Drug Development & Delivery

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The Science & Business of Pharmaceutical and Biological Drug Development

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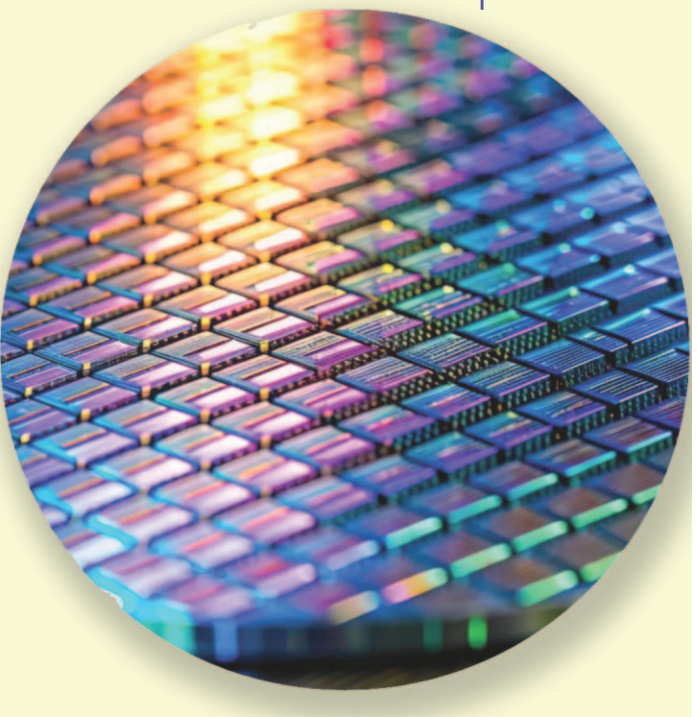
"As mRNA and other nucleic-acid-based therapeutics and vaccines expand beyond liver-targeted applications, the need for precise, tissue-specific delivery becomes increasingly urgent. Protein barcoding offers a transformative leap forward in this effort, one that not only addresses the limitations of current screening technologies but also redefines the scale and efficiency of *in vivo* testing."

p.32



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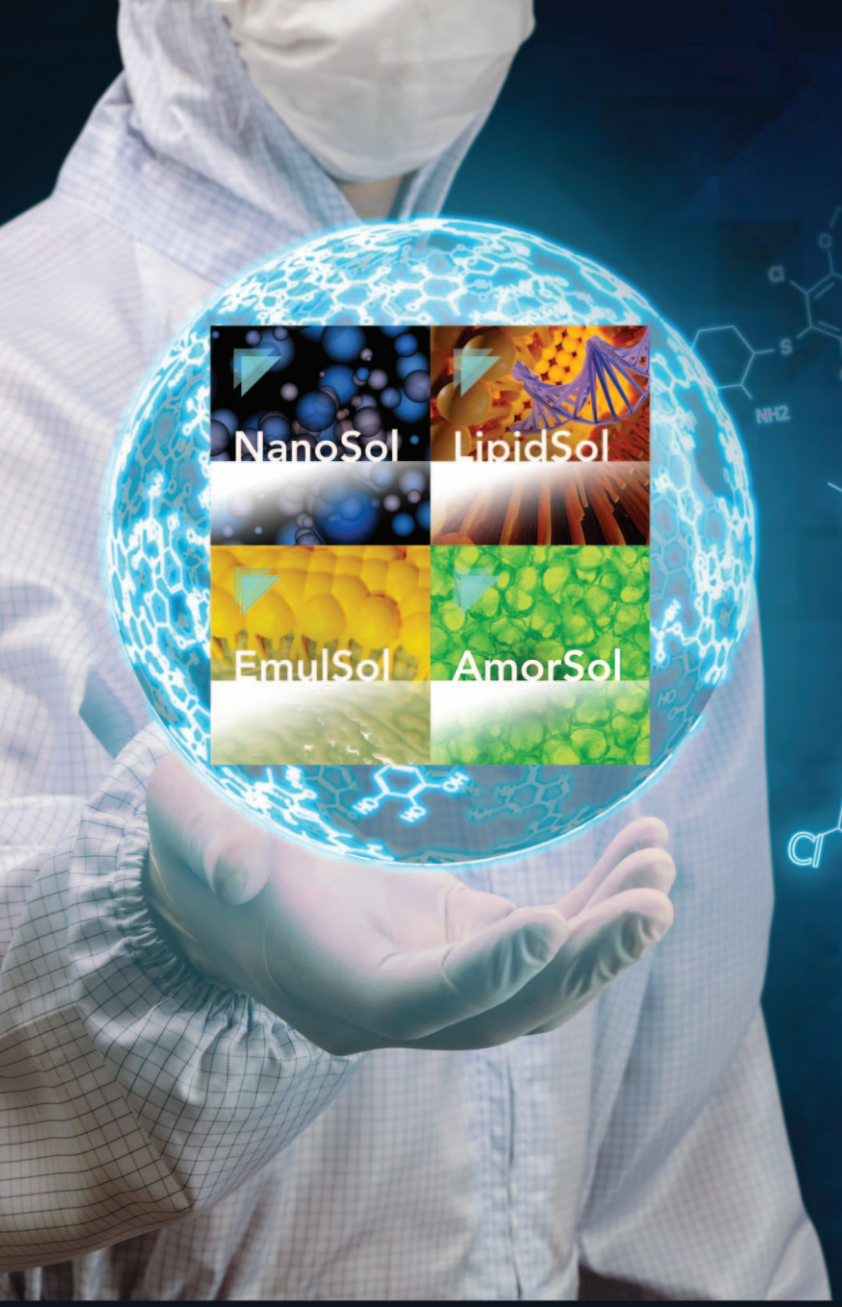

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"Growing R&D activities, personalized medicines, large-scale production of biologics, and access to new technologies are some of the biggest reasons why the contract development and manufacturing organization (CDMO) market is expected to practically double from $168 billion this year to $318 billion by 2034."

p.36

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Nuclera & Cytiva Collaborate to Accelerate Characterization of Proteins for Drug Development

Nuclera recently announced a collaboration with Cytiva focused on accelerating the production, purification, and characterization of proteins required for drug research and development, enabled through the combination of Nuclera's eProtein Discovery System with Cytiva's Biacore surface plasmon resonance (SPR) technology.

Proteins represent 95% of drug targets designed to combat disease. Rapid access to these proteins and understanding how they interact with drug candidates is essential for drug development. Typically, it takes months to obtain and characterize proteins, but Nuclera and Cytiva together have achieved production and characterization within five days. This achievement was showcased at industry conferences Discovery on Target and PEGS Europe, where Nuclera's eProtein Discovery System was used to produce Bruton's Tyrosine Kinase (BTK) and Vascular Endothelial Growth Factor (VEGF). These proteins were subsequently functionally characterized using Cytiva's Biacore SPR system.

Dr. Yvonne Tan, Associate Director of Product Management, Nuclera, said "Collaborating with life science leader Cytiva supports Nuclera in our mission of improving human health. Through this collaboration, we have demonstrated eProtein Discovery's ability to produce clinically significant proteins that can be used in characterization experiments. Combining eProtein Discovery's capability to streamline protein production workflows with Cytiva's Biacore protein characterization systems open a whole new avenue for accelerating drug development."

Anna Moberg, Senior Manager and Project Manager, Cytiva, added "The ability of Nuclera's eProtein Discovery to accelerate protein production and purification complements Cytiva's Biacore SPR technology by streamlining the upstream protein production process. We look forward to continuing our collaboration to further enhance the production of characterizable proteins for drug development."

For more information about Nuclera's eProtein Discovery System, visit https://www.nuclera.com/system/

Nuclera's mission is to better human health by enabling scientists to easily access the proteins they need for drug discovery research. The Company's eProtein Discovery™ benchtop System accelerates protein expression and purification optimization in research labs.

Applying digital microfluidics alongside in situ protein detection assays and cell-free protein synthesis, eProtein Discovery enables rapid, scalable access to high-quality proteins, supporting both cell-free and cell-based expression methods. The System significantly reduces time and cost of these processes by automating construct screening, protein scale-up, and producing purified proteins in under 48 hours for downstream functional testing. The System accelerates workflows, achieving results in days rather than the months required by traditional cell-based methods. Founded in 2013, Nuclera's offices are located in Cambridge (UK) and Boston (US). For more information please visit: www.nuclera.com

At Cytiva, our mission is to advance and accelerate the development of therapeutics. With 15,000 associates in more than 40 countries, we're driven to use our expertise and talent to achieve better flexibility, capacity, and efficiency for our customers. Our broad and deep portfolio of tools and technologies, global scale, and best-in-class service provides critical support from discovery to delivery, for customers spanning researchers, emerging biotech, large-scale biopharma, and contract manufacturers.

Monarch Therapeutics & SNAP Biosciences Enter Licensing Agreement to Bolster Cell Therapy in Oncology

SNAP Biosciences, Inc., a majority-owned subsidiary of Coeptis Therapeutics Holdings Inc., and Monarch Therapeutics Inc. recently announced a licensing agreement to enable the development and commercialization of SNAP Biosciences' proprietary Snap-Car NK cell therapy platform in oncology using Monarch's small molecule adaptor technology.

This agreement grants SNAP Biosciences access to Monarch's novel small-molecule adaptor-based technology platform, significantly broadening the functionality of the Snap-Car universal CAR-based receptor platform. Monarch's groundbreaking small molecule approach, invented by Monarch's scientific co-founders Drs. Jason Lohmueller and Alexander Deiters, enables SNAP-CAR cells to be directed by small molecule-based adaptors, enhancing the system's precision, flexibility, and modular potential across diverse therapeutic areas.

"This agreement underscores the growing recognition of our adaptor technology as a transformative tool for cell therapy," said Christopher Potts, CEO of Monarch Therapeutics. "We are thrilled to have the team at SNAP Bioscience bring this exciting technology to patients with a new generation of NK therapies that have the potential to be both highly targeted and curative."

The Snap-Car NK cells represent a promising platform technology in the cell therapy landscape. By integrating Monarch's small molecule adaptors, these therapies can now be engineered to simultaneously target multiple tumor antigens and modulate their activity in real-time, with an improved manufacturing and regulatory pathway. This advanced functionality offers a significant leap forward in addressing tumor heterogeneity and challenges associated with antigen escape commonly encountered in oncology.

"We are thrilled to incorporate this innovative adaptor technology into our Snap-Car NK platform," said Dave Mehalick, CEO at Coeptis Therapeutics Holdings, inc. "This collaboration positions us to advance more potent, flexible, and scalable NK therapies aimed at transforming outcomes for patients with difficult-to-treat cancers."

Under the terms of the agreement, Monarch will receive an upfront licensing payment and is eligible for future development milestone payments, as well as royalties on net sales.

Monarch Therapeutics is a pre-clinical stage biotechnology company focused on developing next-generation immunotherapies. The company's proprietary adaptor platform enables precise, programmable control of cell-based therapies, expanding their reach and dynamic disease targeting across a broad range of therapeutic areas. With a focus on solid tumors, Monarch Therapeutics implements its adaptor platform to drive universal CAR-T cell therapies with leading tunability, mutli-antigen targeting, and control. For more information, visit https://monarchtherapeutics.com/.

SNAP Biosciences, Inc is a majority-owned subsidiary and one of the biopharmaceutical divisions of Coeptis Therapeutics Holdings, Inc. SNAP Bioscience's is focusing on the development of Snap-Car, a "universal" CAR (chimeric antigen receptor) cell therapy, that uses a SNAP molecule to connect a CAR to tumor cells. This allows for programmable antigen targeting through co-administered antibodies, providing flexibility in targeting multiple antigens and indications. For more information, visit https://snapbioscience.com.

Alvotech & Advanz Pharma Extend Strategic Partnership to Commercialize Three Additional Biosimilars in Europe

Alvotech and Advanz Pharma recently announced they have entered an agreement to expand their commercial partnership to cover three additional biosimilar candidates.

The new agreement covers the supply and commercialization in Europe of biosimilar candidates to Ilaris (canakinumab), a human antibody interleukin-1β blocker indicated for the treatment of various inflammatory diseases, and Kesimpta (ofatumumab), a CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of multiple sclerosis, in addition to a third undisclosed biosimilar candidate. Alvotech will be responsible for development and commercial supply and Advanz Pharma will be responsible for registration and commercialization in Europe. The agreement includes development and commercial milestones for the three products, totaling up to $180 million at current exchange rates (EUR 160 million). In addition, the partners will participate in a revenue share.

"We are very pleased to expand our partnership with Advanz Pharma. We now have agreed to launch proposed biosimilars to more than ten reference products in Europe, starting in 2025 and reaching beyond 2030. This new agreement demonstrates the business development potential and value of Alvotech's growing biosimilars pipeline, that is unrivalled by any other biosimilars developer," said Róbert Wessman, Chairman and CEO of Alvotech.

"By adding canakinumab, ofatumumab and another early-stage program to our strategic partnership with Alvotech, Advanz Pharma now holds European commercial rights to proposed biosimilars referencing more than ten originator biologics. Importantly, two of these three new candidates address rare-disease indications, reinforcing our commitment to broaden access to rare disease and specialty medicines. Biosimilars are a cornerstone of our growth strategy and this expanded collaboration positions us to deliver sustainable value for patients and healthcare systems alike," added Steffen Wagner, CEO, Advanz Pharma.

Alvotech and Advanz Pharma previously entered into partnership agreements, signed in 2023, to commercialize proposed biosimilars to Xolair (omalizumab), Simponi (golimumab), Entyvio (vedolizumab), Eylea (aflibercept) and Eylea HD (aflibercept), Dupixent (dupilumab), Taltz (ixekizumab) and Tremfya (guselkumab). The supply and commercialization agreements cover all 30 member countries of the European Economic Area, as well as the UK and Switzerland. For omalizumab, the agreement additionally includes Canada, Australia, and New Zealand. According to IQVIA, the current addressable market for the proposed biosimilars covered by the partnership agreements between Alvotech and Advanz Pharma in the countries in scope is now at least $13.8 billion.

Alvotech is a biotech company, founded by Robert Wessman, focused solely on the development and manufacture of biosimilar medicines for patients worldwide. Alvotech seeks to be a global leader in the biosimilar space by delivering high quality, cost-effective products, and services, enabled by a fully integrated approach and broad in-house capabilities. Alvotech's current pipeline includes eight disclosed biosimilar candidates aimed at treating autoimmune disorders, eye disorders, osteoporosis, respiratory disease, and cancer. Alvotech has formed a network of strategic commercial partnerships to provide global reach and leverage local expertise in markets that include the United States, Europe, Japan, China, and other Asian countries and large parts of South America, Africa and the Middle East.

Candel Therapeutics Receives FDA Regenerative Medicine Advanced Therapy Designation for CAN-2409 for the Treatment of Prostate Cancer

Candel Therapeutics, Inc. recently announced the US FDA has granted Regenerative Medicine Advanced Therapy (RMAT) designation to CAN-2409 (aglatimagene besadenovec), the company's biological immunotherapy lead candidate, for the treatment of newly diagnosed localized prostate cancer in patients with intermediate-to-high-risk disease. CAN-2409 was also previously granted FDA Fast Track designation for the same indication.

The FDA's RMAT designation is intended to expedite the development and review of regenerative medicine therapies intended to treat, modify, reverse, or cure serious or life-threatening diseases where preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The designation provides opportunities for intensive FDA guidance and organizational commitment to potentially support and expedite drug development. The designation also offers eligibility for mechanisms designed to speed Biologics License Application (BLA) review and approval, with potential opportunities for rolling review and priority review.

The RMAT designation was granted on the basis of the positive data from Candel's phase 3 randomized, placebo-controlled clinical trial evaluating the efficacy and safety of CAN-2409 plus valacyclovir (prodrug), together with standard of care (SoC) external beam radiation therapy, in newly diagnosed, localized, intermediate-to-high-risk prostate cancer.

Data announced by Candel in December 2024 showed that the phase 3 trial met its primary endpoint and demonstrated statistically significant improvement in disease-free survival (DFS) ($p=0.0155$) with a 30% reduction (HR 0.70) in the risk for prostate cancer recurrence or death due to any cause in patients who received CAN-2409 plus prodrug, combined with SoC radiotherapy ($n=496$), compared with patients who received placebo combined with SoC radiotherapy ($n=249$). CAN-2409 improved prostate-specific DFS with a 38% risk reduction compared with placebo (HR 0.62; $p=0.0046$). There was also a significant increase in the proportion of patients achieving a prostate-specific antigen (PSA) nadir of <0.2 ng/ml in the CAN-2409 treatment arm compared to the placebo arm (67.1% vs. 58.6%, respectively; $p=0.0164$). Furthermore, the data showed an 80.4% pathological complete response in the 2-year post-treatment biopsies after CAN-2409 administration compared to 63.6% in the control arm ($p=0.0015$). The safety profile of CAN-2409 was generally consistent with previous studies, with no new safety signals identified. Key aspects of the study design, including the primary endpoint, were agreed with the FDA under a Special Protocol Assessment (SPA).

"Receiving the FDA's RMAT designation underscores the critical unmet need in patients with early, localized prostate cancer and validates the promising clinical activity observed with CAN-2409. This designation further supports the design of our phase 3 study, including the DFS primary endpoint agreed upon with the FDA during the SPA negotiation," stated Paul Peter Tak, MD, PhD, FMedSci, President and Chief Executive Officer of Candel.

Dr. Tak continued, "We look forward to collaborating with the FDA to pursue an expeditious approval of CAN-2409 once we submit our BL – currently anticipated at the end of 2026. Our aim is to introduce a new treatment option for patients at the early stages of prostate cancer, a disease that has seen minimal innovation over the past two decades. We expect the RMAT designation to facilitate the BLA filing process and bring us closer to achieve this objective."

Altamira Therapeutics Announces Collaboration on Circular RNA Delivery

Altamira Therapeutics Ltd. recently announced it has entered into a collaboration agreement with an undisclosed company to evaluate the potential use of Altamira's proprietary CycloPhore platform for the delivery of circular RNA payloads under development by the partner company.

Under the terms of the agreement, Altamira and its collaboration partner intend to test *in vitro* and *in vivo* the use of CycloPhore nanoparticles. The partner will, under certain conditions, have the option to negotiate with Altamira a license agreement to develop and commercialize circRNA nanoparticles with their proprietary RNA payload.

"We are very excited to enter in this first collaboration to explore the utility of our CycloPhore platform," said Covadonga Pañeda, PhD, Altamira's Chief Operating Officer. "CycloPhore was launched only recently specifically for delivery of circular RNA, which has been emerging as a highly promising approach for RNA drug development. For instance, circular mRNA could allow for lower dosing and less frequent administrations than linear mRNA. We look forward to working with our new partner who has strong expertise in circular RNA and the ambition to develop truly life changing therapeutics."

CycloPhore is a versatile platform for safe and effective delivery of circRNA (circular messenger ribonucleic acid) into target cells. It is based on the xPhore technology, comprising a patented 21-amino acid peptide that can engage any type of RNA in rapid self-assembly into a nanoparticle. The nanoparticle has a size, charge, and other physical features that allow it to escape hepatic clearance and thus to reach other target tissues than the liver. xPhore protects the RNA payload from degradation in circulation and allows for rapid cellular uptake, while enabling pH-dependent endosomal escape and cytoplasmic delivery.

Altamira Therapeutics is developing and supplying peptide-based nanoparticle technologies for efficient RNA delivery to extrahepatic tissues (xPhore platform). The versatile delivery platform is suited for different RNA modalities, including siRNA, mRNA and circRNA, and made available to pharma or biotech companies through out-licensing. The company has two proprietary flagship programs based on xPhore and siRNA payloads: AM-401 for KRAS driven cancer and AM-411 for rheumatoid arthritis, both in preclinical development beyond in vivo proof of concept. In addition, Altamira holds a 49% stake (with additional economic rights) in Altamira Medica AG, which owns its commercial-stage legacy asset Bentrio, an OTC nasal spray for allergic rhinitis. Further, the Company is in the process of partnering / divesting its inner ear legacy assets. Founded in 2003, Altamira is headquartered in Hamilton, Bermuda, with its main operations in Basel, Switzerland. For more information,

XOMA Royalty Purchases Mezagitamab Royalty & Milestone Rights Held by BioInvent International for up to $30 Million

XOMA Royalty Corporation and BioInvent International AB recently announced XOMA Royalty has purchased the future mezagitamab (TAK-079) royalty and milestone interests held by BioInvent for $20 million at closing, with a total transaction of up to $30 million.

"This transaction further builds the potential of XOMA Royalty's late-stage royalty portfolio by increasing our economics in a promising Phase 3 program already in our portfolio," said Brad Sitko, Chief Investment Officer of XOMA Royalty. "We appreciate the longstanding relationship with BioInvent stemming from XOMA's legacy technology, which gave rise to mezagitamab. We are pleased to provide BioInvent non-dilutive capital to further advance its proprietary pipeline to a key inflection point."

Martin Welschof, Chief Executive Officer of BioInvent, added "Today's announcement highlights the value to BioInvent of our n-CoDeR platform, which has led to the identification of multiple promising therapeutic antibody drug candidates, many of which are now in mid-to late-stage clinical trials. As well as reflecting XOMA Royalty's expanded interest in mezagitamab, this transaction supports our strategy of creating value via partnerships and gives us a non-dilutive capital injection that bolsters our balance sheet so that we can continue to focus on advancing our own clinical drug development programs."

The future royalty and milestone economics interest in mezagitamab originated from a 2003 cross-licensing agreement covering XOMA Royalty's legacy bacterial protein expression technology and BioInvent's n-CoDeR antibody library. Under the terms of XOMA Royalty's purchase of BioInvent's economic interest in mezagitamab, XOMA Royalty paid $20 million to BioInvent at closing today and will pay an additional $10 million upon mezagitamab achieving a specific pre-defined regulatory milestone associated with receiving marketing approval in the IgA nephropathy indication from the US FDA.

With its existing entitlement, plus the newly acquired economics from BioInvent, XOMA Royalty will be entitled to milestones of up to $16.25 million from Takeda and mid-single digit royalties on future mezagitamab commercial sales.

In its Fiscal Year 2024 financial results, Takeda, the company developing mezagitamab, announced it has initiated a Phase 3 clinical trial in patients with immune thrombocytopenia (ITP). Mezagitamab is a fully human immunoglobulin IgG1 monoclonal antibody (mAb) with high affinity for CD38 expressing cells (including plasmablasts, plasma cells, natural killer cells) resulting in their depletion that has the potential of becoming the best-in-class anti-CD38 mAb.

XOMA Royalty is a biotechnology royalty aggregator playing a distinctive role in helping biotech companies achieve their goal of improving human health. XOMA Royalty acquires the potential future economics associated with pre-commercial and commercial therapeutic candidates that have been licensed to pharmaceutical or biotechnology companies. When XOMA Royalty acquires the future economics, the seller receives non-dilutive, non-recourse funding they can use to advance their internal drug candidate(s) or for general corporate purposes. The Company has an extensive and growing portfolio of assets (asset defined as the right to receive potential future economics associated with the advancement of an underlying therapeutic candidate).

BioInvent International AB (Nasdaq Stockholm: BINV) is a clinical-stage biotech company that discovers and develops novel and first-in-class immuno-modulatory antibodies for cancer therapy, with currently five drug candidates in six ongoing clinical programs in Phase 1/2 trials for the treatment of hematological cancer and solid tumors. The company's validated, proprietary F.I.R.S.T technology platform identifies both targets and the antibodies that bind to them, generating many promising new immune-modulatory candidates to fuel the company's own clinical development pipeline and providing licensing and partnering opportunities.

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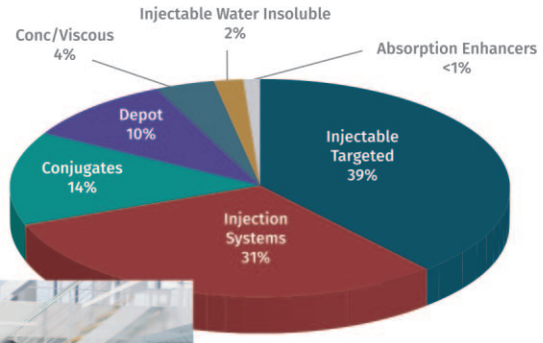
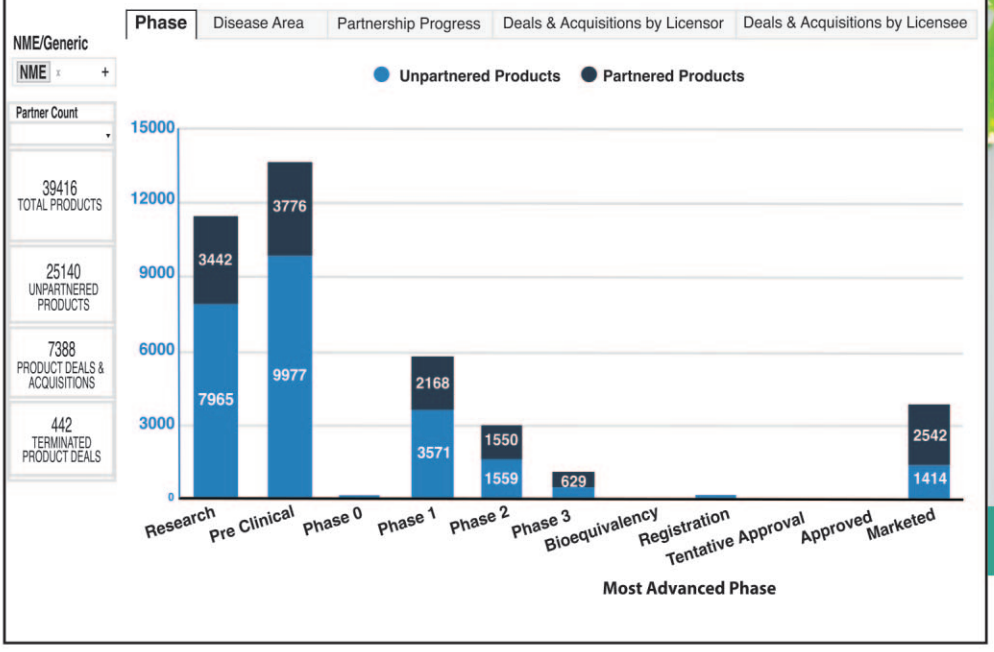
CROSCARMELLOSE SODIUM **(Core/Content)**	30.3 mg
MICROCRYSTALLINE CELLULOSE **(Core/Content)**	75.76 mg
SODIUM STEARYL FUMARATE **(Core/Content)**	29.29 mg
COLLOIDAL SILICON DIOXIDE **(Core/Content)**	7.58 mg
POLYVINYL ALCOHOL, UNSPECIFIED **(Tablet/Capsule coat)**	11.72 mg
POLYETHYLENE GLYCOL **(Tablet/Capsule coat)**	5.92 mg
TALC **(Tablet/Capsule coat)**	4.33 mg
FERRIC OXIDE YELLOW **(Tablet/Capsule coat)**	0.32 mg
TITANIUM DIOXIDE **(Tablet/Capsule coat)**	7 mg
FD&C RED NO. 40 **(Tablet/Capsule coat)**	
FD&C BLUE NO. 2 **(Tablet/Capsule coat)**	

Evaluate New and Promising Technologies



Injectable Drug Delivery Technologies

Screen Potential Partnering and Investment Opportunities



Assess Development Pipeline and The Competitive Landscape

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Formulation Forum

Manufacturing of Solid Oral Dosage Forms by Direct Compression

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

KEYWORDS: Direct compression, SODF, tableting, co-processed excipients, hardness, compressibility, continuous manufacturing.

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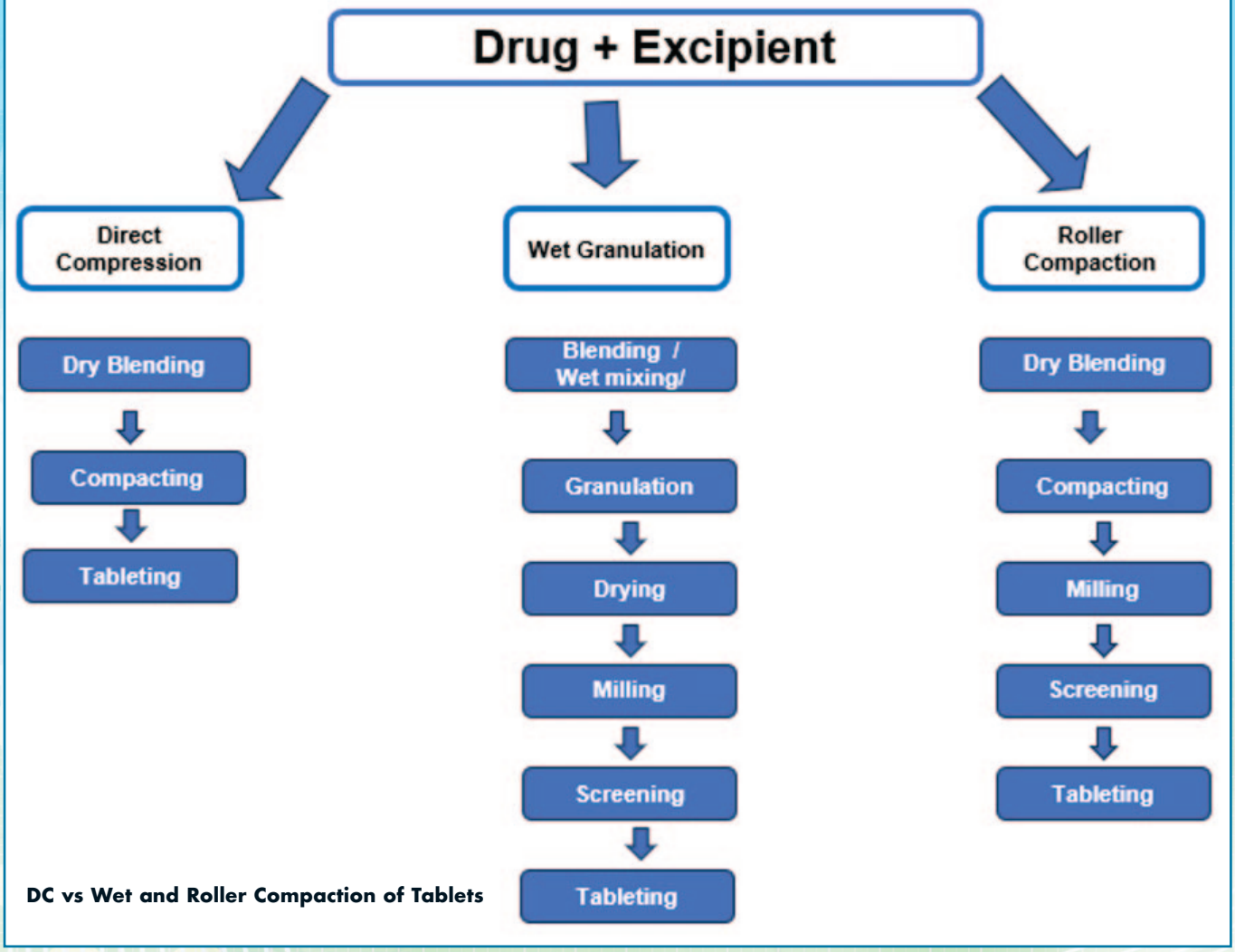
INTRODUCTION

Solid oral dosage forms (SODFs) count for more than 80% of marketed drugs, especially for economical and stability reasons, and for easy manufacturing. SODFs can be achieved by several methods. Of those, wet granulation remains a preferred method for achieving the greater compaction and content uniformity, especially for low to medium doses. However, it requires longer drying and processing times as opposed to dry granulation, by roller compaction, and direct compression, which are most preferred and ideal processes with smaller footprints because of their

FIGURE 1



DC vs Wet and Roller Compaction of Tablets

TABLE 1

Excipient /Composition	Process	Properties
Lactose monohydrate	Spray dried lactose	Uniform, spherical particle size, good flowability, brittle deformation, low compactability
Microcrystalline cellulose and colloidal silica	Co-processed, spray dried	Good flowability, plastic deformation, unstable with strong oxidizing agents,
Lactose and microcrystalline cellulose	Spray dried	Superior flow and binding properties, brittle deformation, incompatible with oxidizing agents
Lactose monohydrate and starch	Spray drying	Good flowability and compactability, hygroscopic, elastic-brittle deformation

A few lactose-based DC-grade excipients: manufacturing processes and properties

simplicity, yielding greater physico-chemical stability and manufacturing efficiency of moisture sensitive drug products.[1,2]

Direct compression (DC) requires blending, mixing, and compression of the ingredients into tablets without going through the wet granulation process that requires milling, drying, screening, and diluting with other ingredients before tableting. Not all excipients are well suited for DC, so challenges remain to find excipients compatible to DC due to certain physicochemical properties associated with poor flowability, lack of plasticity, flexibility, and compressibility. Thus, to enable these excipients with DC properties, additional excipients such as fillers and binders are co-processed to yield highly compressible at low to medium compression forces. The co-processing of two or more excipients may produce new materials with much better properties than individual excipients, making it flexible for greater compressibility with APIs to produce good quality SODFs.[3]

Poor flowability could stem from fine APIs as well as excipient particulates. These could pose challenges for direct compressibility of the powder blends into tablets. Finer APIs could lead to poor flowability, which could lead to particle segregation and obstacles for achieving higher drug loading. Chen, et al (2019) used spherical crystallization to overcome poor flowability and achieve higher drug loading by using free flowing lactose (Lactose 316).[4] Spray drying or granulation remains an alternative method for DC by overcoming many other barriers in tableting.[5]

DIRECT COMPRESSION PROCESS

As outlined in Figure 1, the DC process is simpler and more straight forward for making tablets, provided the right criteria for excipients and drug substances are met. The finer grade drug/excipient particulates lead to aggregation, and poor flowability, and hence poor compressibility with increasing drug loading. These can be addressed by wet granulation and/or dry granulation.[6]

The advantages of the DC process include greater chemical stability, APIs less susceptible to hydrolysis or degradation, time-saving and low manufacturing cost, and faster dissolution. The disadvantages of the DC process include higher segregation risk, higher excipient cost (eg, co-processed excipients), fixed composition, and less compactability.

EXCIPIENTS FOR DIRECT COMPRESSION

There are several classes of commonly used dry binders for DC approved in marketed drugs (Table 1).[7]

Citing an example, Margret and Madhavi (2020) evaluated quinapril in DC as the drug is unstable by wet granulation due to moisture. They evaluated a range of excipients to assess the stability of drug at ambient and stressed conditions, and based on the results, lactose monohydrate, crospovidone, and hypromellose were selected for DC.[8] The powder in pre-blends for DC was characterized by angle for repose, bulk and tapped density, Hausner's ratio, and moisture content. The content uniformity of drug in compressed tablets was consistent for all three blends, and the dissolution profile was also consistent, showing more than >90% release in 30 min.

SPRAY DRYING FOR DIRECT COMPRESSION

Spray drying is a unique process for manufacturing composite particles composed of two or more ingredients with poorly soluble APIs dissolved in common organic and/ aqueous solvents. The resulting co-processed composite bulk powder improves the physico-chemical properties, such as flowability, compatibility, and compressibility with respect to individual components used in the composite blend.[9,10] Spray drying excipients without drug is also used to improve the performance of excipients, combined for tableting and the performances of solid oral dosages (SODs). Like many other marketed excipients, Ludipress®, for example, composed of lactose monohydrate, PVP K30, and

TABLE 2

Drug/Dosage	Excipient	Functional Property	Reference
Acetazolamide/250 mg	None	Improves particle elasticity and tensile strength	12
Chlorothiazide/250 mg-500 mg	None	Improves particle porosity and tensile strength, nanosized particles	13
Ibuprofen/ 200 mg-800 mg	Mannitol, erythritol, maltodextrin, crospovidone, colloidal silica, Polysorbate 80	Improves flowability and compactability	14
Cimetidine/ 200 mg-400 mg	Mannitol, erythritol, maltodextrin, crospovidone, colloidal silica, Polysorbate 80	Improves flowability and compactability	15
Celecoxib/ 50 mg-400mg	Povidone, meglumine	Improves flowability, higher compactability and tabletability	16
Metformin HCl/ 500 mg- 1000 mg	Povidone, copovidone, HMPC, sodium alginate, sodium croscarmellose	Reduced crystallinity, improves compactability, more isodiametric microparticles	17
Naproxene/ 250 mg-500 mg	HPMC	Reduce crystallinity, more isodiametric particles, improved compactability and tabletability	18

List of spray drying of drugs with and without excipients.[5]

crospovidone is used as a directly compressible excipient for tableting of drugs (FDA listing). In the following section, we will focus on spray drying of drugs with excipients for yielding DC tablets, which is achieved by particle engineering of morphology to achieve the desired compressibility in high doses with the appropriate excipients, especially those with poor compressible.[11]

Table 3 shows a number of drugs that can be co-processed in spray dried powder for improved compactability, tabletability, and performance. In the spray drying process, the spray dried droplets coming out of nozzles are affected by atomization and the shear energy applied (inlet and outlet temperatures), which are also dependent on viscosity and surface of the feed solution. In general, high viscosity and surface tension favor larger droplets, on the other hand, high spray energy yields smaller droplets and particulates. APIs sensitive to higher temperatures are most suited because the solvent evaporation in the spray drying process is short, allowing the drug to be less exposed to higher temperatures.

Chaudhari and Gupte (2017) investigated Avicel HFE with additional 35% mannitol to study the picking and sticking issue of a reference drug (compound XY) by direct compression.[19] It was observed that by blending Prosolv 90 with granular mannitol in reduced amounts improved picking and sticking as opposed to using powder mannitol.

Gohel and Jogani (2005) reviewed co-processed DC excipients. The authors evaluated lactose for improving flowability and compressibility via the freeze-thaw method with PEG6000, povidone, and gelatin at different concentrations and compared the performance with diclofenac sodium as a model drug in Microcelac.[6] The results were significantly better compared to lactose monohydrate in terms of flowability, compressibility, and disintegration of DC tablets.

One of the major disadvantages of the co-processed excipient mixture is the ratio of each ingredient fixed, and those ratios might not be ideal for the optimal formulation of an API.[20] Thus, due to lack of pharmacopeial acceptance, some of the fillers and binders might not be added unless their performance significantly helped improve direct compressibility as opposed to individual components in the physical mixtures. Of several, Kollidon® SR, for example, available as co-processed excipient mixture and composed of polyvinyl acetate and PVP K30 as major components, possesses greater flowability and yields much better hardness on DC as opposed to individual components in the physical mixture.[21] Kollidon SR is not monographed, but the DC excipients like Compressuc® MS is monographed as Compressible sugar and composed of 96% sucrose with 2.3% maltodextrin and 1.7% inverted sugar. Thus, changing the ratios of the ingredients for better compressibility with higher drug loading might be challenging.

Plasticity remains an important parameter in DC. In comparison with cellulosic excipients, such as microcrystalline cellulose, hydroxypropyl cellulose and povidone K-30, the plasticity of povidone K 30 is about 80% as opposed to about 70% for MCC and HPMC.[22] The compression date suggests that Kollidon VA 64 (copovidone) is not adversely affected by increasing the compression pressure at 18 kN and 25 kN, while the cellulosic excipients showed far less compressible in DC at 18 kN

TABLE 3

Spray Dried Excipient/ Co-Processed Excipients	Commercially Available, Brand Name
Lactose	FlowLac® 90, FLowLac® 100, Pharmatose® DCL 14
Microcrystalline cellulose	Avicel®, Vibapure®, Emocel®
Calcium Salts	Puracal® DC (calcium lactate pentahydrate), Fujicalin® (dicalcium phosphate), TriCafos® (tricalcium phosphate)
Sugars and Polyols	Compressuc® PS (sucrose), Advantose® 100 (maltose), Partek® M, Pearlitol® SD, Mannogem® (mannitol); Neosorb® XTAB, Partek® SI (sorbitol),
Rice starch	Era-tab®, Primotab ET®
Cellactose® 80	75% lactose monohydrate, 25% cellulose powder (3:1)
MicroceLac® 100	75% lactose monohydrate, 25% microcrystalline cellulose
StarLac®	85% lactose monohydrate, 15% white maize starch
CombiLac®	70% lactose monohydrate, 20% microcrystalline cellulose, 10% white native corn starch
Avicel® HFE	90% microcrystalline cellulose, 10% mannitol
Avicel® CE-15	85% microcrystalline cellulose, 15% guar gum
Avicel® DG	75% microcrystalline cellulose, 25% dibasic calcium phosphate
Prosolv®, Prosolv® EASY tab	98% microcrystalline cellulose, 2% colloidal silicon dioxide
StarCap 1500®	90% corn starch, 10% pregelatinized starch
Emdex®	95% glucose, 5% oligosaccharides (from starch)
Ludipress®	93% lactose monohydrate, 3.5% PVP K30 and 3.5% Crospovidone
Advantose FS95	95% fructose, 5% starch
Compressuc® MS	96% Sucrose with 2.3% maltodextrin and 1.7% invert sugar (USP monograph-Compressible sugar)
Kollidon® SR for Sustained release	80% polyvinyl acetate, 19% povidone K30, 0.7% SLS, 0.3 % colloidal silica
F- Melt® for ODT	Xylitol, mannitol, crospovidone, microcrystalline cellulose
Pearlitol® Flash for ODT	80-85% mannitol, 15-20% maize starch
Ludiflash® for ODT	90% mannitol, 5% crospovidone, 5% polyvinyl acetate

A range of commonly used spray dried excipients and co-processed excipients for DC

and 25 kN. Thus, Kollidon VA 64 plasticity can be used as a marker for higher drug loading of crystalline drugs in direct tableting. For example, ascorbic acid, when directly compressed in crystal and powder with 5% Kollidon VA64, showed the hardness of about 95 N and 130 N, respectively. In another example, highly crystalline acetylsalicylic acid powder (400 mg) when compressed in 516 mg tablet comprised of co-processed Ludipress® (99 mg) with Kollidon CL (15 mg) and stearic acid (1 mg), yielded the hardness of 90 N with friability of <0.4% and >97% dissolution in 30 min. The tablets were stable over 12 months at ambient and accelerated conditions showing less than 0.2% salicylic acid formation.[22]

Ludiflash® – a co-processed directly compressible excipient composed of mannitol, crospovidone, and polyvinyl acetate has been evaluated in orally dispersive tablets. The flowability of Ludiflash with fine particle APIs could lead to particle segregation. In such cases, the addition of 1%-3% colloidal silica improves the flowability in direct compression.[23]

Kollitab® DC 87 L, a DC-grade excipient composed of 84.5%-88.5% Lactose monohydrate, 8%-10% crospovidone (Kollidon CL-SF), 3%-4% PEG-PVA-copolymer (Kollicoat IR) and 0.8%-1.8% sodium stearyl fumarate, a co-processed excipient prepared by spray-drying.[24] In DC with 25% acetylsalicylic acid, Kollitab gives harder tablet with tensile strength of >2 MPa at compression of 200 MPa or higher, suggesting it can be used for high drug loading without compromising the hardness and dissolution properties of the tablets. It is also true with vardenafil HCl tablets comprised of 2% to 8% drug loading with yielding the hardness of >90 N at compression force of 9 kN for 2% drug and 6 kN for 8% drug.

Kollicoat Protect, a co-processed moisture barrier coating polymer, composed of 60% Kollicoat IR and 40% polyvinyl alcohol, was investigated as directly compressible binder with crystalline drugs. In comparison with its parent polymer Kollicoat IR, the hardness of Kollicoat Protect tablets continuously increased with increasing compression force to 6-fold, whereas for Kollicoat IR tablets hardness unchanged (3-4 kP) as the compression force increased to 22 kN.[25]

Other examples include Emedex®, which is a directly compressible grade excipient co-processed with 95% glucose monohydrate and different oligosaccharides from starch (NF, Dextrates) and on compression with 25%

highly crystalline ascorbic acid, yields harder tablets with 70 N hardness as compared to DC-grade sorbitol, isomalt, and granulated lactose.[26]

While spray granulation or drying of the excipients in a co-processed mixture or drug with and without excipients is widely used for preparation of directly compressible dry binders, Chen et al (2019) used a quasi-emulsion solvent diffusion (QESD) method for crystal engineering of a model drug ferulic acid (FA) aimed at attaining bulk crystal powder to achieve high drug loading in a DC tablet.[4] The tablets derived from QESD with <1% HPMC met the criteria for tablet design but; however, the disintegration time was >30 min, which is longer than the required 15 min or less for an immediate tablet. To further improve the disintegration time to <10 min, and the ejection force to <400 N, 0.75% crospovidone and 0.25% magnesium stearate were added. Upon compression, QESD with 99% FA loading showed an excellent compressibility and met all the criteria for flowability, friability, tabletability, and dissolution. In comparison with MCC PH 102, QESD showed over 6-fold higher flowability.

FUTURE PERSPECTIVES & SUMMARY

As more new molecules continue to be discovered, so is the increase in number of innovative co-processed excipients for development of directly compressible tablets. In the past decade, excipient manufacturers have taken steps to launch new co-processed excipients with the interest to use in continuous manufacturing and also to improve the processing time to reduce footprint and lower the cost. DC of co-processed excipient mixture is normally accepted as the best choice for poorly compressible drugs with sluggish flowability and compactability into tablets. Particle engineering by granulation or solvent diffusion, spherical agglomeration, and crystallo-co-agglomeration is often used for improving flowability of crystalline drugs without impacting the physico-chemical properties in DC tablets with high loading.

As continuous manufacturing (CM) comes at the heels of drug manufacturing to reduce cost and to lower the risk of material hold-ups, the industry is moving toward continuous direct compression (cDC) to improve homogeneity with higher yield and greater flexibility to eliminate the traditional steps like granulation, drying, and sieving before tableting or filling in two-piece hard gel capsules.[27-29] Ascendia with its expertise and cGMP manufacturing capabilities with ISO cleanrooms in injectable and oral liquids and SODFs can lead the way in expediting the formulation development of innovative molecules to the clinic faster. Our enabling technologies, AmorSol®, NanoSol®, EmulSol®, and LipidSol™ are aimed at addressing the challenges with poorly soluble drugs in oral and parenteral formulations. ◆

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OUTSOURCING

The Power of Partnerships Fueling Biopharma Progress With Advanced Tools & Expert Support

By: Lisa V. Sellers, PhD

INTRODUCTION

Whether they were working 20 years ago or are shaping the most innovative therapies and diagnostics entering the clinic today, scientists at every phase of the research and development pipeline continue to need robust and reliable tools to work effectively and efficiently. But while today's biopharma stakeholders face many of the same challenges they have for decades, much has changed about how we work in the space, as well as the range of tools and solutions at our disposal. Advances in research tools and critical components have kept pace with the growing number of novel drug modalities and precision medicines.

As biopharma moves faster and new drug approvals reach an all-time high, relationships with critical component suppliers and expert development and manufacturing partners cannot be an afterthought. By supporting biopharma companies with reliable, cutting-edge tools and services and reshaping the drug development process, these organizations will play a critical role in helping biopharma reach its full potential.

A CHANGING LANDSCAPE

One of the most significant recent shifts in the pharma space is a growing reliance on collaboration and outsourcing to develop increasingly complex therapeutics. Early in my career as a chemist, when small-molecule drugs dominated the landscape, drug development efforts were largely managed internally with minimal external support. Groups within pharma companies were directed at designated topical focuses in discovery and development, with research infrastructure maintained in-house.

As more complex small-molecule drugs and biopharmaceuticals have emerged, pharma organizations are seeing the advantage of working with expert development and manufacturing partners for specialized chemistry and biology needs. Rather than building an internal "linker chemistry group" to support an expanding antibody-drug conjugate (ADC) pipeline, for example, a growing number of organizations are instead turning to partners with specialized chemical and biological expertise and linker design capabilities. In doing so, they can access specialized production infrastructure as well as deep knowledge in linker chemistry, de-risking their development process.

This shift has fundamentally changed the way companies work, especially for biotech organizations developing advanced biopharmaceutical modalities. Development partnerships give companies the flexibility to leverage established expertise and infrastructure and focus their resources elsewhere, a vital advantage for early stage organizations with limited capital. The cell therapy field has highlighted the advantages of collaborative development and manufacturing partnerships for driving progress and maximizing resource efficiency. In this nascent industry, there are a limited number of experienced personnel with the special-

ized skills necessary to support cell therapy development and production, leading to persistent challenges in finding and maintaining talent. Additionally, building the internal infrastructure required to produce cell therapy products for clinical or commercial use is a massive investment for any organization. Simply put, it's not realistic or resource-efficient for every company to build in-house capabilities from the ground up.

COLLABORATION, CAPABILITIES & COST EFFICIENCY

The benefits of collaborative, specialized partnerships are also true for vital research tools and product development capabilities. Working with established external partners can help drug developers gain reliable, cost-efficient access to the most advanced techniques and tools and the expertise to best apply them. When it comes to innovative therapies and diagnostics, outsourcing doesn't have to come at the cost of IP ownership — biotech companies can still develop the IP for a product and outsource the process or "recipe" to an external partnership. By emphasizing collaboration and breaking silos, biopharma players big and small can enhance their research capabilities and accelerate product development, getting groundbreaking therapies to patients faster.

The explosion of scientific innovation that has empowered biopharma's biggest milestones over the past 2 decades has now created a new challenge – an overwhelming number of options. Faced with a seemingly infinite range of new choices for tools, techniques, and suppliers, researchers struggle to navigate these options and ensure they're selecting providers with reliable, validated, and cost-effective solutions. It's a similarly daunting task to shopping on Amazon as a consumer today. With virtually countless options for even a single product at our fingertips, it can be hard to sift through these choices to find what we need and know it's coming from a reputable, trustworthy supplier. While biopharma researchers may not be bombarded with a curated social media feed of potentially dubious products, it's not uncommon to rely on a simple internet search to serve up exactly what you need, when you need it. But for something as important as drug or diagnostic development, working with reliable, high-quality tools from the beginning is vital to long-term success. Partnering with reputable, established critical component suppliers can connect drug developers with the tools and reagents they need at every step, from R&D to the clinic.

UNLOCKING NEW POSSIBILITIES

In addition to expanding the global catalog of tools and reagents, innovation in research methodology has transformed the scope of research and made complex techniques more accessible. Technical advances have empowered a deeper understanding of disease etiology than ever before, helping drug and diagnostic developers to identify novel drug targets and mechanisms. We can now probe biological systems at a previously unattainable resolution with a growing range of advanced research techniques and tools available to scientists at every level. Innovations in spatial biology techniques have helped researchers visualize proteomic and transcriptomic data within the context of tissue, opening doors to promising diagnostic and translational applications across cancer, immunology, and more. Recent research has also fostered an appreciation for the role of previously "niche" topics, such as glycobiology, in health and disease. In turn, advances in chemical biology are enabling researchers and drug developers to apply this deeper biological knowledge to work in a therapeutic context. Due to the increase of available tools and expert supplier support, approaches such as click chemistry are now accessible for biopharma players big and small to use successfully.

Artificial intelligence (AI) and high-throughput technologies are further supplementing these advances, helping biopharma companies to deliver on the

potential of promising biomarkers and mechanisms with faster, more efficient research. Sophisticated robotics systems can now support automation in high-throughput screening and experimentation, enabling more efficient selection of candidate compounds to guide drug development. While it seems like we're just scratching the surface thus far with AI and machine learning (ML) in biotech, some exciting applications have highlighted the power of these technologies. In this space, collaborating with specialized partners can also help biotech and biopharma companies gain access to the most advanced tools without investing internal time or resources to build capabilities.

Companies such as Etcembly and Alloy Therapeutics are uniting deep immunology expertise with powerful AI/ML approaches to engineer better immunotherapies. Etcembly, for example, has built a massive and growing database mapping the human immune repertoire, from which it conducts in silico T-cell receptor (TCR) engineering for novel therapies. Rather than relying on manual screening of lead candidates, companies working with Etcembly can leverage AI-based engineering of novel TCR candidates. These can then be applied in new biologics or used to re-engineer and improve existing biotherapeutics. AI/ML guided techniques like these can help speed the path of novel, groundbreaking drugs to the clinic, potentially cutting development timelines in half.

GOING FARTHER TOGETHER

While AI holds undeniably exciting possibilities for advancing medicine, it won't be completely replacing scientists

anytime soon. We can't lose sight of the value of deep experience, expertise, and collaboration between researchers. AI offers so much, but what it still cannot replace is the wealth of information an experienced scientist holds about their failed experiments and missteps in execution. That still resides in the experience of research and translates to the valuable talent of experts across the field. Lessons about failure are just as valuable as insights on success, and sharing both through collaborative relationships can take biopharma further.

There's work to be done yet, and drug and diagnostic developers can continue to advance and fine-tune innovative tools and techniques, including the use of AI, alongside expert development partners and critical component suppliers. As research tools continue to evolve and expand, partnerships between biopharma and specialized providers will play a fundamental role in accelerating the development of new drugs and diagnostics. There is simply too much for pharma to bear alone, and we can all go farther and faster together. ◆

BIOGRAPHY

Dr. Lisa V. Sellers is the CEO of Vector Laboratories. She is an accomplished leader and mentor in life sciences with more than 20 years of experience in the industry. As a top innovator in immunohistochemistry, immunofluorescence, and glycobiology products used for scientific discovery, she drives the company's expansion and business strategies. She earned her PhD in Chemistry from the University of Colorado Boulder and her BS in Chemistry, ACS Certified from Santa Clara University.

ESG STRATEGY

Sustainable Foundations: Embedding ESG Principles at Every Level

By: Benedicta A. Bakpa, MSc

THE IMPORTANCE OF ENVIRONMENTAL SOCIAL GOVERNANCE (ESG)

Sustainability is not a new topic – neither in Pharma nor more widely. Patients are seeking medicines that are more sustainable, from production to packaging, and regulations are adding pressure to favor therapies with a lower environmental impact in order to reduce overall healthcare footprints. This means that drug developers and CDMOs must consider integrating sustainable initiatives throughout their value chain. However, with "greenwashing" a key concern, claims must be backed by concrete evidence and transparent communications about environmental impact using data. As a result, a robust (ESG) strategy is increasingly important for businesses to align with stakeholder values.

By bringing together the three different aspects of business sustainability, ESG provides a holistic way of looking at a company's operations and impact. It therefore also provides a useful framework to guide corporate strategy and decision-making.

At Bespak, we believe that we have a responsibility to make a positive impact in the world, and this means adopting an approach of continual improvement to minimise negative environmental and social impacts across all aspects of our operations.

SUSTAINABLE FROM THE START

ESG has been woven into Bespak's strategy from the very start. Having been spun out from Recipharm in April 2024 with a mission to take a leading role in the transition to low carbon pressurized Metered Dose Inhalers (pMDIs), sustainability and corporate responsibility are fundamental core values.

Our central focus is on driving a reduction in emissions from pMDIs through the adoption of low Global Warming Potential (GWP) propellants, and this is where we have concentrated the bulk of our resources and investment so far. However, we ultimately recognize that this is just one part of a larger picture and are committed to taking a more extensive approach that goes beyond pMDI propellants. For example, we consider sustainability throughout key areas where we can have an impact: the development and manufacturing process, whether a pMDI or one of our alternative inhalation device platforms. And, thinking even bigger, this brings into focus the footprint of Bespak as a whole, considering our impact from every perspective, from global consequences for the atmosphere to local effects on the ecosystems of our sites and our local communities.

These factors are vital to embed in our ESG strategy, coupled with transparent data-driven actions and relevant metrics to monitor and evaluate progress. As a key step, we are releasing our inaugural Bespak ESG Update. This important assessment of our operations allows us to establish benchmarks, identify priority actions and next steps, maintain accountability, and ultimately drive meaningful change.

CONSIDERING THE FULL SUPPLY CHAIN

Another important aspect to consider in terms of overall sustainability is the many different players in the supply chain. This is something we have factored into our ESG strategy, ensuring that our report extends beyond just our in-house operations, for example, through Life Cycle Assessments (LCAs) that include impact from raw materials through to manufacturing. Our supply chain has therefore been carefully built to leverage local expertise, minimizing transport-associated emissions. We also prioritize working with suppliers that match our values and meet our high operational and ethical standards. This not only helps to maintain standards and a consistent alignment on goals, but also offers the additional benefit of increasing supply chain resilience through onshoring.

ENVIRONMENTAL: CONSIDERING PROPELLANTS, RESOURCE USE, BIODIVERSITY & BEYOND

Considering our impact on the environment is an obvious place to start. As a CDMO specializing in inhaled therapies that treat a range of respiratory conditions, the state of the atmosphere is a highly topical concern. Addressing carbon emissions is a priority for Pharma more widely, for example, with seven big pharma companies announcing their shared commitment to accelerating net-zero healthcare in 2022.[1] But an environmental footprint goes beyond air pollution and climate change, to encompass biodiversity, resource use and more.

Transitioning to Low GWP Propellants

The transition to low GWP propellants is a clear priority for the industry, and our most significant priority at Bespak. In 2024, propellant emissions alone accounted for 86% of our direct operational emissions, highlighting the urgent need for change. We are focused on driving this transition and have expanded our facilities with a new high-speed production line capable of producing pMDIs using Honeywell's Solstice® Air HFO-1234ze(E). Our plans to manufacture at commercial scale using Orbia's Zephex® HFA-152a were accelerated during 2024 with the addition of a GMP pilot-scale facility to supply pMDIs utilizing this low GWP propellant into clinical studies. We will continue to develop our expertise and capabilities to drive the switch to low carbon pMDIs, and reduce the inhalation sector's carbon emissions.

Considering Resource Consumption

Consumption of energy and raw materials, and waste generation – including emissions and discarded materials – must also be considered in a holistic approach to environmental sustainability.

We have implemented several initiatives to support greater energy efficiency, from renewable energy (with solar panels providing 7% of our Holmes Chapel site's total energy), to transitioning to LED lighting and upgrading HVAC filters in our cleanrooms. We also implemented carbon accounting software to help track and monitor our Scope 1, 2, and 3 emissions.

To enhance resource efficiency and reduce waste, we are implementing significant sustainability initiatives across device packaging and component manufacturing. These measures include introducing ISCC-certified materials into moulded parts and transitioning to recycled PET (rPET) for device trays, which has reduced CO_2e emissions by 29.3% compared to virgin PET. We're also working to align with circular economy principles, achieving up to 80% rPET content. Additionally, strategies, such as re-using plastic trays and re-assessing the necessity of desiccant sachets in packaging, are being explored to further minimise material use and environmental impact.

LCAs are a critical tool in identifying carbon- and resource-intensive hotspots in our products and processes, highlighting opportunities for improvement, as well as allowing us to integrate sustainability into new product designs from the onset.

Biodiversity Impacts

A potentially overlooked aspect of sustainability is both direct and indirect impacts of business operations on local biodiversity. We are lucky enough to have our Holmes Chapel headquarters surrounded by green landscape, and as such, preserving local ecosystems is particularly important to us. By conducting on-site biodiversity assessments to understand the direct impact, and looking at our overall supply chain to understand indirect impacts, we can find opportunities to reduce our overall biodiversity footprint and environmental impact.

Having now conducted many of our initial assessments, we have established benchmarks from which to set our environmental targets. For example, we are planning to conduct a climate risk assessment to help identify where the business is most vulnerable in terms of climate change and its impact on our operations, supply chains, assets, and markets.

SOCIAL: WELLBEING ACROSS EVERY STEP IN THE SUPPLY CHAIN

People are vital to any business, and at Bespak, we pride ourselves on the quality of our workforce. Collaboration and respect are among our core values, and this extends from the workers in our supply chain, to patients and our local communities. Beyond this, we are committed to continual upskilling and employee support. Our innovative Injection Moulding Academy, which was awarded the Plastics Industry Awards' Best Training and Development Programme 2024, provides specialist training and professional development for our staff and our partners, as well as supporting apprenticeships for the local community. With social impact largely underreported in the pharmaceutical space, we recognize our responsibility to commit to and effectively communicate our social initiatives.[2]

Contributing to a Sustainable Work Culture

There are many different factors that contribute to a sustainable, ethical work culture. Among these are employee health, safety, and wellbeing approaches to recruitment and development, and a commitment to diversity, equality, and inclusion. We have business policies in place to support all of these factors, but at only a year old, we are still making foundational decisions that define Bespak's culture. We are committed to taking the time to get this right, bringing employees into the conversation to shape the future of the Bespak workforce. It's also important to extend ethical standards and values to workers in our value chain, which is why we have developed a supplier code of conduct and evaluation process.

Excellence Across the Value Chain

When considering the full value chain, this should also include patients and other end-users of our products – ensuring that the products they receive are of the highest quality and have positive impacts on their lives. Quality and efficacy are of course non-negotiable in our industry, but we are committed to maintaining our decades-long track record of safe, reliable products, with continuous improvements to our quality systems ensuring that we raise the bar every day.

Engaging With Local Communities

The final aspect of social impact concerns our local communities. Community engagement such as donation matching, sponsorships and volunteering has been a strong part of our historic workplace culture at Bespak. We are now going a step further to contribute to positive impacts on the local communities surrounding each of our sites. We have conducted local community needs assessments in Holmes Chapel and King's Lynn, and will use these going forward to develop a mission-driven community engagement strategy. We are also planning to expand our partnerships with local education providers, offering even more opportunities for apprenticeships and training particularly in STEM subjects.

GOVERNANCE: BUILDING ESG INTO OUR LEADERSHIP

Achieving sustainability ambitions requires governance structures that prioritise them. Our leadership approach works to balance our ESG strategy with our business needs, to ensure the longevity to succeed sustainably.

Assigning Responsibility

We have established governance frameworks with the senior leadership team involved in maintaining a chain of accountability and keeping our sustainability goals front of mind and central to our operations. Our strategy also includes ESG awareness and training sessions to foster engagement and a feeling of responsibility across our workforce.

SETTING THE STAGE

After our first year as a stand-alone inhalation CDMO, it will be important to continue the momentum toward our sustainability goals. Our aim is for Bespak to be a leader in this area, which means going above and beyond regulatory requirements, customer expectations, and industry norms. Our 2024 ESG Update is a critical milestone, as it lays the groundwork for our commitments. With sustainability already a key focus in the inhalation space, due to the transition to low GWP propellants in pMDIs, we look forward to the initiatives and innovations that will help to enhance the impact of the industry on the world. ◆

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- ESG Update 2024 (report)
- Biodiversity report
- LCAs
- Low carbon terminology blog

BIOGRAPHY

Benedicta A. Bakpa is the Head of ESG at Bespak, bringing 15 years of experience in Environmental Management and Sustainability across multiple sectors. She specializes in Net Zero Carbon initiatives, helping organizations achieve their carbon reduction goals and contributing to a more sustainable future. She has successfully led the implementation of numerous environmental and social value initiatives for companies in Africa, the Middle East, and the UK. She earned her Master of Science in Applied Environmental Economics from the Imperial College London and a certificate in Business and Climate Change from the University of Cambridge. She is a Chartered Environmentalist and a full member of the Institute of Environmental Management and Assessment (IEMA).

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Adare Pharma Solutions

ADARE® PHARMA SOLUTIONS

Fast, Flexible, and Focused: The Secrets of a Successful CDMO Partnership

As timelines shrink and therapies grow more complex, sponsors are relying on outsourcing partners with the experience, flexibility, and oral solid dose expertise to bring effective treatments to market quickly. *Drug Development & Delivery* recently interviewed Steven Facer, Senior Vice President of Sales and Marketing at Adare Pharma Solutions, who shares practical insights on what makes CDMO partnerships work and what can cause them to fall short. From managing supply chain disruptions to maintaining a strong customer-first culture, he offers a candid look at the strategies that help turn operational challenges into shared success.

Q: What should sponsors look for when selecting a CDMO partner, and how can the right choice impact long-term success?

A: Choosing the right CDMO is one of the most important strategic decisions a sponsor can make. A strong CDMO partnership can accelerate development, reduce costs, and de-risk the path to market, but the wrong fit can lead to misalignment, delays, and added complexity. Beyond just assessing capabilities and infrastructure, sponsors should evaluate how well a potential CDMO understands their program goals, communicates across functions, and supports cross-disciplinary teams comprising, for example, regulatory affairs, quality, and project management. It's also important to choose a CDMO that is properly scaled for a sponsor's program and can integrate seamlessly with their team and values.

At Adare, we approach every engagement with the mindset of a long-term partner, not just a service provider. Our integrated solutions span the spectrum of CDMO services, from development through manufacturing and packaging, and

we're especially strong in important areas like novel oral solid dosage forms and patient-centric technologies. We're large enough to offer a full range of capabilities, yet agile enough to give every project the attention it deserves. This reflects our customer-centric culture: we listen, we adapt, and we focus on what success means to the customer.

Q: With global supply chain disruptions an ongoing concern, how can CDMOs help sponsors minimize risk and maintain continuity?

A: Global supply chains have faced extraordinary challenges over the past few years, from a global pandemic to tariffs, inflation, and transportation bottlenecks. Such disruptions subject sponsors to intense pressure, so outsourcing partners must provide more stability, greater flexibility, and faster turnaround. A strong global network with responsive infrastructure is the best way for a CDMO to help sponsors safeguard their supply chains and keep projects on track.

Adare has built a network of development and manufacturing facilities in both the US and Europe, the world's two biggest pharma markets. This gives sponsors the regional access and security they need to keep their projects moving with minimal disruptions. We focus on flexible operations and diversified sourcing to ensure that sponsor projects overcome supply chain challenges and maintain momentum. We're also supporting customers who are reshoring manufacturing to the US or strengthening their European operations. We are committed to helping our customers navigate an unpredictable and ever-shifting landscape.

Q: How can CDMOs best support sponsors navigating the increasingly complex drug commercialization process?

A: Sponsors are under ever-increasing pressure to manage timelines, solve technical challenges, and bring products to market efficiently. That's where the right CDMO can make a real difference. The most effective CDMOs don't just offer specialized capabilities, they are strategic partners evolving to meet sponsor needs every step of the way.

Adare's approach is built around that kind of partnership. We offer fully integrated, end-to-end CDMO services, giving sponsors a consistent provider from early formulation through commercial manufacturing and packaging. We understand the real-world challenges our customers face, from patient adherence to therapeutic performance, and leverage our specialized dosage form technologies to help overcome these hurdles. By maintaining close collaboration and clear communication throughout the process, we can streamline transitions, catch issues early, and help accelerate the path to market.

Q: Oral solid dosage forms continue to dominate the global pharmaceutical market. What accounts for their continued popularity?

A: Oral solids are the go-to format for a reason: they're familiar, they're flexible, and they're efficient. They offer sponsors a cost-effective way to deliver precise, consistent dosing. Patients prefer them because they offer a level of convenience that other delivery methods often can't match: they're simple to take, easy to travel with, and don't require any special devices or handling restrictions. From a manufacturing standpoint, oral solid dose is well understood, scalable, and compatible with a wide range of APIs. It's a proven platform that still offers plenty of room for innovation.

Oral solid dosage forms are the foundation of Adare's expertise. We provide sponsors with deep technical capabilities in tablets and capsules as well as novel formats like multiparticulates, orally disintegrating tablets, and sprinkle formulations. Our teams specialize in innovative oral solid dose technologies that efficiently solve challenges like customized release, taste masking, and flexible dosing.

Q: Tech transfer is a critical phase in commercialization. How can CDMOs ensure a smooth and efficient transfer from development to commercial manufacturing?

A: Tech transfer is where a project moves from theory to practice, and small missteps can lead to costly delays, rework, or even regulatory setbacks. To be successful, a tech transfer depends on early planning, clear communication, thorough documentation, and close collaboration between development and manufacturing teams.

Other CDMOs might see tech transfers as a simple hand-off, but Adare approaches tech transfers as a fully integrated process, one that starts long before manufacturing begins. Our commercial manufacturing teams are involved early in development to ensure that scale-up considerations, process design, and quality requirements are aligned from the outset. Technical leads and project managers are dedicated across the

program lifecycle to keep communication seamless and timelines on track. To stay ahead of potential issues we follow a structured, risk-based approach that includes detailed transfer protocols, comprehensive documentation, and frequent cross-functional reviews.

We also have extensive experience helping sponsors seamlessly move existing products into our network. With more than 65 products successfully manufactured across our network, we know how to manage the complexities of commercial-stage transfers while maintaining continuity, compliance, and product quality.

Q: How can CDMOs evolve their capabilities to support the growing complexity of today's drug development landscape?

A: As drug development becomes more complex, it's no longer enough for CDMOs to offer a narrow set of services or operate in silos. Today's sponsors are looking for integrated solutions, flexible capacity, and teams that can pivot quickly as programs evolve. They want to work with partners who embrace new technologies, anticipate potential roadblocks, and offer practical strategies to move their programs forward.

As our customers' needs evolve, we're making sure our capabilities keep pace by investing in tools and technologies representing the future of drug development. A great example is our partnership with Laxxon Medical, which provides 3D screen printing capabilities enabling a new generation of personalized and precision therapies.

We provide pharmaceutical companies of all sizes with the capabilities and technical expertise needed to move quickly and confidently even as the drug development and manufacturing world grows more complex.

Q: What specific advantages does 3D screen printing offer for sponsors looking to develop more complex or targeted therapies?

A: I believe that 3D screen printing represents a transformative opportunity for drug development by enabling complex drug delivery systems that simply can't be achieved via traditional methods.

The 3D screen printing process avoids the scalability and formulation challenges of laser- and nozzle-based 3D printing methods, which have long struggled with high costs, API degradation, and limited production volumes. In contrast, 3D screen printing is a scalable, additive manufacturing process that facilitates precise, layer-by-layer construction of drug formulations.

This allows integration of immediate, extended, delayed, and sequential release mechanisms within a single tablet. We can also use the technology to easily incorporate multiple APIs with distinct pharmacokinetic profiles into one dosage form, offering unprecedented therapeutic flexibility. Importantly, 3D screen printing is designed for scalability: the same process can move seamlessly from lab prototyping to full-scale commercial production without major changes.

As personalized medicine and patient-centric therapies become the norm, we're going to see 3D screen printing play a major role in helping sponsors bring smarter, more targeted products to market.

Q: As global operations become the norm for CDMOs, how can companies keep quality systems aligned and avoid gaps between sites?

A: Maintaining consistent quality across facilities around the world is a major challenge for CDMO networks. Sponsors expect the same level of quality and compliance across geographies.

We've worked hard to build a global quality model at Adare that enables consistency and trust across our sites. We operate under a harmonized approach, incorporating quality-by-design principles into all projects and maintaining consistent practices at all our facilities. Our teams undergo rigorous, continuous training across regions to align and maintain best practices. We manage our global sites as part of an integrated network, not as isolated operations, and we ensure compliance across markets via regular audits, standardized documentation, and extensive communication between sites. We undergo regular inspections by agencies like the FDA, DEA, and AIFA, giving our customers confidence that their products will meet their rigorous quality expectations.

Q: You mentioned a customer-centric culture earlier. Why is that so important in today's CDMO landscape?

A: Bringing a drug product to market is a complex, expensive, and time-consuming process. Sponsors need outsourcing partners who listen, adapt quickly, and deliver tailored solutions. A truly customer-centric culture fosters open communication, faster problem-solving, and streamlined processes.

Every sponsor's needs are different, so at Adare we tailor our approach accordingly. New customers benefit from a personalized onboarding process designed to ensure a smooth transition and immediate connection with our teams. Every customer is paired with a dedicated project manager who provides consistent support throughout the commercialization journey. That continuity facilitates long-term relationships and personalized support that evolves with the project.

Adare's cross-functional teams — spanning commercial, development, manufacturing, quality, and regulatory — stay aligned throughout each program, and we offer extensive support services to help customers navigate challenges that arise along the way. We take a proactive approach to problem solving, flagging potential issues before they become real obstacles. Most importantly, we communicate continuously to keep customers informed, engaged, and confident. A customer-centric partnership is built around one simple idea: when our customers succeed, we succeed. ◆

PROTEIN BARCODING

Streamlining mRNA Therapeutic & Vaccine Development

By: Meredith Carpenter, PhD

INTRODUCTION

Nucleic acid-based vaccines and therapeutics, including mRNA-based platforms, represent a groundbreaking advance in healthcare. A critical determinant of therapeutic efficacy of these treatments is the delivery system, which ensures precise targeting to the intended tissues while also minimizing degradation and off-target effects.

Lipid nanoparticles (LNPs) have emerged as a powerful tool for delivery due to their low immunogenicity compared to viral vectors, along with their ability to encapsulate and protect nucleic acids and facilitate their entry into cells. LNPs are used in the COVID-19 mRNA vaccines, for siRNA delivery, and in numerous clinical trials with a range of payloads. However, the majority of these applications are in liver-focused disease areas simply because that is where LNPs accumulate in the body when administered systemically.[1]

TARGETING LNP DELIVERY

Even subtle changes in LNP lipid composition, ratios, particle size, or surface modifications can significantly alter how the LNP behaves in vivo and thus affect biodistribution, immunogenicity, and expression kinetics. As mRNA therapies move beyond the liver and into applications targeting other tissues, customized LNP formulations are essential for precise and effective delivery.

Directing mRNA to different tissues thus requires high-throughput screening of a vast number of mRNA-LNP formulations. In general, the LNP screening process involves formulating a library of different LNP compositions and administering them, often one at a time, in animal models. Tissues are collected and mRNA expression is measured, typically through protein output or reporter assays (Figure 1). This approach is labor-intensive, low-throughput, and expensive, as each formulation must be evaluated in separate animals or animal groups.

FIGURE 1

Optimizing mRNA delivery and protein expression is a common bottleneck in mRNA-LNP therapeutic development.

The specific steps in the workflow for creating and screening mRNA-LNPs vary depending on the specific assay requirements, but generally include the following:

Select, synthesize, and characterize the mRNA payload: Confirm the mRNA sequence after synthesis, determine purity, and characterize/optimize the 5′ cap and 3′ poly(A) tail.

Select and formulate lipid components: To achieve maximum efficacy, each LNP formulation must be optimized for specific biophysical characteristics such as shape, size, payload density, and surface charge.

Select the screening method: Select in vitro (2D or 3D cell culture) or *in vivo* (animal models) methods.

Select the screening readout: Fluorescence or next-generation sequencing, depending on the reporter used in the mRNA construct.

Encapsulate the mRNA into the LNP: The purified mRNA is combined with the lipid nanoparticle solution, allowing the mRNA to be encapsulated within the LNP's hydrophobic core.

Quality control and characterize the final product: Perform analytical tests to assess the size, stability, encapsulation efficiency, and purity of the mRNA-LNP formulation.

Perform the screen: Based on the method and readout selected.

Draw conclusions: Identify the top candidates from the screen and feed the results back into mRNA and lipid formulations for further studies and optimization.

While different tools are available to support nanoparticle design, formulation, and quality control (steps 1-6), the screening step (step 7), still faces limitations with current methods, which include next-generation sequencing (NGS), mass spectrometry, flow cytometry, ELISA, and Western blotting.[2-7] For example, using NGS for screening is efficient because it allows for the analysis of multiple mRNAs in a single animal. However, a significant limitation of this approach is that it measures delivery – ie, the presence of mRNA – rather than translation of the mRNA into the desired protein.[5,6]

This can lead to inaccurate results and erroneous candidate selection.

In contrast, screening that uses a protein-level readout, such as mass spectrometry (MS) or flow cytometry, provides evidence that the mRNA was both delivered and translated effectively.[7-8]

Limited tools are available for multiplexing at the protein level, which increases costs and reduces efficiency; in the case of flow cytometry, this also results in low sensitivity. Therefore, new tools that facilitate multiplex pooled screening with a direct protein-level readout could substantially improve mRNA-LNP screening and accelerate the development of new nucleic-acid-based therapeutic and vaccine candidates.

Newer techniques, such as protein barcoding, are now being employed to accelerate and scale up this process. This multiplexed approach enables the simultaneous evaluation of mRNA-LNP formulations in a single experiment, significantly accelerating the identification of lead candidates with optimal biodistribution and transfection profiles, at a reduced cost.

TABLE 1

***In Vivo* Studies in Mouse**

Traditional workflow		
Candidate 1	Mouse 1	$500
Candidate 2	Mouse 2	$500
Candidate 3	Mouse 3	$500
Candidate 4	Mouse 4	$500
Candidate 5	Mouse 5	$500
Candidate 6	Mouse 6	$500
Candidate 7	Mouse 7	$500
Candidate 8	Mouse 8	$500
	Current reagents	$1,000
	Animal cost	$4,000
	FTE cost	$1,500
Total		**$6,575***

Platinum Pro workflow		
Candidate 1-8	Mouse 1	$500
	Quantum-Si kit(s) cost per sample	$875
	FTE cost (est)	$500
Total		**$1,875***

Next-Gen Protein Sequencing™ reduces cost by 71% and the number of animals required by a factor of 8

***In Vivo* Studies in NHP**

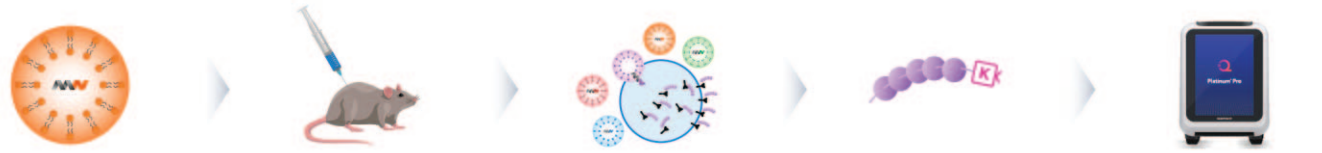
Traditional workflow		
Candidate 1	Monkey 1	$25,000
Candidate 2	Monkey 2	$25,000
Candidate 3	Monkey 3	$25,000
Candidate 4	Monkey 4	$25,000
Candidate 5	Monkey 5	$25,000
Candidate 6	Monkey 6	$25,000
Candidate 7	Monkey 7	$25,000
Candidate 8	Monkey 8	$25,000
	Current reagents	$1,000
	Animal cost	$200,000
	FTE cost	$3,000
Total		**$204,000***

Platinum Pro workflow		
Candidate 1-8	Monkey 1	$25,000
	Quantum-Si kit(s) cost per sample	$875
	FTE cost (est)	$3,000
Total		**$28,875***

Next-Gen Protein Sequencing reduces cost by 86% and the number of animals required by a factor of 8

Multiplexing with barcodes enables more mRNA/LNP candidates to be screened per animal, significantly increasing efficiency and reducing development costs.

FIGURE 2



Cost-effective mRNA-LNP formulation screening using peptide barcodes.

THE BASICS OF PROTEIN BARCODING

Protein barcodes are information-rich short stretches of amino acids that can be genetically added to the coding sequences of proteins. Proteins expressing unique barcodes can be co-expressed together, and desired proteins can be selected for protein engineering, mRNA translation, therapeutic delivery mechanisms, and many other protein-screening applications. Upon protein selection, distinct barcodes associated with each expressed protein can be directly identified and quantified with single-molecule resolution via next-gen protein sequencing (NGPS). This approach has the potential to transform drug discovery and development, similar to how DNA barcodes have advanced the field of genomics. Importantly, NGPS offers significant advantages over the use of MS for decoding protein barcodes. These advantages include a simple, user-friendly workflow on a benchtop instrument that distinguishes peptides based on recognition of specific amino acids rather than mass/charge ratio. Thus, protein barcodes for NGPS readout can be engineered to have highly similar physical properties while remaining distinguishable by their amino acid sequences.

By appending the coding sequences for protein barcodes to each mRNA coding sequence, expressed proteins will have unique tags, despite the proteins themselves having the same amino acid sequence. Sequencing the barcodes on the Platinum Pro® NGPS platform allows rapid identification of which mRNA had the highest expression, resulting in the most abundant protein. These sequencing results can also be used to determine the effectiveness of different lipid nanoparticle delivery systems.

ADVANTAGES FOR *IN VIVO* MRNA-LNP

While *in vitro assays are essential for* early screening, they can't capture the full biological complexity of how mRNA-LNPs behave in the body. Once administered *in vivo*, LNPs interact with endogenous proteins that can coat the particle and significantly influence biodistribution, an effect that is both unpredictable and impossible to replicate *in vitro*. *In vivo* studies are therefore critical to truly understand delivery efficiency and tissue targeting. Protein barcoding offers a powerful solution by enabling multiplex-pooled screens with a direct protein-level readout, increasing the scale of screening while significantly reducing costs and the number of animals required for the all-important *in vivo* studies (Figure 2).

SIGNIFICANT REDUCTION IN *IN VIVO* MRNA-LNP SCREENING COSTS

As summarized in Table 1, a simulated study using multiplexing study with barcodes offers the potential to significantly improve the process economics of mRNA-LNP screening in animal models. By allowing multiple candidates to be tested simultaneously in a single animal, this approach maximizes data output per study and minimizes the number of animals needed. The result is a more efficient screening process that reduces both time and development costs, accelerating the path to identifying optimal delivery vehicles, and aligns with recent FDA plans to reduce animal testing in drug development.[9]

In vivo studies in mice using barcodes and NGPS can reduce costs by 71% and the number of animals required by a factor of eight. In studies with non-human primates (NHPs), the number of animals required can also be reduced eightfold, with an 86% reduction in costs.

PROTEIN BARCODES HELP UNLOCK THE FUTURE OF NUCLEIC ACID THERAPEUTICS

As mRNA and other nucleic-acid-based therapeutics and vaccines expand beyond liver-targeted applications, the need for precise, tissue-specific delivery becomes increasingly urgent. Protein barcoding offers a transformative leap forward in this effort, one that not only addresses the limitations of current screening technologies but also redefines the scale and efficiency of *in vivo* testing. By enabling multiplexed, protein-level readouts within a single animal, this approach dramatically reduces both time and cost while improving the quality of data generated.

More than just a technical advancement, protein barcoding is a catalyst for unlocking the full therapeutic potential of nucleic acid-based medicines. It empowers researchers to rapidly identify the most promising delivery systems, paving the way for safer, more effective treatments that reach beyond the liver and into a broader range of diseases and tissues. In short, protein barcoding doesn't just streamline the development pipeline — it also opens new doors for innovation in genetic medicine. ◆

**Cost estimates provided are for informational purposes only and are based on general assumptions regarding experimental design, throughput, and resource utilization. Actual savings will vary depending on multiple factors, including but not limited to: the specific workflow and protocols used, the scale and frequency of experiments, reagent and consumable costs, labor costs, institutional pricing and discount structures, equipment depreciation, and regulatory or compliance requirements. Quantum-Si makes no guarantees regarding specific cost reductions or financial outcomes. Customers should perform their own cost analysis based on their unique operational parameters.*

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BIOGRAPHY

Dr. Meredith Carpenter is Head of Scientific Affairs at Quantum-Si, where she manages external collaborations and publication strategy. Dr. Carpenter has over 10 years of experience in developing and deploying novel genomics and multi-omics tools in the biotech industry. Prior to Quantum-Si, she held roles as Director of Assay Development at Arc Bio and Senior Director of Strategic Alliances at Cantata Bio. She earned a BS in Biology from Emory University and a PhD in Molecular and Cell Biology from UC Berkeley, and she performed post-doctoral research in the Department of Genetics at Stanford University.

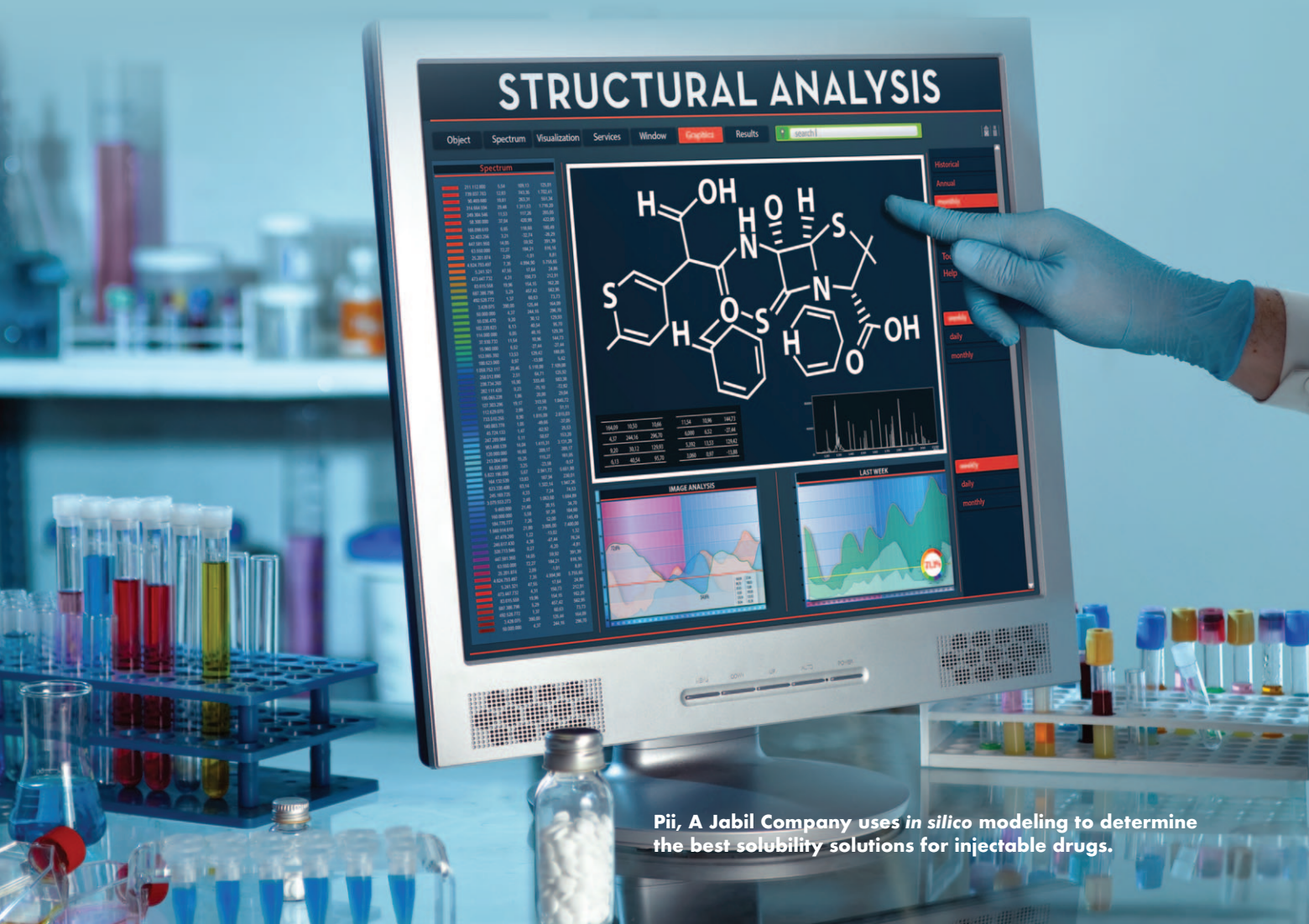
Special Feature

Outsourcing Formulation Development & Manufacturing: CDMOs Are Making Their Supply Chains More Resilient and Secure

By: Cindy H. Dubin, Contributor

Growing R&D activities, personalized medicines, large-scale production of biologics, and access to new technologies are some of the biggest reasons why the contract development and manufacturing organization (CDMO) market is expected to practically double from $168 billion this year to $318 billion by 2034.[1]

"Contract development services are in high demand as pharmaceutical companies face challenges in bringing products from development to market quickly and efficiently," says David Crawford, Associate Director – Manufacturing, Almac Pharma Services. "Companies are increasingly seeking development-driven CDMOs that offer fully integrated services, ensuring a seamless transition from pharmaceutical development to industrial-scale manufacturing. This approach accelerates time-to-market, mitigates risks, and optimizes resources."



Pii, A Jabil Company uses *in silico* modeling to determine the best solubility solutions for injectable drugs.

Mitigating risk and optimizing resources are also presenting challenges for CDMOs, particularly in the current geopolitical environment: the uncertainty of potential tariffs placed on incoming materials; waiting to see if The Pills Act passes; and the passage of The BioSecure Act – the latter two borne out of the pandemic. The PILLS Act (aka Producing Incentives for Long-term Production of Lifesaving Supply of Medicines) was introduced in February by Representative Claudia Tenney (NY-24) to promote the domestic production of generic medicines through tax incentives and reducing reliance on India and China for these drugs. Similarly, The BioSecure Act prohibits executive agencies (i.e., FDA, CDC, and NIH) from contracting or extending loans or grants to any company with current or future commercial arrangements with a "biotechnology company of concern," such as those located in China.

As a CDMO founded in response to global supply challenges during the COVID-19 pandemic, Resilience has a deep interest in the evolving landscape of trade policies and tariff regulations. "We recognize the uncertainty these changes can create for our partners," says Cyril Kelly, Senior Manager, Procurement-Distribution, Logistics, Warehouse and Transportation. "We've begun taking steps to help mitigate concerns. Through continuous, ongoing monitoring, our supply chain team is closely tracking tariff developments and assessing the impact on suppliers and products based on country of origin while also considering how to minimize disruptions to overall supply chain. We're leveraging supply chain engineering to reduce risk exposure and deliver targeted support that helps our partners interpret Harmonized Tariff Schedule classifications, assess general tariff exposure, and maintain compliance with international trade laws. We can facilitate conversations with trusted partners who specialize in cross-border transaction assessments to help further navigate these changes with confidence and help alleviate risk."

In fact, many life science leaders view the current geopolitical conditions as an opportunity. "Contract manufacturing appears to be more in demand, perhaps due to the global geopolitical conditions creating uncertainty in the marketplace," says Janice Cacace, Executive Director Pharmaceutical Development, Bend Bioscience. "With the push toward US manufacturing, and uncertainty in the feasibility of some offshore supply, plus tariff negotiations, we have seen an increase in requests for tech transfer projects for clinical and commercial manufacturing to customers who are looking to de-risk their overseas supply chain. We can no longer rely on the 'just-in-time' operations of previous years, and the tariff situation has become a key risk factor. So, we are shoring up the supply chain and sourcing alternate suppliers as risk dictates. We are derisking by sourcing materials earlier in the development phase through to commercial manufacturing to ensure robust and continuous supply. This has resulted in the discovery that several basic OSD ingredients have different behaviors in formulations, despite being similar in description. Upfront understanding of these differences will save time and decrease risk in any future development program."

In addition to sourcing earlier, CDMOs are strengthening their supply chains in other ways as well. "To navigate these geopolitical uncertainties, we are enhancing our supply chain resilience by diversifying our supplier base and investing in domestic manufacturing capabilities," says Dr. Richard Johnson, Chief Scientific Officer & Founder at Upperton Pharma Solutions. "These measures aim to mitigate risks, ensuring uninterrupted service to our clients."

Likewise, Aragen has proactively implemented a dual-sourcing strategy to improve supply chain resilience for critical active/inactive materials, functional and specialized excipients, consumables and packaging components, particularly those sourced from geopolitically sensitive regions. "We are also expanding our qualified vendor base across multiple geographies, to ensure business continuity and regulatory compliance," says Vaibhav Sihorkar, Vice President & Head – Formulations Solutions, Aragen Life Sciences Ltd. "These efforts are closely aligned with our supply chain digitization and quality risk management practices, allowing us to maintain reliable clinical and development supply timelines for our global clients."

While pharmaceuticals were initially exempt, the possibility of significant tariffs on pharmaceutical imports could have profound implications for the global pharmaceutical industry and CDMOs with operations largely outside the US. By concentrating on cost management, cultivating strategic partnerships, prioritizing robust compliance, proactively managing risk, and embracing holistic supply chain transformation, CDMOs are proactively turning tariff-related complexities into competitive advantages.

At Abzena, for example, the company is reshaping its supply chain

strategy to thrive in a complex global market. "In the current geopolitical landscape, and among recent discussions about tariffs on pharmaceutical products and the BioSecure Act, our fully integrated, US-based manufacturing model offers a strategic advantage, often delivering a 25% price edge over many international competitors," says Dr. Campbell Bunce, Chief Scientific Officer of Abzena. "By leveraging domestic partners for sterile filling, lyophilization, and packaging, we effectively manage the entire supply chain from monoclonal antibody (mAb) production to final drug product within the United States. This approach helps us minimize the unknown risks posed by global trade shifts for our customers."

More insight from these and other life science leaders follows in this exclusive *Drug Development & Delivery* annual report.

Fully integrated formulation and manufacturing support for mAbs, ADCs, AOCs, RDCs, and bi/multi-specifies in the US (Abzena).

Abzena: Fully Integrated Approach Takes Best Molecules to Development

Abzena's flexible and customizable approach across a broad range of formulation and manufacturing services for biologics and bioconjugates enables the CDMO to support a product throughout its entire lifecycle – from initial pre-formulation studies and generation of a formulation to support toxicology, first-in-human (FIH) clinical trials through to clinical in-use studies, formulation optimization, robustness, device interaction studies all the way through commercial scale manufacturing. This enables customers to utilize a single organization for all their formulation, analytical and manufacturing requirements, which streamlines and de-risks the process and allows any experience and learnings to be shared across teams. This first-hand knowledge of the product can then be applied to rapidly solve any complex problems that may arise downstream.

"By offering a fully integrated, 'discovery through manufacturing' approach, and extensive expertise across antibody engineering, analytics, bioassay, bioconjugation, cell line development and scale up, we are able to design, optimize and select the best molecules to take into development, increasing their likelihood of clinical success," says Dr. Campbell Bunce, Chief Scientific Officer of Abzena.

With regard to client success, a customer came to Abzena with a monoclonal antibody (mAb) formulation that had performed well in Phase I clinical trials, but the client wanted to transition from intravenous (IV) to subcutaneous (SC) administration for subsequent clinical studies and commercialization. The target concentration was 150mg/mL, which, while being stable, significantly exceeded the viscosity limit for SC injection devices (20cP). At this concentration, the formulation exhibited a viscosity of 34cP, making it unsuitable for use with standard SC delivery devices, he explains.

To address this, Abzena's formulation team undertook a screening process to identify viscosity-reducing excipients. Several buffers were tested to determine their impact on viscosity without compromising stability. This process revealed an excipient that reduced viscosity to within the acceptable range for SC injection while maintaining the biologic's stability. Stress testing confirmed that the selected excipient did not introduce instability.

"In fact, it marginally improved the protein's resistance to aggregation under accelerated conditions," says Dr. Bunce. "The reformulated product successfully met all requirements for SC delivery and progressed to clinical studies."

He does attribute Abzena's client successes in part to the company's leveraging of artificial intelligence (AI) and machine learning (ML) to create a model that can predict formulation stability over long-term storage using early-stage data. "This model is particularly beneficial in projects with tight timelines driven by customer needs," he says. "Through the generation of high volumes of qualitative data across multiple analytical parameters, we are ex-

panding the potential of AI and ML towards optimizing manufacturing processes, which can dramatically reduce development timelines and costs in ways that were previously unimaginable. By understanding and integrating such advanced tools, there is potential to analyze complex biological systems more precisely, leading to faster and more effective outcomes. At Abzena, we actively seek out and incorporate these new technologies into our processes so that we can offer our customers more efficient development pathways, ultimately helping to bring their products to patients more quickly and at a lower cost."

Adare offers global and regional CDMO capabilities across the US and Europe, from the earliest stages of development through to commercial manufacturing and packaging.

Adare Pharma Solutions: 3D Screen Printing for Personalized & Precision Therapies

Adare Pharma Solutions offers fully integrated CDMO services, from early-stage development through to commercial manufacturing and packaging. The company specializes in innovative oral solid dosage forms – including multiparticulates, orally disintegrating tablets, sprinkle formulations, and other patient-centric technologies – that help sponsors overcome hurdles in adherence and therapeutic performance.

"We're large enough to offer a full range of global capabilities, yet agile enough to give every project the attention it deserves," says Steven Facer, Senior Vice President of Sales and Marketing, Adare Pharma Solutions. "We integrate seamlessly with our customers' teams and values, bringing a customer-first mindset to every engagement. We don't see ourselves as service providers, we see ourselves as long-term partners invested in shared success."

He says that Adare is seeing growing interest is in fully integrated partnerships that span the entire lifespan of a project's journey. As sponsors face increased pressure to manage timelines, reduce risk, and bring complex therapies to market efficiently, they want to work with strategic CDMO partners that can deliver end-to-end support and maintain continuity throughout the program lifecycle.

Adare Pharma Solutions has embraced technology in drug development. A notable example is its partnership with Laxxon Medical to provide customers with advanced 3D screen printing capabilities. "This additive manufacturing technology allows for the precise, layer-by-layer construction of drug formulations with integrated immediate, extended, delayed, and sequential release, all in a single tablet," says Mr. Facer. "It also allows for the incorporation of multiple APIs with distinct pharmacokinetics. Unlike traditional laser or nozzle-based methods, the 3D screen printing process is scalable from lab to commercial production. This offers sponsors a transformative solution for personalized and precision therapies, helping them achieve smarter, more targeted drug delivery without compromising cost or volume."

Adare is also taking proactive steps to structure its operations to help customers navigate global challenges, including the impact of tariffs. Mr. Facer says the CDMO maintains a strong network of development and manufacturing facilities in both the US and Europe to provide flexibility and access while minimizing disruption from tariffs or other trade-related pressures.

"We've also invested in diversified sourcing strategies and flexible operations, and we're actively supporting customers who are reshoring manufacturing to the US or strengthening their presence in Europe," he adds. "Our goal is to help sponsors safeguard supply chains, ensure continuity, and deliver results in an unpredictable landscape."

Almac Pharma Services: Tailor-Made Solutions for Complex Formulations

Almac's formulation development and manufacturing services offer comprehensive support from early-stage clinical development to commercial manufacturing and packaging. Services include formulation development, specializing in developing solid and liquid oral dose formulations, ensuring that drug products meet patient

High-potent, large-scale commercial manufacturing at Almac Pharma Services.

needs. Process Development and Scale-Up provides pre-formulation studies, process development, scale-up, validation, product launch, and ongoing commercial supply. Manufacturing Operations address various dosage forms, including tablets, capsules, stick packs, and sachets.

"What makes us unique is our commitment to quality, our ability to solve complex challenges through a wide range of expertise and experience, and our ability to offer tailor-made solutions for every single client," says David Crawford, Associate Director – Manufacturing, Almac Pharma Services. "By leveraging our single-source platform, clients benefit from reduced timelines and simplified project management, making us a reliable partner in the industry."

Mr. Crawford says that both contract manufacturing and contract development services are in high demand, particularly due to the increasing complexity and variety of drug modalities that require specialized manufacturing capabilities. There is also demand for the development and manufacture of high potent and pediatric medications as well as for personalized medicines.

Almac Pharma Services successfully resolved the development issue for a client who faced challenges with its formulation and GMP manufacturing process. The client wished to develop a low dose, uniform formulation across multiple dosage strengths. The formulation needed to remain stable across the product lifecycle. Almac Pharma Services recommended a detailed development plan, including:

- Powder characterization of both non-GMP and GMP batches;
- Development of lab-scale prototypes with extensive tablet testing (weight, hardness, friability, disintegration, dissolution, and content uniformity);
- Accelerated stability programs to 'stress test' formulations;
- Statistical design of experiments to explore critical process parameters and critical material attributes;
- Engineering batches using GMP equipment to confirm the manufacturing process;
- Comprehensive in-process testing and stability packaging;
- GMP Clinical and Registration batches with associated stability studies;
- Scale up, prototype batches;
- Process Performance Qualification (PPQ) batches, with enhanced sampling and testing regimes to gain better product understanding; and
- A robust Continuous Process Verification (CPV) program to monitor product variables and shifts to aid product knowledge and to enable proactive interventions, if required.

"As a result, we developed a robust manufacturing process and formulation leading to a successful clinical study and product approval," says Mr. Crawford.

Aragen Life Sciences Ltd.: Accelerating the CMC Path with Clinical DP & DS Delivery

Aragen operates as a fully integrated CRDMO, offering end-to-end solutions that take new chemical entities (NCEs) from discovery, through clinical candidate nomination, to CMC, through the phase-appropriate drug substance/drug product development and manufacturing. The company aligns drug substance (DS) and drug product (DP) development under one roof, ensuring that formulation strategies are both scientifically grounded and operationally seamless across the molecule's lifecycle, says Vaibhav Sihorkar, Vice President & Head - Formulations Solutions, Aragen Life Sciences Ltd.

"Within this ecosystem, formulation sciences play a pivotal role, serving as the bridge between exploratory research and clinical execution, and eventually translating discovery into clinic through integrated formulation excellence," he says. "Our for-

mulation CRDMO capabilities begin with pre-formulation support during the discovery phase, offering salt and polymorph screening, solid-state and particle engineering, bio-relevant solubility profiling, excipient compatibility, and pharmaceutical developability assessments. These are tailored to determine whether a molecule is CMC-enabling or CMC-challenging."

Mr. Sihorkar says that this is a critical distinction that shapes the path to the clinic. Formulations designed for preclinical studies must not only achieve target exposures in rodent and non-rodent models, but also withstand the rigor of scale-up, stability, and manufacturability.

"Our deep technical strength lies in solving formulation challenges for a wide spectrum of difficult-to-develop molecules, including poorly soluble 'brick dust' compounds, chemically or physically unstable actives, and high-dose drugs with poor flow or compressibility profiles," he says. Technologies such as spray drying, hot-melt extrusion, nanosizing, lipid-based systems, multi-particulates, and long-acting injectables are applied based on a compound's bio/pharmaceutical needs and physicochemical properties. For instance, in amorphous solid dispersion development, Aragen assesses drug-polymer miscibility using advanced thermal analysis, computational prediction of interaction energies, and solid-state NMR, ensuring molecular-level dispersion and long-term physical stability. Design of Experiments (DoE) is applied to optimize process parameters and control particle size, morphology, and residual solvents – each influencing downstream scalability and bioavailability.

Mr. Sihorkar says Aragen clients are increasingly seeking early, scientifically informed formulation strategies to support IND-enabling studies and de-risk clinical entry. The CRDMO supports this with scientifically sound clinical DP strategy deployment, developing validated analytical methods, clinical batch manufacturing, and packaging for FIH through Phase 2 trials. "Our solutions range from drug-in-capsule (DiC) and drug-in-bottle (DiB) approaches to simple (tablets, capsules) and complex (micronization- and SDD technology-based) oral solid dosage forms, injectables, and modified-release systems," he explains. "This integrated approach allows us to go beyond formulation support and truly accelerate the CMC path with clinical DP and DS delivery."

A recent case illustrates Aragen's problem-solving capability. An NCE with low aqueous solubility failed to meet systemic exposure targets even after prior micro-sizing, nanosizing and SDD attempts by other vendors. The Aragen team reassessed the molecule's developability through comprehensive physicochemical and solid-state profiling, based on principles of molecular pharmaceutics. "We designed tailored polymer selection that provide Tg and/or viscoelastic advantages to optimize and maintain both solubility advantage and extended stability from crystallisation, reformulated it using a refined spray drying strategy," he explains.

The reformulated compound achieved over 3-fold improvement in preclinical exposure, allowing the client to progress through regulatory toxicology and initiate clinical material manufacturing at Aragen's site, all executed under one integrated program. "We also integrated newer and upcoming technologies like Atomic Layer Deposition (ALD), nanostructured lipids and second-generation LAI technologies that offer precise and improved solubility, stability, and release control," he says.

Ardena: Translating Complexity Into Clinical Reality

Ardena is a fully integrated CDMO and Bioanalytical CRO with a core focus on precision medicine and the development of innovative, complex therapeutics. Formulation development and manufacturing services span small-molecule APIs, high-potency APIs (HPAPIs), controlled substances, and advanced drug products, including nanomedicines. Seamless integration of services across the development lifecycle allows Ardena to mitigate risks, ensure smooth project execution, and accelerate time-to-clinic. A dossier-centric approach ensures regulatory considerations are embedded from the outset, aligning scientific development with compliance expectations.

"Today's innovators are seeking flexible, science-led partners who can support fast-moving programs with the right expertise at the right time," says Ariane De Ganck, Chief Commercial Officer at Ardena. "Our integrated model was designed with exactly that in mind: helping our customers translate complexity into clinical reality."

In recent years, the company has observed a growing need for agile and phase-appropriate development. "Early-phase programs often require rapid iteration and adaptability, which our integrated platform is well-equipped to provide," she says.

A testament to Ardena's problem-solving capabilities is its collaboration with Race Oncology in manufacturing the first cGMP batch of bisantrene formulation, RC220. Faced with the challenge of meeting stringent quality standards for intravenous human clinical trials, Ardena provided comprehensive support, ensuring compliance with regulatory requirements from the EMA, FDA, and TGA. "Our inte-

Spray drying process at Ardena.

grated approach facilitated the successful production of the drug product, demonstrating our commitment to excellence in pharmaceutical development," says Ms. De Ganck.

Technological advancements play a pivotal role in enhancing Ardena's formulation development and manufacturing processes. The CDMO is actively incorporating digitization, machine learning, and process automation to support data-driven decision making and enable more agile and dynamic workflows. "Alongside our $23 million investment in a state-of-the-art nanomedicine facility in Oss, the Netherlands, which features GMP-compliant cleanrooms, advanced process development laboratories and integrated analytical capabilities, we are also expanding our bioanalytical services footprint in both Europe and the US," explains Ms. De Ganck. "In bioanalysis, we are deploying machine learning tools to streamline data interpretation and enhance the robustness of complex assay workflows."

In addition to expanding investments in facilities and equipment, Ardena is expanding its ability to address potential impacts from tariffs and regulatory changes such as the BioSecure Act. "We are proactively strengthening our supply chain resilience.," she explains. "Our strategic expansion into North America, marked by the acquisition of Catalent's Somerset, New Jersey facility, enhances our ability to manage material supply and regulatory compliance across regions. This facility, a Center of Excellence for advanced oral dosage forms, complements our European operations and reinforces our global manufacturing capabilities."

Ascendia: Map Out Challenges Early to Optimize Formulations

Ascendia offers enabling formulation platforms for addressing the challenges associated with poorly soluble or bioavailable drugs across all modalities. As more and more new molecules being discovered are poorly soluble and less bioavailable, Ascendia's core technologies can help expedite the development by reducing time and saving cost.

"Our seamless approach offers a unique value proposition for all clients working with high melting and/or higher logP molecules," says Shaukat Ali, PhD, Senior Director, Scientific Affairs & Technical Marketing, Ascendia. "For example, in cases where the molecules behave like brick dust or hydrophobic, AmorSol® requiring the appropriate polymers and solubilizers can be used to further expedite from proof of concept to optimized formulations with the desired solubility and bioavailability. In other cases, if the molecules are lipophilic, EmulSol® or NanoSol® might be better options for bringing those molecules to clinic."

Ascendia's four enabling solubilization technologies offer a 180-degrees holistic approach to resolve the challenges with NCEs. "Tailored formulations for an API coupled with timely delivery are key attractions to our clients," he says. "Building

trust starting with "promises made and promises kept" to meet the deadlines for developing formulations with FDA approved excipients, invaluably expedite the *in vivo* testing for pharmacokinetics (PK) data in animals, which are essentials for IND filing to initiate the human clinical trials. Thus, it is essential to map out the earlier challenges to understand the efficacy of an API in the formulations and to optimize the right ones for scale up for additional pre-clinical data in higher animals like dogs and monkeys among others, and to start the clinical studies."

Ascendia's contract manufacturing capability handles controlled substances (Category 3-5) and highly potent molecules (OEL 1-4). In addition, clean rooms are specifically designed to handle aseptic with fill-finish coupled with lyophilization capabilities with 50L manufacturing batches for clients working with small and large molecules and biologics. Furthermore, Ascendia's capabilities utilize a Delta Vita Gamma Vita for nanosuspensions wet milling in ISO 5 clean rooms, offering additional values for clients interested in scaling up larger batches ranging from 600mL to 25L and 100L for clinical trials and commercial manufacturing. LipidSol®-enabling technology is unique for small and large molecules encapsulated in lipid nanoparticles and polymeric nanoparticles for modified and extended release, and long-acting injectable drugs. Dr. Ali says: "Coupled with our new microbial lab and latest water for injection (WFI) plant with 1000's of liters of capacity offers a unique value proposition for our clients for seamless transition from early phase to later phase clinical development."

Leveraging its technical expertise and manufacturing practices for injectable and oral drug products under cGMP, Ascendia continues to play an important role in developing drugs for clinical trials and commercial manufacturing. Located in the northeast region of the US, Dr. Ali says that Ascendia is well positioned to handle projects – both aseptic and non-aseptic – despite new regulations, tariffs, and the BioSecure Act. "Drug manufacturers with intent to expedite challenging molecules are looking for CDMOs to streamline time and save cost without compromising clinical trials and drug products," he says.

Bend Bioscience: *In-Vitro* Permeability Ranks Formulations

Bend Bioscience was formed in 2024 through the merging of Bend Bioscience, Oregon, with CoreRx, Florida, and Societal CDMO, Georgia, to broaden the new company's capabilities to include early development, spray drying, and solubility enhancement, and expanded solid dose commercial-scale manufacturing. The new company offers clinical-scale development for spray drying, particle engineering solutions, suspensions and microsuspensions, solid dose development, and clinical and commercial manufacturing of capsules, tablets, mini-tablets, granulates, and particulates. These services are built across vertical integration of design – formulation and process determination based on the Target Product Profile (TPP); develop – process scale-up and analytical; and manufacture – at clinical and commercial scales.

"As a CDMO, we encounter development issues on a regular basis," says Janice Cacace, Executive Director Pharmaceutical Development, Bend Bioscience. "Whether from solubility or physical properties, new molecules don't often behave as expected during formulation and/or scale-up."

For example, a client was not achieving the bioavailability results they wanted for a suppository dosage form. One of the tools Bend uses for formulation selection is *in-vitro* permeability through a biomimetic membrane, which was used to evaluate the *in-vitro* permeability of the API out of different suppository formulation

Bend Bioscience Senior Operations Specialist Adam Glines carefully inspects bottles for quality assurance prior to tablet packaging in a controlled manufacturing environment.

bases, alone, and with permeability enhancers.

"We were able to discern that concentration and particle size were not contributing factors, but that the root cause was the API had a preference to stay in the original lipophilic suppository base and not diffuse, making it unavailable," she explains. "The *in-vitro* permeability results enabled us to rank formulations from different bases and enhancers, leading ultimately to a lead product that displayed improved bioavailability."

Bend Bioscience is developing tools that enable the ability to 'learn' from the breadth of drug delivery, and in particular structure-formulation patterns with respect to TPPs and then apply that knowledge to active development programs to save time and decrease risk. For instance, in development, AI is helping to understand and predict scale-up parameters in the spray drying process. "Our goal is to incorporate AI tools in process design and, ultimately, for it to be the 'holy grail' in automating and managing our processes throughout commercial manufacturing operations," she says.

BioDuro: Delivering *In-Vitro/In-Vivo* Results In Just 4 Weeks

BioDuro delivers integrated preformulation, formulation development, and manufacturing services. Its formulation team is co-located with the API and DMPK teams, enabling accelerated IND-enabling services through seamless cross-functional collaboration.

"Our preformulation services are grounded in rigorous scientific analysis," says Dr. Hong Li, Vice President of Formulation at BioDuro. "We conduct comprehensive physicochemical profiling – assessing pKa, logP, stability, and hygroscopicity assessments – to support optimal candidate selection and proactively address potential delivery challenges."

Spray drying process using PSD-1 spray dryer at BioDuro.

For example, strategic salt and polymorph screening is employed to enhance crystal form stability and drug performance and advanced bioavailability enhancement techniques – including amorphous dispersions, co-crystals, and lipid-based formulations, which enable effective delivery of poorly soluble compounds.

BioDuro's formulation capabilities support a broad range of dosage forms, including oral solids, injectables, topicals, and ophthalmics. A proprietary Solution Engine solubility platform is designed for speed and flexibility, with more than 100 successful IND filings. Dr. Li says: "We routinely deliver IND-ready formulations in 8-12 weeks, including animal PK studies. Utilizing cutting-edge enabling technologies such as spray-dried dispersions and hot-melt extrusion, we provide phase-appropriate formulations tailored to each stage of development, from preclinical through to commercial production."

In fact, Dr. Li says there is increasing demand for integrated IND programs that can reduce both development timelines and overall costs. She says this can be attributed to a rising number of projects stemming from orphan drug designations and fast-track programs where CMC timelines are becoming more compressed.

BioDuro also has seen growing demand for development services, driven largely by the increasing complexity of drug molecules and the emergence of new therapeutic modalities such as GLP-1s, peptides, and antibody-drug conjugates (ADCs). Dr. Li explains that these innovations require advanced formulation strategies and highly customized development approaches, capabilities that many pharmaceutical companies may lack in-house.

In addition, the growing prevalence of poorly soluble compounds has led to heightened interest in proven bioavailability enhancement technologies such as spray-dried dispersions and hot-melt extrusion. When paired with *in vivo* PK studies, these services are becoming increasingly popular for their ability to accelerate and de-risk development.

As an example, one biotech client approached BioDuro with a highly challenging early-phase API characterized by extremely poor solubility, limited available material, and an accelerated development timeline. "Speed and precision were essential, as the compound needed to advance rapidly toward preclinical evaluation," says

Dr. Li. "Due to the molecule's poor solubility, we identified amorphous solid dispersion (ASD) as the optimal strategy to enhance bioavailability. Spray drying was selected as the enabling technology, given its shorter development timeline and minimal material requirements."

BioDuro's team began with comprehensive *in silico* modeling, screening more than 20 polymer/API combinations. "This virtual approach enabled rapid excipient selection without consuming any API and was completed within a single day," she says.

Guided by the modeling results, the team minimized experimental screening by focusing only on the most promising API/excipient pairs. With a strategically designed experimental plan, a formulation was developed within two weeks using less than 100mg of API.

Subsequently, the DMPK team conducted two rounds of rodent pharmacokinetic (PK) studies to select the optimal ASD formulation. Compared to *in vitro* dissolution alone, *in vivo* PK data provided a more accurate assessment of product performance, she says. This stage was completed in less than 10 days.

"The result was a complete data package, including both *in vitro* and *in vivo* results, delivered in just four weeks," says Dr. Li. "The final formulation demonstrated over a 12-fold improvement in bioavailability compared to the unformulated (neat) API. With robust PK data in hand, the client was able to initiate drug product manufacturing with us and move confidently toward IND filing."

Bora: Improved a Drug Product's Stability Up to 12 Months

Bora offers development and manufacturing services for a broad range of dosage forms including OSD, semi-solid, liquid, ophthalmic and sterile injectable products. In Maple Grove, MN, Bora houses quality control labs and dedicated R&D to support phase-appropriate product and analytical development, and seamless scale-up to cGMP clinical and commercial production of oral solids, powders, and liquids.

"Our expansive global network includes facilities across the US, Canada, and Taiwan, with the flexibility, global capacity, and robust infrastructure to support complex development and manufacturing for a broad range of drug products," says Helen Clark, PhD, Senior Technical Director, Bora. "With our experience in scale up, and expansive global network of commercial-scale capacity, we are seeing demand from clients looking to establish domestic supply centers, and from "friendshoring" (a preference for manufacturing and sourcing from countries considered geopolitical allies) initiatives for regional supply."

One client recently approached Bora to establish a formulation strategy for an oral solution. The client's API was not stable at high temperatures and high humidity. To fully understand the reasons, Bora conducted API stress studies to confirm the reaction pathway. These included a complex forming agent (betadex) to facilitate the solubility of the API and provide better stability of the drug product. The study is ongoing, but at room temperature conditions Bora has helped improve the drug product's stability up to 12 months, explains Dr. Clark.

Within Bora, technologies are transforming formulation development by enhancing precision, speed and data-driven decision-making, which can significantly reduce the time and costs associated with early-stage R&D, she says. In manufacturing, for example, the use of automation, such as isolator-based technology for aseptic fill/finish, can help streamline complex tasks and reduce human error and contamination risks, enabling faster, safer, and more efficient manufacturing of essential therapies.

"With integrated data systems and AI-powered operational efficiency, development and manufacturing teams can make proactive, predictive, and data-driven decisions at every stage, from formulation to fill/finish, ultimately accelerating timelines and bringing high-quality, life-saving products to market faster and at scale," says Dr. Clark.

Catalent: Formulation Strategies Meet Aggressive Timelines

Catalent provides comprehensive formulation development and manufacturing services across all major therapeutic modalities, including small molecules, biologics, and advanced therapies. Services span the entire product lifecycle, from preclinical formulation design and analytical method development through clinical manufacturing to commercial production and global distribution. William Wei Lim Chin, PhD, Senior Manager, Scientific Marketing, Catalent, says that what distinguishes Catalent is its integrated, end-to-end approach. Scientific and technical teams collaborate across development, analytics, delivery, and supply to reduce complexity, accelerate timelines, and support formulation strategies that meet patient and program needs.

Catalent offers comprehensive formulation development and manufacturing services across all major therapeutic modalities.

He says: "Whether designing modified-release oral forms for chronic conditions, scalable fill-finish processes for biologics, or supply logistics for cell and gene therapies, Catalent adapts technologies and workflows to fit clinical and commercial goals."

Digital tools, automation, and artificial intelligence are being implemented across Catalent's network to improve client responsiveness, process control, and data integration. In aseptic processing, Catalent has implemented real-time viable particle monitoring systems that detect contamination risks early and allow quicker resolution through automated tracking and traceability. Embedded process analytical tools like Raman spectroscopy provide real-time process visibility and support upstream quality assurance.

Modern laboratory information systems enable automated calculations and continuous trend analysis. "This gives quality teams reliable insights faster and supports proactive decision-making," says Dr. Chin. "In cell therapy, Catalent has automated high-throughput assays for flow cytometry, cytotoxicity, and cytokine release, replacing manual testing and improving consistency."

Catalent has observed greater demand for contract development, especially from emerging biopharma companies. Dr. Chin says these organizations often seek partners who can provide both scientific insight and operational execution early in development to reduce risk and move programs forward faster. This demand is driving increased interest in integrated programs that combine formulation design, process development, and GMP manufacturing. Catalent supports this need with flexible, phase-appropriate services that enable rapid iteration, reliable tech transfer, and efficient transitions from early-stage work to later-phase manufacturing, he says.

Catalent recently supported a sponsor with a poorly soluble API and limited supply that needed to complete Phase 1 trials under aggressive timelines. Traditional fixed-dose manufacturing would have required excessive capsule counts and lengthy stability testing, which would have delayed the study and consumed valuable API, Dr. Chin explains.

"We implemented an on-demand manufacturing approach using a lipid-based formulation and extemporaneous softgel capsule filling at the clinical site," he says. "Two fill concentrations were developed to cover a 75-fold dose range. Rather than producing multiple finished strengths, intermediate fill material was manufactured under GMP conditions and shipped to the clinical site."

Clinical pharmacists at the contract research organization were trained by Catalent to fill and seal softgel capsules using manual techniques. Training included proper handling of nitrogen-filled lipid formulations, capsule sealing methods, fill accuracy, adherence to in-use stability timelines, and batch record documentation. "This ensured consistency, dosing precision, and regulatory compliance during trial execution," he says.

Intermediate stability data and well-characterized materials supported regulatory approval of this approach. The program reduced API usage by more than 50%, minimized unnecessary batch production, and enabled the successful completion of the trial within the required 30-week timeline.

CuriRx, Inc.: Integrated Approach Combines Advanced Science With Early-Stage Manufacturing

CuriRx, Inc. is a woman-owned small business and full-service CRDMO specializing in injectable formulation development, analytical testing (GMP and non-GMP), and pre-clinical batch manufacturing for clients worldwide. Its expertise spans a range of molecule types, including complex biologics. CuriRx offers end-to-end services from pre-formulation through dosage form development, including advanced delivery systems such as lyophilized products, nanoparticles, lipid nanoparticles (LNPs) for mRNA, liposomes, micelles, and complexation-based

formulations. The company supports non-GMP manufacturing for early-stage stability and animal studies, including prefilled syringe (PFS) fills.

"Our integrated approach – combining advanced formulation science with early-stage manufacturing – helps clients de-risk development and accelerate timelines," says Indu Javeri, PhD, President & CEO of CuriRx.

Currently, CuriRx's contract development services are in high demand, particularly among early-stage biotech companies seeking solutions for complex delivery challenges and scalable processes. "Our reputation for solving formulation issues – especially for biologics and advanced delivery systems – has made us a preferred partner for preclinical and IND-enabling programs," she says.

Analytical capabilities include chromatography, spectroscopy, USP/EP methods, and high-resolution LC-MS. CuriRx operates under GLP and cGMP standards and is ISO 9001 certified. Its scientists have contributed to the development of commercial products like Humira, Synagis, Blincyto, and Gattex. CuriRx also formulated a personalized peptide vaccine for terminal melanoma patients, whose results were published in Nature.

In collaboration with IAVI and Rockefeller University (funded by the Gates Foundation), CuriRx developed high-concentration antibody formulations (150mg/mL) for subcutaneous injection, achieving acceptable viscosity and injectability.

"We also helped a client overcome adsorption issues in a bispecific antibody formulation, developing a stable lyophilized product with over two years of shelf life allowing for patent application by the client," says Dr. Javeri. "In addition, our analytical methods enabled accurate quantification, supporting successful Phase 2 trials."

Gattefossé: Optimizing Pre-Clinical Lipid-Based Formulations

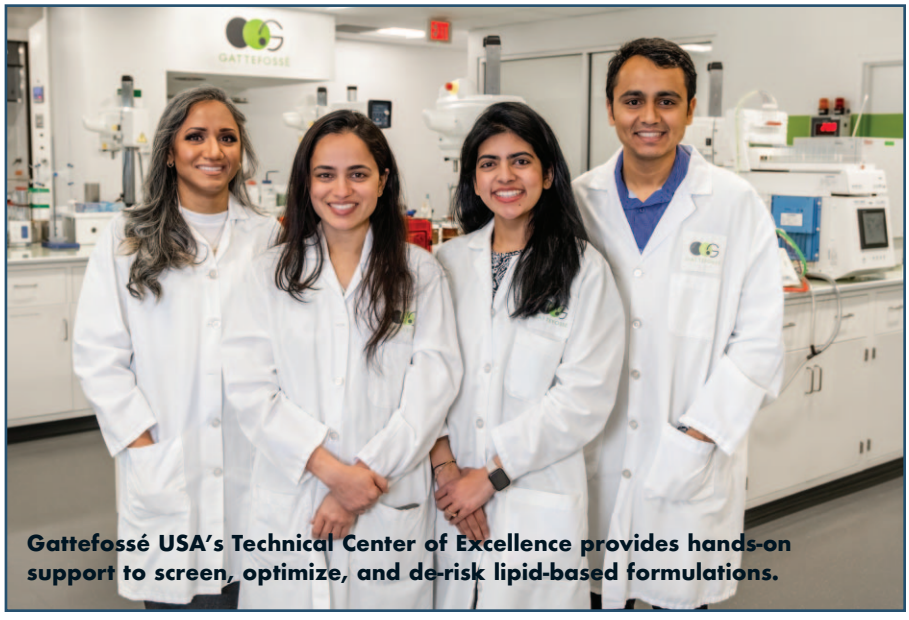
As drug discovery efforts accelerate, formulators are under increased pressure to advance large pipelines of challenging molecules – often ones with solubility and permeability limitations. Lipid-based formulations offer key benefits across several routes of administration. These benefits include improved solubility and enhanced *in vivo* absorption via the oral route as well as penetration enhancement and effective, patient-friendly formats for topical/transdermal products. Gattefossé has established four Technical Centers of Excellence (TCE Labs) in France, the US, India, and China. These labs aid in the selection and optimization of pre-clinical lipid-based formulations; provide tailored, hands-on customer support; and advance lipid knowledge through education and training, explains Nick DiFranco, Senior Marketing Manager – Pharmaceuticals, Gattefossé USA.

"We have taken on a wide range of projects in recent years, including lipid screening for poorly soluble drugs, troubleshooting of existing formulations, and optimization of late-stage projects prior to clinical and commercial scale-up," he says. "While many projects involve early-stage screening and optimization, we also work with customers to troubleshoot and optimize existing lipid-based formulations."

Technical capabilities range from screening/compatibility studies for liquid and semi-solid excipients to the development of binary and ternary systems that utilize multiple lipids to optimize drug loading, maximize drug exposure, and improve product performance. Mr. DiFranco says that Gattefossé also performs *in vitro* lipolysis and Franz cell diffusion testing to simulate *in vivo* conditions and guide both oral and topical formulation selection.

"Our TCE labs serve the unique purpose of streamlining early-stage pre-clinical development to ensure a seamless transition to clinical and commercial formulations," he says. "Gattefossé's TCE scientists act as an extension of our customers' R&D teams, providing hands-on support to overcome difficulties associated with challenging APIs."

Recently, a customer approached



Gattefossé USA's Technical Center of Excellence provides hands-on support to screen, optimize, and de-risk lipid-based formulations.

Gattefossé with a clinical-stage lipid-based formulation that was facing inconsistent dissolution and capsule compatibility issues on stability. "After fully investigating the client's formulation and with our deep knowledge of lipid chemistry, we identified that oxidation was the main cause of these formulation challenges," explains Mr. DiFranco. "Gattefossé TCE Lab worked to identify the best antioxidants along with recommended levels to address the formulation issues and allow the client to successfully complete their clinical trials."

In addition to oral offerings, Gattefossé specializes in creating topical and transdermal solutions. Mr. DiFranco says clients benefit from hands-on development support and access to prototype formulations for creams, lotions, gels, and ointments. "We enable clients to create effective, patient-friendly products, improving API solubility and skin penetration while optimizing key sensory attributes such as texture, rub-in, absorption, and after-feel."

LATITUDE Pharmaceuticals Inc.: Formulating Challenging Compounds

LATITUDE Pharmaceuticals Inc. specializes in innovative drug formulation development and GMP manufacturing services. LATITUDE offers tailored formulation development for a variety of drug formats, including injectable, oral, topical, ophthalmic, and inhalation products. LATITUDE is particularly adept at producing complex liquid formulations like nanoemulsions, liposomes, and nanoparticles.

"LATITUTDE distinguishes itself through a small-company approach that includes in-depth expertise, direct connection with our project scientists, flexibility, and rapid provision of quality deliverables," says Matthew A. Singer, PhD, Vice President, Head of Business Development, LATITUDE.

The company has successfully formulated challenging compounds, addressing issues like poor solubility, instability, and bioavailability. When appropriate, LATITUDE can employ proprietary technologies such as ClearSol™, a solubilization platform for difficult APIs, and PG Depot™, a phospholipid gel depot for sustained injectable drug release. LATITUDE also provides GLP and GMP-compliant analytical testing services, supporting clients from preclinical studies through Phase 1 and Phase 2 clinical trials.

Since its founding in 2003, LATITUDE has completed more than 1,400 formulation development projects for more than 300 clients, "building a reputation for creative problem-solving, reliability, and rapid turnaround," says Dr. Singer. "For the many clients that come to LATITUDE with solubility (and often bioavailability) issues, we offer a well-defined set of approaches that are highly effective to produce a quality drug formulation."

He says that while both contract manufacturing and development are both in demand. "LATITUDE offers both easy transition of our clients' formulation projects to LATITUDE's GMP manufacturing, as well as just one or the other service, if that is the need of our clients," he explains. "And, like most things, demand goes in cycles. For much of the second half of 2024, our contract manufacturing was in greater demand by established clients, as seed investment in pharma was slow. However, by the end of 2024 and into 2025, LATITUDE is seeing normal demand for both formulation development and GMP manufacturing."

Lifecore Biomedical: Taking On Tough Projects Others Won't

Lifecore Biomedical is a US-based injectables CDMO providing clinical to commercial process development and manufacturing along with end-to-end services like on-site testing and stability as well as packaging, handling, and sterilization options. The company also manufactures sodium hyaluronate, which is used in some of the formulations produced for its partners.

"We're generally recognized as the 'ones who do the tough stuff' that others can't or won't undertake," says Ryan Swanson, PhD, Director of Process Development, Lifecore Biomedical. "We work with many products that are difficult to fil-

Lifecore Biomedical is a US-based injectables CDMO known for tailored process development and fill/finish services.

ter and fill, especially complex and high-viscosity formulations (>100,000 centipoise). But we also handle products that are not as challenging. Partners in all stages and with products of varying complexity choose us because we can handle the unexpected."

One of these tailored solutions was a biologic formulation that required precision process engineering. During formulation, the molecule needs controls for temperature, light, and shear sensitivity. It involves a multi-step chemical reaction within a sterile mixing environment, and a process that is controlled to within 10 seconds. Post-mixing, the final formulation has a gel consistency that is difficult to fill. While these individual process steps and controls may not be challenging, the combination of all of them created a complex process that involved building a custom formulation skid and multiple programmable logic controls (PLCs). "We transferred this formulation into Lifecore as a bench scale process, scaled it for clinical GMP batches, and then scaled it again for commercial supply," he says.

When it comes to supplies, Lifecore's customers and prospects understand the current macroeconomic environment that is adding uncertainty to supply chains. Dr. Swanson says that technical transfer experience and ability to scale are becoming more valuable as a result. "These companies are considering alternative geographies for manufacturing their products and they appreciate agility in responding with solutions," he says. "They appreciate Lifecore's ability to offer flexible options like plant-in-plant concepts or dedicated filling lines that give them a means of gaining control over supply chain uncertainty."

Lonza: Advanced Synthesis Addresses Unmet Medical Needs

In recent years, small molecules and bioconjugates segments have shown a steady increase to an already high level of outsourcing, and current estimates suggest this trend will continue. There is a sustained high level of outsourcing originating from Big Pharma players, but the segment growth is driven by small and emerging companies, many of which lack extensive in-house manufacturing capabilities. These companies are advancing new products across various modalities, including small-molecule active pharmaceutical ingredients (APIs) of any potency and bioconjugates, including antibody-drug conjugates (ADCs).

Lonza collaborates with its business partners to embrace innovation and manufacture drugs by delivering integrated offerings that meet the complex needs of global customers. In Advanced Synthesis, Lonza leverages its expertise in classic and complex chemistry and biochemistry to manufacture APIs and ADCs, addressing the unmet medical needs in oncology, autoimmune diseases, diabetes, and more.

"Our recent collaborations and investments in Advanced Synthesis reflect our commitment to pioneering next-gen APIs and ADCs using cutting-edge science, smart technology, and lean manufacturing for our customers and their patients," says Christian Seufert, Head of Advanced Synthesis, Lonza.

Within the last decade, 70% of new molecular entities approved by the FDA were derived from small-molecule APIs. Global trends, like population growth and aging, are accelerating the need for faster, more efficient drug development. Artificial intelligence (AI), machine learning (ML) and robotics are driving optimization of developing and manufacturing of APIs. Their structural complexity presents a challenge in drug development, particularly synthetic route design. In general, APIs often require complex synthesis that may exceed 20 steps, resulting in extended lead times, increased raw material management, and heightened supply chain vulnerability. To tackle this, pharmaceutical developers are increasingly using AI to

Lonza's bioconjugation facility in Visp, Switzerland.

streamline synthetic route design and predict viable pathways that experienced process chemists can use to optimize synthetic routes and reduce complexity, he explains.

Lonza recently launched its AI-Enabled Route Scouting Service, combining the company's process R&D expertise, proprietary commercial supply chain databases, and computer-aided synthesis planning technologies. "With access to global chemical supply chain intelligence bolstered by the predictive power of AI, the Route Scouting Service streamlines API development by optimizing synthetic pathways, enhancing supply chain resilience, and ultimately, enabling faster and more cost-effective drug development," says Mr. Seufert.

In addition, recent ADC commercial launches have driven the ramp-up of commercial volumes and intensified pipeline development. This growth, driven by emerging companies, is increasing demand for CDMO support to meet challenging timelines while maintaining high innovation, managing complex supply chains, tight timelines, and overcoming regulatory hurdles.

To solve these challenges, Lonza is making strategic investments and collaborating with research-based partners. For example, a new bioconjugation suite at Lonza's Ibex® Biopark will support the manufacturing, handling, and containment of highly-potent modalities. In addition, the integration of AI and predictive tools into its ADC development toolbox (including Synaffix offerings) will help accelerate the design and development of next-generation ADC pipelines.

Mikart: Catering to Complex Products

Mikart's formulation development services encompass pre-formulation studies, drug-excipient compatibility assessments, and the application of Quality-by-Design (QbD) principles to ensure robust and scalable formulations. The company recently expanded capabilities with the addition of a state-of-the-art liquids and suspensions suite, enabling the development and manufacturing of complex suspension products, including extended-release formulations.

Mikart has made substantial investments to enhance its formulation development capabilities, particularly in response to client demand for robust and reliable liquid dosage forms. The new liquids and suspensions suite in Atlanta exemplifies this commitment. This facility supports a wide range of volumes, from 50L to 4,000L, catering to the development and manufacturing of complex suspension products, including extended-release formulations. These advancements are especially beneficial for pediatric and geriatric product development, areas where Mikart has seen increased demand. Moreover, Mikart's strategic investments in advanced equipment, such as the Korsch XM12 tablet press and the FlexPack NF-150 Horizontal Sachet-Packaging Machine, bolster its development and manufacturing capabilities.

Mikart has embraced digital transformation to enhance decision-making in formulation development and to create more dynamic manufacturing processes. The company transitioned from paper-based quality processes to a digital platform by implementing TrackWise Digital eQMS. This shift streamlined document approvals and training management, reducing approval times from days to less than a day and improving visibility into training compliance. Investments in state-of-the-art equipment, such as the Fette® double-sided tablet presses, have enhanced Mikart's manufacturing capabilities. These machines offer advanced features like automatic weight control and real-time monitoring, enabling precise and efficient production of complex oral solid dose products.

Mikart partnered with Nano Pharma-Solutions to utilize their NanoTransformer™ technology, a solvent-free, nano-granulation process that enhances the solubility of active pharmaceutical ingredients (APIs). This collaboration allows for the development and manufacturing of nanomedicines, addressing solubility challenges in drug development.

Gus LaBella, Director of Formulation Development of Mikart, explains that one client recently had a prototype formulation of an amphiphilic drug with very poor water solubility. The formulation used a high concentration of propylene glycol that acted as a co-solvent for the API as well as an anti-microbial agent. However, due to safety and regulatory concerns, it was required to decrease the propylene glycol concentration below a certain level. Various solubility enhancers and surfactants were screened, and they were not effective, he says. Application of heat was not recommended for the API stability. Eventually, maintaining the original ratio of propylene glycol to water was tried by reducing the overall concentration of propylene glycol by 3 to 5 times in the prototype. Because the API is amphiphilic in nature, a specific solvent polarity is required to maintain its solubility with less co-solvent. This co-solvent system exhibited monomeric solubilization making it a

more robust and stable form of solubility enhancement. Although the reduced propylene glycol was not sufficient to act as an anti-microbial, it effectively solubilized the preservatives added to the drug product. The formulation remained simple and efficient, avoiding the need to introduce multiple additional excipients.

Aeronose™ *in vitro* nasal regional deposition model (Nanopharm).

Nanopharm: Developing Stable Formulations for Oral & Nasal Drug Products

Nanopharm is a specialized contract development organization focusing on orally inhaled and nasal drug product (OINDP) development services, including preformulation and formulation development, device selection and characterization, and *in silico* modelling of regional deposition and systemic bioavailability. The company also offers GMP fill/finish and release/stability studies for early clinical development.

"Nanopharm has significant experience working with generic OINDPs and has collaborated with FDA for the past 10 years on developing clinically relevant *in vitro* and *in silico* methods to accelerate approval," says Gemma Budd, General Manager, Nanopharm.

There is a growth in the market for OINDP due to an interest in targeting local delivery to the lungs or nose, as well as repurposing drugs to offer faster onset or higher bioavailability compared to oral dosage forms, and to overcome patient resistance associated with injections – or even to target direct delivery to the brain. Growth in biologic molecules also makes it more difficult to deliver orally, so nasal and inhalation dosage forms are increasingly popular.

"The kinds of projects we work on cover challenges, such as developing a stable formulation with much higher concentrations of drug compared with oral or injectable dosage forms, as well as optimize the device and formulation holistically to enable aerosolization," she says. "This requires sophisticated formulation strategies, as well as consideration of formulation enhancers to increase retention time or accelerate absorption, or particle engineering to preserve drug stability while facilitating delivery and deposition. Furthermore, some customers want to target certain regions of the nose or lungs, so we have to optimize the droplet or particle sizes to target these regions and still get high efficiency of dose delivery, which is a very niche area of expertise that not many other CDMOs have."

In silico modelling capabilities, such as Simhalation™ and SmartTrack™, allow Nanopharm to factor in disease-specific variables and patient-to-patient variability, which helps to derisk clinical development and refine dosing strategies – a service not available from most CDMOs, she says.

Nano PharmaSolutions: Single Nanoformulation for All Phases With No Solvent or Polymers

Poor solubility remains one of the greatest challenges in pharmaceutical development. More than 70% of new chemical entity (NCE) candidates have poor solubility and therefore poor bioavailability, which remains one of the main causes of failure for Phase 1 First-in-Human trials. While the number of methods for enhancing drug solubility continues to increase, most of the formulation work is performed after Phase 1 clinical trials due to often-long development time and high quantities of drug required for these solubility enhancement technology options. However, the regulatory requirements for bridging the safety and human PK studies for introducing enhanced bioavailability formulation after the initial Phase 1 study are costly in terms of development time and resources. "Solubility-enhancing technology that is suitable at early development stages is more highly desirable now than ever," says Dr. Kay Olmstead, CEO of Nano PharmaSolutions.

NanoTransformer™ is a scalable drug nanosizing technology that generates

GMP NanoTransformer™ Equipment (Nano PharmaSolutions).

nanoparticles of BCS Class II and IV drugs in the 100-300nm medial particle size range. This process uses a physical vapor deposition process used in the aerospace industry to nano-coat these insoluble drugs onto regular excipients using gentle heat and extremely low pressure (<10-6 torr). This N-granulation™ process may be used for animal safety studies as aqueous suspensions as well as for Phase 1 clinical trials without changing the formulation, but instead filling the N-granules into capsules, powder-in-capsule, or powder-in-bottle; and as compressed tablets for later-stage clinical trials. Using the same nano-granulation for the base dosage form in all phases of clinical trials removes the need for bridging PK studies required by regulatory agencies for formulation changes during the development phase, Dr. Olmstead explains. "A solvent-free nanoformulation for animal safety studies will ensure the same good exposure of drug is maintained in both animals and humans."

The NanoTransformer N-granulator is a high-vacuum drug nano-coater, enabling the production of nanodrugs under cGMP conditions. The development time for nanoformulation is rapid and requires very little API, making this process suitable for preclinical studies as well. Industrial vacuum nano-coaters can generate hundreds of kilograms of nanoparticles; therefore, scale-up to production-sized batches is achievable.

"Solubility and bioavailability enhancement outperforms solid dispersion techniques like spray drying," she says.

Nano PharmaSolutions offers GMP manufacturing of clinical supplies of nanomedicines at its co-manufacturing facility at Mikart, LLC (Atlanta, GA). Mikart is a contract development and manufacturing organization (CDMO) with capability in developing and manufacturing oral solid and liquid dosage forms. "GMP operation of NanoTransformer technology at Mikart with smooth tech transfer from Nano PharmaSolutions and manufacturing capability for finished dosage forms for various formats (capsules, tablets, nanosuspension, pediatric formulations, etc.) provide an easily scalable solution for difficult formulations in all development stages," says Dr. Olmstead. "This differentiated, solvent-free, nano-granulation process for drug development and manufacturing provides biotech and pharmaceutical companies with a new solubility enhancement technology that has environmental sustainability, well suited for new drug development as well as life cycle management of commercial drugs."

Pii, A Jabil Company: Delivering Agility When It Counts

In silico modeling is changing how formulation development happens at Pii, a Jabil Company. "Instead of purely lab-based trial and error, our scientists use computational simulations to predict how drug candidates behave – how they dissolve, interact with excipients, or degrade over time," explains John Fowler, CEO, Pii, A Jabil Company. "This early insight helps reduce risks, saves valuable API, and focuses lab efforts on formulations with the highest potential, speeding up development while improving confidence."

On the manufacturing side, robotics play a growing role, especially in fill-finish operations for parenteral drugs, like ADCs and biologics. Automated systems bring speed, precision and consistency, reducing human error and contamination risk. Mr. Fowler says: "They allow for faster line changeovers and easier validation, which is critical when working with small batches or complex drug products. This dynamic manufacturing approach helps meet tight timelines and ensures product quality remains high."

He says that what sets Pii, a Jabil Company, apart is the seamless integration of drug and device development and manufacturing. Mr. Fowler explains that this combined capability simplifies supply chains and accelerates time to market – especially for complex combination products like autoinjectors or prefilled syringes. "Having both drug formulation expertise and advanced device engineering in-house means we can collaborate closely to optimize product design, regulatory pathways, and commercial-scale manufacturing," he says.

Supply chain resilience is a key focus as well. The BioSecure Act and ongoing

tariff uncertainties have pushed many to rethink where and how they source materials. Pii leverages Jabil's deep supply chain network and multi-source procurement strategies to mitigate risk. "Our onshore and near-shore manufacturing sites keep critical processes close to patients, reducing delays and increasing oversight," he says. "This approach supports regulatory compliance and provides agility to navigate disruptions without sacrificing cost or continuity."

By integrating digital modeling, advanced automation, combined drug-device expertise, and strategic supply chain management, Pii and Jabil are shaping more informed, flexible, and reliable pharmaceutical development and manufacturing processes, claims Mr. Fowler. "It's about making smarter decisions early and having the operational agility to deliver when it counts."

Quotient Sciences: Using Technology to Bridge Studies & Formulations

Quotient Sciences has a breadth of formulation and manufacturing services for small molecules and synthetic peptides across a range of dosage forms. Matt Paterson, Chief Strategy Officer, says that Quotient Sciences' Translational Pharmaceutics® platform – a disruptive approach to drug development that integrates drug product formulation and manufacturing with clinical testing – sets the company apart. "The integration of services improves decision-making while reducing time and white space, so milestones can be achieved as efficiently as possible, shortening drug development timelines as a whole."

Asma Patel, Vice President, Integrated Development Services at Quotient Sciences explains how the platform addressed a product development challenge for one client. "We worked on a project for Rigel Pharmaceuticals, which was developing R552, a small molecule RIPK1 inhibitor for autoimmune and inflammatory disorders. Preclinical data showed potential solubility issues and, therefore, the client wanted to evaluate a range of formulations for the first-in-human (FIH) study. Leveraging the Translational Pharmaceutics platform, we conducted an adaptive FIH study to develop lipid and solid dispersion (SDD) formulations to enhance solubility. These formulations underwent rapid, iterative testing, allowing for immediate adjustments and optimization."

The study found that R552 was generally safe and well-tolerated, with linear pharmacokinetics and no significant food effect. The SDD formulation proved effective in overcoming solubility challenges. Bridging studies were then conducted to transition from a suspension to a more patient-friendly SDD tablet formulation. "Using this approach, Rigel was able to achieve proof-of-concept milestones in a more streamlined and efficient manner," she says.

Translational Pharmaceutics is commonly used to bridge from simple formulations suitable for FIH studies to drug products that are scalable for proof-of-concept and later stages of clinical testing. To take this a step further, Mr. Paterson says Quotient Sciences also has an ongoing AI program aimed at improving decision making and productivity in formulation design. "Combining our extensive clinical experience and modelling and simulation expertise, the integration of AI will enable more informed and efficient decision-making, hence optimizing the formulation development process."

Recipharm: Modeling Platform Accelerates Development

Recipharm has a fully integrated offering for drug substance and drug products (for development and commercial supply), oral formulations, and sterile fill finish. Its complete offering ranges from API route scouting to commercialization.

Recipharm's ReciPredict platform accelerates process development and technology transfers. "ReciPredict combines statistical modelling and simulation to facilitate product development, technology transfer and manufacture of drug products efficiently and reliably," explains Dr. Uwe Hanenberg, PhD, Head of Product Implementation, Recipharm. "It enables data driven, informed decisions by applying data science and digital technology to develop and manufacture drug products."

ReciPredict was recently applied when Recipharm experienced a 'sporadic' Out of Specification (OOS) in the assay of a sterile liquid formulation in vials. Dr. Hanenberg says: "By translating the manufacturing process and the analytical process into a mathematical model and using historical data to feed into it, we were able to identify and eliminate the root cause for the sporadic OOS."

Resilience: Robust Data Platform Eliminates Inefficiencies

Resilience provides development and drug substance and drug product manufacturing for biologics, vaccines, cell and gene therapy, and nucleic acids, hands-on support and regulatory guidance, and scale-up to commercial drug product manufacturing – all within North America. Resilience's quality procedures and regulatory experience safeguard BLA filings, prioritizing overall program success. Their network of facilities was designed to meet

the highest industry standards, ensuring quality assurance and regulatory integrity that mitigate risks for its partners' IND filings and clinical trial timelines. They are ready to support new platform technologies, process and analytical development programs, or drug substance or drug product manufacturing needs, while meeting timelines with dedicated capacity, and the ability to tailor resources to support innovative projects.

The CDMO is witnessing growing demand in cell therapy, drug substance biologics, and sterile fill/finish for injectable products, particularly where downstream manufacturing and commercialization expertise are critical. One especially promising opportunity is the accelerating momentum behind GLP-1 therapeutics, which have expanded beyond diabetes management to include obesity, weight loss, and even conditions like sleep apnea.

Resilience has built a data platform that supports data processing and helps to increase efficiencies by streamlining cross-organizational communications between procurement, finance, supply chain operations, project management, and more. The program interconnects 30 data products across six domains, enabling near real-time reporting for more than 25 applications and reducing human error by eliminating the need for manual data transfer and transcription.

"This allows us to provide a transparent and centralized visibility of quality, ERP, lab, and process monitoring data to our clients in almost real-time and allows us to accelerate manufacturing timelines by reducing batch cycle times," says Chuck Lemire, Vice President, Enterprise Systems, Resilience. "While currently used as an internal tool, Resilience is now transforming our cloud-based capability into an app that clients can utilize to remotely and securely access their data, see the status of their program, and integrate to their own systems."

Following tech transfer for development, a client approached Resilience with an incredibly tight timeline to produce a small drug substance batch. Their process was not yet very robust and was at risk for fairly routine failures, explains Mr. Lemire. The Resilience team was enlisted to fortify the process to help ensure the run would be successful so they could maintain their timeline.

"Utilizing our industry-leading Data Platform allowed us to monitor critical attributes in near real-time, with automated alerts for any trend towards out of specification," he says. "Additionally, we synced video of the bioreactor to the data sets to provide our scientists immediate observation into the operation. This empowered them to take action the moment an alert was sent. As we anticipated, there were issues during the run, however our team was able to intervene immediately and prevent any batch failure. Additionally, given the data sets recorded, we were able to provide development feedback to the client on how to improve their manufacturing process further. Overall, the combination of data, automation, and our experienced scientists facilitated successful completion of a critical asset and led to rapid improvement of their process."

Samsung Biologics: Synchronizing Systems & Experience

Samsung Biologics adapts a stepwise screening matrix to find the best formulation condition. As biologic modalities evolve, the company continues to update that matrix by leveraging the scientific expertise and experience of its formulation scientists.

"Our capabilities and technical readiness can cover liquid and frozen formulations as well as lyophilization for drug substance (DS) and drug product (DP)," says Heonchang Lim, Director of Formulation Development, Samsung Biologics. "Since the launch of our services, we have implemented around 100 projects for diverse molecules – from monoclonal and multi-specific antibodies to Fc-fusions – and successfully formulated all of them."

The growing molecular complexity of biologics has propelled Samsung Biologics to develop a data-driven approach to identify the ideal formulation type for each molecule. Its approach synchronizes cutting-edge systems and cumulative project experience. To further enhance the reliability and efficacy of the product, a tailored formulation strategy is developed with a high-throughput developability assessment. Additionally, a collection of data-driven insights – critical for issue identification, process traceability, and agile problem-solving – can be simultaneously implemented during formulation via simple forced degradation studies upon client request.

Mr. Lim says: "Our formulation scientists are responsible for performing the developability assessment, formulation development, and small-scale non-GMP DP manufacturing. The most critical responsibility is development, as the primary goal is to attain optimal formulation conditions regardless of a molecule's characteristics."

Attaining a higher concentration can be challenging. Instability at high concentrations, pH shifts, and viscosity issues can emerge at any stage of formulation. "Several months ago, we managed to achieve

a concentration level of 266mg/mL, surpassing the 200mg/mL target," he says. "But, the pH condition was also adjusted to 0.51. Extrapolating a solution from our cumulative project experience, we promptly decided to leverage offset buffers to tackle the issue. The optimum, stable pH condition was achieved after implementing tangential flow filtration with the offset buffers."

In terms of technological advances, Samsung Biologics leverages robot handlers – equipped with cameras that can identify visible particles, color, and turbidity – to reduce human error in formulation sample screening. A smart lab notebook system conducts robust data collection and analysis, adhering to good document practice standards. Generated data are recorded, sorted, and analyzed, enabling audit trails and process traceability tests.

Serán: Spray Drying Experience Makes or Breaks a Program

Developing complex molecules to treat human disease presents unique challenges. Serán helps clients overcome these obstacles by offering a range of drug delivery and formulation strategies designed to optimize bioavailability. Final dosage forms include capsules, tablets, multi-particulates, and powder-in-bottle formats. Solid dosage forms are engineered to address solubility challenges and enable controlled or extended-release profiles.

"With decades of experience in particle engineering, including advanced techniques like spray drying, Serán brings deep expertise to every stage of development," says Rod Ketner, PhD, Serán. "Our solid-state analytical capabilities allow for thorough characterization of crystalline and amorphous APIs and drug products.

Engineer preparing clinical production equipment at Serán.

These services are supported by comprehensive analytical offerings and a GMP-compliant QC lab for release testing and stability studies.

Our strength lies in our scientific foundation, technical expertise, and collaborative team culture, ensuring smooth transitions from early development to commercial manufacturing."

Serán focuses on the clients' target product profile to make improvements in processes and delivery methods that help well-formulated medicines reach patients faster, says Dr. Ketner. "Innovation moves technology forward, but it's our ability to apply proven strategies to new problems that drives success," he says. "This is especially critical with complex technologies like spray-dried dispersions (SDDs), where experience can make or break a program."

While known for spray drying and enhancing bioavailability, Serán also supports a range of conventional oral dosage forms. Dr. Ketner says: "Our focus is always on choosing the simplest, most effective solution tailored to the client's molecule, the patient population, and their development goals."

ten23 health AG: A Holistic Approach to Primary Packaging

ten23 health offers development services for sterile dosage forms for molecules such as biologics, peptides, oligonucleotides ADCs, viral vector, including formulation, process, and analytical development. Dr. Hanns-Christian Mahler, Chief Enablement Officer & Board Member, ten23 health AG, explains that the company's formulation development approach is holistic and includes the choice of primary packaging, and leverages relevant processes to ensure suitability and representativeness.

ten23 also provides manufacturing services for sterile drug products – from manufacturing of preclinical study material to stability study material to reference standard. Isolator-based GMP filling lines process RTU primary packaging and produce clinical to commercial sterile products, including vials, syringes or cartridges.

Dr. Mahler is proud that ten23 health moves programs from development into GMP manufacturing, facilitating such (possibly challenging) handovers for customers, that would otherwise transfer between CDMOs. "Our GMP manufacturing system is high-end technology, using

Next Generation Impactor (NGI) in use at Upperton Pharma Solutions' Research & Development laboratories.

robot-assisted filling of RTU containers, that, together with a clever choice of manufacturing processing materials and process, enables the precision of filling and stopper setting.

He describes a couple of instances where ten23 health has successfully helped clients with formulation challenges. "We have customers approaching us for specific issues they encountered with their formulations and process (developed elsewhere)," he says. "One was when the biologics API was precipitating upon dilution on sodium chloride bags. The prior formulation was developed closely to its edge of failure and with a focus of only 'thermal stability,' with the stabilizers having been diluted too much in the infusion bag. We supported an immediate 'quick-fix' solution and embarked on developing a sufficiently robust, and usable formulation."

In another example, ten23 health assessed polysorbate degradation, leading to particle formulation and non-compliance. The company supported troubleshooting of the customer's process to improve product quality.

Upperton Pharma Solutions: Finding the Best Nasal Device for Your Formulation

Upperton provides comprehensive nasal formulation development services, covering both liquid and dry powder formats for multi-dose and single-dose delivery. Capabilities include selecting the most suitable nasal device for a formulation from a range of options, ensuring optimal delivery performance, says Dr. Richard Johnson, Chief Scientific Officer & Founder at Upperton Pharma Solutions. Upperton also offers in-house characterization of the final dosage form, including performance testing in nasal models such as the Alberta Idealised Nasal Inlet (AINI).

"Our team has deep expertise in particle engineering, enabling us to develop and manufacture dry powder formulations for nasal delivery – especially relevant for biologics, peptides, and vaccines," he says. "A key differentiator is our work at the forefront of nose-to-brain delivery, including partnerships involving proprietary devices in this emerging area. This work builds on our broader experience across other challenging dose forms, such as oral solids (tablets, capsules), pulmonary (single- and multi-dose), and sterile injectable liquids and powder products."

Clients developing dry powder nasal products face a challenge when scaling up from milligram to gram and eventually kilogram-scale production at a time when API supplies are likely to be limited, he explains. This is particularly challenging as particle size and morphology needs to be maintained at all stages of development. "In one case, we addressed this by applying a stepwise scale-up strategy using our spray drying technology and expertise, allowing us to match particle specifications at small and intermediate scales," says Dr. Johnson. "This approach enabled us to manufacture small batches for early testing and seamlessly progress into the clinic. The outcome was faster clinical entry, with a scalable process that consistently delivered the same particle quality – batch after batch."

Over the last two years, several high-profile products, such as Neffy, approved by the FDA in 2024, have demonstrated that drugs traditionally delivered by injection can be effectively administered nasally, says Dr. Johnson. "This shift has sparked significant interest in nasal delivery, especially for emergency-use and treatments that require fast-onset of action," he says. "As a result, we've seen growing demand for early-phase formulation development, particularly for Phase 1 and Phase 2 programs. Companies are increasingly exploring nasal routes for biologics, peptides, and other small molecules, driven by the potential for improved patient compliance, rapid onset, and non-invasive delivery. This trend is also pushing more of these types of projects into late-stage manufacturing."

Upperton has introduced automated

device filling capabilities using Fill2Weight technology, which allows for precise and consistent filling of nasal delivery devices – both liquid and powder formulations. This system ensures high fill accuracy and efficiency, especially important for single- and multi-dose nasal products. On the assembly side, Upperton is expanding capabilities to support semi-automated and automated assembly of nasal devices, including integration of components and in-process checks. He says: "These technologies help us maintain tight quality control, reduce manual handling, and support scalable manufacturing as products move into later phases." ◆

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Drug Development
EXECUTIVE

Chris Gilmor
VP, Sales
Sanner of America

SANNER

Sanner Group: Building a Suite of World-Leading Services for its Customers

Shortly after Sanner Group announced its acquisition of Gilero, the medical device design, developer, and manufacturer based in Durham, NC, *Drug Development & Delivery* recently interviewed Chris Gilmor, Vice President of Sales, Sanner of America, to discover how its Advance with Agility™ program helps its partners achieve faster development times and reduce time to market, and how the company embeds sustainable practices into its global business.

Q: To set the scene for our readers, can you please describe Sanner's business?

A: Sanner GmbH was founded in 1894, and we are now known as a global market leader for desiccant closures and effervescent tablet packaging. As the business has grown, most recently with the acquisition of Springboard Pro in Cambridge, UK, we have become a sought-after provider of customized solutions in the areas of medical devices and diagnostics, pharmaceuticals, and consumer healthcare.

Q: I believe most readers would agree our industry has seen a lot of disruption, yet development pipelines are healthy and there's a lot of innovation. How has your business adapted?

A: Innovation has always, and will continue to be, the hallmark of this industry. It is the responsibility of companies such as Sanner to evolve accordingly by augmenting its products and services to meet new market needs.

During the past decade, specifically between 2011 and 2016, the pharmaceutical industry experienced the "patent cliff" with the largest number of

patented drug product expirations in history. This greatly changed the competitive landscape between innovators and generics for oral solid dose (OSD) delivery. Concurrently, the industry embraced the rise of innovative biologic therapeutics presented in small-volume, high-value, parenteral formats that have different packaging, dosing, and administration requirements. Sanner is uniquely positioned to support companies across these and other routes of administration with our comprehensive contract design services and manufactured solutions.

Q: How has Sanner responded to those demands?

A: Though market share has changed, from 2017 to 2022, 182 of the 293 (close to 62%) of the new chemical entities approved by the FDA were small molecule OSD drugs. Furthermore, small molecule OSD formulations still represent about 38% of the drugs in Phase 3 clinical trials, many of which will be susceptible to moisture mediated chemical and/or physical degradation requiring the use of a desiccant with primary packaging to ensure drug safety and efficacy.

Historically drug manufacturers have used probe stability studies to determine the type and amount of desiccant required to ensure product shelf-life required by global regulatory agencies. These probe stability studies, designed as a matrix of various desiccant types, amounts, and packaging materials conducted under real time testing conditions can take between 6 and 12 months, depending on the number of iterations required. With each stability test estimated to cost upward of $225,000, this approach costs significant time, money, and testing waste.

Sanner provides a Quality-by-Design (QbD) approach for our customers in our Advance with Agility value proposition that combines our moisture management prediction program, Atmo Guard System®, with industry recognized predictive stability modeling by FreeThink Technologies' ASAPprime®. The Atmo Guard System evaluates the primary drug package with or without built-in desiccant to USP <671> moisture testing standards at 23°C/75% RH, thereby characterizing all aspects of moisture ingress for a given packaging design (ie, assembly joints, interference fit between cap and bottle). These results, when used with ASAPprime and empirical measurements (adsorption/desorption isotherms) on a unique drug product formulation, elucidate stability outcomes for the drug product and proposed packaging configuration modelled. This approach enables drug manufacturers to quickly and correctly select successful packaging during Phase 2B clinical trials, reducing or eliminating the need for long and costly probe stability testing. Reducing development time provides innovators a shorter commercialization timeline, allowing earlier revenue recognition for new products while providing a competitive edge in generic industry where the US first-to-file advantage provides the successful company with a 6-month exclusivity window in which they can recognize upward of 60% of their profits for that drug product alone.

Our Advance with Agility program doesn't end with the faster determination of the required stability solution, but provides consultative guidance on the designation of a commercially available desiccant product, the design of a custom, built-in, desiccant solution if requested, through to dispensing guidance for commercial packaging operations to optimize packaging uptime with unparalleled quality and efficiency.

Companies not only value Sanner's understanding of primary packaging design, materials of construction, moisture ingress, sorbent technology, and packaging operations, but the consultative approach in which we ensure all key stakeholders from formulation, R&D, package engineering, packaging operations, procurement, quality, and regulatory are engaged so all needs are addressed with efficiency and effectiveness. Advance with Agility is our promise to our customers to provide faster development, packaging changes, and time to market.

Q: As a provider of moisture control solutions for medical devices, diagnostics, and pharmaceutical products, does Sanner find itself at odds with environmental considerations?

A: The primary purpose of healthcare packaging is to preserve and protect products, ensuring they are safe and effective when used. As OSD formats remain a core focus, both physical and chemical stability challenges will persist making the elimination of plastics such as HDPE and PVC in primary packaging presentations with related desiccant use difficult to avoid.

We recognize there is a move toward sustainability across the board in the pharmaceutical industry, including both prescription and OTC products, with a significant rise in attention to the amount of plastic waste and the impact it is having on our global environment and public health. While the elimination of plastic in healthcare packaging is not readily viable, alternate sustainable solutions exist that include material selection, but forward-thinking design considerations and

regionalization of supply chains as customers aim to minimize their carbon footprint and de-risk supply chain risk that the recent COVID-19 pandemic highlighted.

Sanner offers BioBase®, the first package designed for effervescent tablets that is made from renewable and responsibly sourced raw materials. BioBase is nearly free of petroleum-based fossil raw materials, made from 94% plant-based material and responsibly sourced biopolymers, offering a substantially lower carbon footprint than the traditionally used polyethylene or polypropylene alternatives. BioBase has been proven to run efficiently on existing filling and packaging lines, supporting traditional labels, off-set print or in-mold labeling applications while being suitable for common recycling streams. Most impressive is that the BioBase solution offers improved moisture barrier, up to 40% longer shelf-life, than the traditional polypropylene tubes.

The cornerstone of our product development process is based around an understanding of, and interactions between resources, material efficiency, recyclability, and the design of biobased packaging options. Product development is governed by our IDP-Process, or Idea-Design-Product, which carefully evaluates all stages from the initial idea through to finished product by looking at: concept, design, prototyping, industrialization, commercialization, and life-cycle management. This stage-gate process empowers our team to ensure our cornerstone mandates are incorporated into every product we design at each stage of the development for our customers.

Sanner is committed to sustainability in a more comprehensive manner than the few examples I have provided here. We publish an annual sustainability report, which is available on our website. Of particular interest, Sanner has recently completed moving into our new flagship state-of-the-art facility located in the Green MedTech Park of Bensheim, Germany.

Q: What's next for Sanner?

A: Sanner Group's goal is to focus on building a suite of world leading services for its customers across the drug delivery, diagnostic, nutraceutical, and medtech device sectors. The recent acquisition of Gilero in Durham, and that of Springboard Pro, further position the business as a leading provider of end-to-end services across drug delivery, diagnostics, and medtech device sectors.

As we look to the future, Sanner Group will have a significant local presence in the North America CDMO industry anchored by Gilero and our new US manufacturing site in Greensboro, NC. This new facility, (60,500 square feet/5,620 square meters), on track to commence commercial production this summer (2025) will also support our current and evolving product portfolio in the pharmaceutical packaging and moisture management sector. Our investment in the North American market is an indication of Sanner's commitment to the industry by providing local, in-market, design, engineering, regulatory, quality, sales, and manufacturing support and expands our global manufacturing presence with sites currently in Germany, France, Hungary, and China.

Our US-based manufacturing site also addresses the comment I made previously regarding the regionalization of supply chains. Companies are increasingly aware of the cost of transporting goods, particular over great distances from one continent to another. This problem can be further exacerbated based on the type of product being transported. Our desiccant canisters have a high packaging density providing improved economics and carbon footprint over effervescent tubes that are akin to shipping "air". Our US site will provide our customers the ability to source key packaging solutions for their global manufacturing and packaging sites, greatly reducing their carbon footprint from transportation. A network that includes multiple manufacturing sites also fundamentally de-risks supply chain concerns. Should a disruption occur in one facility, our customers know we can continue to support their needs from another facility. The future will surely be an exciting time for Sanner and our customers. ◆

DRUG ADMINISTRATION

Protecting Patient Data in Cell & Gene Therapy: The Role of Tech Platforms

By: Matthew Lakelin, PhD

SAFEGUARDING PATIENT DATA IN THE CGT LANDSCAPE

Cell and gene therapies (CGTs) hold immense promise for treating previously incurable diseases, but their development and commercialization present unique challenges, particularly in safeguarding patient data. The sensitive nature of data used in CGTs, often involving personalized treatments and handling of genetic information, requires heightened attention to patient privacy and data security.

Protecting patient data is obligatory, and unique challenges are associated with managing sensitive information related to CGTs, including patient identification, chain of custody and identity, and the longitudinal nature of the patient journey. This journey encompasses various touchpoints, from diagnosis and starting material collection to manufacturing, treatment administration, and long-term follow-up.

Technology platforms are pivotal to the modern era of healthcare for safeguarding patient data and ensuring compliance with evolving regulations. This is essential given the diverse range of stakeholders involved in the CGT supply chain, from healthcare professionals, approved treatment centers (ATCs), and manufacturers to couriers and technology specialists, all of whom have a role to play in ensuring data security. However, the growing number of CGT products and their associated IT systems has led to healthcare providers experiencing "portal fatigue," with multiple platforms and logins creating confusion and inefficiency.

The following provides expert insights into the evolving landscape of patient data protection in CGT. It explores the need for robust and adaptable solutions to address the unique challenges of this field, emphasizing the importance of collaboration, standardization, and user-centric design in ensuring patient privacy and security throughout the CGT journey.

THE DATA-DRIVEN PATIENT JOURNEY

The patient journey in CGTs is a complex, data-intensive process, spanning from diagnosis and treatment selection to long-term follow-up. Each stage generates a wealth of data crucial for patient care, treatment efficacy, and regulatory compliance.

KEY TOUCHPOINTS IN THE CGT PATIENT JOURNEY

Diagnosis & treatment selection: Patient medical history, genetic information, and diagnostic tests are gathered to determine eligibility for CGT.

Sample collection: Data are captured regarding the collection, labelling, and transport of patient samples (e.g., blood or tissue) to the manufacturing facility.

Manufacturing: The manufacturing process generates data on cell processing, quality control, and batch records, ensuring the final product meets stringent quality standards.

Logistics & delivery: Data are tracked throughout the transport and delivery of the CGT product, including temperature monitoring, chain-of-custody records, and delivery confirmation.

High-Level Clinical Trial Supply Chain for Autologous Cell Therapies.

Treatment administration: Data are captured regarding the date, time, dosage, and any adverse events associated with the administration of the CGT product.

Post-treatment monitoring: Long-term follow-up data are collected to assess treatment efficacy, monitor for any long-term side effects, and contribute to ongoing research and development efforts.

The longitudinal nature of the CGT patient journey, often spanning months or even years, necessitates continuous data tracking and monitoring. However, the use of disparate systems and processes across different stakeholders can lead to data fragmentation and siloed systems. This fragmentation hinders efficient data management, making it difficult to gain a holistic view of the patient's and the drug product's journey and potentially compromising patient safety and treatment outcomes.

Orchestration platforms offer a solution to these challenges by providing a centralized system for managing data across the entire patient journey. These platforms can integrate with various systems and stakeholders, streamlining data flow and ensuring data integrity. By unifying data management, orchestration platforms enable real-time visibility into the patient's progress, facilitate better decision-making, and ultimately contribute to improved patient outcomes.

ENSURING CHAIN OF CUSTODY & IDENTITY FOR CGTS

Accurate patient identification is essential to the inherent personalized and time-sensitive nature of CGTs. The chain of custody and identity are vital throughout the complex CGT supply chain, and any errors or misidentifications can have a devastating impact on patient safety and treatment outcomes.

This CGT supply chain involves a vast network of stakeholders, from healthcare providers and manufacturers to couriers and testing laboratories. This intricate network presents a challenge in maintaining a secure chain of custody and identity, with a high risk of errors or misidentification. Such errors can lead to incorrect patient treatment, product contamination, or regulatory non-compliance.

To mitigate these risks, technology platforms, especially orchestration platforms, are critical for ensuring accuracy throughout the CGT supply chain. These platforms can leverage unique identifiers, such as ICCBBA's Chain of Identity (CoI) Identifier and other tools to track the CGT product at every step, from sample collection to treatment administration. For instance, a unique identifier can be assigned to each patient given therapy, allowing it to be tracked as it moves through the manufacturing process, quality control checks, and final delivery to the patient. This ensures that the right product is administered to the right patient at the right time.

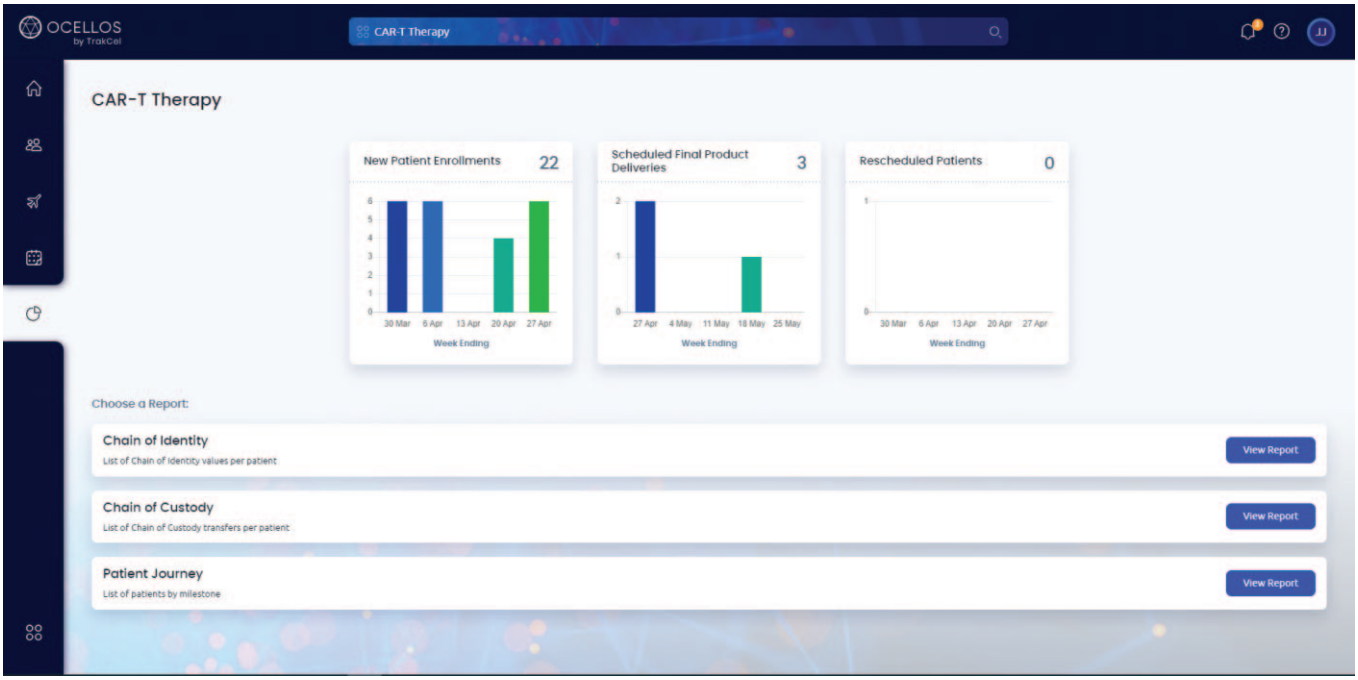
Technological integration has also been key in replacing paper-based systems that are not sufficient for a compliant chain of identity or custody when commercially supplying CGTs. Electronic systems utilizing orchestration platforms offer a more secure and reliable method for tracking and managing patient data, mitigating the risk of errors, and ensuring compliance with regulatory standards.

These orchestration platforms offer numerous advantages in maintaining the chain of custody and identity:

Centralized data management: These platforms provide a centralized system for managing patient and product data, ensuring that all stakeholders have access to the necessary accurate information.

Real-time tracking: Orchestration platforms allow for real-time tracking of the CGT product throughout the supply chain, providing complete visibility into its location and status.

Reduced risk of errors: By automating data capture and tracking, these platforms minimize the risk of human error and ensure data accuracy.



Screenshot Showing Analytics for a CAR-T Therapy From OCELLOS, TrakCel's Orchestration Platform

Improved compliance: Orchestration platforms help ensure compliance with regulatory requirements by providing auditable records of the chain of custody and identity.

PATIENT DATA PROTECTION & SECURITY: SAFEGUARDING SENSITIVE INFORMATION

The generation of data surrounding genetic information, medical history, and other personally identifiable data highlights the need for patient data protection and security in CGTs. The regulatory landscape surrounding patient data protection is constantly evolving, fuelled by the advancement of technologies and an increasing number of ways to collect and apply these data. Regulations such as the General Data Protection Regulation (GDPR) and the Health Insurance Portability and Accountability Act (HIPAA) set stringent standards for data privacy and security. For example, GDPR mandates the pseudonymization or anonymization of personal data whenever possible, which can be particularly challenging in CGTs where treatments are often tailored to individual patients. HIPAA, on the other hand, requires the implementation of safeguards to ensure the confidentiality, integrity, and availability of electronic protected health information (ePHI), which includes CGT patient data.

The healthcare sector is a prime target for cyberattacks and data breaches, which can have severe consequences for patients, including identity theft, financial loss, and reputational damage. To mitigate these risks, technology platforms handling CGT patient data must implement robust security measures:

Data encryption & anonymization: Encrypting data at rest and in transit helps protect it from unauthorized access, while anonymization techniques can help de-identify sensitive information.

Access controls & user authentication: Implementing strong access controls and multi-factor authentication helps ensure that only authorized personnel can access patient data.

Regular security audits & vulnerability assessments: Conducting regular security audits and vulnerability assessments helps identify and address potential security risks.

Disaster recovery & business continuity plans: Having comprehensive disaster recovery and business continuity plans in place ensures that patient data can be recovered and operations can continue in the event of a cyberattack or other disruption.

Single sign-on (SSO): Implementing SSO can improve security by reducing the number of passwords users need to remember, making it less likely that they will use weak or easily guessed passwords. It can also

make it easier for users to access multiple applications, which can improve efficiency and productivity.

In addition to these technical measures, appropriate policies and procedures are essential to ensure that patient data is handled responsibly and ethically. This includes training staff on data privacy and security best practices, establishing clear procedures for data access and disclosure, and regularly reviewing and updating these policies to reflect the evolving regulatory landscape, threat landscape and best practices in data protection.

THE ROLE OF ORCHESTRATION PLATFORMS IN PROTECTING PATIENT DATA

Orchestration platforms can play a crucial role in safeguarding patient data throughout the CGT journey. These platforms act as a central hub for managing data from various sources and stakeholders, streamlining the data management process and enhancing security.

Key features and functionalities of orchestration platforms that contribute to data protection and security include:

Robust chain of custody & identity tracking: Orchestration platforms can track the chain of custody and identity of patient samples and CGT products at every stage, from sample collection to treatment administration. This helps prevent errors and ensures that the right patient receives the right treatment. Orchestration platform design should incorporate a full risk assessment of proposed new features to ensure that these do not introduce a risk of data breaches.

Secure data storage & access controls: These platforms provide secure data storage and access controls, ensuring that sensitive patient data is protected from unauthorized access. They can also help organizations comply with data privacy regulations such as GDPR and HIPAA. For example, systems should employ role-based data access to ensure that personally identifiable information is only visible to personnel who need to see it.

Real-time monitoring & alerts for potential data breaches: Orchestration platforms can monitor data in real-time and generate alerts if any suspicious activity is detected, helping to prevent and mitigate data breaches.

By centralizing and streamlining data management, orchestration platforms can help CGT providers improve patient safety, treatment outcomes, and compliance with data privacy regulations. This not only benefits patients but also helps build trust and confidence in the CGT industry.

A COLLABORATIVE APPROACH TO CGT DATA PROTECTION

Protecting patient data is vital and obligatory in the rapidly evolving CGT landscape. As therapies become more personalized and complex, the need for robust data management and security measures intensifies. Technology, especially orchestration platforms, plays a vital role in addressing the unique challenges of CGT data management, including chain of custody, identity verification, and secure data transfer.

However, technology alone is not enough. Ensuring patient privacy and security requires ongoing vigilance and collaboration among all stakeholders in the CGT ecosystem. This includes healthcare providers, manufacturers, technology developers, regulators, and, most importantly, patients. Open communication and collaboration are crucial to staying ahead of the curve in this dynamic landscape. By sharing best practices, challenges, and solutions, stakeholders can collectively contribute to a more secure and efficient CGT environment.

We encourage further exploration of data protection best practices and the use of orchestration platforms in CGT. By working together, we can ensure that these life-changing therapies reach patients safely and effectively while safeguarding their sensitive data. ◆

BIOGRAPHY

Dr. Matthew Lakelin is Head of Consultancy Services & Co-Founder of TrakCel. He earned his PhD in Pharmacology and has over 20 years of experience working in the pharmaceutical and biotechnology industry. He has led the deployment of TrakCel's software to a wide range of advanced therapies (including CAR-T, TILs, personalized immunotherapies, neoantigen cancer vaccines) and in his role as Head of Consultancy Services is a key spokesperson and responsible for ensuring that TrakCel solutions continue to evolve to meet industry needs.

FACILITY DESIGN

Holistic Facility Design in Injectable Fill-Finish Operations

By: Chad Hafer

INTRODUCTION

The implementation of the EU's Annex 1 regulations has introduced new standards for contamination control and sterility assurance in injectable fill-finish operations, encouraging the industry to adopt more advanced, automated systems that reduce human intervention. While meeting these standards is crucial, it is just one part of the larger picture. Companies need to consider a more comprehensive approach that not only ensures compliance but also incorporates cutting-edge technologies and prioritizes sustainability.

FROM REACTIVE COMPLIANCE TO PROACTIVE PLANNING

A reactive approach to regulatory compliance in fill-finish operations involves retrofitting existing facilities to meet new standards. While sometimes necessary, this method can lead to increased costs, operational inefficiencies, and potential quality risks. The introduction of Annex 1 offers an opportunity to reconsider this approach.

Annex 1, a crucial component of the European Union's Good Manufacturing Practice (GMP) guidelines, specifically addresses the manufacture of sterile medicinal products. Revised significantly in 2022, it sets forth stringent requirements for contamination control and sterility assurance in pharmaceutical manufacturing. The updated Annex 1 places a strong emphasis on quality risk management, introducing the concept of contamination control strategy (CCS) as a holistic approach to maintaining sterility throughout the manufacturing process.[1]

Key aspects of Annex 1 include:

- Enhanced focus on a quality risk management approach
- Implementation of contamination control strategy (CCS)
- Increased emphasis on the use of barrier technologies and closed systems
- Stricter environmental monitoring requirements
- Greater attention to personnel training and behavior in cleanroom environments

The revised Annex 1 guidance represents a paradigm shift in how sterile products are manufactured, emphasizing a proactive, risk-based approach rather than a reactive one. Compliance with Annex 1 is not just about meeting regulatory requirements; it is about fundamentally improving the quality and safety of sterile medicinal products. By reducing the risk of contamination, Annex 1 aims to enhance patient safety and product efficacy.

Rather than viewing Annex 1 compliance as a hurdle, forward-thinking companies are viewing it as a chance to innovate. By adopting a more holistic approach that considers compliance, technology, and sustainability from the outset, these organizations are not just meeting current standards — they are preparing for future changes as well.

HOLISTIC FACILITY DESIGN

A holistic view of facility design is central to a future-forward mindset. This approach envisions comprehensive systems engineered with Annex 1 compliance and future adaptability as foundational principles. Facilities designed with this holistic perspective incorporate several key features that set them apart from traditional manufacturing sites.

First and foremost, these facilities integrate compliance into

A rendering of an Annex 1 compliant fill suite containing isolator technology.

every aspect from the ground up. Annex 1 standards are not afterthoughts but are woven into the basic design, influencing everything from the overall facility layout down to individual process steps. This integrated approach to compliance reduces the need for future retrofitting and ensures that regulatory requirements are met efficiently and effectively.

Technology readiness is another crucial aspect of this holistic design philosophy. Recognizing the rapid pace of technological advancement in the pharmaceutical industry, these facilities are designed with the flexibility to adopt new technologies as they emerge. This foresight creates spaces that can accommodate new equipment and processes without requiring major renovations, thus future-proofing the facility against technological obsolescence.

Sustainability considerations are also a key component of this holistic approach. Environmental factors are carefully considered in the facility design, from the implementation of energy-efficient isolator technologies to the optimization of resource use. This focus on sustainability not only reduces the environmental impact of pharmaceutical manufacturing but can also lead to significant cost savings over the long-term.

Risk reduction is a primary focus in every aspect of these holistically designed facilities. By going beyond current regulatory requirements and anticipating potential future standards, these facilities are designed to minimize contamination risks at every stage of the manufacturing process. This proactive approach to risk management helps ensure product quality and patient safety while also preparing the facility for potential future regulatory changes.

Finally, operational flexibility is built into the core of these facilities. In an industry characterized by changing market demands and evolving regulatory landscapes, the ability to adapt quickly is a significant advantage. Facilities designed with this holistic perspective can more easily adjust to new product lines, manufacturing processes, or regulatory requirements, providing a competitive edge in a dynamic industry.

By embracing this holistic approach to facility design, pharmaceutical companies and CDMOs can create manufacturing environments that are not only compliant with current regulations but are also well-positioned to meet the challenges of the future. This forward-thinking strategy represents a significant shift in how the industry approaches fill-finish operations, emphasizing long-term sustainability, adaptability, and excellence in pharmaceutical manufacturing.

TECHNOLOGY INTEGRATION

While automation has been a topic of discussion in the industry for some time, holistic facility design takes this concept further. The goal is to create an integrated technological ecosystem, not just to automate individual processes.

ADVANCED ISOLATOR TECHNOLOGY

A cornerstone of technological integration in modern fill-finish operations is advanced isolator technology. This innovation represents a significant leap forward from traditional cleanrooms or basic restricted access barrier systems (RABS), offering a level of contamination control that is particularly well-suited to meet the stringent requirements of Annex 1.[2]

Modern isolators provide complete physical and aerodynamic separation between operators and the critical aseptic processing area. This separation is achieved through a fully enclosed, highly controlled environment that significantly minimizes the risk of human-borne contamination. The isolator's design typically includes glove ports for manipulations, transfer ports for materials, and a sophisticated air handling system that maintains a sterile environment.

One of the key advantages of isolator technology is its ability to maintain a consistent, high-quality environment. Unlike traditional cleanrooms, which can be subject to fluctuations due to personnel movement and other factors, isolators provide a stable, controlled space that can be more easily validated and maintained. By providing a physical barrier between the product and potential sources of contamination, isolators address one of the pri-

mary concerns of Annex 1 regulations. Moreover, the closed nature of isolator systems allows for more effective decontamination procedures, further enhancing sterility assurance.

Beyond compliance and risk reduction, isolator technology offers significant operational and sustainability benefits. These systems typically require less energy for environmental control compared to traditional cleanrooms. The smaller volume of space that needs to be maintained at critical environmental parameters (temperature, humidity, particulate levels) translates to reduced HVAC requirements and lower energy consumption.[3]

The implementation of isolator technology does come with its own set of challenges. The initial capital investment can be significant, and staff require specialized training to operate these systems effectively. Additionally, the design and validation of isolator systems require careful consideration to ensure they meet all regulatory requirements and operational needs.

Despite these challenges, the benefits of advanced isolator technology in meeting Annex 1 requirements, reducing contamination risks, and improving operational efficiency make it a key consideration for companies adopting a holistic approach to fill-finish operations. As the pharmaceutical industry continues to evolve, isolator technology is likely to play an increasingly important role in ensuring the quality and safety of sterile products.

EXPANDING AUTOMATION

The industry is exploring more advanced automation, with robotic systems capable of performing complex tasks within isolators. These robots can handle delicate components and perform precise manipulations, further reducing the need for human intervention in critical processes.

An isolated syringe filling line. To go next to advanced isolator technology paragraph.

For example, automatic bag opening systems are helping to eliminate the variability and potential contamination risks associated with manual handling. These systems consistently open sterile barriers, reducing the chance of accidental contamination or damage to packaging materials.

ENHANCING QUALITY ASSURANCE THROUGH AI/ML

Artificial intelligence (AI) and machine learning (ML) are beginning to play a role in fill-finish operations. AI algorithms can analyze large amounts of data to identify potential quality issues before they occur, allowing for preventive actions. This shift towards more proactive quality management represents a significant step forward in ensuring product consistency and safety.

ML models have the potential to optimize process parameters in real-time, helping to ensure consistent product quality even under varying conditions. This dynamic process adjustment capability could help reduce waste and improve overall operational efficiency.

EVOLVING QUALITY MANAGEMENT

The holistic approach to fill-finish operations requires a fresh look at quality management systems. The goal is to integrate quality considerations into every aspect of the operation.

Electronic batch records (EBR) systems represent an important advancement in quality management. These systems provide real-time tracking of interventions, help ensure compliance with standard operating procedures, and maintain accountability throughout the manufacturing process. The digital approach can enhance data integrity, reduce the risk of human error in documentation, and provide a clear audit trail for regulatory inspections.

Complementing EBR systems, advanced video monitoring and microstep analysis technologies are improving risk assessment capabilities. These tools allow for continuous process monitoring and can detect subtle deviations that might be missed by human observation. By identifying potential issues early, these technologies contribute to more proactive quality management.

Process Failure Mode and Effects Analysis (PFMEA) is also becoming in-

creasingly important. This systematic approach to identifying potential failures is being integrated earlier in the design phase of new facilities and processes. By anticipating potential issues and designing mitigation strategies from the outset, organizations can create more robust and reliable fill-finish operations.

SUSTAINABILITY AS A DESIGN CONSIDERATION

In the past, sustainability was often a secondary consideration in pharmaceutical manufacturing. However, in advanced facilities, it's becoming a more integral part of the design process, influencing various aspects of the operation.

The shift to isolator technology not only enhances sterility assurance but can also reduce energy consumption. Isolators typically require smaller HVAC systems compared to traditional cleanrooms, which can lead to energy savings.

Purpose-built facilities are often designed with an eye towards minimizing water usage and overall utility consumption. By adopting lean methodologies, these facilities can reduce waste, optimize resource use, and improve overall operational efficiency. This not only reduces the environmental impact but can also contribute to long-term cost savings.

THE POTENTIAL OF GEOGRAPHIC LOCALIZATION

Geographically optimized production is emerging as a strategy for potentially reducing both costs and environmental impact. Centrally located facilities can minimize transportation risks, which is particularly important for temperature-sensitive biologics. Fewer touchpoints in the distribution process may also reduce the risk of product tampering or diversion and could allow for quicker adaptation to market demands and supply fluctuations.

A holistic approach can extend beyond the physical facility to encompass a range of services. Comprehensive, end-to-end services can provide a single point of contact for multiple needs, potentially simplifying communication and problem-solving. This can allow for a more unified quality system and a cohesive approach across the production process. By reducing the need to coordinate multiple vendors, integrated services may help reduce time-to-market for new products.

PREPARING FOR FUTURE SHIFTS

While Annex 1 compliance is a current focus, a holistic mindset for facility design considers potential future regulatory changes as well. This forward-thinking approach aims to ensure that these facilities can adapt to new requirements without major overhauls, which could provide a competitive advantage.

The future of injectable fill-finish operations involves not just meeting current standards but creating adaptable, efficient, and sustainable operations that can evolve with the industry. By adopting a holistic approach that considers compliance, technology, and sustainability from the ground up, pharmaceutical companies and CDMOs can position themselves well within the industry.

Advanced fill-finish facilities represent more than just a new way of manufacturing; they embody an approach that prioritizes quality, efficiency, and environmental responsibility. As the industry continues to evolve, those who embrace this holistic approach find themselves well-positioned to navigate an increasingly complex and demanding market.◆

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BIOGRAPHY

Chad Hafer is the Director of Technical Operations at Kindeva Drug Delivery, bringing over 10 years of experience in aseptic operations. Currently, he is spearheading the design and construction of Kindeva's aseptic injectable fill-finish facility in Bridgeton, MO. He earned a Bachelor of Science degree in Chemistry, a Master of Science degree in Project Management, and a Master of Engineering.

CLINICAL TRIALS

Solving Clinical Trial Challenges Through Sub-Population Optimization and Modeling Solution

By: Adrian Kizewski, MSc, MBA

INTRODUCTION

Clinical trials are the foundation of medical research, paving the way for groundbreaking therapies and treatments. However, these trials often face significant challenges, including high failure rates, substantial costs, and complex patient recruitment. In recent years, a revolutionary approach known as Sub-population Optimization & Modeling Solution (SOMS) has emerged to transform the landscape of clinical trials and offer new hope for more efficient and successful studies.

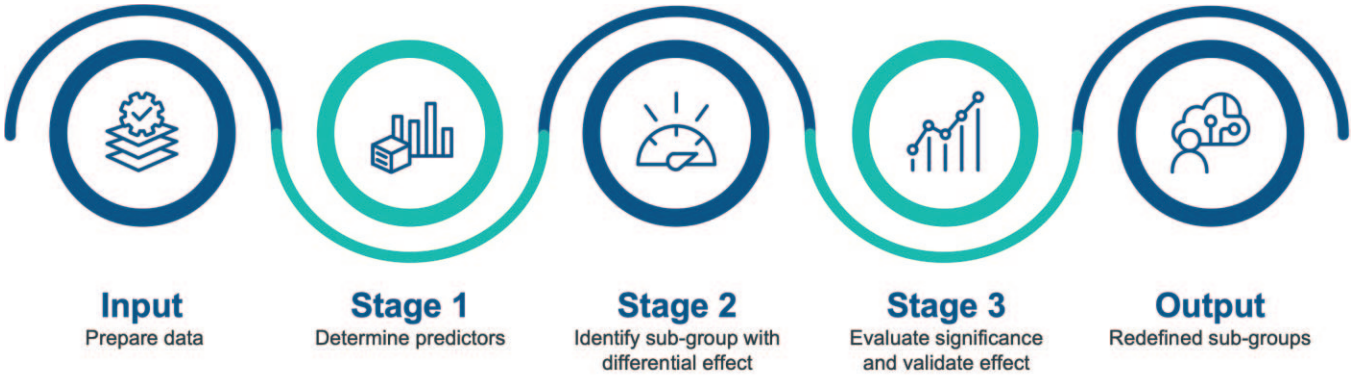
WHAT IS SOMS?

SOMS represents a shift in how clinical trials are conducted and analyzed. A sophisticated tool, SOMS leverages artificial intelligence (AI) and advanced analytics to identify biomarkers within specific patient subgroups that can predict treatment response. This capability helps researchers identify patient subgroups with higher efficacy and/or risk for adverse events, which significantly boosts the likelihood of trial success.

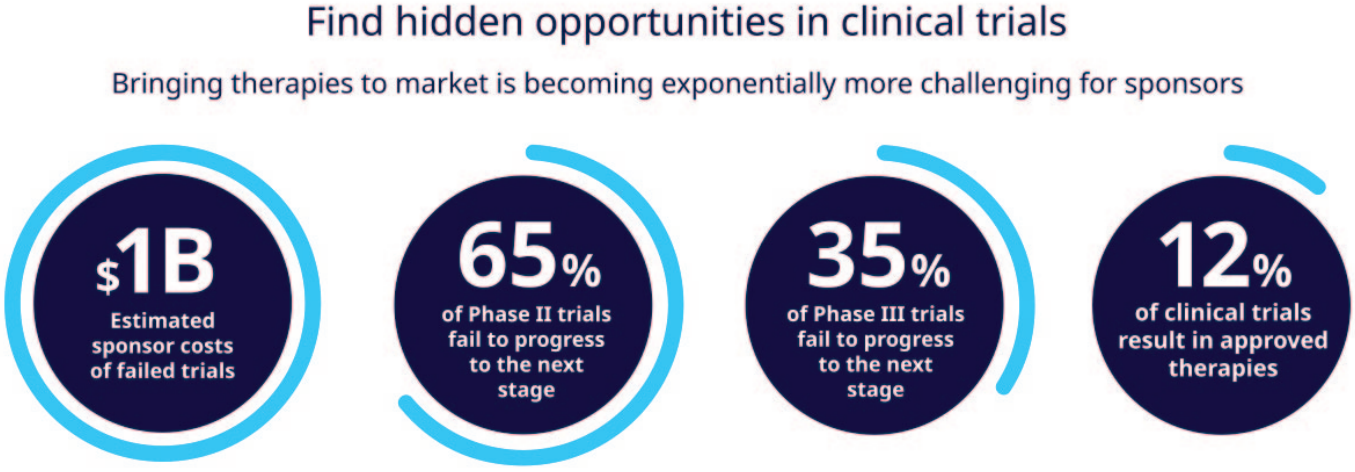
A MULTITUDE OF BENEFITS

One significant advantage of SOMS is its ability to progressively enhance trials throughout the process. From the outset, researchers can track subgroups, validate initial hypotheses, and run ongoing biomarker analyses to uncover new subgroups. This dynamic approach stands in stark contrast to traditional methods, which often rely on predetermined variables and static analysis. Trials that do not start with SOMS can still benefit from its introduction later, especially in cases of slow patient recruitment or minimal differences in treatment responses between treatment and placebo groups.

The power of SOMS includes real-time analysis, trial simulation, and benchmarking. Using simulated or real-world data, researchers can predict trial outcomes based on specific patient pool characteristics. This feature allows sponsors to simulate various scenarios and incorporate historical data to create more accurate patient pools. Moreover, SOMS can compare standard treatments or other therapies in a specific therapeutic area/indication to provide important insights into the potential performance of a new therapy in real-world situations.



A Typical SOMS Process



Taking a molecule to market is becoming exponentially difficult for sponsors every year.

The importance of SOMS becomes particularly apparent when considering the substantial costs and high failure rates associated with clinical trials. Taking a therapy through all trial stages can exceed $1 billion, with failure rates of 65% in Phase 2 and 35% in Phase 3. Even more concerning, only 12% of therapies that complete Phase 3 receive FDA approval.[1] In this challenging landscape, SOMS offers a lifeline, helping to optimize trials and control for elements that might otherwise go unnoticed or take too long to identify.

One of the key strengths of SOMS lies in its AI integration. In contrast to traditional statistical methods in which statisticians decide variables beforehand, SOMS uses a data-driven approach to analyze multiple variables at once. This allows the AI to evaluate exponential permutations and comprehensively analyze all possible patient subgroups that might respond better to therapy or have improved safety profiles.

SOMS demonstrates impressive processing efficiency. Once data has been prepared, SOMS can generate analyses within 30 seconds for Phase 1 and Phase 2 data, or within a couple of hours for larger Phase 3 datasets. A comprehensive analysis, including data preparation, can be achieved within a week. This translates to a significant, near 20x reduction in analysis time compared to traditional methods, enabling continuous optimization throughout the trial lifecycle.

SOMS's credibility stems from its use of validated, open-source algorithms with a proven track record, which lends weight to results presented to health authorities. The system also offers flexibility, allowing users to modify various criteria as needed. Its repeatability across trials within a portfolio, with consistently prepared data and adapted algorithms, has proven effective across multiple therapeutic areas.

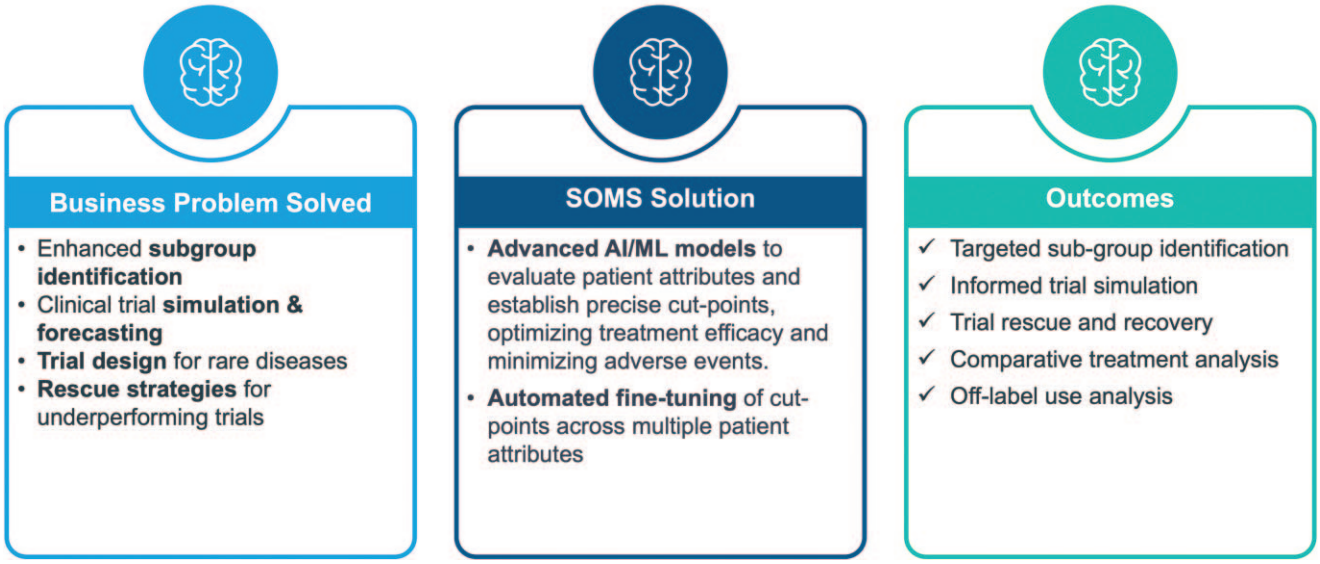
KEY REAL-WORLD APPLICATIONS

One of the most critical applications of SOMS is to implement rescue strategies for struggling clinical trials. Common indicators of a trial in distress include unexpected adverse events or lack of efficacy in the treatment group. When such issues arise, SOMS can intervene with targeted rescue strategies. For instance, in a Phase 3 trial with serious adverse events in a subset of patients, SOMS can quickly analyze the data to predict which subgroups are more susceptible to these events.

A real-world example of SOMS's effectiveness is from a Phase 3 trial in multiple myeloma that needed to identify patient subgroups at increased risk for cardiac failure. Using SOMS, researchers analyzed 25 various biomarkers, including demographic and disease characteristics. The analysis revealed two specific biomarkers within the patient population that indicated an increased risk of cardiac issues. This data empowered sponsors to focus on high-risk groups, implement protective measures and introduce interventions to mitigate the incidence of cardiac failure.

SOMS's ability to identify and optimize effective subgroups within a trial is another crucial feature. To address various analytical needs, the platform offers three versions of the core algorithm, called Subgroup Identification Based on Differential Effect Search (SIDES). These variations include the basic SIDES algorithm, fixed SIDES and an adaptive SIDES. These algorithmic methods enable SOMS to analyze trial data with high accuracy and configurability to effectively identify patient subgroups with precision.

While SOMS excels at finding patterns when they exist, it is important to note that



Deploying SOMS' advanced AI/ML solves tangible business problems with tangible outcomes.

not every trial will have clear subgroup distinctions. The impact of SOMS-driven safety measures on trial integrity and success rates depends on several factors, including the specific findings for each trial, the nature of the identified risks, and how researchers choose to act on the information SOMS provides.

When addressing patient recruitment challenges, SOMS takes a unique approach. Rather than directly improving recruitment numbers, SOMS enhances the quality and relevance of the recruited patients. This "fewer but right" approach can lead to better trial outcomes in the long-term, including potentially faster recruitment due to a more focused pool.

The therapeutic and financial outcomes of using SOMS in clinical trials are significant. In one instance, a Phase 3 trial for a new antibacterial treatment initially showed no overall treatment effect. By analyzing 26 biomarkers, SOMS identified a subpopulation with a strong enough response to secure FDA approval. This intervention not only resulted in a successful drug launch for a particular patient subgroup but also prevented a late-stage failure, potentially saving pharmaceutical companies hundreds of millions of dollars.

SOMS offers valuable support to sponsors throughout clinical trials, from design to closeout. Its versatility allows application across the entire trial lifecycle, with a particularly significant impact between Phase 2 and Phase 3. In Phase 1, SOMS can leverage existing data from the therapy in different indications or from similar compounds to simulate patient responses. The simulated data helps inform Phase 2 design and patient selection.

The transition from Phase 2 to Phase 3 often sees the greatest impact of SOMS. By analyzing data from both Phase 1 and Phase 2, SOMS can refine inclusion/exclusion criteria, identify responsive subgroups, and ultimately optimize overall trial design for Phase 3. These capabilities significantly increase the chances of trial success and regulatory approval. SOMS's value extends beyond Phase 3. It can also be used in post-approval phases to benchmark the therapy against standards of care.

LOOKING AHEAD

SOMS holds significant promise for the future of clinical trials. While SOMS currently operates independently, future developments aim to integrate it with data management systems. This will enable real-time analysis as data streams in, allowing for dynamic trial management with identification of emerging risks and opportunities. In addition, incorporating SOMS into risk-based quality management tools will enhance risk prediction and mitigation to leverage automated workflows.

The evolution of algorithms is also a critical area. Currently, SOMS uses a generalized approach across various indications. The future lies in specialized algorithms for specific therapeutic areas. These will provide more nuanced and accurate insights, especially in early signal detection. Custom algorithms tailored to specific contexts are being developed to better predict efficacy and safety events, leading to more precise insights for different therapeutic areas and trial types.

As AI and advanced analytics mature, their role in clinical trial optimization will grow significantly. The trend is toward

more integrated, intelligent, and responsive systems. AI is likely to impact various aspects of trial design, conduct, and analysis, including sophisticated predictive modeling, automated patient matching and recruitment, real-time data analysis and AI-assisted protocol design.

Advanced analytics hold the potential for targeted approaches leading to adaptive trial designs that evolve based on incoming data. This could significantly reduce the time and cost of bringing new treatments to market. Integrating diverse data sources, like real-world evidence and genetic information, could lead to a more comprehensive understanding of treatment effects and patient responses, with AI playing a crucial role in synthesizing insights from these complex datasets.

As these technologies evolve, ethical considerations and explainable AI will be increasingly important. AI-driven decisions in clinical trials must remain transparent, interpretable and aligned with patient safety and regulatory requirements. The future of clinical trial optimization with tools like SOMS and other AI-driven solutions points toward more efficient, precise, and adaptive trials. This has the potential to revolutionize how new therapies are developed and brought to market.

SOMS is a powerful solution for many clinical trial challenges. By leveraging advanced analytics and AI, it offers a data-driven approach to optimizing patient subgroups, predicting outcomes and enhancing overall trial efficiency. As the field continues to evolve, SOMS and similar technologies are poised to play a crucial role in shaping the future of medical research and drug development, ultimately leading to better treatments and improved patient outcomes. ◆

REFERENCE

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9293739/

BIOGRAPHY

Adrian Kizewski is Associate Director of Product Management at IQVIA. He brings expertise spanning R&D and clinical life sciences, business analysis, process design and improvement, and product implementation. He is currently a lead for IQVIA's Clinical Data Analytics Solution (CDAS) as well as Subpopulation Optimization and Modeling Solution (SOMS). He earned his MBA from the McDonough School of Business at Georgetown University, in addition to his MSc in Pharmacology from The Johns Hopkins University School of Medicine and a BSc in Biochemistry from Temple University.

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