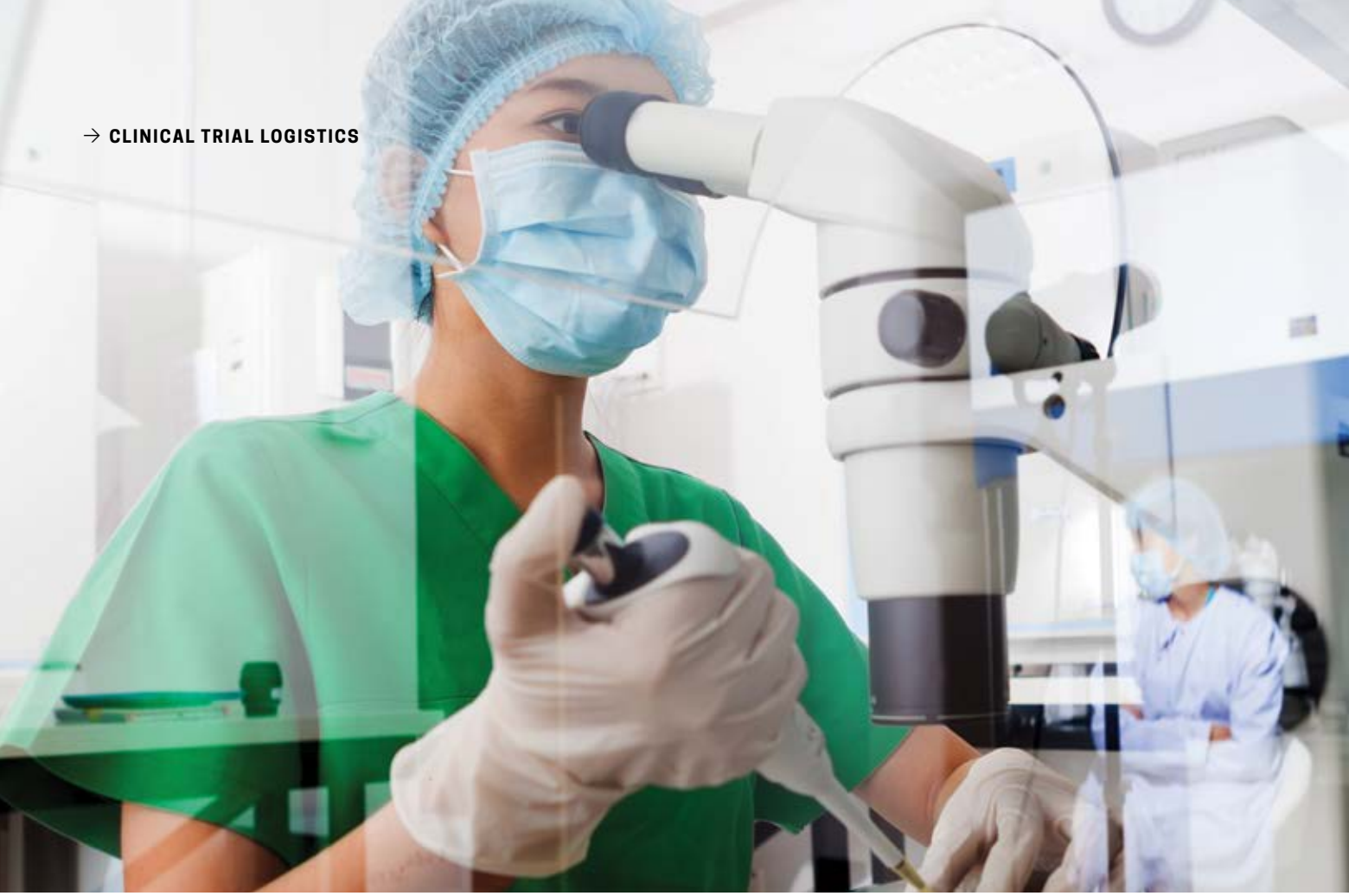

FACILITATING COMPLEX CLINICAL TRIALS FOR RARE DISEASES

→ BY **ARIETTE VAN STRIEN,** MARKEN

Developing drugs to treat diseases creates opportunities to simultaneously address the urgent unmet medical needs of patient populations and access new markets. The challenging clinical trials landscape for drugs continues to achieve new efficiencies due, in part, to streamlined regulatory processes, decentralized clinical trials models and next-generation technologies, all supported by a flexible and evolving supply chain.

RARE DISEASES CONTINUE TO IMPACT THE INDUSTRY

Though individual orphan diseases are rare by definition, the 7,000 identified diseases collectively affect an estimated 25 million people in the United States and 30 million in Europe.[1]

The market impact of rare diseases and their available treatments becomes clear when considering return rates; between 2000 and 2012, orphan drug companies had a 9.6% higher return on investment than non-orphan drug producers.[1] Orphan drugs can yield dramatic results and may provide a faster road to approval. "There's an opportunity to generate convincing clinical safety and efficacy data with very limited patient populations…," says James Wilson, director of the University of Pennsylvania Orphan Disease Center, "which means the cost of development would be a fraction of what it could be for more common diseases."[1]

In 2018, orphan drugs accounted for almost 60% of new drug approvals,[2] and global orphan drug sales are predicted to grow at a CAGR of 11.3% through 2024 – compared with 6.4% for pharmaceuticals overall – to eventually capture one-fifth of global drug sales.[3] Beyond the reduced R&D costs and accelerated approval times, there are favorable patent life and pricing incentives for developing orphan products. Among the 100 best-selling drugs in the U.S. market in 2016, the cost per patient per year for an orphan drug was $140,443, compared with $27,756 for a non-orphan drug.[3]

Orphan drug approval can be achieved following trials enrolling fewer than 50 individuals, which is significant in comparison to clinical trials for more common conditions or vaccines that might be introduced into the general population, which require thousands of trial participants. A demonstrative example of this was a phase III trial that included a very small number of participants.[1] In addition to abbreviated timelines, orphan drugs also have a 5% higher likelihood of regulatory success compared with more traditional drug products.[1]

SHIFTING THE CLINICAL TRIALS PARADIGM TOWARDS PATIENT CENTRICITY

In general, the industry is driving toward more patient-centric clinical trials, with more options for patients. Traditional trials, however, can present intrinsic logistical challenges including small or geographically dispersed patient populations, which has led the clinical trials landscape to shift toward site-less trials or hybrid trials. Marken's direct-to-patient (DTP) clinical drug delivery and direct-from-patient (DFP) sample pick-up, combined with Home Health Care (HHC) services by a global network of licensed providers, facilitates these patient-centric trials. Next-generation, patient-specific treatments and precision medicines are taking center stage, with DTP services offered as an option in many clinical trials occurring worldwide. These new models facilitate investigating drugs and supporting populations that were previously unfeasible, but they impose new demands on the logistics of the underlying supply chains.

While all clinical trials pose challenges surrounding enrollment and retention of patients throughout the trial, recruitment is typically the most time-consuming phase of any given trial, with almost 80% of trials failing to meet initial targets.[4] Even once enrollment has reached its goals, 30% of traditional clinical trial participants drop out, nearly 20% of trials end before completion because of participation shortfalls and many trials take two or three times as long to complete as anticipated. Unlike traditional clinical trials, which require frequent patient visits to a central investigational site, remote clinical trials run using a virtual/hybrid model are based in the patient's home, enabling patients with mobility issues – such as the elderly or disabled – or patients who live in remote areas with limited transportation options to participate in the trial.

Virtual and hybrid trials using a DTP approach can make conducting clinical trials more cost-effective. Implementing mobile technologies to support DTP trials can potentially reduce costs: 8% for phase I, 12% for phase II, 12% for phase III, and 13% for phase IV.[4] Pharma companies are taking advantage of this new efficiency model, with DTP trials predicted to increase from 24% of all clinical trials in 2017 to 33% by mid-2019.[5]

Cost-savings notwithstanding, patient centricity remains the primary driver of adoption of virtual/hybrid clinical trials, with stakeholders identifying improved patient retention (38%), the ability to reach dispersed populations (19%) and improved communication (17%) as the top three reasons for adopting DTP trials models, according to a survey conducted by Arena International Research. The same respondents listed concerns associated with loss of cold-chain control (28%) as the primary barrier to embracing DTP, underscoring how critical reliable logistical support is in realizing these new approaches to clinical trials, especially in the last mile.[5]

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DTP models present unique challenges associated with temperature control, requiring that drivers, nurses and patients take responsibility for maintaining the cold chain and reporting any excursions. Tracking the chain of custody for trial kits and ensuring patient data blinding – as mandated by the Health Insurance Portability and Accountability Act (U.S.) and the General Data Protections Regulation (EU) – are further logistical challenges associated with DTP clinical trials that require new protocols and specialty courier training to protect patient confidentiality and maintain blinding. To truly facilitate such complex clinical trials, pharma companies and CROs must partner with supply chain organizations that manage intelligent, flexible networks that continually provide agile and adaptive solutions.

TECHNOLOGY IS BREAKING DOWN BARRIERS

As clinical trials and tracking software become more sophisticated, so has the support infrastructure for documentation, processing, randomization, communication and supply management that is fundamental to decentralized clinical trials, including wearables, mobile apps,

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Interactive Response Technology (IRT) and e-Clinical Outcome Assessments (eCOAs).

One clear benefit of these technologies is improved patient adherence. Companies are focused on bringing the lab into the real world with a host of mobile tracking products. Sensing technologies are now capable of tracking bioparameters regularly monitored in trials, such as heart rate, glucose levels and blood pressure – any unusual activity or metabolism changes are then flagged by artificial intelligence. Mobile platforms can track adherence through facial recognition algorithms. After patients submit a video of themselves swallowing a pill, artificial intelligence can validate that the correct patient has taken their prescribed drug. Incorporating mobile technologies into trial design can also boost retention of clinical trial participants; according to decentralized technology provider Science37, known for its strategic alliance with Novartis, the firm's virtual trials boast an impressive 97% retention rate and are completed 30% faster than traditional trials.[7]

Drone technology has also entered the real world for diagnostic drug delivery or sample recovery and may one day advance trial execution. Recent examples from UPS include a mock drug delivery from Beverly, Massachusetts to an island located three miles from the Atlantic coast. UPS drones have also been used for humanitarian endeavors, having successfully brought blood and vaccines to remote areas of Rwanda. These drones also have the ability to check inventory on high storage shelves in depots and at storage facilities, including at drug-manufacturing locations.

DELIVERING ON THE PROMISE OF PERSONALIZED MEDICINE

In the age of personalized medicine, the Marken network is designed for patient-centric trials. The complexities of a global DTP/DFP program – particularly in the last mile – require a supply chain solutions provider with the ability to anticipate potential points of risk. Marken is a leading provider of DTP/DFP services, managing a large portfolio of 360 DTP trials over the past 24 months, including global trials with more than 20,000 patients. Marken is experiencing continued growth of client requests for DTP/DFP and HHC components for new clinical trials.

Our Patient Communication Center (PCC) supports these efforts as a 24/7 call center dedicated to meeting the logistics needs of patients participating in home-based clinical trials. Along with the unique global HHC nursing network, Marken is now moving to the next level with the launch of a global nursing network technology system that allows nurses to electronically record visit documentation in a GDPR-, HIPAA- and 21CFR Part 11–compliant and validated system. The nurses access patient details to schedule the visit and also capture all visit data within the system. The system will also track major milestones within a patient's progress throughout a trial, and sponsors will be able to view (blinded) details in order to make assumptions and any adjustments throughout the trial.

Next to home-based trials, the industry's other major focus is cell and gene therapy trials. In response, Marken has expanded our cryogenic (liquid nitrogen) service locations to nine facilities globally. We are the chosen provider for the past five years for global cell and gene trials and work closely with global partners to provide full chain of custody and identity for every trial.

We have additionally developed an automated closed-loop packaging solution that allows temperature-controlled clinical trial materials to be transported to any global location with an automated packaging returns process, allowing for reconditioning and repositioning with more efficiency.

FLEXIBLE SOLUTIONS

As the clinical supply chain subsidiary of UPS, Marken provides reliable, flexible, agile and effective solutions for the evolving demands of clinical trials to support the pharma industry and leading supply chain solutions for personalized medicines and next-generation therapies. P

ABOUT THE AUTHOR

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As Chief Commercial Officer at Marken, **Ariette van Strien** is responsible for the global sales, pricing, marketing and project management teams across the globe. She has been instrumental in building strategic relationships with companies throughout the pharmaceutical industry. Through her expertise, management and guidance, Ariette has helped to double the size of Marken in the past eight years and is spearheading Marken's newest service, Home Health Care (HHC), which is a unique addition to the Direct To/From Patient (DTP/DFP) service launched in 2012.

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REFERENCES

1. Kwon, Diana. "How Orphan Drugs Became a Highly Profitable Industry." *The Scientist*. 1 May 2018. Web.
2. Daghlian, Marie. "Report: Cost of Drug Development for Orphan Drugs Less Than for Non-Orphan Drugs." Global Genes. 14 Jan. 2019. Web.
3. *World Preview 2018, Outlook to 2024.* Rep. EvaluatePharma. Jun. 2018. Web.
4. *Assessing the Current and Future State of Clinical Trial Supplies.* Rep. Arena International Research. 8 Mar. 2017. Web.
5. "The Benefits and Challenges of Virtual Clinical Trials." Anju Software. n.d. Web.

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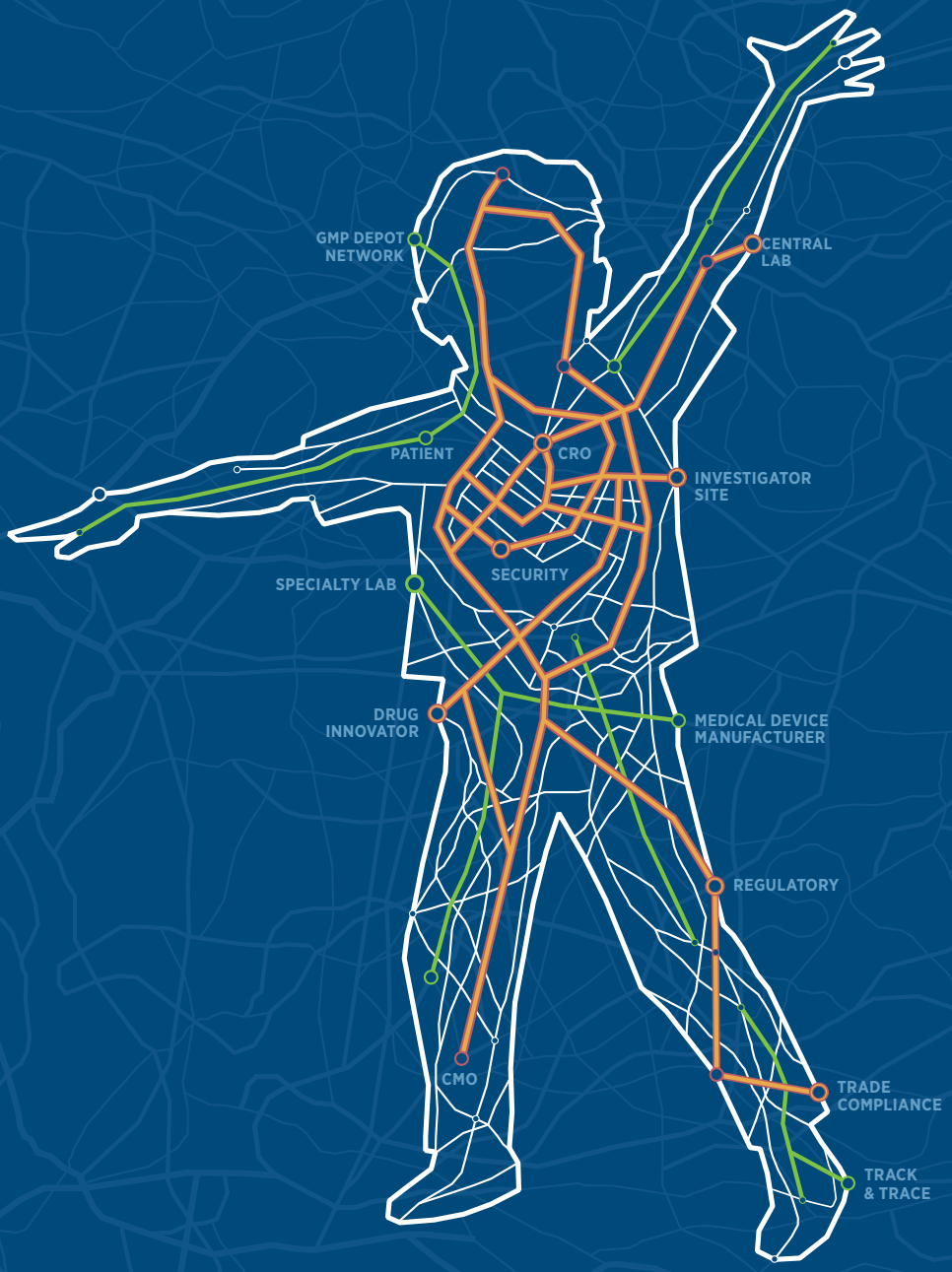

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