Drug Development & Delivery

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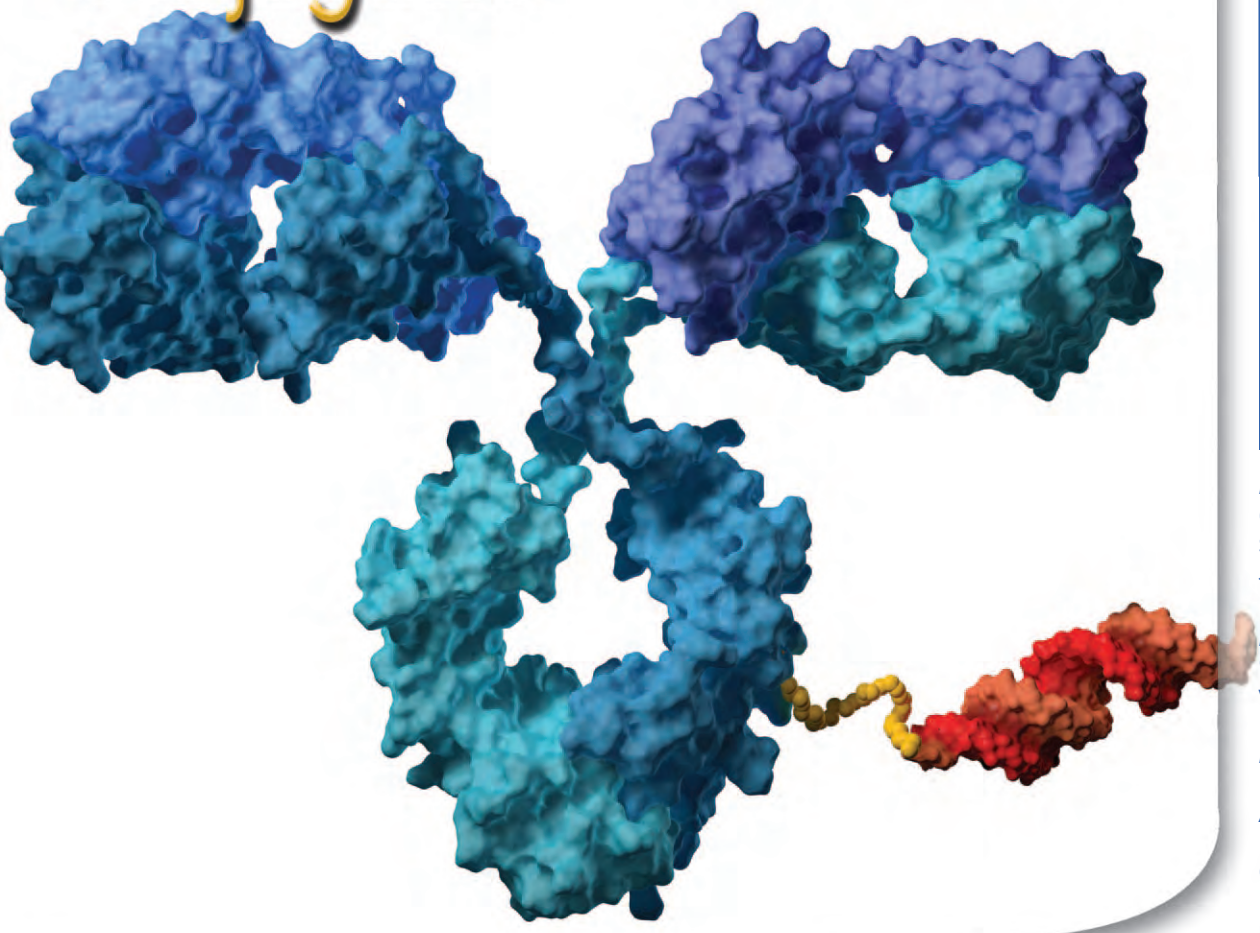
Antibody Oligonucleotide Conjugates



The Science & Business of Pharmaceutical and Biological Drug Development

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Special Feature

Outsourcing Formulation Development & Manufacturing: Going Beyond the Science to Become True Partners

By: Cindy H. Dubin, Contributor

Contract Development and Manufacturing Organizations (CDMOs) are critical partners for pharma and biotech companies when it comes to providing innovative solutions that advance the next generations of therapies. To that end, CDMOs are seeking to modify contracts to maintain competitiveness and maximize revenue growth. The top three contract modification priorities are adding more indices, extending contract durations, and ensuring adaptability to shifting market requirements.[1]

Small-molecule specialized CDMOs with expertise in complex formulations, such as (HPAPIs)are growing in importance. The global small-molecule CDMO market will reach almost $85 billion in 2032, up from $45 billion in 2022.[2] While not growing quite as significantly, the global large-molecule CDMO market was valued at $11.6 billion in 2023 and is expected to jump to almost $20 billion in 2029. This market revolves around biologics, monoclonal antibodies, therapeutic proteins, and biosimilars.[3]

Both play a critical part in process development, complex manufacturing processes, and regulatory compliance. "As we continue

Sterile vial filling in Eurofins' closed robotic isolator via filler.

to see the industry evolve post-COVID, 2023 continued to be a difficult year when it came to rising inflation impacting biotech funding and M&A," says Dr. Andrew Lewis, Chief Scientific Officer, Quotient Sciences. "One major takeaway from 2023 was evident: with the best science, it's possible to weather the storm and make truly ground-breaking advancements. We are already seeing turnarounds in 2024, with CDMOs increasingly viewed as strategic partners."

For instance, contractors are providing less off-the-shelf programs, and are instead going deeper to work on the science needed to enable all parts of a program. He says: "The scientific acumen of the outsourcing provider and quality of scientific output can be the deciding factor in a program's success or failure."

In this exclusive, annual report, leading CDMOs speak with *Drug Development & Delivery* about how they are adapting to bio/pharma client needs, their capabilities in handling complex molecules, and how they are transforming from specialist contractors to true partners.

Abzena: A Two-Pronged Approach to Formulation

Abzena offers a customer-centric approach across a range of formulation and manufacturing services that support a biopharmaceutical product throughout its entire lifecycle, from the initial preformulation and generation of a formulation to support toxicology and first-in-human (FIH) clinical trials through to clinical in-use studies, formulation optimization, robustness, and device interaction studies. This enables customers to utilize a single organization for all their formulation and manufacturing requirements, which

Using key technologies, like the Prometheus Panta, Abzena generates critical stability data that aids in the candidate selection process and streamlines formulation development activities.

streamlines and de-risks the process and allows any experience and learnings to be shared across teams, says Gary Watts, PhD, Senior Manager of Analytics at Abzena. This first-hand knowledge of the product can then be applied to rapidly solve any complex problems that may arise downstream.

Broadly speaking, Abzena applies two approaches to formulation studies: First-in-Clinic approach, which is a streamlined methodology focused on enabling the customer to obtain FIH results in the shortest time possible; and a Best-in-Clinic approach, focused on providing a superior product format to the competitors, often applied after Phase 1.

"A practical example of these approaches is where a customer applies the streamlined approach to get to the clinic quickly using a simple formulation at low drug concentration (for intravenous administration), utilizing frozen storage," explains Dr. Watts. "The aim is to ensure there are no adverse events when the drug is administered. The same drug would then be reformulated to provide a 'best-in-clinic' product once known to be safe and efficacious, which could involve concentration of the drug to allow for subcutaneous administration, and optimization of the formulation to maintain a viscosity that is readily injectable, and a product stable to long-term storage at refrigerated temperatures."

He describes how one customer acquired a novel monoclonal antibody (mAb) that was formulated at another CDMO where the approach did not assess the fundamental properties of the mAb. This resulted in phase separation and gelation during refrigerated storage. "These issues were resolved by warming to room temperature (without any apparent impact on quality), however, this was not ideal from a regulatory perspective or for patient administration," Dr. Watts says.

A study was designed to evaluate the fundamental factors crucial to formulation stability and an optimal formulation was identified that showed the desired physical and chemical stability, and was clear, colorless, and free of visible particles after >6 months storage at 2-8°C. In addition, Watts says solubility was sufficiently improved to allow the concentration to be increased to 100mg/mL from 50mg/mL, in line with the customer's requirements.

Over the last couple of years, the proportions of projects based on antibody-

drug conjugates (ADCs), multi-specifics, and vaccines have increased noticeably, making it more important for suppliers to offer customers a streamlined approach to the clinic. "To that end, Abzena's mission is to move new medicines forward to patients faster and we've been investing in our capabilities and forming strategic partnerships to support that," says Dr. Watts.

For example, for the newly launched cell line development platform, AbZelect™, Abzena forged a partnership with ProteoNic Biosciences BV to license their premium protein expression technology, 2G UNic®. This vector technology will significantly improve the production of high-yielding CHO cell lines for Abzena's customers, he says. "By partnering with ProteoNic, we further enhance our existing offering by providing customers with a premium solution that increases the production levels for even the most challenging and complex proteins."

For customers with complex biologics in discovery, the DRIVE-Bio partnership with OncoDesign Services offers an ecosystem of support. Dr. Watts says: "DRIVE-Bio leverages the skills and expertise to develop antibodies in oncology and inflammation through a privileged collaboration that combines Abzena's discovery, development, and manufacturing support of biologics and ADCs with OncoDesign Services' capabilities in optimization to lead selection of naked or pay-loaded preclinical candidates vs target product profile."

Adare Pharma Solutions: Setting Standards in Patient-Centric Solutions

Adare Pharma Solutions is a global technology-driven CDMO providing end-to-end, integrated services, from early-stage development and formulation to commercial-scale manufacturing and packaging. The company has amassed decades of small-molecule expertise focusing on a variety of oral dosage forms including solid dose, capsules, and liquids. The company's technology platforms provide taste masking solutions, customized dose-release profiles, solubility enhancement, and patient-centric dosing solutions. From its seven facilities in the US and Europe, Adare has developed and manufactured more than 65 products that are marketed worldwide.

One customer is a mid-size pharma company with an effective drug product for the treatment of tremors and other persistent, uncontrolled body movements associated with certain neurological conditions. An estimated 5% to 10% of patients with these neurological conditions have dysphagia, which is difficulty swallowing or the inability to swallow.

"Working with the customer, we developed a sprinkle form of the drug that addresses the needs of dysphagic patients," explains Nathan Dormer, Director, Drug Product Development & Site Leader at Adare Pharma Solutions. "These oral granules can be mixed with food or liquid and easily swallowed, improving medication adherence and patient comfort."

Approved by the FDA in April 2024, the sprinkle form is now available in North America, with clinical trials underway for expanded global markets. Dr. Dormer says: "This patient-centric solution highlights Adare's commitment to addressing real-world patient needs, enhancing quality of life, and setting a new industry standard."

Adare is also setting some standards for how it deploys Artificial Intelligence to advance scanning capabilities, giving fresh perspectives on molecules and formulation characteristics. The company is using AI to predict how formulations and molecules will perform in the clinic, guiding partners to focus resources on the most promising candidate formulations and giving the program the highest probability of success in subsequent clinical studies, saving the sponsor time and money.

"Looking to the future, Adare recently reviewed over 25 AI applications and prioritized further focus on those most likely to differentiate our services to clients and speed programs to the clinic, and ultimately to patients," he says.

Adare also embraces ESG principles, driving ethical standards and positive impact across its operations. "With safe and effective solutions, these principles prioritize stakeholder satisfaction, spanning patients, healthcare providers, employees, investors, and communities," says Dr. Dormer. "Our strategy focuses on continuous improvement, setting measurable goals in each ESG pillar to minimize environmental impact, maximize social contribution, and ensure long-term financial resilience."

Almac Pharma Services: Specialized & Flexible for a Range of Formulations

Almac Pharma Services offers a range of formulation, process development, manufacturing, and commercialization capabilities for a variety of oral dosage forms. Through its expert teams, Almac offers product development experience associated with molecule development from candidate selection through to scale up and commercialization. Its range of equipment is aligned to enable batch sizes that are typically required for Phase I clinical phases through to >300kg commercial

Pharmaceutical development at Almac.

batch sizes. Manufacturing capabilities include capsule filling, wet and dry granulation, compression, and film coating. Almac also offers a range of specialized equipment and expertise associated with molecules requiring high containment, bio-enhancement or for specific patient populations such as pediatrics or older patients. Almac designs drug products based on solid fundamental scientific understanding and a consideration of the patients' individual and unique requirements.

Recently, a client required a fixed-dose combination pediatric product. The product contained three active ingredients and the capabilities of the patient to administer the dosage form were a key consideration of the dosage form design. After considering the properties of the drug substance, the dosing regimen, and the patients' needs, a mini-tablet combination product was developed. Mini-tablets of each active ingredient were manufactured, coated, and filled into stick packs at appropriate quantities. The final drug product is then sprinkled onto appropriate food to enable oral administration. The next milestone for this product will be commercialization and ongoing supply.

In addition to pediatric formulations, Almac can handle highly potent molecules. "Our unique capability to handle high potent molecules enables our expert teams to build close partnerships with a number of pharmaceutical and biotech companies," says Terry Ernest, Director, Manufacturing Science and Technology, Almac Pharma Services.

Handling high potent molecules requires complex manufacturing operating processes and procedures, significant engineering controls, and various operational supporting infrastructure. Almac recently invested in this area with new, custom-built facilities being built to expand existing capabilities for handling and processing high potent molecules.

"This specialized manufacturing is best handled by experts providing Almac with the opportunity to build strong partnerships with clients, to enable development and commercialization of their highly potent assets," he says.

Handling a variety of formulations means Almac needs to be flexible in its equipment and facilities to increase capacity. "Providing flexibility to our clients within development discussions as milestones are reached and data is generated ensures that we are approaching projects in an agile way to facilitate adaptations and modifications as projects progress," Mr. Ernest says. "We recognize that planning activities in R&D is not easy, and projects may slow down or accelerate. By communicating regularly with our clients and building trust, we are able to offer maximum flexibility while also maintaining high quality and efficiency within our manufacturing facilities. Within the development process, we aim to scope out experiments with various scenarios in mind so that alternative plans have been pre-discussed and do not delay activities."

ARx: Proprietary Enhancer Promises More Complex Therapies

Leveraging more than 60 years in adhesive and film formulations and manufacturing, ARx specializes in oral thin film and transdermal patch dosage forms. Its expertise in polymers and technology, combined with a proprietary *in silico* preformulation model, allows the company to select the appropriate excipients to meet the targeted pharmacokinetics with a patient-centric design.

"ARx supports partners with specialized capabilities in formulation development, *in vitro* permeation testing, analytical method development, validation, and testing, as well as with clinical, registration, and commercial manufacturing," says Megan Greth, Director of Marketing & BD for ARx. "From a manufacturing standpoint, we have flexible batch sizes of several hundred to millions of finished dose units. As an FDA-ap-

ARx's oral thin film and transdermal patch manufacturing capabilities.

proved manufacturer of several branded and generic prescription drug products, we invested to nearly double our capacity and are a fully integrated partner, delivering serialized cartons and cases."

Customization of formulations and flexibility in partnering are pillars of the ARx partnership model. Each drug substance, as well as its interactions with the body are different, requiring a formulation strategy that starts with the Quality Target Product Profile. In addition, ARx recognizes the business needs of its partners require flexible project plans, batch sizes, timing, and continuous review of risk-based scenarios for progressing development. To reduce risk, production capabilities successfully scale from 3L to 1,000L batch sizes, with the same operating principles, she explains.

When beginning formulation development, ARx leverages proprietary predictive algorithms to streamline and reduce the number of iterations required for selecting the most optimal excipients and enhancers, unique to each API. Ms. Greth says: "This enables us to achieve the targeted results faster and more efficiently; thus, reducing overall time to file new drug products."

ARx recently invented a new formulation and manufacturing technology for oral thin films to solve a delivery issue during formulation development. The client had a unique application that required quick onset of a highly potent active. Delivering micrograms of drug quickly was not achievable with the traditional drug in film matrix technology. Therefore, ARx invented a method to apply the active ingredient to the film surface. This technology was commercially scaled and automated in less than three years from its inception.

"Transdermal patches and oral thin films are specialized dosage forms that have unique abilities to address complex therapeutics by avoiding the first-pass metabolism and, thereby, increasing bioavailability and avoiding adverse events; however, not all molecules easily permeate the mucosal or skin membranes," Ms. Greth explains. "ARx recently discovered a novel enhancer package on a partnered program that allowed for the delivery of a highly prescribed anticoagulant. Without the proprietary enhancer package invented by ARx, the program was not feasible. ARx is excited about utilizing our knowledge in selecting enhancers to allow for more complex therapies to be feasible in the future."

BioDuro-Sundia: Adapting to Meet Client Needs & Schedules

BioDuro-Sundia has been an industry leader in amorphous solid dispersions (SDD and HME) and modified release. This enables development of complex and challenging formulations and processes, along with the traditional solid oral dosages intended for oral administration. In fact, the company recently manufactured a Phase 1 SDD product from formulation development to release testing of the product in three months.

"This makes us one of the few CDMOs that can deliver to client expectations based on technical quality and expertise," says Magdalena Mejillano, Senior Vice President, Clinical Development and Commercial Manufacturing, BioDuro-Sundia. "We are one of the very few CDMOs that can perform pre-clinical to commercial drug product manufacturing in one site. In addition, our site has the permits to handle large amounts of organic solvents for spray drying and coating."

In addition to complex therapeutics, BioDuro-Sundia supports small-volume drugs for rare disease and orphan indications. "We have a wide range of equipment with different capacities that can support these types of products," she says. "We have forged at least three partnerships for commercial drugs using proprietary equipment and technology that will be provided by the client and manufacturing conducted at our facility. These clients will have dedicated suites modified according to their specific requirements."

BioDuro-Sundia will even modify ex-

BioDuro-Sundia specializes in amorphous solid dispersions (SDD & HME) and modified release.

isting suites to enable the installation of client equipment and train staff on their operation. The company has also supported, and continues to support, specialized technologies that are not necessarily in its core competencies by allowing clients to bring in their own specialized equipment and install in customized dedicated suites.

"Our clients' feedback has consistently been about our flexibility in terms of adapting to client needs or meeting a very aggressive schedule," says Dr. Mejillano. "We have two work shifts in manufacturing, but can activate two 10-hour shifts or three 8-hour shifts, if needed. There is also extensive cross-training between formulation and process development staff and manufacturing operators, both clinical and commercial."

Some of the more challenging projects BioDuro-Sundia has conducted that have been resolved and went into successful clinical trial manufacturing include: low solid content, low soluble fast crystallizing API in an SDD formulation (~2-3% solids), optimized process conditions to achieve <7um (D90) particle size of an inhalable product; optimized process and secondary conditions to spray acetic acid solvent mixtures and achieve below-ICH limit residual solvents; and optimized a process to spray (aqueous-based) heat-sensitive biological actives to achieve stable products.

Celanese: Partnering with CDMOs to Enhance Patient Outcomes

According to reports from Fierce Pharma, the pharmaceutical industry is witnessing a remarkable trend: the accelerated growth of CDMOs, which is outpacing the broader market. This surge highlights the critical role CDMOs play in the sector, a dynamic that has been increasingly recognized for its strategic importance.

"At Celanese, our engagement with CDMOs is not merely transactional; it is a deliberate strategic focus to advance our specialized capabilities in material science and drug delivery technologies, particularly in controlled-release applications for biologics," says Tom Quinci, Senior Manager – External Partnerships, Celanese.

Celanese aims to help pharmaceutical companies develop their products by offering the VitalDose® EVA Drug Delivery Platform and formulation expertise for sustained molecule release. "As early research and development efforts scale up into clinical research, we then transfer our initial formulations technology to CDMOs," he explains. "The Celanese internal laboratories and scientists are pivotal in establishing the basic feasibility of these early research efforts. They lay the groundwork for detailed product development, targeting a pharmaceutical company's target product profile. Trusted partnerships and collaborative relationships are essential to this process."

He adds that CDMOs provide comprehensive chemistry, manufacturing, and controls (CMC) services necessary for producing clinical-grade drug products. Partnering with them allows Celanese to efficiently produce and screen for formu-

Celanese scientist testing for drug release.

lations that can be scaled up. This capability ensures that Celanese's innovations are seamlessly transitioned from concept to clinic, ultimately benefiting patients globally.

"Combining Celanese's advanced material polymer and formulation expertise with a CDMO's process development and manufacturing scale-up expertise allows us to work synergistically to achieve success for our mutual pharmaceutical partners," says Mr. Quinci. "This collaboration results in a potent combination where innovation meets execution, providing the industry with high-value, comprehensive solutions particularly vital in the treatment of solid tumors, retinal diseases, and neurological disorders."

As the influence of CDMOs grows within the pharmaceutical industry, so too does the opportunity for strategic partnerships. By aligning Celanese's technological capabilities with the operational excellence of its CDMO partners, he says Celanese is driving innovation and emphasizing a commitment to improving patient outcomes through the value of optimized drug delivery.

Curia: Working Within Tight Formulation Constraints

Curia offers a full range of parenteral formulation development services, as well as clinical and commercial manufacturing of drug product. Formulation development is a critical stage in the drug development process, which involves the optimization of the physical and chemical properties of a drug, including its stability, solubility, and compatibility with different drug delivery systems.

"When envisioning the first-in-human development space, most programs that are brought to our scientists have significant questions yet to be answered, and often times the molecules are new and unique," explains Tyler Jones, Director, Formulation, at Curia. "This provides not only numerous challenges, but also opportunities to develop novel and groundbreaking solutions. A key to success in this ever-changing space is the ability to develop emerging formulations that not only stabilize the molecule but also lead to viable drug products."

These challenges are often related to the molecule itself, but can also be created by the target product profile or route of administration. For example, Curia undertakes projects for intrathecal delivery, which comes with a very controlled formulation space. Being able to work within these tight formulation constraints, while still developing stable and successful formulations, is a necessary skill for success, he says.

As advances in Lipid Nanoparticle (LNP) applications continue to revolutionize the industry, the ability to readily screen and manufacture candidate formulations at phase-appropriate scale is advantageous. "In our experience, we have found that customers often prefer to stay within a technology family (such as microfluidics, jet impingement, T-mixing, etc.) as they progress from early research into clinical drug product supply," says Dr. Jones. "This process continuity through the early development phase streamlines scale-up while protecting material and timeline considerations." Curia's clinical drug product sites have invested heavily into these technologies, offering a full suite of LNP services from bench scale-up to, and including, GMP fill/finish using microfluidics systems.

As therapeutic applications are becoming more complex, CDMOs working in the early development and first-in-human clinical supply area must be flexible, as immediate goals are often changing based on new data, funding, prioritization, and other external forces not under the CDMO's control. "At Curia, we are well-versed in accommodating unique needs and requests to help our partners achieve results," he says. "These requirements range from extremely short timelines to customized experiments looking to answer molecule-specific questions. Building out a knowledge base and making data-driven decisions is the key to successfully advancing programs through the critical early stages of development."

CycloLab Ltd.: Understanding the Nature of Complexation

In the realm of cyclodextrin host-guest complexes, understanding their intricacies is paramount. CycloLab is dedicated to unravelling the mysteries of these complexes using a diverse array of analytical techniques such as nuclear magnetic resonance (NMR) spectroscopy, isothermal titration calorimetry (ITC), phase solubility studies, and capillary electrophoresis (CE).

"NMR stands as a cornerstone in our quest for molecular elucidation," says Dr. Levente Szöcs, R&D director at CycloLab. "By analyzing chemical shifts, coupling constants, and spin-spin interactions, NMR provides invaluable insights into the structure, dynamics, and stoichiometry of cyclodextrin complexes."

To understand the molecular recognition process adequately, determining the stoichiometry of the selector–select and complexation is essential. CycloLab uses the continuous variation method (Job plot) to quantify the stoichiometry of the inclusion complex. "In this experiment, we

maintain the sum of the concentration of the guest and cyclodextrin constant while measuring the 1H NMR chemical shifts (δ) at different guest concentration/CD concentration ratios," he explains.

In most cases, it is 1:1 molar ratio, but CycloLab has examples for 1:2 and 2:1 as well as stoichiometries of higher order. In another set of experiments that resembles a titration, the company can determine the stability constant(s) of the complex.

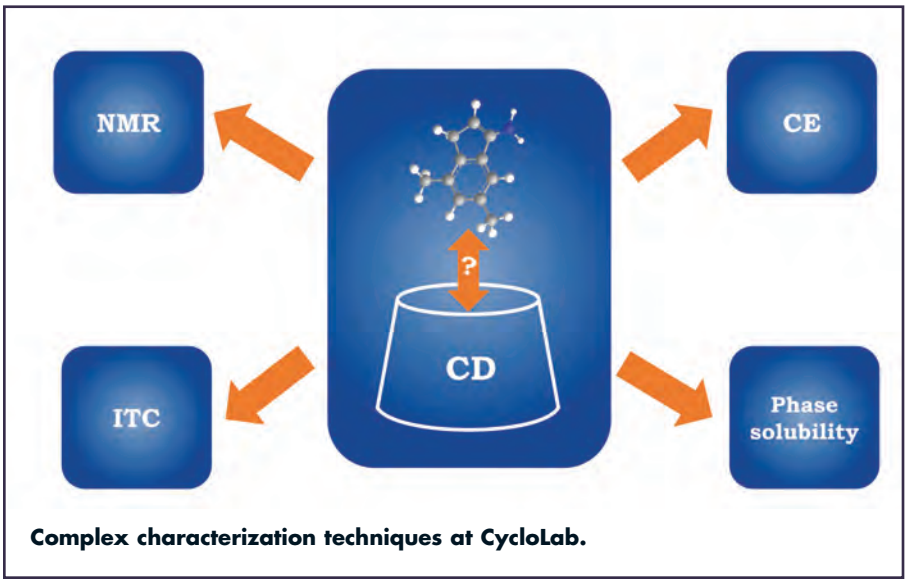
With 2D NMR experiments, like the so-called ROESY, the structure of the complex can be determined. The rationale of these experiments is the nuclear Overhauser effect (NOE), a manifestation of cross relaxation between two non-equivalent nuclear spins that are relatively close (<5Å) in space. Thus, this experiment can confirm inclusion complex formation and also offers insight into the geometry of the complex.

"This spectroscopic study will give detailed information on the weak interactions of host-guest complex formation at the atomic level and unambiguously confirm (or disprove) the formation of an inclusion complex," says Dr. Szöcs.

In the pursuit of understanding binding affinities and thermodynamic parameters, ITC emerges as a powerful tool. Through precise measurements of heat changes upon complex formation, ITC sheds light on the energetics driving cyclodextrin guest binding, offering crucial information for drug formulation and optimization.

Phase solubility studies serve as a cornerstone for quantifying complexation constants and assessing the solubilizing efficacy of cyclodextrins. By plotting solubility profiles against guest concentrations, these studies elucidate the stoichiometry and stability of host-guest complexes, aiding in the selection of optimal cyclodextrin formulations.

Capillary electrophoresis is also a versatile technique for evaluating the interaction strengths between cyclodextrins and guest molecules. Through the separation and quantification of complexes based on electrophoretic mobility, capillary electrophoresis offers valuable insights into complexation kinetics, charge interactions, and chiral selectivity.



Complex characterization techniques at CycloLab.

Eurofins BioPharma Product Testing: Early-Phase Formulation & Sterile Filling

Eurofins BioPharma Product Testing's San Diego site has developed and manufactured a range of drug products from sterile injectables to oral solutions to topical creams. The team is focused on early-phase and small-batch manufacturing, which puts the company in a position to provide the support that challenges large commercial-scale manufacturers.

"Our fully GMP lab has extensive analytical capabilities, enabling our experts to rapidly design and test formulations to arrive at the most stable, clinically-presentable formulations," says Joe Page, PhD, President, Eurofins BioPharma Product Testing San Diego. This spans modalities, including mAbs, mRNA, oligonucleotides, and small molecules.

Additionally, in its BSL2 lab, Eurofins BioPharma Product Testing San Diego has worked with AAV drugs and tissue-derived samples. The company provides GMP sterile fill/finish services (up to 3,000 vials) to advance clients into clinical trials.

"Complex therapies, such as mRNA, mAbs, ADCs, AAV, and oligonucleotides, require an understanding of the critical quality attributes to effectively develop and formulate these modalities," says Dr. Page. For example, excessive antibody aggregation or high levels of mRNA unbound from the LNP could render these treatments ineffective. In addition, these high-value drugs require the greatest level of assurance of sterility that is best achieved by isolator technology in the fill/finish process.

"We have worked with many clients to develop techniques to test these emerging drugs to ensure optimal formulations," he says. "For example, we have tested formulation variants for PS80 levels and tested

the corresponding antibody aggregation levels. These techniques accelerate stability studies conducted on candidate formulations. We collaborate with our sister site in Toronto, Canada, Eurofins Alphora, to source complex APIs, and our Lancaster, PA, site for cell banking, leveraging our network of laboratories to propel our clients' drug journeys. We've also built strong collaborations and relationships with biopharma companies that provide drug substances such as oligonucleotides, mRNA, and DNA."

Eurofins views IT solutions as a key differentiator, which is why the company has continuously developed its software platforms. This allows Eurofins to scale its business, harmonize globally, and customize solutions specific to a client's needs.

As a provider to early-phase clinical clients, flexibility is a critical component to the service. "We understand the need for flexibility and customization and collaborate with our clients during formulation development by recommending excipients and process steps to deliver both a clinically-acceptable, and cost-effective formulation," says Dr. Page.

As formulation development is a strength, one client had an insoluble API that, despite the use of cyclodextrin, still suffered from solubility issues. The Eurofins team worked through the issue and revealed that hold times during the initial dissolution were important to long-term solubility. Dr. Page says: "This seemingly simple, yet critical change enabled this product to move into clinical trials."

Another client's product had solubility and degradation issues. Eurofins discovered that the order of addition was important to minimizing formulation-induced degradation. "We then prepared 12 formulation variants with varying levels of ethanol and polysorbate," he says. "An accelerated stability study resulted in a formulation appropriate for the clinic."

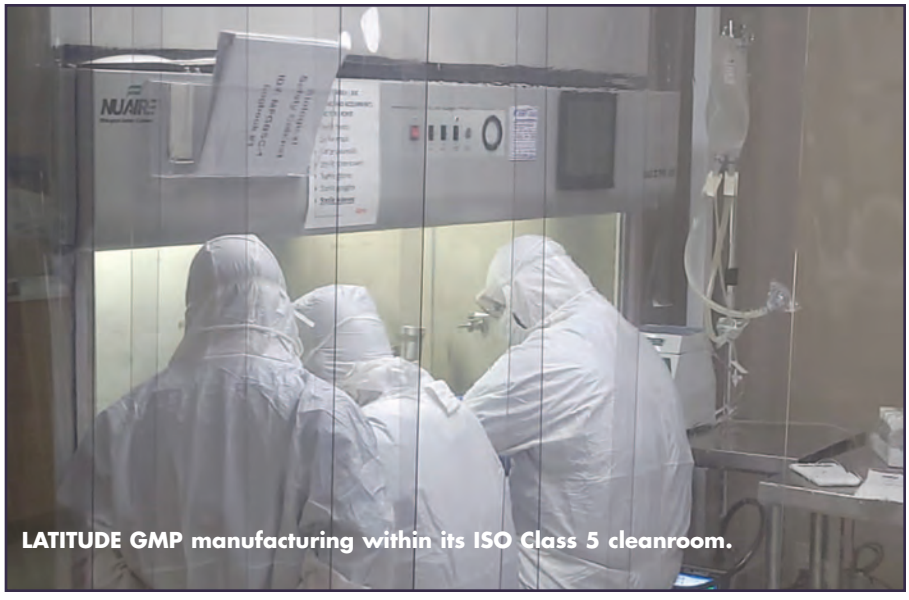
LATITUDE Pharmaceuticals: Flexible & Customized Formulations

LATITUDE Pharmaceuticals is a small California-based CDMO – starting in 2003 as a formulation development CRO – and has strong experience with injectables, oral solids and liquids, ophthalmic, intranasal, and inhalation formulations. Formulation services support clients from preformulation to preclinical and clinical development, including full in-house analytical support and method development. LATITUDE has particular expertise with complex injectable formulations, including nanoparticles, nanoemulsions, and liposomes.

LATITUDE added GMP manufacturing for Phase 1 and Phase 2 clinical trial materials in 2019. GMP capabilities include the manufacture of sterile injectables (vials, bottles, prefilled syringes), oral solids and liquids, and ophthalmics (eyedropper bottles), as well as full method development and validation. Of particular note is a recently added space for GMP aseptic lyophilization to enable even poorly-stable formulations to rapidly enter human clinical trials, says Matthew Singer, Vice President of Business Development. LATITUDE.

LATITUDE prides itself on its flexibility to easily pivot according to clients' changing needs. Clients interact directly with project scientists and each formulation is custom-developed. LATITUDE works with companies of all sizes. One recent client needed to develop an interarticular injection formulation with sustained release of the API. He says that LATITUDE developed a PLGA microsphere-based formulation that provided the PK profile desired by the client, including the necessary analytical methods, and provided the material necessary for animal testing.

In other areas, LATITUDE has worked with numerous clients for oral solid and liquid development, solving issues of solubility and bioavailability with nanoparticles, nanosuspensions, self-emulsifying delivery systems, and LATITUDE's proprietary ClearSol™ solubilization platform.



LATITUDE GMP manufacturing within its ISO Class 5 cleanroom.

Lifecore Biomedical: Handling Process Development & Manufacturing Complexity

Lifecore Biomedical is known for a flexible approach to collaboration, allowing customers to "define the starting line" and be as involved as desired while remaining ready to provide technical expertise. "We offer on-site, person-in-plant camera access for batch manufacturing, as well as remote camera access for clients who can't be on site," describes Alex McDonah, Technical Manager of Business Operations, Lifecore Biomedical. "During all project phases, we welcome face-to-face visits as a key contributor to the establishment and maintenance of close relationships with customers."

From a technical perspective, Lifecore Biomedical has worked with molecules and process fluids across the spectrum of viscosity, pH, light, heat, sterilization sensitivity, and filtration feasibility. Through decades of experience and more than 20 commercial products, the company has developed broad experience and deep knowledge in formulation, filtration, aseptic processing, filling, and finishing. Mr. McDonah says: "We support production processes from simple thaw, filter, and fill/finish to complex formulations with multiple, aseptic processing and formulation steps for solutions that cannot be terminally sterilized or filtered – and everything in between."

An example of complex process development work by Lifecore was recently undertaken for multiple customers requiring the ability to aseptically process materials through homogenization to ascertain specific particle size distribution. In these instances, sterile components were formulated and processed aseptically all the way through to the final drug product.

Supporting projects from simple to complex, Lifecore maintains a responsive approach to unique customer needs.

Lonza: Enhancing Capacity and Technologies to Accelerate Customers' Timelines

Lonza is a global partner to the pharmaceutical and biotech markets with expertise in biologics, small molecules, cell and gene, and capsules and health ingredients. Integrated services and products support from early-phase discovery to custom development and manufacturing of active pharmaceutical ingredients and innovative dosage forms.

To offer customers a more integrated bioconjugates offering, Lonza acquired Synaffix B.V. The acquisition will enable access to Synaffix's payload and site-specific linker technologies. In March 2024, Lonza signed an agreement to acquire Roche's manufacturing facility in Vacaville, CA, which will add significant new capacity to its global network and support the growing global need for large-scale mammalian manufacturing.

"Over the past two years, Lonza has significantly continued to strengthen its development and manufacturing network as well as its technology portfolio to better support customers from the earliest stages of development to market," says Jean-Christophe Hyvert, President, Lonza Biologics.

As is true for most industries today, artificial intelligence (AI), machine learning (ML), and robotics drive the industry forward. Lonza is adopting digital technology


Scientist at Lonza's facility in Visp, Switzerland.

and automation to streamline operations, decrease manual involvement, and improve data-driven decision-making. For example, by leveraging its experience of more than 150 tech transfers, Lonza is investigating the potential of AI and ML applications in product technology transfer.

"Throughout a product lifecycle, manufacturers encounter different scales and different equipment setups during technology transfers," he says. "The number of process variables and critical quality attributes involved in technology transfers add another dimension of complexity. AI and ML applications can be used to predict process performance or critical process steps in such technology transfers, helping to address these complex challenges."

Lonza is also investigating the use of AI and ML in deviation management and change control applications. Such applications can add significant value as transactional intelligence systems. In addition, Big Data, ML, and AI are routinely used in areas such as R&D, computer-aided drug design, protein profile assessment, engineering mammalian expression systems with DNA element design, and in predicting side effects for novel therapy forms.

In downstream processing, spectroscopical methods like Raman are used in combination with an ML algorithm to monitor critical process parameters, allowing production process performance to be monitored without taking a manual sample if an in-line spectrometer probe is installed. Mr. Hyvert says: "This impacts process performance through decreased contamination risk and increased manufacturing speed."

Mikart: Addressing the Demands for Complex Formulations

Mikart offers comprehensive formulation development and manufacturing services for pharmaceutical products, specializing in solid oral and liquid dosage forms and providing end-to-end solutions from development to production. Their focus on quality, flexibility, compliance, and customer service sets them apart in the market. Over the past two years, Mikart has addressed the growing demands for complex therapies in the pharmaceutical industry. The company has focused on expanding its capabilities in both solid oral and liquid oral formulations.

In 2021, Mikart invested in the Korsch XM12 tablet press. This technology enhances the company's ability to develop and produce complex oral solid dose products. It supports the development of fixed-dose combination products and potent compounds, offering advanced compression technology for bi-layer and mini tablets. This acquisition underscores our commitment to meeting client demands for complex formulation development and production of oral solid dose products.

In early 2023, Mikart unveiled a state-of-the-art liquids and suspensions suite. This investment is designed to develop and manufacture robust liquid dosage forms, including complex suspension products and extended-release formulations. The suite is equipped with various temperature-controlled tanks, enabling the handling of a wide range of volumes from 50L to 4,000L, which supports both pediatric and geriatric product development.

Mikart has signed a collaboration agreement with Nano PharmaSolutions, Inc. (NPS) to produce clinical trial materials using the NanoTransformer™ technology. This technology enhances the solubility of pharmaceutical APIs. "By incorporating the NanoTransformer technology, Mikart can address API solubility issues, formulation development, and commercialization of the finished product," says Nazar Elkarim, Vice President of Product Development Services for Mikart. "This unique, solvent-free, nano-granulation process for drug development and manufacturing offers biotech and pharmaceutical companies an alternative solubility enhancement technology and complex therapies."

Dr. Elkarim says that Mikart's goal is to provide value without compromising on quality or service. "We address the need for flexibility by offering customizable solutions to meet the specific needs of pharmaceutical companies and work closely with our partners to develop tailored manufacturing and packaging solutions that

Empowering Pharmaceutical Innovation: Customizable and Cost-Effective Solutions by Mikart.

align with their unique requirements," Gus LaBella, Director of Formulation Development, Mikart, says. "This approach allows biotech and pharma companies greater control over the production process. It ensures that their products are manufactured in an efficient and sustainable way."

Nano PharmaSolutions, Inc.: Single Nanoformulation for All Phases with No Chemical Additives

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 the leading cause for failure of Phase 1 First-in-Human trials. While the number of methods for enhancing drug solubility continues to increase, trade-offs in forms of cost, development time, and formulation bridging animal and PK studies make optimal solutions elusive.

Nanoformulation is an attractive alternative to solid-form solutions like spray drying or hot melt extrusion technologies to enhance solubility and bioavailability. However, nanoformulation is not widely utilized in early drug development of solid oral formulation due to fears of long development time and poor flow characteristics of submicron-size drug particles.

NanoTransformer™ is an easily scalable nanosizing technology that generates drug nanoparticles in the 200-600nm (D50) range. This process uses gentle heat under low pressure to evaporate solid drug substance to gas phase, and subsequently deposit them as drug nanoparticles on the surface of a common hydrophilic granulation excipient (e.g., mannitol, lactose, microcrystalline cellulose). These nano-granules may be used for animal safety studies as aqueous suspensions; for Phase 1 clinical trials as capsules, powder-in-capsule, or powder-in-bottle; and as compressed tablets for later-stage clinical trials – all without changing the base formulation. Using the same nano-granulation for the base oral 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. A solvent-free nanoformulation for animal safety studies will ensure the same good exposure of drug is maintained in both animals and humans, says Dr. Kay Olmstead, CEO, Nano PharmaSolutions.

The NanoTransformer granulator is a high-vacuum nano-coater, commonly used in the semiconductor and aerospace industries, enabling the production of nanodrugs under cGMP conditions. "The development time for nanoformulation is rapid and requires very little API, which is suitable for preclinical studies," she says. "Industrial vacuum nano-coaters can generate hundreds of kilograms of nanoparticles; therefore scale-up to production-sized batches is easily achievable."

Nano PharmaSolutions offers GMP manufacturing of clinical supplies of nanomedicines at its co-manufacturing facility at Mikart, LLC. Mikart is a CDMO focusing on developing and manufacturing oral solid and liquid dosage forms. Dr. Nazar Elkarim, Vice President, Drug Development Services, Mikart, says that 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, pediatric formulations, etc.) provides an easily scalable solution for difficult formulations in all development stages. "This differentiated, solvent-free, nano-granulation process for drug development and manufacturing provides biotech and pharmaceutical companies with an alternative solubility enhancement technology."

Particle Sciences, Inc.: Collaborating to Expand Capabilities to Meet Client Needs

Particle Sciences, Inc. (PSI, an Agno Pharmaceutical company) develops patient-centric complex dosage forms, which include long-acting injectables, implantables, and drug-eluting devices. These dosage forms are developed for challenging APIs, such as water-insoluble, DEA-controlled substances, and highly potent compounds. Examples of form factors include PLGA microspheres, implantable rods, intravaginal rings, and API nano/microparticles. PSI works closely with clients, and in some cases, adds capabilities to support clients' programs, such as commercial aseptic powder filling. Additionally, the company will be building a commercial, aseptic nano-milling line. All capabilities and dosage forms are supported by in-house analytical services (including physicochemical characterization tools), providing a one-stop-shop for clients' target product.

Feasibility programs for drug-eluting devices, nanomilling, and PLGA microspheres are designed to be low-cost, entry screening programs to assess if a clients' API is amenable to one of the stated technologies and to establish some proof-of-concept, explains Onajite Okoh, Director, Drug Device Development for Particle Sciences, Inc., an Agno Pharmaceutical company. "PSI then takes clients into formal development, through cGMP manufacturing and, if it makes sense for both parties,

Particle Sciences Inc. can be a partner for intravaginal ring design.

we may offer them the option of supporting their commercial production. We have partnered with equipment manufacturers to place specialized equipment at PSI to support specific formulation forms, for example, a hot melt extruder to support the development of biodegradable ophthalmic implants. Our parent company, Agno Pharmaceuticals, has added sterile API and excipient commercial manufacturing at the request of our clients."

In addition to meeting client requests, PSI partners with clients to address their needs. "There is a willingness to invest and expand our capabilities to meet the clients' need and timelines," says Shreya Shah, MS, Associate Director, Pharmaceutical Development for PSI. "An example of this is onboarding sterile API commercial manufacturing and sterile powder filling capabilities at the request of one of our clients. We also utilize a phase-appropriate quality approach that has been shown to accelerate our client's development programs, hence eexpediting the timelines to their clinical trials."

Robert Lee, PhD, Senior Vice President, Business Development for PSI, adds: "A collaborative approach that may include co-investment in capabilities that we don't currently have offers risk mitigation for our client." One example is Agno building a single-product, sterile suspension commercial manufacturing PFS line on an exclusive basis for a client.

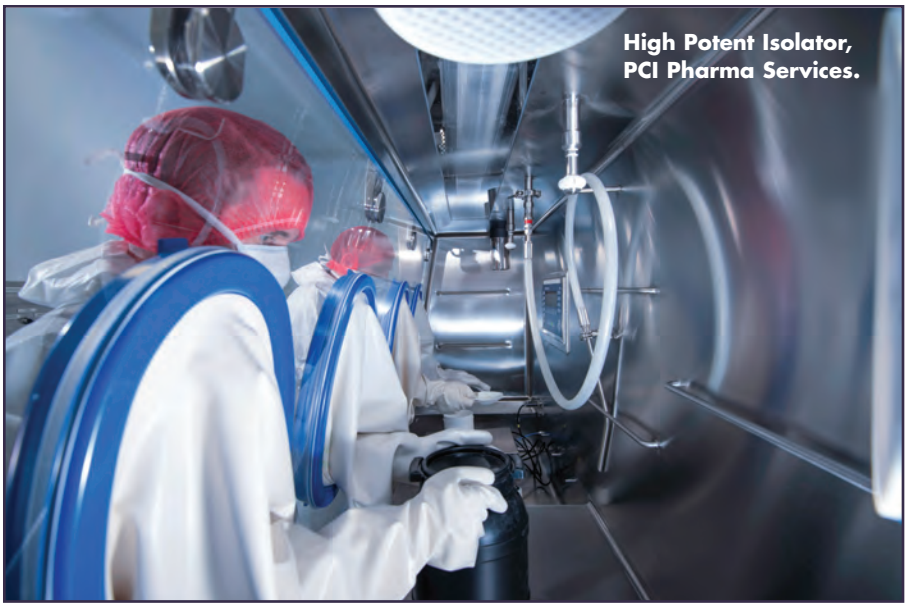
PCI Pharma Services: Fully Equipped Labs & Regulatory Support

PCI provides development and manufacturing services for both sterile and non-sterile dosage forms. Sterile services include formulation development (including complex formulations), lyophilization cycle development and optimization, geometric scale-up and process development, aseptic fill/finish, and lyophilization (plus non-aseptic, including bulk, medical device and intermediates), and bulk lyophilization. A recently expanded Contained Manufacturing Facility in the UK handles APIs to an OEL of 0.01μg/m3, with services including small- and large-scale granulation suites, Xcelodose® drug-in-capsule manufacturing technology, roller compaction, high-volume tablet compression and encapsulation, and oral liquids to support pediatric therapies.

Underpinning these core services are fully equipped analytical laboratories, extensive regulatory support, and a global distribution network for clinical and commercial supply. PCI has forged several key partnerships with equipment suppliers to ensure best-in-class technologies to support the development and manufacture of complex therapies. For example, PCI's partnership with S3 led to the recent supply of the Enclony Planet 6GP-TC High-Speed Tablet and Capsule Vision Inspection Machine, allowing visual inspection of tablets and capsules for clients.

Observation is indeed critical. There was a history of punch sticking observed during the development stage tablet compression of a drug product developed by PCI. Punch sticking occurs when powder material sticks to the punch face and leaves a defect on the tablet face, or material previously stuck to the punch face transfers to the next tablet causing a defect, explains David O'Connell, Director of Scientific Affairs, PCI. It's commonly caused by adhesive properties of the API or other materials in the formulation or by insufficient lubrication. The issue can be exacerbated by tooling design, in particular the design of the embossing.

"This issue was initially resolved by adjusting the amount of lubricant used during manufacture; however, when the tooling design was changed for the commercial image to create a debossing effect on the final tablet, the punch sticking issue re-emerged," he says. As additional lubrication can have a negative impact on product dissolution, the issue was resolved by adjusting the tooling embossing, and introducing chromium nitride coated tool-



High Potent Isolator, PCI Pharma Services.

ing, with support from the tooling supplier. The lubricant level was then further assessed during pre-validation trials to ensure process robustness prior to commercialization.

"A history of punch sticking is an important factor to consider when the drug product requires debossing," says Mr. O'Connell. "Certain characters or designs create a space on the tooling that can easily collect material through the batch compression." For example, characters such as; 0, P, A, and 4 are prone to the center portion of the character sticking to the punch. Tooling suppliers can often advise on alternative designs or considerations that minimize this risk, which becomes a key consideration if debossing is required for a drug product in tablet form.

Quotient Sciences: Helping to Accelerate Drug Development

Quotient Sciences provides integrated CDMO/CRO services to work for clients, ranging from candidate selection, drug substance synthesis and manufacturing, and preclinical formulation development, through to commercial drug product manufacturing. The company's flagship Translational Pharmaceutics® platform integrates formulation development, on-demand and adaptive GMP manufacturing, healthy volunteer clinical testing, data analysis and full regulatory support within a single organization.

"By controlling the full drug development value chain, including implementing adaptive clinical trial designs, we can transform the traditional model of drug development and accelerate a molecule on its route to market," says Dr. Andrew Lewis, Chief Scientific Officer, Quotient Sciences. "For example, within the First-in-Human (FIH) study, we can bridge from a fit-for-phase drug product to a POC-ready formulation. This reduces risk to the development program – something particularly powerful for drugs on accelerated approval pathways."

Artificial Intelligence also plays a role in accelerated pathways, having a notable impact in drug discovery. "Quotient Sciences is working with technology providers on applications that are 'quick wins' requiring minimal disruption, but with short-term impact on efficiency or productivity. We are also considering transformational, longer term use cases for AI, all aligned with our mission to accelerate drug development," says Dr. Lewis.

He adds that while there is no one-size-fits-all strategy to develop a drug, the desire to advance quickly through development is a common theme for nearly all. Programs should be designed to meet the needs of the client, molecule, and patient population. He says: "Using adaptive clinical trial designs in early development can help rapidly advance a fit-for-phase formulation to a POC-ready format, optimize performance of a drug product in response to emerging clinical data, and gain valuable data to inform the next stage of development."

Over the past 16 years, Quotient Sciences has conducted more than 500 Translational Pharmaceutics® drug programs, all ultimately resulting in expedited delivery of medicines to patients. A recent application was a collaboration with YourChoice Therapeutics in hormone-free family planning products.

"Having established a scale-up ready synthetic route for the YCT-529 API at our Alnwick, UK, facility, we developed the initial product formulation and the FIH clinical protocol in parallel," he explains. "Once approved, this allowed our Nottingham, UK, facility to perform on-demand drug product manufacturing for precision dose escalation, which removed extensive and costly up front product manufacturing. We are excited to see the potential of this first hormone-free male birth control pill as it progresses to patient trials."

Resilience: Technology & Processes Aim to Cut Timelines by 30%

Resilience provides customers with several solutions to route their program to the market. The company offers hands-on

support and regulatory guidance for development and drug substance manufacturing, and scale-up to commercial drug substance and drug product manufacturing. Resilience boasts an RFP process that aims to reduce timelines by approximately 30% compared to industry standards for First-in-Human materials, says Evan Pasenello, Vice President & Business Head – Biologics & Vaccines, Resilience.

Resilience is focused on a collaborative approach to partnership. One such partnership involved a complex therapy that required the development of a vaccine product containing aluminum adjuvants. Aluminum adjuvants (known as aluminum salts or alum) are added to many vaccines based on their ability to improve the overall potency, explains Milan Tomic, PhD, Senior Director – Process Development, Resilience. "For this program, Resilience employed its Process and Analytical Development division, which supports clients in designing their final drug formulation buffer. Their innovation resulted in a highly specialized system used when mixing the alum. The primary goal of the project was to ensure that the client could progress to clinic with a formulation that was appropriate to continue past Phase I and into later phases, with the ultimate goal of advancing towards a market-level formulation."

A client came to Resilience with a process that was too low yield to manufacture and commercialize in a cost-effective manner. The process development team resolved the issue by increasing the process productivity by almost a magnitude. "All of this was achieved in under three months by utilizing automated high throughput tools and our continuous high-density perfused batch (HDPB) process platform," says Ethan Bossange, Scientist I – Process & Analytical Development. "Continuous manufacturing is known for being flexible, reconfigurable, and having significantly lower cost of goods. However, the complexity of fully continuous biomanufacturing often brings lengthy development cycles, complicated control strategies, and new risks. Resilience's HDPB platform offers simplicity with a careful balance between speed to clinic, productivity gains, and risk mitigation."


Resilience brings together minds in science and engineering to deliver advanced technologies.

Risk is also mitigated with flexibility. Mr. Pasenello says that Resilience has designed a platform called ResIQ, which allows clients to complete a smart logic-based questionnaire that immediately generates a proposal for internal review. "The program is designed to continually adapt and collect the most relevant and important information to build an accurate and transparent guide as a first step to working with our team, whether your program is focused on process and analytical development or drug substance or drug product manufacturing," Mr. Pasenello says. "From there, dedicated business development, project management, and technical project leads are assigned to the program and serve as single points of contact and oversight throughout the project's lifecycle."

Resilience has strategically designed its digital ecosystem to focus on data enablement, aiming to provide both the company and its clients with a comprehensive, real-time perspective on operations and product lifecycle management. Such connectivity allows Resilience to trace lot and product genealogy. "This means that from any finished product batch, it is possible to access extensive lifecycle details, such as related experiments from process development, associated consumables and costs, resource allocation for development and manufacturing, pertinent quality data, physical storage locations, linked data files, and historian data," says Brian McNatt, Digital Sites Head – Research and Process & Analytical Development, Resilience.

Serán: Early & In-Depth Understanding of API Properties

Innovators are under increased pressure to reduce development timelines and deliver more challenging molecules. This molecular complexity includes increasing molecular weight, multiple active binding ligands (such as protein degradation and

molecular glues), and limited bioavailability due to decreasing solubility and permeability. This new reality requires an early in-depth understanding of API properties and formulation risks in order to develop a robust, scalable formulation.

"Serán's approach to developing early clinical drug product formulations has been successful in identifying over 50 FIH formulations, many of which have progressed to late-stage clinical trials without significant formulation changes, thus reducing the need for expensive API and time-consuming reformulation or scaleup trials and bioequivalence studies," says Rod Ketner, PhD, Vice President, Business Operations, Serán.

At Serán, collaboration begins with a tailored workplan to understand key API physiochemical properties – from a drug product delivery viewpoint – and identify opportunities and risks to development. The API characterization includes solid-state and materials testing, solubility measurements of both the crystalline and amorphous forms of the API in biorelevant fluids and may include salt and polymorph testing. Dr. Ketner says: "This hypothesis-driven approach leads to a science-based formulation screening to identify derisked technology selection and drug product formulations early in development."

If enabling technology is potentially required to achieve target drug exposure at projected doses, Serán's team screens a variety of formulation approaches using particle engineering. These approaches include API particle size control with dry or wet milling, use of functional excipients such as surfactants and acidulants, amorphous solid dispersions including spray dried dispersions (SDDs) and hot melt extrusion (HME), lipid formulation screening, and solid lipid nanoparticles. "All work is done with a material sparing approach, often requiring only a few hundred milligrams to fully characterize an API, select the technology approach, and screen amorphous SDD formulations, including supplying initial pre-clinical PK studies," he explains.

Oral solid tablet or capsule formulations are also screened using a material sparing, materials science-based approach that leverages experience, equipment, and characterization tools for direct compression or dry granulation-based formulations and manufacturing processes. The use of a dry granulation and tablet compaction simulator, and a representative granulator, enables facile and scalable formulation screening of prototypes that can be tested in biorelevant dissolution studies to ensure performance and screened for chemical and physical stability. This approach typically requires 5-25g, regardless of whether the API is crystalline or part of an enabled intermediate, such as an SDD. Lead formulations are then directly scaled, using material properties, to process scale equipment from Bohle, Gerteis, Korsch, O'Hara, and MG2. Compaction simulator, envelope density pycnometer, shear cell, and other tools characterize intermediates and finished dosage forms, including establishing ranges for manufacturing clinical trial material.

Dr. Ketner says: "Whether considering enabling technologies (particle size reduction, SDD, or HME), lipid formulations, or conventional approaches, Serán's team comprehensively assesses technology options rapidly with minimal API use to arrive at scalable drug product formulations and processes."

Simtra BioPharma Solutions: Collaborative Approach to Robust Molecule Production

Specializing in injectables, Simtra BioPharma Solutions supports products in all phases of development, from early clinical to commercial. The company handles complex, highly potent molecules (as well as standard molecules), and helps clients develop a formulation and then establish a manufacturing process that is robust, repeatable and scalable. Having its R&D and manufacturing co-located on the same campus helps expedite testing and minimize disruption of manufacturing, says Benoite Angeline, Vice President, Head of Marketing, Simtra BioPharma Solutions.

Serán's Leistritz ZSE 18 HP-PH Twin Screw Extruder for Hot Melt Extrusion and granulation.

"Many companies turn to us for the manufacturing of their ADC portfolios," she says. "Fill/finish of these products requires sterile and contained environment due to HPAPI in line with cGMP standards, which is capital intensive and requires specialized training of personnel. This is a growing segment of the market as seen by the acceleration in ADC approvals, the indication expansion for existing ADCs, and their use as both first and second line of therapy." Currently, Simtra has experience with more than 50 ADC projects that have been transferred into Simtra, including five commercial ADC programs.

She explains that Simtra BioPharma uses a collaborative, tailor-made approach for handling a multitude of molecule types with various toxicity profiles. The teams in tech transfer, supply chain, project management, quality, and R&D work collaboratively with each client to collect the information required for a successful transfer, and to communicate real time to help solve challenges and overcome hurdles that would cause delays. "Many clients come to us without an established process," says Ms. Angeline. "We try to learn as much as we can about our clients based on what we are provided, share whatever resources we have in our laboratories, in our manufacturing sites, and collaborate with them so that we can build a robust process that will lead to successful production."

Vial filling at Simtra BioPharma Solutions' Bloomington, Indiana facility.

Singota Solutions: Understanding the Needs of Small Biotechs

Singota Solutions specializes in providing formulation, analytical, and process development services to small biotech firms working in the injectables space. Singota understands the characteristics of its start-up clientele and has built its business structure to address these factors, explains Will Powers, Senior Director Business Development and Marketing at Singota. "Having a cGMP-compliant facility with storage, sampling and dispense, up-to-date analytical and manufacturing facilities are a must."

The use of robotics and the associated benefits of repeatability, increases in precision, and the reduction of human error increase the chances of project success and reduce timelines by avoiding delays caused by deviations. Manufacturing equipment designed specifically to minimize line loss, and techniques used in analytical methods and testing, can be devised to minimize the amount of API/drug substance/drug product consumed.

He says that personnel aligned with common goals across the organization, and competent, well-trained project managers who can inform and quickly coordinate a variety of moving parts from all sections of the organization helps move client projects along. "A predisposition to utilizing frequent and effective communication, and a collaborative, non-siloed approach to solving problems is important," Mr. Powers says. "The mindset and characteristics of the employees is critical. Having a team of smart, positive, disciplined, self-motivated employees with good interpersonal and teamwork skills at all levels of the organization makes for an organization that can get things done, and accomplish those tasks correctly."

One task that Singota recently performed was for a small biotech's formulation and process development project. A formulation change, which included adding a preservative, was identified by the client fairly late in the project timeline. This additive was identified as having compatibility issues with one of the polymers in use in the flow-path for aseptic filling. The Singota formulation and process development teams researched the problem, executed mixing and compatibility studies, and a workable solution was identified using the existing flow path. This enabled the project to be completed on time with the new formulation.

ten23 health: Leveraging Technology & Humans to Balance Development Parameters

ten23 health offers integrated services for the development, manufacturing, and

Singota Solutions of Bloomington, IN, specializes in aseptic filling, formulation, analytical, and process development services for small biotech firms in the injectables space. The cGMP-compliant facility features advanced robotics for precision, reduced human error, and minimized line loss, ensuring project success and faster timelines.

testing of sterile drug products. The company develops formulations, methods, manufacturing processes, and supports selection of primary packaging and device, provides stability material, and data. On the manufacturing side, ten23 can supply technical material, clinical, and commercial GMP materials.

"Our expertise is of specific value for complex formulations, such as high concentration formulations for subcutaneous or intravitreal use and highly precisely filled syringes, cartridges or vials – from preclinical to clinical to commercial stages," says Prof. Hanns-Christian Mahler, CEO Chief Enablement Officer at ten23 health.

ten23 health partners and collaborates along the value chain, supporting integrated into parenteral drug/device combination products with device specialists, such as SHL, West Pharma or Ypsomed.

"We partner with customers ranging from small academic spins or virtual startups to large corporate pharma companies, that we can equally support with our expertise and knowledge," says Dr. Mahler.

In collaboration with partner Elio, ten23 leverages artificial intelligence to support process design from a sustainability perspective. He says: "Additionally, ten23 leverages digital solutions, such as electronic lab journals (paperless lab). The company also utilizes the human to balance the various parameters for a highly customized outcome to ensure a sterile product designed for its very specific target parameters. Formulation Development is an art and science, requiring complexity management and problem solving, and understanding the interface of data with product design requirements, the human interface, and other important factors."

As a result, ten23 formulation programs are highly customized and tailored to the specifics of a given project, depending on molecule, target indication, quality target product profile and other criteria, while ensuring regulatory requirements. Dr. Mahler explains that the company supports customers with a variety of formulation and stability issues. Example include: understanding the degradation of surfactants in formulations and designing mitigation around this; tackling aggregation and particle issues in formulations; designing a formulation product to improve defects caused by lyo fogging; designing and assessing how the product can be administered safely to patients, while ensuring product stability (clinical administration setup and testing, CSTD evaluations); converting lyo products into liquid products by adequate formulation development; and developing subcutaneous and intravitreal-high concentration formulations (in syringes or cartridges) and converting from early-stage IV low-concentration formulations to later-stage development. ◆

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