing. The goal: make work easier, faster, and more efficient.
- AI for Process Transformation – Solutions that rethink workflows and significantly improve efficiency. An example would be robotic process automation.
- AI for Strategic Differentiation – Initiatives that strengthen the business model and secure its future relevance.

"In short, AI can deliver impact on multiple levels — from incremental efficiency gains to strategic realignment," says Mr. Ottinger. "Whether it's analyzing large datasets, optimizing processes or enabling predictive maintenance, AI adds value wherever patterns can be detected and risks are identified early."

However, he says, AI does not replace experience, judgment, or accountability — especially in a highly regulated environment like the biopharmaceutical industry. "One of the greatest myths surrounding AI is that technology alone can think, decide, or lead," he says. "In reality, AI is a powerful enabler, but its success depends on the people who guide and apply it responsibly."

Vetter embeds appropriate technology features in its corporate strategy to navigate disruption, build resilience, and enhance competitiveness. As a CDMO, the company leverages AI technologies, such as Natural Language Generation and Robotic Process Automation, to streamline quality and controlling processes, minimize risks of human errors, and accelerate reliable decision-making.

"These tools can optimize workflows and free up resources, ultimately leading to improved precision and reliability," says Mr. Ottinger. "Looking ahead, we see the greatest potential of AI in predictive maintenance, remote services, and intelligent assistance systems — solutions that not only can boost operational efficiency but also contribute to better patient outcomes. The key lies in balance: using technology where it strengthens us — while maintaining a clear human compass. In the end, it's not about Artificial Intelligence, but about real responsibility."

VectorSeek: Conversational Search for All Your Documentation

A persistent myth in the pharmaceutical industry is that organizations need bespoke AI systems before they can meaningfully benefit from the technology. In reality, many of the bottlenecks slowing drug development stem not from a lack of advanced modeling, but from the inability of teams to find and use the data they already have.

This is where VectorSeek, a private, domain-specific AI search platform, delivers immediate value. Rather than replacing existing infrastructure or forcing teams into rigid new workflows, VectorSeek indexes an organization's entire internal knowledge base or external website and transforms it into a secure, conversational search engine. Scientists and operational leads can ask questions in natural language and receive citation-backed answers sourced directly from their own controlled content.

The result is dramatically faster access to institutional knowledge, which directly supports the very AI-driven acceleration the industry is striving toward.

"I like to think of it as 'un-generative AI,' because it's not making up new stuff, it's pointing you to data that you already have," says Mike Walker, Co-founder. "In drug development, where precision and compliance matter, AI shouldn't replace your expertise, it should be used as a tool to make your company more efficient."

VectorSeek emphasizes privacy and governance and the model can operate on a customer's proprietary data without using it to train any external systems, addressing a core concern among CDMOs, CROs, and pharma organizations evaluating AI adoption.

In a landscape where AI promises unprecedented speed, VectorSeek enables the clarity, traceability, and informed decision-making that allows that speed to translate into real-world impact, without sacrificing scientific rigor or regulatory confidence. Domain knowledge specific to your company and the products you're creating may be buried in various documents, VectorSeek makes that expertise available to everyone in your organization. ◆

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Drug Development
EXECUTIVE

Joel Latham
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Incannex Healthcare: Pioneering the Future of Cannabinoid & Psychedelic Therapies

As global interest in psychedelic and cannabinoid-based therapies accelerates, one company stands at the intersection of scientific innovation and regulatory advancement: Incannex Healthcare Inc. (NASDAQ: IXHL). Led by CEO Joel Latham, Incannex is developing a diverse pipeline of treatments targeting some of the most challenging and underserved indications in medicine, including Obstructive Sleep Apnea, Rheumatoid Arthritis, and Generalized Anxiety Disorder. What sets Incannex apart is its commitment to rigorous clinical validation, international regulatory engagement, and a vision for multimodal drug delivery that blends emerging science with patient-focused outcomes.

Drug Development & Delivery recently interviewed Mr. Latham who shares how the company navigates complex global regulatory pathways, building strategic collaborations, and forging a path toward commercial success that balances both scientific rigor and therapeutic optimism.

Q: Can you provide a high-level overview of your company's mission and what makes you stand out in the drug development landscape?

A: At Incannex Healthcare, our mission is to develop and commercialize innovative therapies that address persistent and underserved medical conditions. We focus on diseases where current treatments are inadequate or come with significant drawbacks, and we approach them with a science-driven, clinically rigorous strategy.

What makes us stand out is our dual focus on cannabinoid-based pharmaceuticals and psychedelic-assisted therapies. Unlike many companies in this emerging space, we're committed to advancing our therapies through FDA and TGA-regulated clinical trials, ensuring that our treatments are not just promising, but provably effective and approvable.

We also prioritize fixed-dose combination therapies, which allow us to target complex conditions through multiple mechanisms, improve outcomes, and develop strong intellectual property. For instance, our IHL-42X program combines dronabinol and acetazolamide to treat Obstructive Sleep Apnea (OSA), an approach we believe could reshape the current standard of care.

With a seasoned team and strategic partnerships in place, we're efficiently moving assets through the pipeline. At the end of the day, our goal is to bring forward prescription therapies that are novel, effective, and capable of making a real difference in patients' lives.

Q: Let's talk about IHL-42X, your lead candidate for OSA. Why is this such a compelling target, and what have you seen in clinical trials so far?

A: OSA is a massive public health issue, estimated to affect over one billion people globally. Yet, there are no FDA-approved pharmacological treatments. The standard of care, CPAP devices, suffer from notoriously poor compliance, and that is the gap we aim to fill with IHL-42X.

IHL-42X is a fixed-dose oral combination of acetazolamide and dronabinol, designed to reduce the Apnea-Hypopnea Index (AHI), the gold-standard measurement of OSA severity. In our Phase 2 trial, we saw significant improvements, particularly with the lowest dose, which reduced AHI by 51% on average. Importantly, 25% of participants experienced reductions of over 80%. That's a huge signal. We're now conducting a global Phase 2/3 trial, called RePOSA, involving patients who are either non-compliant with, or intolerant to, CPAP. We're optimistic that IHL-42X could become the first approved pharmacotherapy for OSA.

Q: Another exciting area is your work in Rheumatoid Arthritis (RA). What is the science behind IHL-675A, and how does it differ from other anti-inflammatory drugs on the market?

A: RA is a complex autoimmune condition where inflammation plays a central role. Current treatments often don't work for everyone and can come with significant side effects. IHL-675A is our investigational therapy that combines two active agents: hydroxychloroquine (HCQ), a long-established immune modulator, and synthetic cannabidiol (CBD), which is known to exert anti-inflammatory effects through the endocannabinoid system.

What makes this exciting is the synergistic mechanism, HCQ dampens overactive immune responses, while CBD inhibits pro-inflammatory cytokines and prostaglandins. Together, they target both immune and inflammatory pathways. Preclinical models showed substantial reductions in inflammation, and our Phase 1 data confirmed a favorable safety profile and bioequivalence. Now, we're advancing IHL-675A into Phase 2 trials to evaluate its efficacy in RA patients. If successful, it could offer a new oral, non-opioid alternative for patients struggling with disease-modifying antirheumatic drugs.

Q: You're also exploring psychedelic-assisted therapy for Generalized Anxiety Disorder (GAD) with PSX-001. What's your perspective on the future of psychedelics in mental health care?

A: There's growing recognition that traditional psychiatric drugs, especially SSRIs and benzodiazepines, aren't working for everyone. Psychedelics like psilocybin have shown promise in helping patients "reframe" deeply rooted patterns of thought and behavior, particularly when paired with professional psychological support.

Our candidate, PSX-001, is a synthetic, oral psilocybin formulation that's being studied in combination with psychotherapy. In our Phase 2 trial, 44% of participants experienced a clinically meaningful reduction in anxiety, at least a 50% drop in anxiety scores. That's significant for a patient population often left behind by conventional treatments. The therapy was also well-tolerated with no serious adverse events. What sets Incannex apart is that we're not just conducting clinical research, we're focused on pharmaceutical-grade manufacturing, controlled dosing, and regulatory pathways. We believe PSX-001 can become

Q: Cannabinoids and psychedelics are emerging fields, but also heavily regulated. How does Incannex approach clinical development and regulatory strategy to meet FDA and international standards?

A: We're not in the wellness or dispensary business. Incannex operates strictly as a pharmaceutical company. That means adhering to Good Manufacturing Practices (GMP), submitting Investigational New Drug (IND) applications, and conducting randomized, placebo-controlled trials.

We work closely with regulators in the U.S., Australia, and Europe to ensure our studies are designed for eventual

marketing approval. Our team includes experienced regulatory professionals and advisors who've brought drugs to market globally. We also benefit from being based in Australia, where we can run trials more efficiently and access the FDA via Project Orbis and other international collaboration pathways.

Ultimately, our goal is to be among the first to bring cannabinoid and psychedelic drugs through traditional regulatory pipelines, with the same rigor as any small molecule or biologic.

Q: From a business perspective, how is Incannex positioning itself for long-term success? Are you exploring partnerships, licensing, or vertical integration?

A: We're building a business with global scalability, and we recognize that partnerships will be an important part of that equation. Our priority today is to demonstrate strong clinical results and de-risk our pipeline, particularly as we approach pivotal trials and eventual New Drug Applications (NDAs). That gives us leverage for potential collaborations.

At the same time, we've invested in IP protection, proprietary formulations, and efficient trial execution, all of which make us attractive to larger pharmaceutical players. We're certainly open to strategic partnerships or licensing agreements, especially as we complete later-stage trials. That said, our current focus remains on advancing our programs and generating high-quality clinical data.

We're also exploring complementary technologies and delivery systems that could enhance patient outcomes or expand our pipeline in the future. The long-term goal is to be a category-defining leader in psychedelic and cannabinoid drug development, much like how biotech pioneers established the first wave of immunotherapies or gene therapies.

Q: How do patient perspectives shape your clinical programs, and how are you ensuring that your therapies align with their real needs?

A: At Incannex, patient needs are the north star guiding our development strategy. We deliberately focus on conditions where current therapies are inadequate, inaccessible, or non-existent, such as OSA, RA, and GAD, because these are the areas where patients are underserved and often overlooked by larger pharmaceutical companies.

From the earliest stages of program design, we listen to patients and clinicians to understand where current options fall short. For example, with OSA, poor adherence to CPAP machines has continued to be documented, yet the pharmaceutical industry has largely ignored it. That's why we're advancing IHL-42X as a potential first-in-class oral therapy, an option that better aligns with how patients want to manage their condition.

We also design our clinical trials with patient experience in mind. That means minimizing treatment burden, ensuring our protocols are tolerable, and building in meaningful endpoints, such as real-world functionality and symptom relief, not just biomarker data. In our psilocybin-assisted therapy program for GAD, the inclusion of psychological support isn't just a regulatory requirement; it's an essential part of helping participants feel seen, safe, and empowered.

Ultimately, we don't just want to meet regulatory endpoints, we want to transform lives. That's the lens through which we evaluate every program we advance.

Q: Looking ahead, what milestones should stakeholders watch for in the near future?

A: The next year is expected to be a big one for Incannex. In parallel, we are initiating the Phase 2 trial for IHL-675A in RA, which will help validate our unique combination therapy model. We also expect to report key clinical results from the Phase 2 trial of PSX-001 for GAD in the near future, another major catalyst for us.

On the corporate side, we'll continue to engage with regulators and explore global licensing and commercialization strategies. If all progresses as planned, we will be well-positioned for late-stage development, strategic partnering, or even submission for marketing approval in some regions.

Overall it really is an exciting time; we believe we're at the forefront of a shift in chronic disease treatment, and we look forward to sharing our journey with the broader scientific and investment communities.

As Incannex Healthcare continues to advance a robust pipeline of cannabinoid and psychedelic therapies, it is staking out a unique and disciplined path in an industry full of promise, and pitfalls. Joel Latham's insights reflect not only the company's scientific ambition but its commitment to regulatory rigor and patient impact. With multiple data readouts on the horizon, Incannex is a company to watch closely as the future of mental health and chronic disease treatment continues to evolve. ◆

CELL & GENE THERAPY

What the Industry Can Learn From Baby KJ About Optimizing CRISPR Development

By: Venkata Indurthi, PhD

INTRODUCTION

In just May 2025, six-month-old "Baby KJ" became the world's first patient to receive a personalized CRISPR gene editing therapy, which was fast tracked to be developed for him after his CPS1 deficiency diagnosis, a life-threatening genetic disorder that caused ammonia to build up in his bloodstream. Children's Hospital of Philadelphia and the University of Pennsylvania worked closely with several companies to create the CRISPR therapy, which corrected the defective gene.

Aldevron, a global leader in the production of DNA, RNA and proteins, was one of the companies that contributed to this effort, and we believe the success of Baby KJ provides a model that could be replicated many times over to treat people with ultra-rare genetic diseases. Creating more of these "N of 1" therapies will be far from simple, however.

The main challenge of personalized cell and gene therapy is not scaling it up, but rather scaling it out – establishing efficient workflows that researchers in any setting can use to create therapies for small patient populations, often on compressed timelines. Right now, the biopharmaceutical industry is set up to manufacture products for millions of patients, and attempting to adapt those workflows to N-of-1 development would be time-consuming and costly.

Optimizing CRISPR development to serve patients who need rapid, personalized therapies for ultra-rare diseases will require novel approaches to everything from how editing tools are delivered into the body to how CRISPR therapies can be manufactured at extremely small volumes. By working together, academic scientists and biopharmaceutical developers are continuing to innovate novel solutions to these challenges.

HOW MRNA IS ADVANCING CRISPR

One key to the success of KJ's CRISPR therapy was the development of a novel guide RNA sequence and an mRNA-encoded base editor, designed in collaboration with Integrated DNA Technologies (IDT), which, like Aldevron, is part of the Danaher company family. Delivering CRISPR gene-editing tools in mRNA form helps to improve efficiency and lowers the risk of off-target editing.[1]

The ability to quickly develop mRNA-encoded CRISPR without compromising safety represents a major challenge. One method for accelerating this process is by limiting the size of the quality-control panel. For example, researchers could consider starting with 10 candidates, and select the top three from those. They could then test for purity and efficacy, and then move on.

In KJ's case, the development team coordinated with the US FDA from the beginning, facilitating the simultaneous completion of several steps of the process. In the first three months, the most precise gene-editing approach was established. Months four through six were spent manufacturing the CRISPR batch for toxicology studies, performing safety studies in mice and nonhuman primates and manufacturing the batch that would be brought to the clinic.[2] Future development of N of 1 therapies will require similar close coordination between regulators and developers.

INNOVATIONS IN CRISPR DELIVERY

The most commonly used vehicle for delivering DNA into the body is adeno-associated virus (AAV). The problem is, AAVs are limited in the size of the cargo they can carry and their ability to target cells beyond the liver. AAVs can also raise the risk of immunogenic reactions.[3]

Several promising alternatives to AAV delivery are under development. They include lipid nanoparticles (LNPs), which have a well-documented safety profile due to their use in COVID-19 mRNA vaccines. LNPs have been demonstrated to protect mRNA constructs from degradation and to aid in tropism, or the delivery of CRISPR tools to the intended targets.[4] Baby KJ's mRNA CRISPR treatment was encapsulated in liver-directed LNPs.

Other alternatives for CRISPR delivery that are starting to gain traction include extracellular vesicles and virus-like particles. What's promising about these options is that they can carry larger cargos than AAVs typically can, and they can target cells beyond the liver.[5]

CRISPR components are typically transported into target cells using plasmid DNA backbones, which are effective but potentially cytotoxic. Novel plasmid DNA backbones are smaller than traditional plasmids, and they are free of antibiotic markers that have traditionally been used in plasmid DNA. These attributes lower the risk of toxicities and transgene silencing. In a 2022 study, Genentech compared the efficiency of three DNA donor templates for generating CD8 T cells using CRISPR. They reported that the smallest of the plasmid vectors generated twice the number of edited cells as did a traditional plasmid and three times as much as a linear double-stranded DNA donor template.[6]

IMPROVING EFFICIENCY & TARGETING

Since the earliest development of CRISPR, the enzyme Cas9 has been the preferred enzyme for cutting DNA. But it's not always the best choice because it is often inefficient and it can cause off-target editing. There are now several alternative enzymes that can reduce errors and improve efficiency. For example, dCas9 fusions are deactivated mutants of the enzyme that can improve targeting. Also available are non-Cas9 nucleases such as Cas12a, which can often target genomic sites that may not be reachable with Cas9.

In the effort to help more patients like KJ, CRISPR developers are searching for other ways to make the technology more adaptable to a wide range of genetic disorders. In some cases, that may require not just removing faulty genes, but also inserting therapeutic genes. The most widely used insertion strategy is homology-directed repair (HDR), which is often inefficient. One promising alternative is microhomology-mediated end joining (MMEJ), which involves using programmable nucleases to create double-stranded DNA breaks and then inserting the genes at those sites. In studies, MMEJ has been shown to be up to three times more efficient than HDR. Another advantage of this process is that it is active in all phases of the cell cycle. That could provide more opportunities for introducing therapeutic genes into patients' genomes, potentially widening the universe of diseases that can be targeted with CRISPR.

EMBRACING AUTOMATION

The ability to industrialize N of 1 CRISPR development to help tens of thousands of patients with ultra-rare diseases will require several innovations on the process side. Basically, everything the industry does now must be scaled down to accommodate smaller batch sizes. Automation will help us get there.

One innovation that could make it easier to replicate the process that led to KJ's cure can be described as "RNA in a box"—the ability to use one tool to move quickly from a digital sequence to the final CRISPR product. It would be a true plug-and-play approach: With the use of a single machine, researchers could put in DNA and enzymes, hit "play," and receive an RNA drug packaged in a nanoparticle. This isn't a reality yet, but several companies are working on technology to realize this vision.

To manufacture N of 1 therapies efficiently, developers need to reduce reaction volumes to move from producing several hundred milligrams to under 100. This is a challenge, because normally a drug is advanced from the reaction stage into a purification system, which can cause a lot of the volume to be lost. When the final volume is several hundred milligrams, losing a small amount is generally not problematic. But with smaller batch sizes, manufacturers can't afford to lose any amount of product. Reducing the complexity of the flow path will prevent product loss. Innovations on the equipment side to accommodate small batch sizes will be critical.

THE EVOLVING ROLE OF AI IN CRISPR DEVELOPMENT

Artificial intelligence could improve every stage of N of 1 CRISPR development, further enhancing efficiencies. KJ's development team didn't rely on AI to complete the CRISPR therapy in six months, but it's easy to see how the technology could compress timelines even more. Designing personalized CRISPR therapies for robust expression and stability with low off-target editing risk takes many rounds of in silico and in vivo experimentation. AI-enabled tools can help researchers optimize these characteristics faster. AI can also help developers quickly determine which manufacturing parameters will result in high rates of purity and yield.

Today, CRISPR still requires largely manual processes that can be time-consuming and expensive. The closer we can get to full automation of all steps, from design through manufacturing, the faster we'll be able to develop N of 1 therapies. We'll also drive down costs.

Most scientists, myself included, keep our emotions in check. But because it's rare to see one's work contribute directly to significant milestones, I couldn't help but feel satisfied by KJ's positive outcome. Most importantly, I am encouraged that this experience will light a path towards further advances in CRISPR therapeutics. From this experience, scientists in academia and industry can apply lessons learned to future innovations, so there can be millions more KJs that can be cured with CRISPR. ◆

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BIOGRAPHY

Dr. Venkata Indurthi is Chief Scientific Officer of Aldevron, a Danaher Life Sciences company that works with CRISPR innovators from early research through clinical use, providing custom nucleases, next-generation plasmid vectors, RNP complexing and analytic services, and more. He has been a member of the Aldevron team since he earned his PhD in Pharmaceutical Sciences from North Dakota State University, Fargo, ND, in 2016.

PLATFORM TECHNOLOGY

How PolyPid's PLEX Unlocks the Potential of Local & Prolonged Release

By: Dikla Czaczkes Akselbrad

A GLOBAL HEALTH CRISIS DEMANDS NEW SOLUTIONS

In the current world of surgery, hospitals are grappling with two escalating challenges: surgical site infections (SSIs) and antimicrobial resistance (AMR). According to the U.S. Centers for Disease Control and Prevention (CDC), more than 2.8 million antibiotic-resistant infections occur each year in the United States alone, causing over 35,000 deaths. Globally, SSIs remain among the most common healthcare-associated infections, affecting millions of patients annually by prolonging recovery times, while adding billions in avoidable healthcare costs.

Despite considerable attempts over recent decades, prevention strategies have not fully solved the problem. Intravenous antibiotics administered prior to surgery quickly become ineffective once an incision cuts the blood supply to the operated area, leaving patients vulnerable during the critical healing period. Systemic approaches, which can be effective, may also drive resistance by exposing the entire body to antibiotic pressure. The question facing drug developers and healthcare systems alike is clear – how can we deliver drugs more effectively, sustainably, and precisely?

THE ORIGIN OF PLEX TECHNOLOGY

At PolyPid, we confronted this challenge by rethinking the problem at its core. What if, instead of relying on systemic delivery, we could create a platform that anchors drugs directly at the site of need and controls its release over weeks or months? That vision led to the development of our PLEX (Polymer-Lipid Encapsulation matriX) platform.

PLEX is a proprietary, biodegradable structure composed of alternating layers of lipids and polymers. These layers self-assemble to encapsulate active pharmaceutical ingredients and release them gradually in a predictable, linear manner. Acting like a protective reservoir, it ensures a consistent delivery of highly concentrated medication exactly where it is needed, and nowhere else.

This may sound simple, but the implications are profound. By localizing drug delivery, PLEX enables higher concentrations at the target site, while lowering systemic exposure to reduce toxicity and resistance risk. It can also protect fragile molecules like peptides and proteins, which would otherwise degrade rapidly, and offers durability with drug release lasting from several days to months, depending on the formulation.

FROM CONCEPT TO CLINIC: D-PLEX100

The first application of PLEX, D-PLEX100, is designed to prevent surgical site infections. These remain a stubborn global problem that complicates recovery, increases costs and, in some cases, can prove fatal. D-PLEX100 incorporates the antibiotic doxycycline into the PLEX matrix, which provides 30 days of constant local protection at the surgical site.

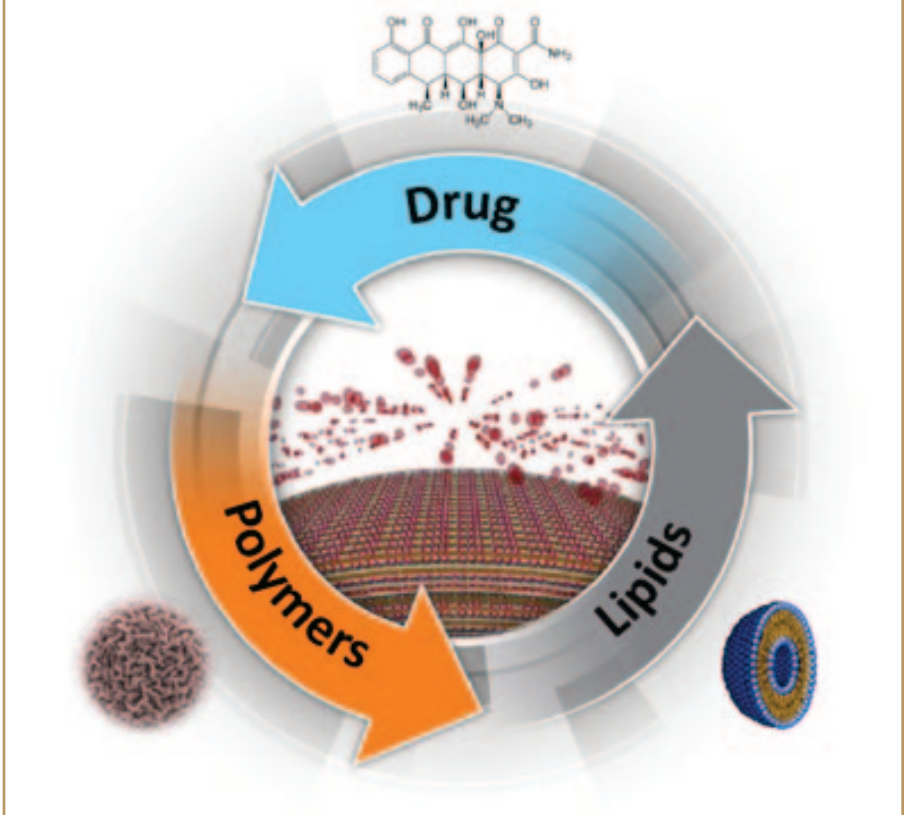
What differentiates D-PLEX100 is its ability to maintain therapeutic concentrations in tissue long after systemic antibiotics have dissipated. It is fully biodegradable, takes minutes to apply, requires minimal training, and integrates seamlessly into existing operating room workflows.

Its potential has been demonstrated in late-stage clinical de-

velopment. In July 2025, a pivotal Phase 3 SHIELD II trial reported positive topline results, marking a significant milestone for both D-PLEX100 and the broader PLEX platform. The study met its primary endpoint as well as all key secondary endpoints. Importantly, D-PLEX100 has shown close to 60% reduction in SSI ($P<0.005$) compared to standard of care while reinforcing its favorable safety profile. PolyPid is expected to submit an NDA for D-PLEX100 in the beginning of 2026.

These results validate years of development and demonstrate the potential of a localized, prolonged-release approach to infection prevention. They further illustrate how PLEX can deliver meaningful clinical impact in areas where systemic therapies have long struggled, highlighting both the potential of D-PLEX100 and the platform's broader value in addressing unmet medical needs.

FIGURE 1



Selected composition raw materials: from countless potential combinations in the non-ordered liquid stage, only a few optimally meet a specific API and medical need.

EXPANDING HORIZONS: BEYOND ANTIBIOTICS

Beyond its effectiveness in fighting SSIs and AMR, PolyPid's solution is highly versatile and not confined to antibiotics. As a delivery platform, it can be applied to multiple classes of therapeutics that struggle with stability, toxicity, or dosing frequency under traditional systemic administration.

One example is oncology. Cancer therapy often requires a delicate balance between aggressive treatment and risk of systemic toxicity. PolyPid's intra-tumoral cancer therapy delivery solution is designed to release immuno-oncology agents like STING agonists directly into tumor resection cavities or into tumors themselves. By keeping these potent molecules localized, the delivery platform can prolong intra-tumoral exposure, strengthen anti-tumor activity, and reduce the systemic side effects that often limit treatment intensity.

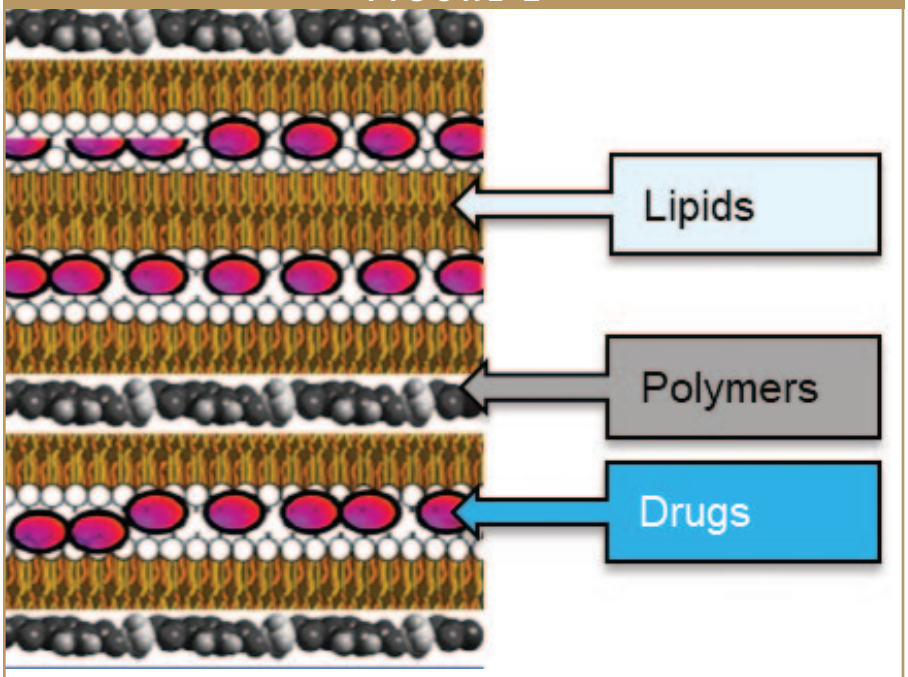
Preclinical studies of PolyPid's docetaxel-based oncology program have shown promising results, and the company has completed a successful pre-IND meeting with the FDA as this program advances toward clinical development in glioblastoma multiforme (GBM) and potentially other hard-to-treat cancers. PolyPid also partnered with ImmunoGenesis to evaluate a novel local delivery system for immuno-oncology molecules such as STING agonists, further demonstrating the adaptability of its technology in oncology.

Another promising frontier is metabolic disease and weight management. While GLP-1 receptor agonists have transformed diabetes management and obesity care, they continue to face challenges with adherence. Current GLP-1 therapies require weekly or even daily injections, which can be burdensome for patients. PolyPid's GLP-1 program leverages the knowledge gathered from its PLEX platform to create a long-acting subcutaneous delivery system capable of maintaining steady therapeutic levels for approximately 60 days. This consistent release profile avoids peaks and troughs in drug concentration, reducing side effects while improving patient adherence. Additionally, extending the release period to two full months has the potential to significantly reduce injection frequency, improve compliance and enhance patient outcomes. As the demand for GLP-1 therapies continues to increase, a delivery system that reduces treatment burden while maintaining efficacy could

present a major advance for millions living with chronic metabolic disorders.

These are just two examples that highlight the versatility of PolyPid's delivery platform and potential application across multiple therapeutic classes. Whether in the operating room, the oncology clinic, or in the management of chronic metabolic disease, the principle is the same: local and prolonged release allows medicines to achieve their full potential. Together, these advances demonstrate how local and prolonged release can reshape treatment paradigms across surgery, oncology, and chronic disease management.

FIGURE 2

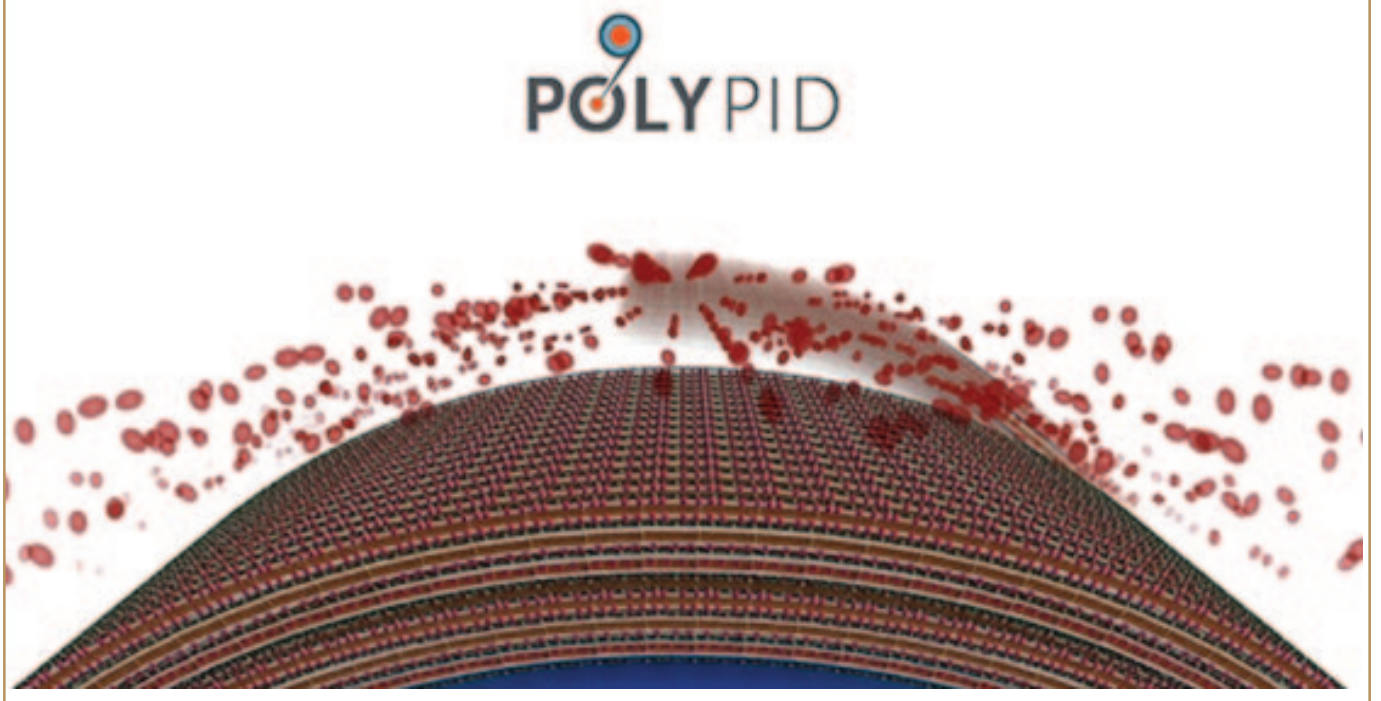


Highly ordered matrix: entering solid-stage production through self-assembly driven by weak forces.

THE ROAD AHEAD

PolyPid's work is only beginning. As D-PLEX100 advances through late-stage trials, OncoPLEX moves toward clinical studies and our GLP-1 program opens new therapeutic horizons, we are building a pipeline rooted in one principle: local and prolonged drug delivery improves outcomes. We also see strong interest from partners across the pharmaceutical industry, with multiple R&D collaborations underway to explore how our platform can be applied to peptides, proteins, and other complex molecules.

FIGURE 3



Organized disassembly: transitioning from solid to a novel liquid state in vivo, enabling controlled and prolonged drug release layer by layer.

A PLATFORM OF HOPE

At PolyPid, we believe the future of medicine is not only about what drugs are discovered, but how they are delivered. By anchoring therapeutics at the site of disease and controlling their release over time, we redefine what is possible for patients, clinicians, and healthcare systems.

Looking ahead, we are determined to continue pushing the boundaries of local and prolonged release until the day that infections are effectively prevented, cancers treated more safely and chronic conditions easier to manage. In the end, it isn't just about technology, it's about giving patients the best chance to heal. ◆

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BIOGRAPHY

Dikla Czaczkes Akselbrad serves as the Chief Executive Officer of PolyPid after serving as the company's EVP and CFO since 2017, leading the company's initial public offering on the Nasdaq Global Market in June 2020. Dikla brings more than 20 years of experience leading life sciences companies through critical international strategic, financial and business transitions, including raising over $350 million in various forms in her prior executive roles.

MAB FORMULATION & FILL-FINISH

Obstacles in Monoclonal Antibody Formulation & Fill-Finish

By: Nandkumar Deorkar, PhD, MBA

INTRODUCTION

Since the first monoclonal antibody (mAb) was approved in 1986, these protein therapeutics have become a cornerstone of healthcare, offering targeted treatment options across a broad range of indications, including oncology, autoimmune disorders and infectious diseases. In recent years, the landscape of antibody-based therapeutics has expanded well beyond traditional mAbs. This therapeutic class now includes multispecifics: bispecific and trispecific antibodies designed to engage multiple targets simultaneously, antibody-drug conjugates (ADCs) that deliver cytotoxic payloads directly to diseased cells, and Fc-fusion proteins that enhance half-life or biological activity. Additionally, engineered antibody fragments and Fc-only formats offer new possibilities for tissue penetration and alternative routes of administration.

As the number and variety of mAb-based therapeutics in development pipelines continue to grow, so does the need for greater operational efficiency, manufacturing flexibility and scalability. Addressing these imperatives must encompass not only upstream production and downstream purification, but also the final manufacturing steps, namely formulation, sterile filtration, and fill-finish. Robust formulation and fill-finish strategies are essential to ensuring product quality, long-term stability, and patient safety. From selecting the right excipients to managing complex aseptic filling processes, drug developers face a host of technical and logistical hurdles that can ultimately impact the efficacy, availability, and success of these life-saving biologics.

The following explores some of the key challenges in mAb formulation and fill-finish, offering practical insights to help developers navigate complexity and ensure success. Considerations related to operational efficiency, flexibility and scalability are also highlighted.

OVERCOMING TECHNICAL CHALLENGES

Intravenous (IV) and subcutaneous (SC) routes have been the primary methods for administering parenteral biologic formulations, each with distinct advantages and limitations. IV administration allows for low-dose formulations and ensures rapid absorption into the bloodstream, offering precise control over the amount and rate of drug delivery. It bypasses barriers associated with oral and intramuscular routes, making it ideal for treating cancers and viral infections.

In contrast, SC injection is limited by small delivery volumes, necessitating high-concentration formulations. Although absorption is slower and bioavailability lower, SC delivery is increasingly favored for chronic conditions such as asthma, psoriasis and autoimmune diseases due to its convenience and potential for self-administration.[1] The growing interest in biosimilars and patient-centric care models also drives innovation in SC biologic delivery. However, SC delivery requires formulations with high protein concentrations, often greater than 100 mg/mL, which introduces significant formulation and manufacturing challenges related to viscosity, protein aggregation and chemical degradation.[1]

Protein viscosity increases exponentially with concentration

due to electrostatic and hydrophobic interactions. This poses hurdles for both manufacturing and drug delivery, particularly in prefilled syringes or autoinjectors, where high viscosity can affect dose accuracy and patient comfort. Addressing these challenges requires careful selection of formulation excipients to ensure the final product is stable, safe, and practical for use. Therefore, viscosity reducers are often employed to alter electrostatic interactions by masking protein charges or binding to protein surfaces, affecting hydrophobic interactions.[2] For example, sodium chloride can lower the viscosity of a formulation by shielding protein charge and decreasing electrostatic protein-protein interactions. Arginine, another excipient used to reduce viscosity, works by directly binding to a protein's surface by interacting with aromatic residues.[2] However, formulation scientists are facing difficulties developing drug formulations using currently available excipients, as some are not a one-size-fits-all solution for therapeutic proteins.

Excipients, including amino acid derivatives, can be leveraged to reduce viscosity, protein-protein interactions, and influence the physical and chemical stability of mAbs. Two such excipients being investigated, bis-acetyl lysine and propyl serine, have been shown to both reduce viscosity at mAb concentrations up to 250mg/mL and control the rate of physical and chemical degradation by reducing mAb deamidation under accelerated stability conditions.[3] Various computational molecular modeling and simulation tools are currently available that can also be used to select an appropriate excipient based on a protein's behavior in its presence; Schrodinger Suite, for example, can predict specific excipient effects on protein folding, aggregation, or surface charge.[4] Additional decisions related to the choice of surfactants and buffers, along with optimization of buffer conditions, must also be made. For example, biologic drugs delivered subcutaneously are often formulated at an acidic pH with a variety of stabilizing agents and buffers designed to mitigate injection-site pain.[5]

Once the formulation strategy is defined, fluid handling and filtration systems designed to ensure accurate and aseptic handling of the therapeutic are essential. Selecting the right components, with the right raw materials of construction and pressure capabilities, mitigates the possible physical degradation of the protein due to mechanical agitation and shear forces and contamination with leachables and extractables.

Finally, reliable sterile filtration processes using customized/configurable assemblies and appropriate filtration pump skids to control differential pressure help to maximize product recovery and maintain sterility in the final filling process. Pre-use post-sterilization integrity testing (PUPSIT) may be considered to detect potential integrity defects in the filter and avoid contamination of the final product. During filling operations, accurate transfer and dosing of fluids is paramount, as is the ability to adjust flow speed to prevent foaming and splashing. Manufacturing challenges of high-dose biologics pose their own unique set of challenges, specifically back-pressure on tangential flow filtration (TFF) equipment, filter clogging, and fill-rate accuracy. This can impact processing time, further emphasizing the need for careful excipient selection during formulation development.

ENSURING REGULATORY COMPLIANCE

Adherence to stringent quality standards and regulatory frameworks is pivotal at this final manufacturing stage. While the same chemicals are used in other phases of mAb manufacturing, meeting critical quality attributes is equally as important in formulation to assure product efficacy and safety.

Identifying the right supplier of high-quality chemicals that have been extensively tested, documented, and meeting regulatory requirements contributes to patient safety and helps to avoid product loss. Use of a single excipient grade in multiple process steps can further reduce risk and may offer additional operational benefits.

Suppliers of fluid handling systems and assemblies need to demonstrate an adeptness in navigating the complexities of regulatory and quality compliance. At a minimum, they should provide an assessment and summary of potential material impurities, along with their risk assessment and documentation, including analytical test data, such as lot release testing, in-process controls, and validation processes. Trusted, qualified suppliers will further help manufacturers reduce risk through comprehensive process understanding, equipment selection, equipment qualification, and documented current good manufacturing practice (cGMP) processes for material traceability.

GAINING EFFICIENCY & FLEXIBILITY

Operational efficiency has become a critical success factor in mAb formulation

Pre-mixed and concentrated buffers streamline preparation, reduce variability and accelerate turnaround in high-throughput biopharma production.

and fill-finish. Even when the right compendial excipients are selected and formulation design is sound, process inefficiencies can derail development timelines, inflate costs and delay regulatory approval.

As the industry shifts toward more agile, high-throughput production models, speed and labor reduction are front and center. Companies are adopting strategies like pre-mixed or concentrated buffer solutions to streamline preparation and reduce variability, while innovations, such as direct dispense systems, are minimizing manual handling during fill-finish. In many cases, the rate-limiting step is no longer the production of the drug substance itself, but rather the turnaround time between campaigns or the labor-intensive process of buffer preparation. These operational pain points are where targeted process innovations can make the greatest impact, enabling faster, more scalable and resource-efficient production.

Flexibility is also essential in today's formulation and fill-finish operations, especially as the biopharmaceutical landscape evolves to include a growing array of antibody-based modalities, ranging from traditional mAbs to bispecifics, ADCs, and Fc-fusion proteins. Each format presents unique requirements for stability, viscosity, and dosing, demanding tailored formulation strategies and adaptable fill-finish solutions. At the same time, manufacturers are moving away from single-product facilities in favor of multimodal platforms that can accommodate a diverse pipeline. This shift calls for fluid handling systems and equipment that can easily adapt to different processes and facility layouts while minimizing cross-contamination risks and product loss. By building flexibility into both infrastructure and process design, companies can better respond to shifting priorities, reduce downtime, and future-proof their operations for whatever comes next.

POSITIONING FOR SCALABILITY

Scalability is a growing priority in formulation and fill-finish, as manufacturers look to bridge the gap between early stage development and commercial production with greater speed and confidence and less risk. The focus today is less on breakthrough technologies and more on integrated, adaptable solutions that support smart, efficient scale-up. Decisions made early, such as material choices, formulation strategies, and equipment selection,

can have far-reaching implications. Using consistent technologies across scales helps reduce variability, streamline tech transfer, and minimize regulatory risk. Modular equipment platforms, for example, that deliver the same performance and user experience at different volumes allow teams to scale production seamlessly without retraining staff or redesigning workflows. In a dynamic environment where product pipelines and demand forecasts can shift quickly, scalable formulation and fill-finish solutions offer the agility and reliability needed to meet both clinical and commercial needs.

INCREASING SUPPLY CHAIN RESILIENCE

A high-quality source of cGMP chemicals and customized/configurable fluid handling equipment is of no value unless those materials are available on time, in the required quantities. Specific to formulation, capacity gaps related to excipients, such as amino acids, salts, and buffers, create the risk of production delays and slow time to market.

Drug manufacturers can apply a range of strategies to overcome supply constraints, including smart forecasting, dual sourcing for redundancy, and collaborative planning. Having trusted suppliers with global networks and multiple regional sites qualified for cGMP raw materials critical to formulation and fill-finish enhances redundancy and strengthens business continuity.

Supply partners that continually invest in increasing production capacities of indispensable chemicals that meet the highest demands of quality and performance ensure a robust and secure supply chain. Such strategic investments, backed by a local footprint, minimize disruptions and ensure product consistency when bringing new therapeutics to patients.

SUMMARY

Formulation and fill-finish are critical steps in the successful development and delivery of mAbs and other antibody-based therapeutics, yet they remain some of the most complex and risky phases of biomanufacturing. As biologic pipelines diversify and patient demand increases, manufacturers must navigate formulation challenges, such as high viscosity, protein aggregation and solubility limitations, while ensuring fill-finish operations remain sterile, precise and compliant.

Success at this stage of manufacturing depends not just on technical expertise, but on the ability to drive operational efficiency, enable flexible manufacturing and scale successfully and intelligently. These imperatives are increasingly interdependent: efficiency is driven by flexible solutions that reduce labor and turnaround time; flexibility enables the same infrastructure to support multiple modalities; and scalability is achieved through standardized, modular systems that perform consistently from clinical to commercial scale.

Achieving this level of integration and reliability requires the right partners with proven experience in bioprocessing, a deep understanding of regulatory requirements and a commitment to innovation and supply chain resilience. The right partner for formulation and fill-finish can help guide raw material selection and fluid path design and provide customizable/configurable, cGMP-ready systems. Importantly, the partner should also be able to ensure the supply of necessary materials and components for formulation and fill-finish.

This type of relationship will ensure that formulation and fill-finish steps contribute to accelerated timelines, minimize risk and ensure the delivery of safe, effective therapies to patients worldwide.◆

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BIOGRAPHY

Dr. Nandkumar Deorkar is Senior Vice President, Biopharma Production Research & Development for Avantor. He is responsible for innovation strategy and planning, and execution of new products and technology development. During his 25+ year career in research & development, he has been leading teams working on various aspects of upstream and downstream bioprocessing, single use systems, chemical/polymer R&D, drug development, formulation, drug delivery technologies, process development, and technology transfer. He has published more than 30 articles and holds more than 20 patents. He earned his PhD from Indian Institute of Technology, Mumbai, India, and his MBA in Marketing from Fairleigh Dickinson University, Madison, NJ.

Drug Development
EXECUTIVE

Chris Ehrlich
CEO & Chairman
CERo Therapeutics

CERo Therapeutics: A Novel Approach to Treating Cancer

Acute Myeloid Leukemia(AML) is one of the deadliest and most difficult blood cancers to treat. It accounts for about one in three adult leukemia cases and about 1% of all cancers, yet progress in survival outcomes has been painfully slow. Treatment options remain limited, and relapse rates are high. A first-in-human Phase 1/1b clinical trial that began in early 2025 is hoping to change that treatment paradigm.

CERo Therapeutics is developing a completely novel approach to treating various types of cancer, starting with AML. T cells have specialized functions for killing targeted cells, showcased by the natural working of the human body's immune system. CERo's platform takes a patient's own immune cells and re-engineers them to create macrophage-like capabilities that can target and eliminate cancer cells. Macrophages are white blood cells that engulf and digest pathogens, including cancer cells. By combining the forces of cell killing (T-Cells) and phagocytosis (Macrophages), CERo's unique CER-T-Cells overcome the limitation of existing therapies to selectively target patients own specific cancer cells leading to a potentially safer and more efficacious means of cancer treatment.

CERo's first-in-human trial is now underway, with dosing already started and initial patient data showing positive results. The study is being held across three separate trial sites across Texas, Colorado, and Tennessee, with The University of Texas' MD Anderson Cancer Center dosing the first patient. The open-label trial will evaluate CERo's lead candidate CER-1236 in patients with AML that is either relapsed/refractory, or in remission with measurable residual disease, or newly diagnosed patients with TP53 mutated MDS/AML. The trial has started with dose escalation to establish safety and optimal dosing, followed by an expansion phase to assess early signs of efficacy. Additionally, CER-1236 was recently granted orphan drug designation by the US FDA.

The Company isn't going to stop there. In preclinical data, CERo has demonstrated tumor-killing capabilities in both liquid and solid cancers, and in parallel, the team plans to initiate trials in ovarian and non-small cell lung cancers before the end of this year in a similar fashion to the AML trial. Drug Development & Delivery recently interviewed Chris Ehrlich, CEO of CERo Therapeutics, to discuss the company's science, clinical program, the treatment landscape, and more.

Q: Can you tell us a little bit about CERo Therapeutics?

A: CERo Therapeutics is a clinical-stage company founded in 2016 with the goal of expanding the potential of engineered T cell therapy into hard-to-treat cancers by merging aspects of the innate and adaptive immune system into a single cell. This idea led to the development of CER-T technology, which combines traditional CAR-T signaling components that harness the potency of the T cell with an innate immune receptor binding domain and signaling domains that allow the T cell to "see" and "eat" tumors like an innate phagocyte would.

Q: How does CERo's CER-T technology platform work, and how is it different from traditional CAR-T therapy?

A: CER-T cells work by redirecting a patient's own T cells so that they can recognize and kill cancer cells. What makes CER-T cells unique compared to traditional CAR-T therapy is twofold. First, CER-T cells target TIM-4-L, a novel target that hasn't been investigated in cell therapy. TIM-4-L is frequently overexpressed on malignant cells, such as AML, ovarian cancer, or NSCLC, but is absent on healthy cells. We believe this pattern of expression will enable CER-T cells to be exquisitely focused against cancer with minimal off-target toxicities. Second, CER-T cells have been designed with the ability to phagocytose target cells, which is not a typical function of T cells. This gives the cells a second mode of anti-tumor killing that complements the traditional mechanisms of T cell-mediated killing. Interestingly, CER-T cells can even act as antigen-presenting cells after phagocytosis, potentially allowing them to bolster this critical immune function that is frequently dysregulated in the tumor microenvironment.

Q: What indications have you targeted for this type of treatment to date and do you expect this to be applicable to more indications in the future?

A: Currently, we are targeting AML, ovarian cancer, and non-small cell lung cancers. These diseases have high unmet need and have been difficult to target with engineered T cells, and express high levels of TIM-4-L making them ideal candidates to test CER-1236. However, we have observed TIM-4-L expression on a wide range of other cancer types and are excited to determine if CER-1236 has pre-clinical anti-tumor effect in these cancer types to support expanding what indications CER-T cells might treat in the future.

Q: Can you tell us about the progress of CERo's current clinical programs?

A: Since the acceptance of CERo's AML IND, we've moved quickly to onboard three sites and a number of CROs to initiate our trial. We've successfully treated four patients to date in the dose escalation phase and those patients are being carefully monitored for safety and efficacy. We plan to share more data as the trial progresses. In the meantime, we are gearing up to initiate our second clinical trial in solid tumors, including ovarian and non-small cell lung cancer, and are working to expand our manufacturing capacity to support these trials through future phases.

Q: What makes this new type of T cell therapy so exciting for your clinical team and partners like MD Anderson?

A: The great success of CAR-T cell therapies in B cell malignancies has been difficult to translate into other indications, including AML. Because the cancerous cells in AML share so many cell surface markers with healthy bone marrow progenitor cells, off-target toxicity has been a frequent problem. Additionally, recent work suggests that AML blasts have mechanisms that confer some resistance to T cell killing. The innovation of engineering an additional killing mechanism, phagocytosis, allows CER-T cells kill a cancer cell via multiple non-overlapping adaptive and innate mechanisms, which we

believe will overcome some of resistance seen in AML. The selection of TIM-4-L as a target is also a novel and very promising feature of CER-T cells. TIM-4-L is a class of ligand that has never been targeted by cell therapy, and the biology of TIM-4-L really restricts its expression to cancer cells, while healthy cells avoid expressing it. We believe this will reduce the off-target toxicities that have been stymied AML CAR-T therapies in the past.

Q: What should we expect to see from CERo Therapeutics over the next two to three years?

A: CERo is very positive about the potential for CER-T cells, and we are fortunate to be starting our initial clinical trial at doses that could functional and therapeutic. For AML, we are investigating subsets with defined paths to FDA approval. We hope in two to three years we will be pursuing pivotal trials or FDA approval for CER-T cells in AML and potentially solid tumors shortly after, and initiating trials in other indications, including rare cancers without good CAR-T targets, to expand the application of the CER-T technology. ◆

MRNA THERAPEUTICS

Strategies for Enhanced Stability, Targeted Delivery & Safe Translation

By: Carsten Rudolph, PhD

INTRODUCTION

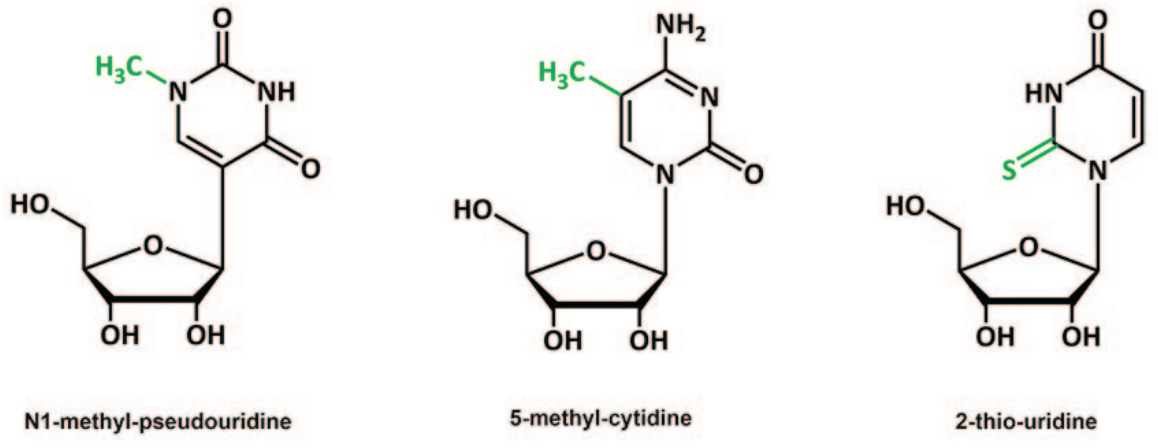
Messenger RNA (mRNA) therapeutics have rapidly advanced from conceptual promise to clinical reality, catalyzed by the success of COVID-19 vaccines and a growing ambition to treat complex diseases – including genetic metabolic disorders, rare diseases, conditions benefiting from protein replacement therapies, and respiratory conditions, among many others. Yet, the field's progress has been shaped as much by its challenges as by its triumphs. The journey from bench to bedside has required not only innovation in molecular design and delivery, but also a rigorous response to issues immunogenicity, translation fidelity, scalability, manufacturability, stability and optimal delivery. This article explores each of these challenges and the solutions offered by novel technology platforms, providing insight into the evolving landscape of mRNA drug development and its potential as a future transformative modality.

THE CHALLENGE OF MRNA IMMUNOGENICITY & TRANSLATION FIDELITY

At the heart of mRNA therapeutics lies the challenge of molecular fragility and translation fidelity, the accuracy with which the genetic information encoded in mRNA is converted into a functional protein.

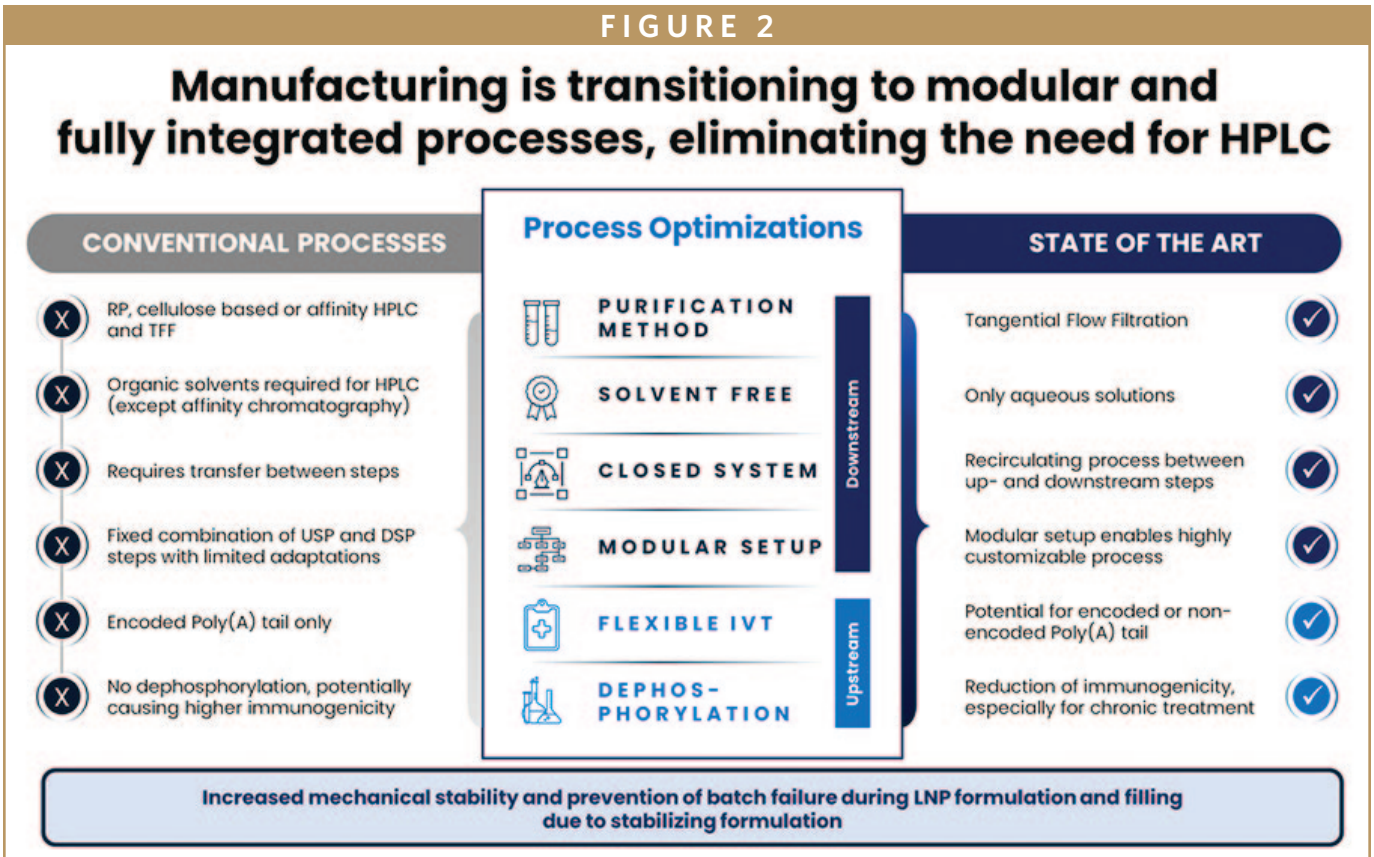
Unmodified mRNA is highly susceptible to enzymatic degradation and can provoke robust innate immune responses. The

FIGURE 1



Examples of modified nucleotides: Modified nucleotides are essential building blocks for mRNA therapeutics. They enhance mRNA stability, reduce unwanted immune responses, and increase protein production in cells, making mRNA drugs and vaccines more effective and better tolerated in patients.

FIGURE 2



Process optimizations of RNA-LNP manufacturing: After mRNA synthesis and modification through enzymatic reactions, tangential flow filtration (TFF) is used to wash, purify and concentrate the mRNA, allowing for solvent-free, continuous and scalable depletion of residuals at a smaller footprint as well as reduced costs and process times.

immunogenicity of mRNA therapeutics is a double-edged sword, which limits its practical utility as a drug. While immune activation is desirable for vaccines, it can be problematic for protein replacement therapies and chronic treatments, where repeated dosing is necessary. Minimizing innate immune activation and the risk of anti-drug antibodies is critical for therapies targeting chronic diseases. This can be achieved by careful chemical modification of the mRNA and optimization of sequence design to remove immunogenic motifs.[1,2]

A variety of strategies to address mRNA immunogenicity issues have been explored over the years, with the goal of ensuring reduced immunogenicity and the highest safety. For example, early strategies focused on chemical modifications- most notably, the incorporation of nucleoside analogues such as N1-methyl-pseudouridine (N1mΨ)-which have been shown to decrease recognition by innate immune sensors and enhance protein expression. However, it was seen that those modifications resulted in the production of off-target protein products through "ribosomal frameshifting" during translation, occurring when the ribosome slips out of the correct reading frame. This off-target products may elicit unintended immune responses [3], a phenomenon particularly relevant for conditions needing chronic or high-dose applications. While no adverse outcomes have been reported to date with mRNA vaccines, technology continues to improve especially for its application in chronic or high-dose settings.

As such, advanced mRNA platforms such as Ethris' non-immunogenic messenger RNA (SNIM®RNA) technology have adopted a multifaceted approach: the use of non-immunogenic, sequence-optimized mRNA. This is achieved through the careful selection and partial incorporation of modified bases beyond N1mΨ, together with proprietary sequence optimization strategies that reduce the likelihood of frameshifting without altering the encoded protein's amino acid sequence.[4] This rigorous attention to translation fidelity, combined with *in vitro* and *in vivo* validation, is critical for ensuring that mRNA therapeutics produce only the intended therapeutic protein and remain both functional and safe, without provoking significant inflammatory responses or anti-drug antibodies- a critical feature for therapies that require long-term dosing such as in chronic disease management. By minimizing innate immune activation through chemical modification and careful se-

quence design, mRNA therapies can be both potent and well-tolerated over multiple doses.

MANUFACTURABILITY & SCALABILITY

As mRNA therapeutics transition from niche applications to mainstream medicine, scalability and cost-effectiveness become paramount to reducing the complexity of bringing mRNA therapeutics to market. This includes addressing the high cost of cGMP-grade reagents required for in vitro transcription, the need for rigorous quality control to remove immunostimulatory by-products such as double-stranded RNA, and the lack of standardized production pipelines. Ongoing efforts to optimize manufacturing processes, such as HPLC (high performance liquid chromatography)-free purification steps, or the development of standardized protocols, are critical for ensuring the affordability and accessibility of mRNA medicines on a global scale. For instance, tangential flow filtration (TFF) is being used as an alternative purification method to HPLC, given it is more scalable, less labour intensive, and has lower operational costs.

STABILITY: LYOPHILIZATION & SPRAY DRYING

One of the most persistent challenges in mRNA therapeutics is ensuring product stability during storage and distribution. Most commercial mRNA vaccines require ultra-cold storage, complicating global access and logistics.[5]

Lyophilized and spray-dried formulations have emerged as promising solutions, as they not only enhance long-term stability at room temperature but also streamline manufacturing and distribution, making it feasible to produce and deliver large quantities of mRNA drugs worldwide without the need for a cold chain.

Spray drying, in particular, offers the advantage of scalability and is the standard technique for producing inhaled drugs. Spray-dried formulations achieve low water content and high stability, with ongoing studies aiming to confirm equivalence to lyophilized products in terms of shelf life and efficacy. These advances are crucial for inhaled therapeutics and vaccines, where stability at ambient temperature can dramatically expand global reach and reduce waste.

However, lyophilization and spray drying present their own technical hurdles. During lyophilization, lipid nanoparticles (LNPs) can deform or aggregate, and mRNA can break or lose integrity, leading to reduced encapsulation efficiency and therapeutic potency. mRNA products need to be formulated to withstand the stresses of drying and reconstitution, maintaining nanoparticle integrity and biological activity for extended periods. Optimization of the lyophilization process, including the use of stabilizing excipients and tightly packed LNPs, such as Ethris' SNaP LNP® technology, has been shown to mitigate these risks, resulting in drug products that remain stable for up to six months at room temperature and for over 18 months in lyophilized form.

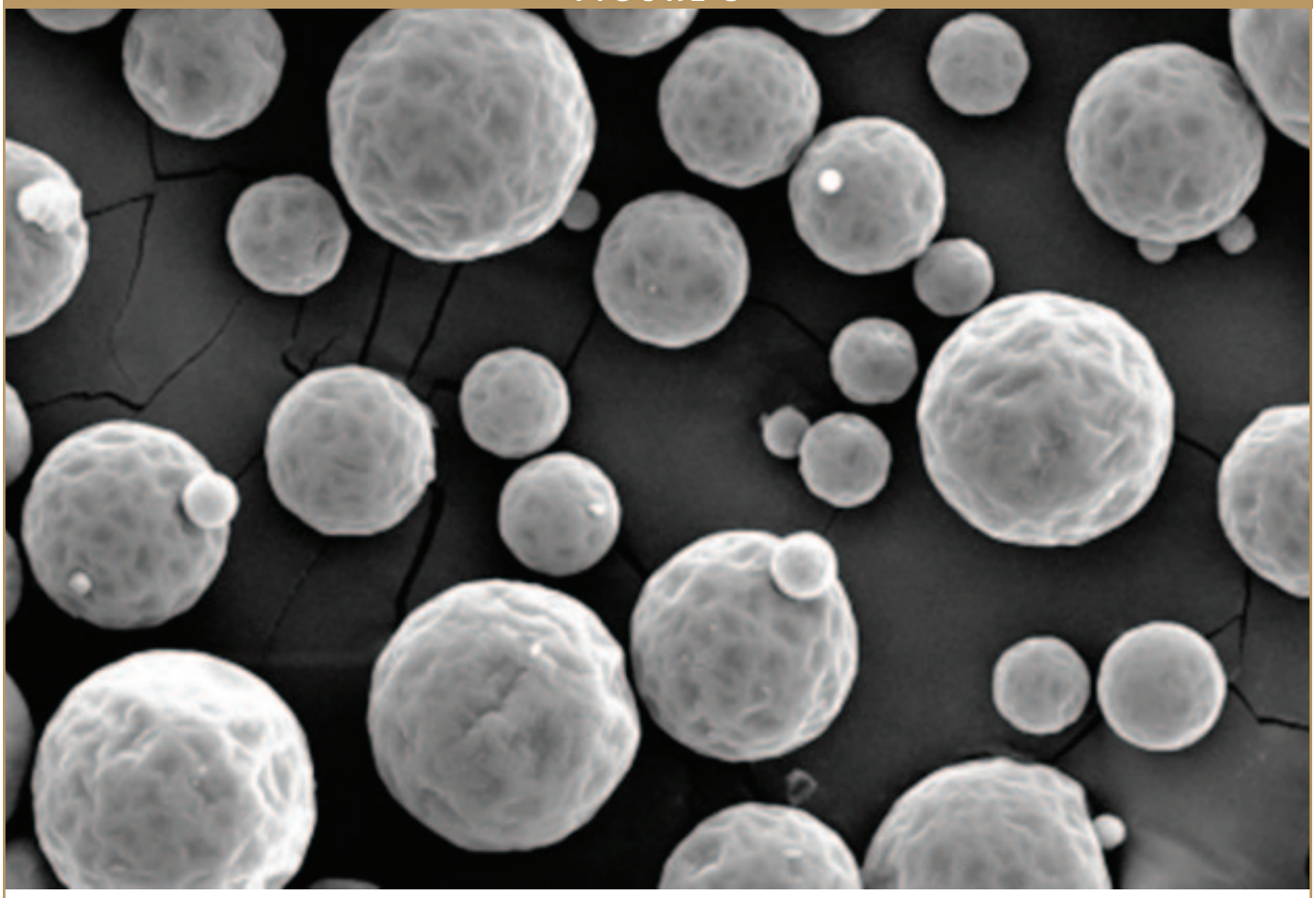
Spray dried formulation of LNPs facilitate a highly scalable manufacturing process. For inhaled therapeutics and vaccines, they can also improve patient convenience, allowing patients to carry their drugs easily in their pockets while traveling, without the need for a cold chain, as the dried formulation can be stored at room temperature.

DELIVERY: FROM SYSTEMIC EXPOSURE TO TARGETED LUNG DELIVERY

In addition to stability, unleashing the full potential of an mRNA therapy is dependent on a delivery system that protects the cargo mRNA during transport to the target cells, facilitates entry through the cell's membrane and efficiently releases it into the cell. The delivery of mRNA to the target tissue and cell type remains one of the most significant technical hurdles in the field.[6] LNPs have emerged as the leading vehicle for mRNA delivery, protecting the cargo from degradation and facilitating cellular uptake. However, conventional LNPs tend to accumulate in the liver following systemic administration, limiting their effectiveness for diseases outside the hepatic system. Likewise, dissemination following local administration may confer unwanted expression in non-target organs. For respiratory diseases, direct delivery to the lungs via inhalation is preferred, but this route introduces new challenges: the pulmonary mucus barrier, mucociliary clearance, and the risk of LNP aggregation during nebulization or spray drying, as explained previously.[7,8]

To overcome these challenges, particularly for inhaled delivery, researchers have developed LNP platforms that utilize tightly packed specific lipidoid formulations and stabilizing excipients, such as those described above, to create nanoparticles with enhanced stability and resistance to mechanical stress. Such design allows for efficient packaging of mRNA,

FIGURE 3



Micrometer-sized dry powder particles incorporating nanometer-scale lipid nanoparticles (LNPs) where mRNA is enclosed.

improved resistance to aggregation during nebulization, and targeted delivery to the respiratory tract allowing penetration of the mucus barrier and achieve even distribution within the respiratory tract.

These advances have also demonstrated the ability to localize protein expression to the nasal epithelium without significant systemic spillover, a key step in minimizing off-target effects and maximizing therapeutic impact. This precision in drug delivery is a game-changer, as it enhances treatment efficacy and reduces adverse reactions. Clinical data have shown that such approaches can result in localized protein expression in the respiratory tract with minimal systemic exposure, supporting the safety and efficacy of targeted mRNA therapies.

FUTURE DIRECTIONS: INTEGRATION & INNOVATION

The evolution of mRNA platforms is far from complete, with the next step moving from vaccines to therapeutic applications. Some pioneering companies have already made significant strides by developing in-house technologies that not only enhance the delivery of therapeutic payloads to the lungs and other organs but also address key challenges that have historically hindered treatment efficacy.[9] At Ethris, for instance, we look forward to continuing to advance our program targeting the upstream triggers of asthma exacerbations and chronic obstructive pulmonary disease (COPD) by encoding interferon lambda (IFNλ), a protein essential innate antiviral host immunity in the respiratory tract. Phase 1 trials have demonstrated not only safety and tolerability but also localized induction of antiviral pathways in the respiratory tract, supporting the potential for mRNA therapeutics to address both chronic and acute lung diseases.

Inhaled mRNA platforms are also being applied to rare genetic disorders such as primary ciliary dyskinesia, where inhaled mRNA can deliver corrected genetic instructions directly to the affected tissues, potentially restoring normal function and halting disease progression. These advances underscore the versatility and promise of mRNA medicines in addressing a wide range of respiratory conditions

Beyond respiratory therapies and vac-

cines, mRNA therapeutics can be used for a broad and rapidly expanding range of medical applications. Their versatility comes from the ability to encode virtually any protein, allowing for targeted treatments across multiple disease areas.

To expand this potential, future directions include the integration of artificial intelligence and high-throughput screening in sequence design and formulation development, enabling more precise targeting and improved safety profiles. Personalized mRNA medicines, tailored to individual genetic or immunological profiles, are on the horizon, particularly in oncology and rare diseases.

Ongoing research into alternative delivery vehicles, such as polymeric nanoparticles, lipid-polymer hybrids, and peptide/protein conjugates, is additionally expanding the toolkit for mRNA delivery and enabling more precise targeting of specific cell types within the lung and other organs. We are only at the beginning of an mRNA revolution. ◆

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BIOGRAPHY

Dr. Carsten Rudolph is Co-founder and Chief Executive Officer of Ethris. He is a pharmacist by training and a leading expert in mRNA technology. As CEO of Ethris, he leads the company' efforts to develop innovative mRNA-based medicines for diseases such as asthma and rare pulmonary conditions, as well as vaccines, focusing on inhaled delivery systems and novel RNA stabilization technologies. He is the principal inventor of Ethris's proprietary SNIM® RNA platform, who led to the founding of the company, and co-inventor of 15 drug delivery patent applications. He has authored more than 120 scientific publications. In 2005, he received the prestigious BioFuture Award of the BMBF, which is the highest endowed young investigator award in Germany. He is also affiliated with the Dr. von Haunersche Children's Hospital, part of Ludwig Maximilian University in Munich. He earned his pharmaceutical degree from the Freie Universität Berlin and his PhD from the Department of Pharmacy at the same university.

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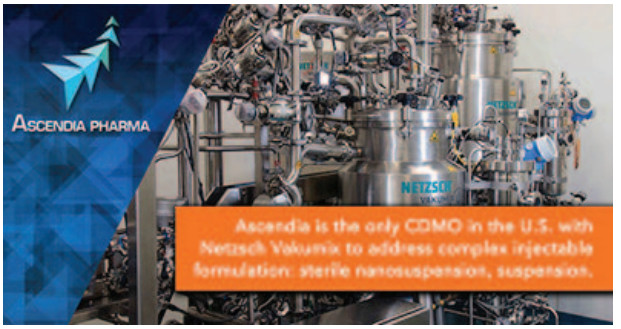

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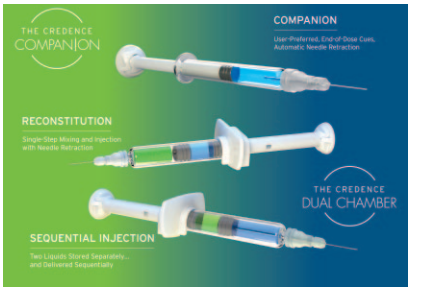

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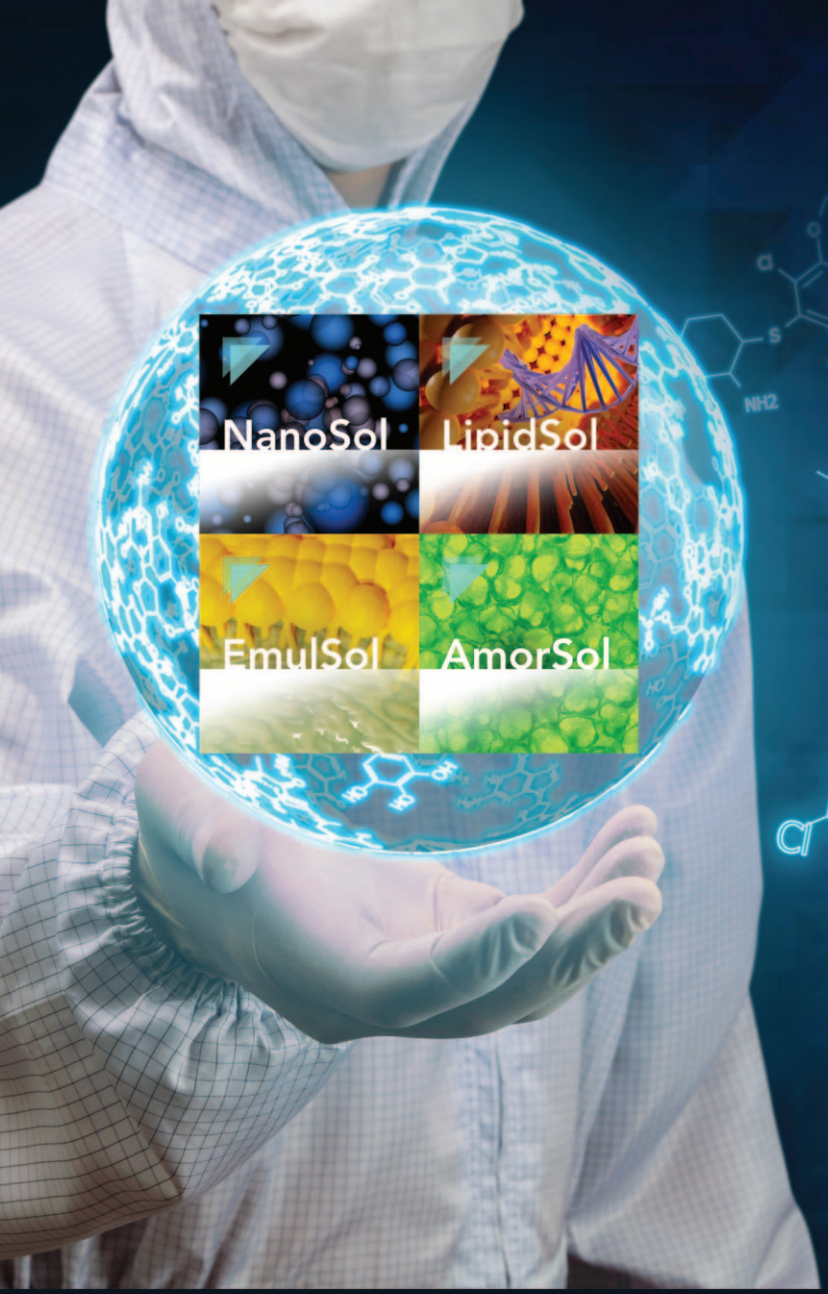

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