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Scrip Asks...What Does 2024 Hold For Biopharma? Transformative Technology

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Foreword

'This time it's different' is a common refrain that usually ends up in disappointment. However, unless the vast majority of the 75 industry executives and experts who shared their predictions are wrong, 2024 really could be the year when transformative technologies impact the pharmaceutical industry in ways that will change it out of all recognition.

For one thing, lessons have been learned about from where the first generation of digital sometimes failed to deliver. Instead, companies and their financial backers are investing with realistic expectations for more sustainable change. There is also a growing realization that it is necessary for them to adopt new technologies across the board.

Improvements in digital platform technology have made it possible to break down the siloes in data that have been the Achilles' heel of the industry for so long. Data from all sources can be captured and aggregated in ways that capture the full power of artificial intelligence (AI), machine learning (ML) and advanced analytics tools. As a result, drugs will be developed faster, but there will also be other bonuses, such as more inclusiveness in patient recruitment for clinical trials.

The use of AI in drug discovery, drug development, manufacturing, and other fields was the dominant theme mentioned by interviewees but gene editing, cell therapies, and new targeting modalities were also highlights. Antibody-drug conjugates (ADCs) were the stars of 2023 and remain strong; RNA-based therapies have also seen considerable interest; and research in CRISPR technologies is creating outstanding opportunities, to name but a few. At the most basic level, AI can also help to improve patient adherence.

It's not a free lunch for the industry, of course. Pressures are growing from the US Inflation Reduction Act and the continued downward pressure on health budgets. Technology making it possible to do the previously impossible creates regulatory expectations in itself. And AI is of little use without the data to apply it to; more information going in does not guarantee better results coming out unless we find the right way to combine new automated capabilities with the human brain. On issues like these the future will be decided.

Dr Andrew Warmington
Manufacturing Editor - Citeline

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AI And Data Science

"Many people have heard about artificial intelligence (AI) and ChatGPT but do not yet quite understand the opportunities and challenges that these new technologies may provide," observed Paul Lammers, CEO of T-cell therapeutics developer Triumvira Immunologics, Inc.

"The old saying 'Innovation is an imperative' in drug development still holds true and the use of AI will only help this process, as AI can help in accelerating at all levels of research and development, assist in analyzing ever growing information databases, and support effective decision making (remember another old saying in biopharma: 'kill often, kill early'). We are on the cusp of a better and more in-depth understanding of the use and proper application of these technologies and that process will significantly expand in 2024."

The possibilities are broad, he noted. "Several examples of this expanded use are the use of machine learning (ML) in the discovery of small molecules that might provide better targeting profiles against certain disease targets; assisting physicians in providing immediate differential diagnoses when evaluating patients presenting with complex sets of signs and symptoms and suggesting the proper diagnostic tests to run; and more optimally managing logistics and supply chain planning for products used in clinical trials or commercially."

"Today, many companies in the life sciences sector are adopting new technologies for applications ranging from process automation to in silico drug and biomarker discovery and development, in order to create value from the vast amounts of data gathered over years of research. Clearly, digital transformation in the life sciences industry will continue to grow rapidly," predicted Liesbeth Ceelen, CEO of biomedical data science specialist BioLizard. "In the coming year, we expect to see the pharma sector build up its data infrastructure to enable high-quality data analytics, while implementation and utilization of AI will ultimately remain the task of the small number of experts with both biological and data analytics expertise."

But new technology brings new problems, Lammers noted. "On the challenging side, scientific and

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> LIESBETH CEELEN, BIOLIZARD

medical journals already have to deal with providing guidance to peer reviewers of journal articles on how to uncover the use of ChatGPT and how that might influence copyright and plagiarism issues. Similarly, company employees need to understand that any use of ChatGPT to rewrite a text, automatically puts all written information into the public domain, including any confidential information."

And BioLizard's Ceelen emphasized that the machines should not be left to their own devices: "Creating

valuable biological insights will always require the right research questions, data and expert evaluation – putting the combination of computational power with human input and collaboration at the core of making the best data-driven decisions."

Meanwhile, the data itself may provide the challenge, as underscored by John Shon, chief technology officer at immune-focused drug discovery service firm Serimmune Inc. "We've seen the continued boom of AI/ML technology throughout the field of life sciences. But what we're not always accounting for or considering is the additional data necessary to fuel innovation in this industry," he said. In particular, he pointed out that immunology is ripe for development in this area. "Immunology is the new kid on the block with regards to adding further insights into those areas that have boomed under the molecular and genomic era of data generation. In the past, immunology has been used clinically in a very general way to indicate exposure to pathogens or increased or decreased activation of immune cells."

Shon highlighted "the next phase of immunology, precision immunology, where we have the potential to uncover our unique immune history, building a broader and deeper understanding of how we as individuals and as a population respond differentially to a variety of environmental and pathogenic exposures. These insights will bring about a new era in drug discovery and development as well as early detection and even disease management."

"Data is only as good as the insights we can glean from it – and that's most true in health care. The year ahead will be defined by the convergence of data sources to advance precision health," said Scott Burke, chief technology officer at Verily, Alphabet Inc.'s life sciences research company, formerly known as Google Life Sciences. "There are three keys to this happening: collecting and organizing longitudinal data from outside the four walls of the doctor's office; implementing technology platforms and systems to handle this multi-modal data complexity; and creating curation and quality processes by skilled clinical, data science, and research teams to generate valid insights from the data."

For Alister Campbell, vice president and global head of science and technology at R&D software firm Dotmatics, "Intellectual property (IP) becomes more critical than AI. Over time, AI in discovery will become table stakes. In its current incarnation it will move the needle only slightly in early optimization but as yet it is not addressing the challenges in

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later stage development and clinical studies. IP is a pharmaceutical company's lifeblood. It represents the company's unique knowledge, gained through decades of tireless work by researchers and scientists. The increasingly digital nature of the drug discovery process means that IP is now encoded in data. Conversely, AI is a commodity. Vendors are building exciting AI products on top of public knowledge. Their models make it easier to glean relevant insights from chemical structures and properties of molecules. These products push the starting point for research forward – for every company that buys them."

Campbell went on: "AI only becomes a unique advantage when it's deployed atop a foundation of proprietary data that is optimized for use in R&D. Optimization, in this context, refers to both technology and governance. AI needs clean, standardized, organized data to produce usable outputs. In turn, companies need a strong data governance culture

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to ensure that the data produced and collected by different teams are consistent. But when computational models are used to design new drugs, the debates will ensue around who owns the IP if it was derived from AI."

At Sumitomo Pharma America, chief analytics and digital officer Bill McMahon was energized by AI's potential. "Nearly everyone has heard about recent advances in large language models (LLMs), and many people are using them daily in their personal lives, but essentially all companies have had to figure out the legal and security requirements to adapt these models for corporate use. For many AI-focused companies, that work completed in 2023. Now the exciting part begins: training these models on internal data and giving the majority of employees (who cannot code) access to deep insights contained within huge company databases," he said. "The breadth of data that can play a role in improving decision-making in pharma but that currently is inaccessible makes it likely that the disruptions in our industry will be significant."

Also excited about AI was Gil Bashe, managing partner, chair global health and purpose at FINN Partners and executive committee member of Galien Foundation. "Used wisely and to its fullest (positive) potential, AI can extend the empathy quotient, making the wise healer more expansive. AI can unlock tremendous insight and perspective for the savvy, self-aware health provider and accelerate drug discovery and clinical trial inclusion decision-making go/no decisions."

However, he also had a warning. "What of the company that prioritizes using this transformative technology to become more efficient and faster – using powerful tools like ChatGPT and GenAI to primarily bolster the bottom line without adding value? Without policy bumper guards, AI will become a 21st-century dehumanizing sharp pencil in dispassionate bureaucrats' hands."

Jeffrey Lu, CEO and co-founder of precision medicines company Engine Biosciences, foresaw "accelerating adoption of AI in biopharma R&D across the value chain. Not only has the 2023 AI boom opened the world's eyes dramatically, application-specific tools that have been built rigorously over the past several years in uses cases like small-molecule screening, target selection, protein design, and patient stratification are reaching greater maturity in technology validation and operational deployment." "It is estimated that the global market size for AI

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> GIL BASHE, FINN PARTNERS

in biopharma will reach $9bn by 2029, with 25% a compound annual growth rate (CAGR) between 2021 to 2029," said Anselmo Chung, partner, life science and healthcare strategy at EY Parthenon, referring to research by Precedence Research and Grand View Research.

Like many others, Chung emphasized the technology's potential across the multiple areas of activity. "For example, AI has helped identify novel disease-related targets and predict new drug designs much more efficiently and can conduct clinical trials up to 20% faster. Additionally, AI-powered digital manufacturing plants have helped biopharma improve quality control and reduce yield loss by up to 30%, while generative AI-powered dynamic customer segmentation and marketing content creation have helped improve doctor targeting accuracy by 45%. We expect to see a significant increase in innovative AI applications in the coming years that will further transform the biopharma industry."

Nandu Deorkar, senior vice president of biopharma production R&D at Avantor, which provides products and services to biopharma customers, identified manufacturing as likely to benefit from AI this year. “2024 will accelerate digitization and automation to enable adoption of generative AI models (versus multivariate mathematical models) by using extensive data sets to drive manufacturing operational efficiency, to improve supply chain visibility, and to meet and exceed quality standards – all necessary for biomanufacturers in an era where speed-to-market wins and patients ultimately benefit,” he said.

For Dotmatics’ Campbell, data science will unleash the power of information that was not previously in a useful state. “Life science companies will start to see the fruits of digitalization as they increase the use of drug repurposing, making it easier to navigate the swaths of data that have previously been locked away in silos, unlocking the potential of drugs that have been shown to be safe but missed initial clinical endpoints.”

He added: “Health care companies have increased their digital capabilities more than any industry except consumer goods since 2019. Under pressure to deliver new treatments and to be multi-modal in their research, life sciences companies will continue to break down silos that impede data sharing and digital collaboration. Pharma companies did the hard work of establishing a shared vision for digital — now they need to make that vision a reality so they can reap the benefits of AI. They need to push each other and the vendors that support them toward use of technologies that ultimately support multi-modal research driving toward an AI future.”

“No matter the field, function, or area of drug development scientists, clinicians, regulatory, manufacturing, and medical writing professionals are involved in, 2024 will see an increased focus on the use of AI and ChatGPT. For the biopharma industry to fully capture the opportunities of these technologies, we need to invest significantly in the education of our workforce on the pros and cons so that we can maximize the benefits and let them assist all of us in creating the next wave of medicines to treat patients in need,” declared Triumvira’s Lammers.

“The current drug discovery process is complicated and inefficient: bringing a single drug to market costs around $2.5bn, takes ten years, and for every drug that gets approved, 10,000 compounds will fail. Industry research has found that over the past 20 years, large pharmaceutical companies have spent an average of $6.16bn per drug approval,” said Campbell.

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> **PAUL LAMMERS, TRIUMVIRA IMMUNOLOGICS**

“Technology and innovation is now helping life science companies shorten the drug discovery funnel and reduce the costs of drug therapy R&D from billions to millions of dollars.”

According to Engine Biosciences’ Lu, success will come in the form of evolution rather than revolution. “Importantly, AI tools that are designed to be integrated with, rather than trying to upend, existing R&D processes, stage gates, and decision-making will be better embraced.”

He concluded: “What will be valued is real impact on pressing industry-wide needs. The strong desire for novelty and differentiation, capital efficiency and easing pain points across all R&D phases means fundamental demand is robust.”

AI In Drug Discovery

“In 2024, the biopharma field is poised for transformative advancements, particularly in drug design and AI,” said Laksh Aithani, co-founder and CEO of AI-based drug discovery firm CHARM Therapeutics. “The rise of tools like RosettaFold All-Atom, AlphaFold and ChatGPT are poised to transform drug discovery.”

Artin Moussavi, chief business officer at Leucid Bio, agreed. “The life sciences sector is undergoing a significant transformation, driven by the advent of Generative AI (GenAI). This technology, exemplified by AlphaFold [developed by Alphabet Inc. subsidiary DeepMind], is poised to accelerate drug discovery and development by rapidly analysing extensive datasets for potential therapeutic candidates,” he said. “AlphaFold’s remarkable ability to predict protein structures revolutionizes our understanding of biology and aids in drug target identification.”

“The convergence of AI and biotechnology will continue to enhance drug discovery by identifying novel drug targets and drug structures for optimizing drug development,” said Dan Passeri, CEO of cancer immunotherapy developer Cue Biopharma, Inc. “We have much greater insight and capacity to elucidate functional pathways driving disease and define points of intervention for developing new therapies. In the oncology space, we have tremendous enhancements in understanding the cancer systems biology and intersection with the immune system. I anticipate ongoing advancements in precision immune modulation with the development of novel protein therapeutics to enhance the specificity, effectiveness, and safety of immunotherapies, providing an improved treatment experience and quality of life for patients.”

“In the year ahead, I foresee that finally we will start seeing more and more assets coming out of discovery and research harnessed by the power of AI, ultimately accelerating the availability of new medicines for the patients who need them,” predicted Elcin Barker Ergun, CEO of Menarini Group. “Equally important to this equation is accuracy, and what better way to use AI than to help with ensuring more precision? If researchers can provide transformative therapies to people more quickly, while improving the accuracy and quality of data, our industry will be a step closer to achieving the goal of providing enhanced and longer lives to all.”

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> **JEN NWANKWO, 1910 GENETICS**

Jen Nwankwo, founder and CEO of drug discovery firm 1910 Genetics, cautioned that “There is a desire to label everything as AI these days, but what we have today is ML, not true intelligence. Current ML models are trained on data of existing structures and, in many cases, will re-generate known molecules.” She went on: “True intelligence is learning from a dataset, understanding the patterns, and being able to reason through and extrapolate to new contexts to generate novel, but also meaningful, molecules. I predict that in 2024 we will see GenAI achieve true intelligence, not only in chemistry and materials science, but importantly, in drug discovery.”

"Drug discovery naturally has a high level of data and analysis required for vast numbers of potential compounds. There have been some early-stage success stories with money raised for AI platforms, and others where it forms part of an integrated service offering. The winners in this category will be demonstrating repeated success in bringing new candidates through the clinic, or turning off unsuccessful candidates early. In 2022, there were 18 AI-created drugs in clinical trials, a growing trend," James West, MD at investment bank Lincoln International, said.

"We are in the midst of a digital revolution in biology. Advances in AI and ML have now made it possible to program novel proteins not previously found in nature with targeted biophysical, biological and therapeutic properties. This breakthrough in generative biology is an important step in accelerating how protein therapies will be discovered," said Gevorg Grigoryan, co-founder and chief technology officer of another AI-powered discovery firm, Generate:Biomedicines.

"Soon we will see new drugs entering the clinic that have been completely computer-generated. Those medicines will transform the entire value chain from lab, to clinic, to regulatory approval, to the patient's bedside. ML has brought us to the brink of this revolution – we anticipate seeing the first clinical proofs of concept in 2024," said Grigoryan. "Generative biology has the power to create medicines faster, more precisely, and at a fraction of the cost of traditional approaches, thus increasing patients' access to innovative, transformative, and novel therapeutics."

And, said Leucid Bio's Moussavi, "GenAI is becoming crucial in personalizing medicine, tailoring treatments to individual genetic profiles to enhance efficacy and safety. In medical imaging, GenAI enhances fields like spatial biology, offering deeper insights into disease mechanisms and progression, vital for the development of advanced therapies. This shift towards GenAI is propelling health care into an era of increased efficiency, precision, and patient-centric care, with groundbreaking advancements in predicting protein structures, transforming how we approach drug discovery and structural biology research."

AI In Development

"Whereas 2023 was a year of progress for AI-enabled drug discovery, it's important to look beyond the discovery stage to the equally complex and data-rich preclinical development stage," said Kent Wakeford, co-CEO of computational biology company Form Bio. "We can expect to see biopharma companies taking their 2023 learnings from early pursuits in AI drug discovery, and applying those lessons and new capabilities to their downstream efforts.

"We're seeing more advancements in task-based modeling, biomanufacturing optimization, regulatory data normalization, drug product characterization standards, and more. And, importantly, biopharma companies are beginning to leverage AI to chip away at the many years and millions (or billions) of dollars it takes to get discovered drugs approved and into the clinic. 2024 will usher in the systematic integration of in silico task-based AI insights and bench science to enable biopharma companies to rapidly address efficacy, safety and manufacturability – to more rapidly advance therapeutics from discovery to the clinic."

"Looking to 2024 and beyond, we expect to see AI embedded across all solutions to improve speed and efficiency in clinical trials," said Tom Doyle, chief technology officer of clinical trials software as a service provider Medidata, a Dassault Systèmes company. "Transformative technologies break the transactional experience for patients, instead, engaging with patients longitudinally beyond a single clinical trial. Medidata is also embedding AI to increase diversity and access to research by decentralizing trials, simplifying enrollment, and enabling new site models. We are using generative AI to create synthetic data that provides clinical researchers with access to rich data and insights while safeguarding patient privacy and intellectual property. We're excited about a future where AI will further reduce patient burden, accelerate the pace of clinical reach, power tomorrow's innovation of research, and create a better experience for patients and researchers alike."

Jane Reed is director of life sciences at Linguamatics, an IQVIA company that delivers a health care AI platform based on natural language processing. "Pharmaceutical companies will increasingly look

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> **TOM DOYLE, MEDIDATA**

to artificial intelligence-based technologies such as natural language processing (NLP) to accelerate drug development and discovery," she said. "Many critical drug development processes, such as finding specific targets for a compound, creating target profiles, incorporating patient voice into clinical trial design, and predicting safety and risk-benefit profiles, can be lengthy, expensive, resource-intensive tasks. NLP enables researchers to sift through and organize massive amounts of data to extract important insights that deliver benefits across the entire drug development lifecycle, from pre-discovery to clinical trials to regulatory review and post-marketing safety and market access."

Simulation

“AI isn’t the only answer as biopharma processes continue to evolve, and digitization and characterization efforts in pharma 4.0 will be more significant, like digital twins,” predicted Avantor’s Nandu Deorkar.

“The first AI-enabled digital twins will emerge in specific therapeutic areas, with the long-term potential to revolutionize health care by making it more sustainable, predictive, and preventive,” said Nathan Price, chief scientific officer of personalized supplement and health testing company Thorne. “Digital twin technologies can provide integrated simulations of health and disease processes across lifespan. Particularly in disease prevention, digital twins are revealing the limitations of traditional trials that focus on single-compound interventions. These trials often fail as most individuals are non-responders. Personalized sets of interventions can lead to more people responding effectively, with significantly better outcomes. This approach will not only improve the effectiveness of prevention strategies but also substantially reduce the costs associated with such trials by reducing the number of people needed.”

“I believe 2024 will be a transformative year for how the industry approaches and validates targets in preclinical investigations of potential drug candidates,” said Keith Murphy, founder of Organovo, and founder and CEO of Viscient Biosciences, both companies focused on 3D bioprinting for R&D. “While 3D human models have been used in place of animal models to some extent already, next year, the first drugs that have been discovered with and developed with the help of 3D human models derived from primary cells of diseased patients will enter Phase II. With sufficient transcriptomic and clinical compound result data validating a specific model, it’s reasonable to assume a much higher probability of success in Phase II studies. I anticipate this resulting in a larger shift among industry to rely on 3D human models to validate targets, better predict drug efficacy in lead optimization, and improve data sets available to aid clinical trial design.”

“For 2024, I predict that organ-on-a-chip (OOC) and microphysiological systems technologies will become an integral part of drug development workflows, as they do a better job of mimicking human biology and predicting human drug responses than many current in vitro and I approaches,” said Tomasz Kostrzewski, chief scientific officer of OOC company CN Bio Innovations Ltd. “The longer companies delay adoption, the more it will cost in time and money, especially for human-specific drug modalities, where the use of animals is less effective. Generally, we envisage animal use becoming more limiting and costly. To circumvent this OOC systems can be utilized as ‘a bridge,’ providing mechanistic data to refine preclinical in vivo experimental design, reducing the number of molecules progressing through such that only the best proceed will help to maintain cost-effective workflows.

> *Digital twin technologies can provide integrated simulations of health and disease processes across lifespan.*
>
> **NATHAN PRICE, THORNE**

“We are now seeing the first lead candidates that have harnessed OOC data to support human efficacy predictions successfully entering the clinic. The benefits of this approach are being increasingly realised across the industry and by regulatory bodies, with ground-breaking legislative changes made this year, paving a way for more widespread adoption in 2024.”

Patient Data

Andrew Burns, chief growth officer at DrFirst, which provides health care technology solutions to prescribers, hospitals, pharmacies, payers and others, sees great potential for AI and ML in engaging with patients. “Just as the retail industry uses AI and ML to transform the customer experience, expect to see the health care industry leverage these tools in the coming year to transform the patient experience and improve health outcomes,” he said.

“Retailers successfully use AI to remove friction for purchasers with chatbots, personalized recommendations, and abandoned cart reminders, to name a few. With the health impact of one in four prescriptions never being picked up, what can the health care industry learn from these examples to help patients start and stay on their prescribed medications? For one, AI and ML could use the interplay of patients’ demographics, social determinants of health, medication history, and insurance benefits to make recommendations to health care providers during the prescribing process, improving the likelihood that patients will take their prescriptions. Then, after the prescription is sent to the pharmacy, AI could use the same data to connect with patients, offering relevant education and financial assistance.”

“Stakeholders now demand tangible data demonstrating our ability to reach the right audiences and achieve meaningful outcomes,” observed Ramita Tandon, chief clinical trials officer at Walgreens. “The direct access to patients that companies like Walgreens possess enables them to refine trial designs, product launches and strategies for patient identification and engagement. Real-world data (RWD) and real-world evidence (RWE), particularly those addressing social determinants of health, are playing a key role, offering invaluable insights into the longitudinal care journey of patients. Notably, several new therapies have successfully integrated RWD and RWE into FDA submissions, indicative of a broader industry trend. This has sparked a keen interest from the FDA in further incorporating these elements into the standard clinical research process to inform regulatory decisions. This move beyond discussions to concrete, personalized approaches informed by patient demographics and experiences, is poised to shape the future of clinical research,” she predicted.

> *RWE and HEOR are becoming increasingly powerful for new drug approvals. Technology can accelerate disease understanding through data capture and analysis, alongside detailed health care system modelling and impact on patients, payers and pharma.*
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> **JAMES WEST, LINCOLN INTERNATIONAL**

Kim Perry, chief growth officer at emtelligent, which provides NLP software to health systems, payers, and life sciences companies, also highlighted RWD.

“Pharmaceutical companies are starting to buy deidentified, real-world data from electronic medical record (EMR) companies to mine for actionable insights. However, gaining value from RWD requires the ability to not only access that data, but to cleanse, normalize, and structure it at scale,” she said. “The

emergence of medical-grade AI that can unlock the value of EMR data – particularly unstructured data, which comprises 80% of all digital medical information – will give pharma companies an opportunity in 2024 and beyond to leverage available EMR data for post-marketing studies and drug development."

Lincoln International's James West agreed: "RWE and health economics and outcomes research (HEOR) are becoming increasingly powerful for new drug approvals," he said. "Sponsor budgets are growing and there has been a focus on the importance of this workstream, particularly with rare, complex, or advanced therapy products. Technology can accelerate disease understanding through data capture and analysis, alongside detailed health care system modelling and impact on patients, payers and pharma."

"When I think about the transformative technologies that are needed, it continues around data, and 2024 will be the year that GenAI will enable us to lean in to understand more about rare diseases," said Kim Moran, SVP, head of US rare disease at UCB S.A. "The plethora of data, and the power of data analytics, will unlock the right insights to have a much fuller picture in terms of what we are trying to understand in the care and support journey for individual patients. This is especially critical in rare diseases, where there is no stereotypical journey: each and every patient has a unique way of experiencing their disease."

"In oncology, we are just scratching the surface of what ML can bring to drug discovery and development. The next-generation techniques now being applied to cancer samples – including advances in RNA sequencing, liquid biopsies for circulating tumor and cell free DNA, and spatial transcriptomics – have yielded a veritable treasure trove of data from patients, before and after standard of care therapies, for researchers to mine," said Catherine Sabatos-Peyton, CEO of precision cancer immunotherapy company Larkspur Biosciences. "The most transformative opportunity in this space will be testing key biological hypotheses – informed by our understanding of the interaction between cancer and the immune system – in the models we are developing through ML. This application can yield not only key targets to pursue, but also inform precision strategies for delivering medicines to the specific patient population that is most likely to benefit."

"Integrating digital health solutions, including new, innovative remote patient monitoring (RPM) and virtual care technologies, as 'digital health companions' alongside novel pharmaceutical therapies will be transformative," said Lishan Aklog, CEO of Lucid Diagnostics, Inc., which is developing a rapid, office-based diagnostic test for biomarkers of esophageal cancer. "Better post-market surveillance using real-world data will facilitate improved safety profiles and measure long-term efficacy and effectiveness allowing expanded access to these high-value, higher-risk therapeutics such as CAR-T therapy and bi-specific antibodies therapy.

"The real-world data collected by these digital health companions have key strategic value for the biopharma industry as therapy developers can use the data to consider indication expansion, targeted marketing, and support product life-cycle management," he noted.

Digital Health Solutions

"For our industry, AI stands as a beacon of transformation which can redefine support systems for patients. The industry must leverage the eruption of AI innovation to improve treatment pathways and address delays. Crucially, delays to drug access can worsen the patient's condition. As the industry propels forward, digital therapeutics which provide personalized interventions via digital platforms, will work to maximize impact and tailor patient care to the individual," said Angelini Pharma's chief medical officer, Agnese Cattaneo.

"At the heart of this is AI. AI-driven solutions are starting to revolutionize pharmacy operations, automating tasks from precise medication dispensing to providing personalized digital therapeutics. This will help drive timely and impactful care, particularly pivotal for fragile patients such as those affected by epilepsy, where every moment matters. Embracing this transformative technology paints a hopeful picture, promising speedier support and brighter outcomes for those in need."

Rosalind Picard, professor at MIT Media Lab and chief scientist of its health monitoring platform spinoff Empatica Inc., also saw transformative potential for digital health, particularly in the field of mental health.

"In 2024, clinical wearable device technology, powered by AI, is predicted to revolutionize mental health care by personalizing treatment strategies, enhancing patient-clinician conversations, and potentially preventing many cases of mental illness. This transformative technology enables real-time monitoring of symptoms, provides objective data beyond traditional clinician interviews, and can estimate changes in symptom severity," she said.

"The potential of wearable data and AI goes beyond treatment; it can also predict and be used as a preventive measure against mental illness, shifting our current 'sick-care' system to a proactive 'health-care' system. Furthermore, by allowing individuals to self-monitor their mental health and detect symptom changes early, it can significantly expand the reach of limited mental health resources, making services more accessible, and bridging the gap in mental health care. The technology also helps identify who needs clinical visits and when, and enables better monitoring and tailoring of effective treatments."

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> AGNESE CATTANEO, ANGELINI PHARMA

Justin Schreiber, chairman and CEO of telehealth company LifeMD, took a similar view, but focused on weight management. "In our digital era, personalization is expected. When it comes to weight management, the most successful programs are those offering patients a combination of excellent clinical perspectives in conjunction with one-on-one coaching, nutrition programs, an introduction to healthier habits, and community support," he said.

> *In 2024, emphasizing technical and clinical validation for digital health is imperative. The pharmaceutical industry's regulatory requirements mandate strong evidence, proof of efficacy, and high safety standards. Prioritizing clinical studies for digital health solutions is essential to establishing efficacy and safety of these products.*
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> **STEPHEN RANJAN, ROCHE PHARMA**

will be especially important for patients seeking holistic health care for chronic diseases, such as those that stem from weight management issues."

Amid the hype, it is important to be rigorous about quality and standards, warned Stephen Ranjan, global head of digital health for Roche Pharma. "In today's convergence of science and technology, data and analytics are transforming digital health delivery into a comprehensive experience that is designed to provide the best care for every individual. Access to patient data enables personalized care, from early detection to treatment planning. However, we are in an era where many digital health products that are marketed lack robust clinical validation," he said.

"In 2024, emphasizing technical and clinical validation for digital health is imperative. The pharmaceutical industry's regulatory requirements mandate strong evidence, proof of efficacy, and high safety standards. Prioritizing clinical studies for digital health solutions is essential to establishing efficacy and safety of these products, learning much from the pharmaceutical industry standards. This approach ensures that digital health products meet rigorous requirements, providing validated solutions. With this as a focus, we can show the true transformative potential of data in revolutionizing health care in the coming year."

"Based on the challenges they've faced when trying to access a primary care provider, patients are seeking out better and more direct ways to get care, even if it means turning to urgent or emergency care. The rise of telehealth is a sign of an overdue industry paradigm shift that puts the emphasis on providing care the way patients want to receive it and as a result benefits stakeholders across the entire care pathway, including physicians and insurers."

Schreiber expected to see "a significant increase in accessibility with the adoption of telehealth services across demographics, based on prior use cases. This

Diagnostics

Transformative technology could play a role in areas including oncology and virus detection, according to some executives. "With more data, richer patient histories, and predictive modeling AI has the potential to radically change the way we think about difficult-to-treat disease. As AI takes a larger role in diagnostics, we may see a shift in the kinds of patients doctors are meeting at diagnosis," said Liz Barrett, president and CEO of UroGen Pharma, Ltd.

"What if the majority of cancer patients were consistently diagnosed at the earliest stages? What if we were able to identify trends unrecognized before, in the massive amount of data collected? This changes the kinds of therapeutic advances required to address future patient needs and shifts the entire paradigm of treatment. It's exciting to imagine but also highlights the delicate nature of responsibly handling patient data, incorporating AI into practice, and preparing as organizations to address patient needs in a very different way."

"In 2024, I believe the diagnostics industry will double down on embracing AI and predictive analytics to better address evolving global public health needs and ensure patients have increased access to the appropriate therapies needed to treat their conditions," said Dave Persing, chief medical and scientific officer at molecular diagnostics company Cepheid. "For example, it is the job of viruses to mutate as they move from person to person, which makes it progressively more difficult for diagnostic tests to detect these natural shapeshifters. Technology can help providers stay a step ahead to get their patients accurate diagnoses. Predictive analytics and AI will likely be used more routinely to see around corners and ensure our diagnostic tools are staying ahead of that genetic drift so a patient presenting with a newer strain of a virus can be treated with the right antiviral therapy."

"Workforce shortages in health care have reached crisis levels in recent years and are expected to continue into 2024. This will force health care organizations to do more with less, and biopharma will play a key role in helping to preserve resources via innovative technologies. A great example of this is playing out in oncology diagnostics, specifically in prostate cancer detection," said Bob Rochelle, chief commercial officer at Cleveland Diagnostics, Inc.

> *In 2024, I believe the diagnostics industry will double down on embracing artificial intelligence and predictive analytics to better address evolving global public health needs and ensure patients have increased access to the appropriate therapies needed to treat their conditions.*
>
> **DAVE PERSING, CEPHEID**

"Health care professionals regularly navigate the in-between of providing optimal care for patients while avoiding unnecessary procedures and health care costs. Recent advancements in proteomic approaches to cancer screening are set to transform the industry by providing accurate, definitive diagnoses and thus minimizing follow-up or unnecessary, invasive biopsies. Breakthroughs such as these will go a long way in reducing physician burnout, driving better patient outcomes, and fortifying our health care system from the inside out."

Owlstone Medical Ltd. CEO Billy Boyle noted that "breath technology is rapidly advancing into a routinely useable biomarker analysis platform, representing a huge opportunity to support drug discovery, validation and diagnostics, and the coming years will be crucial in its deployment for clinician and patient use.

"Breath contains biomarkers from throughout the body, allows large volumes to be collected to improve test sensitivity, and enables flexible, at-home, sample collection, supporting decentralized trial designs and non-invasive longitudinal monitoring," he said. "Also, the use of exogenous probes to target specific biological processes shows great promise for the detection of conditions including lung cancer, liver disease, and digestive diseases. This results in the release of unique chemicals on breath to drive better test performance, and we anticipate significant progress in this technology in 2024."

Finally, he said: "Efforts are underway to generate reference databases of human breath that can accelerate the identification and validation of novel breath biomarkers to further support disease diagnosis and monitoring."

For Peter Bauer, chief medical and genomic officer at Centogene NV, bioinformatics will be the key to change. "Over the past year, we have witnessed remarkable developments in AI and ML – from ChatGPT to proprietary solutions across the industry. Going into 2024, I expect to see us leveraging these technologies even more and integrating them further into workstreams, particularly in the realm of bioinformatics as the connecting point between data and a true understanding of human diseases," he said.

"This evolution is driven not only by technological advancements, but also by the increasing trend of localization in health care. These bioinformatic pipelines play a crucial role in decentralizing diagnostics, making it more efficient and accessible. As we navigate the path to 2024, the integration of automation into bioinformatics becomes imperative, aligning with the industry's need for localized solutions. This shift ensures that diagnostic processes are streamlined, adaptable, and capable of meeting the demands of a health care landscape that values precision and accessibility."

Genomics

"The personalized medicine market is expected to grow by over 11% each year to reach $869.5bn by 2031. It will be increasingly supported by pharmacogenomics, testing that shows how genetic variations affect metabolism, action, and tolerability of medications. Through faster and less-expensive sequencing of the human genome, pharmacogenomics can lead to the best treatment plan for a specific patient and can identify individuals who may be at a higher risk of serious adverse reactions to certain drugs," said Stella Vnook, CEO of cell therapy formulation specialist Likarda.

"This practice has applicability to treat patients with a variety of heterogeneous diseases like mental disorders, cancer, and cardiovascular disease. We hope to see widespread adoption and availability of personalized medicine as education and training increases. Pharmacogenomic information empowers both patients and health care providers to make more informed decisions about treatment options. This shared decision-making process can enhance patient engagement and satisfaction," she added.

Sequencing-based genomic screening of apparently healthy newborns is an area of clinical value ripe for exploitation, thought Madhuri Hegde, chief scientific officer of Revvity, the rebranded diagnostics and life sciences business of PerkinElmer Inc. "The use of proactive genomic screening [of newborns] would enable health care professionals to uncover a wide range of risks for looming pediatric onset conditions, allowing for earlier interventions and personalized treatment plans based on individual genetic make-up. As next-generation screening becomes more accessible to the general public, harnessing this tool could have a profound impact on the health and wellbeing of families and future generations."

"In 2024, the biopharma landscape is poised for a revolutionary leap into the dark genome, reshaping drug discovery. With evidence highlighting that genetic insights double the likelihood of drug approval, I believe that the industry's focus will continue to extend beyond protein-coding genes, to unlock the value of the still largely untapped 90% of disease-associated genetics changes located in this uncharted territory," predicted Danuta Jeziorska, CEO of Nucleome Therapeutics Limited.

> *In 2024, the biopharma landscape is poised for a revolutionary leap into the dark genome, reshaping drug discovery.*
>
> **DANUTA JEZIORSKA, NUCLEOME THERAPEUTICS**

"By looking at the genome in 3D perspective – beyond its linear sequence – the connectivity between genes and the genetic changes that affect their expression at a distance can be unveiled. This has a potential to map the cell type-specific disease-affected pathways, laying down the foundation for understanding complex disease biology and constructing drug discovery hypotheses rooted in genetics."

Gene And Cell-Based Technologies

There was much excitement among our surveyed executives for anticipated developments in the field of gene and cell therapies.

In particular, many referenced the recent FDA approval of Vertex Pharmaceuticals Inc. and CRISPR Therapeutics AG's CRISPR-based gene editing therapy Casgevy (exagamglogene autotemcel) for sickle cell anemia and transfusion-dependent beta thalassemia, which Mahesh Karande, CEO of Omega Therapeutics, Inc., described as "one of the most rapid translations of concept to approved therapy in the history of drug development."

"This is a monumental milestone for biomedical innovation, and it is just the beginning of the future of CRISPR-based applications," said Jon Terrett, head of research at CRISPR Therapeutics.

"Ex vivo cell therapy clearly has led the way, but in vivo CRISPR editing therapies are also in clinical trials and showing signs of benefit in rare diseases and the cardiovascular setting. We will continue to see ways to build upon the CRISPR technology and delivery tools with the goal of enabling even more disease areas," Terrett went on. "The next generation of gene editing has arrived: highly multiplexed allogeneic CAR-Ts are already in the clinic and soon new gene editing and delivery modalities could reach patients too. This could include areas such as all-RNA gene correction, whole gene insertion and non-viral delivery of DNA. Development of more CRISPR-based medicines for the treatment of both common and rare diseases is already underway and I'm excited for all that is to come."

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>
> **JON TERRETT, CRISPR THERAPEUTICS**

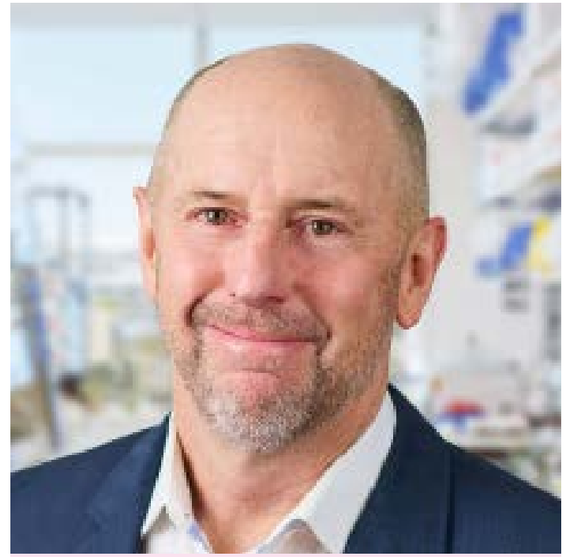
Drew Hope, qualified person and compliance consultant at eXmoor pharma, also underscored the broad potential of the technique. "This autologous cell-gene therapy approach can be used for gene-corrections in a wide range of inherited diseases such as hemophilia, fibrosis and Tay Sachs," he said. But he is also looking forward to the use of CRISPR in allogeneic cell therapies. "The technology is being applied in cancer therapies; there are many CRISPR-based T-cell products in clinical development, the majority of which are allogeneic. The approach may overcome the T-cell malignancy concerns relating to viral transduction used commonly in CAR-T cells. Also, there are numerous medicines in development combining CRISPR gene editing technology and induced pluripotent stem cells (iPScs) to engineer allogeneic stem cells that differentiate into products to hit therapeutic targets across the range of unmet indications."

For Joe Truitt, CEO of in vivo gene-editing specialist iECURE, Inc., Casgevy's approval "highlights the tremendous technical progress that genetic medicine developers have made in the six years since the first gene therapy for a genetic disease was approved," commented. "With other gene-editing approaches independent of CRISPR poised to enter the clinic in 2024, the possibilities for curing diseases that have been intractable to traditional gene replacement techniques have never been closer bringing so much hope to patient communities."

"While genome editing is a new frontier of medicine, it is far from the last," commented Omega's Karande. "The field of controlled epigenomic modulation is emerging as the next breakthrough technology promising to pre-transcriptionally control gene expression while preserving genomic integrity. As the underlying biology has come into clearer focus over the last few years, multiple approaches tapping into the epigenome have emerged. We've already achieved the first-ever clinical proof-of-concept data demonstrating desired downregulation of the previously undruggable oncogene MYC. This feat underscores the real potential of precision epigenomic control to unlock new targets for drug development. As data leveraging this approach accumulates in 2024 and beyond, we will see expanded applications and further evidence of the tremendous value of this new therapeutic class."

"In 2024, the biopharmaceutical field will continue to be transformed by genetic medicines," predicted David Kirn, CEO of 4DMT, a genetic medicine discovery and development company. "The challenges associated with the in vivo delivery of genetic medicine technologies, specifically through use of adeno-associated virus (AAV) vectors, are poised to be overcome by innovative solutions. The limitations with delivery efficiency, genetic medicine expression, and immunogenicity will be addressed by cutting-edge technologies that go beyond conventional methods. This technological leap holds significant promise for superior efficacy in targeted tissues, reduced toxicity and lower doses required. The power of targeted vector technologies is expected to unlock the full potential of genetic medicines for numerous rare and large market populations, including for diseases that were previously deemed too expensive to treat. This not only could open doors for potential cures but also eases the treatment burden on patients, providing hope for populations with significant unmet medical needs in 2024 and beyond."

"Although the funding environment is challenging now, the longer-term trends around transformative technology have never been brighter. The pace of scientific discovery and its application in drug development has never been faster. For example, a significant amount of new investment has been made in the past couple of years to address the challenges in the delivery of genetic medicines to extra-hepatic tissues," said Antonin de Fougerolles, CEO of Evox Therapeutics Ltd.



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>
> **DAVID KIRN, 4DMT**

"For all the value created to date by RNA and genome editing companies, delivery constraints mean drugs can only be delivered to one or two tissues, leaving 95% still untapped. The progress being made on delivery is quickly picking up pace and accompanies an increasing need for RNA and gene-editing companies to create differentiated products that are not solely hepato-centric," he added.

"I predict we'll continue to see promising clinical data in genetic medicines targeting conditions beyond those mediated by the liver," said R. Nolan Townsend, CEO of Lexeo Therapeutics, which is developing genetic medicines to cure cardiovascular diseases and Alzheimer's disease. "For example, a substantial body of evidence now demonstrates the high transduction efficiency of AAVs in cardiomyocytes. These findings pave the way for continued advances in cardiac precision medicine, offering potential treatments for a

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> *Just as we have seen an overall shift to precision medicine in therapeutic areas like oncology over the past decade, we expect to see substantial R&D investment into broader conditions with genetic markers of disease, like cardiovascular disease.*
>
> **R. NOLAN TOWNSEND, LEXEO THERAPEUTICS**

variety of genetically defined cardiovascular diseases, a field that has seen limited industry investment to date relative to the opportunity size. Just as we have seen an overall shift to precision medicine in therapeutic areas like oncology over the past decade, we expect to see substantial R&D investment into broader conditions with genetic markers of disease, like cardiovascular disease."

"The discovery and development of genetic medicines have been accelerating dramatically, and I expect that trend to continue. The well-known barrier to extrahepatic delivery of this important class of therapeutics is finally being funded, and talented teams are going after the problem," said Shawn Davis, CEO of Liberate Bio, which develops non-viral delivery technologies. "I'm hopeful that the combination of talent, science, and funding will result in breaking through this barrier and the industry having access to multiple new vehicles to address the areas of the highest unmet need rather than the organs to which we can currently deliver."

"Most currently approved genetic medicines, as well as many in clinical development, are 'traditional' gene therapies that utilize viral vectors as a delivery platform," commented Alex Nichols, president and chief operating officer of gene delivery specialist enGene Inc.

"Correspondingly, most suffer from the intrinsic limitations of therapies based on a live, infectious vector, including handling and preparation challenges, complex manufacturing, a tendency to generate anti-vector immunity, and longstanding safety concerns. As the field looks to extend the reach of genetic medicines, such as by targeting tissues outside of the liver, non-viral delivery methods continue to generate excitement amongst clinicians and patients. I anticipate that non-viral delivery technologies will take center stage as the next frontier in genetic medicine, with several candidates already in mid- to late-stage development."

For Julian Hanak, CEO of Purespring Therapeutics, Ltd., "One of the biggest developments I anticipate in gene therapy in 2024 and beyond is an increasing focus in the use of the gene therapy in non-monogenic disease. The ability to engineer vectors to carry multiple genetic cargoes and address non-monogenic pathologies, combined with improvements in treatment delivery systems, opens up opportunities to target a much broader range of indications, and we think that this is going to drive a wave of innovation."

"One area I really see transformative technology taking hold in 2024 is in cell-based therapies," said Omid Veiseh, faculty director of the Rice Biotech Launch Pad, Houston, Texas-based Rice University's biotech accelerator. "Despite the considerable promise these therapies have for treating a wide range of diseases, challenges persist in ensuring the survival of cells to produce effective treatments. Presently, numerous ongoing studies are dedicated to tackling these hurdles, particularly in technology to enhance oxygen production – a crucial factor influencing cell viability and potency. Prolonging the health of cells allows for greater autonomy in producing therapeutics within the body. Existing options are inefficient at addressing these problems, necessitating additional technology in this area to make these therapies truly viable."

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"Despite the establishment of CAR-T cell therapies as approved therapies in hematological malignancies, large unmet medical need remains for solid tumors," said Selwyn Ho, CEO of German immuno-oncology developer Medigene AG. "Here, T-cell receptor engineered T-cell (TCR-T) therapies with their ability to target a wider range of tumor antigens and their persistence in the body with potential for durable responses, offer hope towards future curative therapies. The first TCR-T is expected to be approved in 2024.

"The next generation of TCR-T therapies currently under development will bring three major improvements: 1) Optimal TCRs that target newly identified tumor-specific antigens. 2) Enhanced and armored TCR-T therapies with the ability to survive and thrive in the immunosuppressive solid tumor microenvironment. And 3) Improved drug product composition for the development of safe, efficient, and cost-effective therapies."

Peter Maag, CEO of Kyverna Therapeutics, meanwhile, highlighted CAR-T therapy's potential beyond oncology. "CAR T-cell therapy has shown impressive outcomes in hematologic cancers. Now we are seeing early scientific evidence suggesting this modality may also transform the treatment of autoimmune diseases, which impact one in five Americans, and oftentimes cannot be treated effectively with current therapies," he said.

"Recently, researchers reported in the Lancet Neurology the first successful treatment of a patient with myasthenia gravis, a debilitating and chronic disease, using an investigational CAR-T developed for B-cell mediated autoimmune diseases. Other published research found promising outcomes with CAR-T in refractory systemic lupus erythematosus and dermatomyositis, two other autoimmune diseases. I'm optimistic the research momentum will continue in 2024 and may soon enable physicians to offer potentially paradigm-shifting therapeutic options to their patients impacted by autoimmune diseases," said Maag.

Another executive drew attention to a different focus in cell therapy. "In 2024, I believe industry will look for smarter ways to program immunity, particularly new methods to engage dendritic cells more physiologically. Mellman-Chen's 2023 update of their cancer immunity cycle highlighted a growing appreciation for the importance of dendritic cells in sustaining anti-cancer immunity. However, to date, industry attempts

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> **PETER MAAG, KYVERNA THERAPEUTICS**

to develop immune cell therapies have placed an understandable premium on rudimentary efficacy at the expense of safety. The result is relatively unspecific therapies that have attracted huge investment but struggle to progress beyond their innate limitations," observed Justin Duckworth, CEO of Transimmune AG.

"Ultimately, to restore immunological surveillance, we need to revisit dendritic cell engagement. We know there are limitations in how these rare cells have been made in the past that has impacted efficacy. However, with the support of institutions like the Gates Foundation and ARPA-H, new approaches for in vivo and ex vivo engagement are being advanced, providing fresh optimism for a more ambitious generation of cell therapies."

RNA-Based Therapies

"Since the completion of the Human Genome Project, scientists have sought to treat diseases at the genetic level, including by using RNA. Historically, one of the biggest hurdles for RNA-based therapeutics has been delivery to a target tissue," said Vasant Jadhav, Alnylam Pharmaceuticals Inc.'s chief technology officer. "We arrived at a crucial moment for RNA-based medicines when Alnylam scientists invented two transformative delivery platforms: lipid nanoparticles and GalNac conjugates. These enabled liver delivery and led to the approval of six RNAi therapeutics – a new class of medicines. The delivery platforms have also been used for other RNA-based medicines, including mRNA COVID-19 vaccines."

Jadhav went on: "Building on liver delivery lessons, scientists are now making progress in other tissues, including the central nervous system (CNS), adipose and muscle. We expect RNAi therapeutics will rapidly progress toward treatment of many rare and common conditions."

"Advances in RNA drug development are a major area of rapid and exciting progress. Recent research is changing both the ways we develop RNA medicines and their potential to target more diseases safely and effectively," said Sarah Boyce, CEO of Avidity Biosciences, Inc.

"Advances in the use of antibody-oligonucleotide conjugates (AOC) therapeutics that combine the proven technology of monoclonal antibodies with the precision and potency of oligonucleotide therapies are leading to an era where we can access many previously untreatable tissue and cell types. The field experienced a major milestone in 2022 when researchers at Avidity Biosciences delivered RNA to muscle tissue – the first time that delivery of an RNA therapeutic was successful outside the liver. Building on this research, we can now potentially target a much wider range of diseases with RNA therapeutics, including many that could not be targeted previously, in 2024 and beyond."

"RNA editing offers the potential to impact and treat both genetic disorders and common conditions," noted Daniel de Boer, CEO of ProQR Therapeutics N.V. "The transient nature of editing at the RNA level offers flexibility and potential safety benefits,

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> **SARAH BOYCE, AVIDITY BIOSCIENCES**

opening therapeutic opportunities that were not accessible before. While it is still early in its evolution, RNA editing is based on a wealth of experience with the proven modality of oligonucleotides to recruit a novel mechanism of action and is well-positioned to sustain momentum in 2024, with more indications and programs dedicated to advancing clinical development. We look forward to seeing significant developments in the RNA editing space, bringing transformative treatments to patients with unmet need."

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Akihiro Ko, CEO of Elixirgen Therapeutics Inc., was also "looking forward to seeing how scientists continue to expand the use of transformative technology in the RNA space beyond COVID-19 vaccines."

He said: "There's a lot of work being done with how the technology can be used for other infectious diseases, cancer, and rare diseases. One of the important things to think about when designing RNA technology is how to deliver it safely and effectively since RNA is so prone to degradation. Lipid nanoparticles (LNPs) have emerged as a critical tool for delivery and are currently being used in the COVID-19 vaccines. There are ongoing conversations about the manufacturing, proper storage, and immunogenicity of LNPs in addition to organ-specific delivery that we look forward to seeing advance in the next year."

"In 2024, I think antisense oligonucleotide (ASO) technology will become a more important drug modality within the field of targeted therapies," said Konstantin Petropoulos, chief business officer at Secarna Pharmaceuticals, which is developing antisense therapies using a proprietary ASO discovery platform. "This technology has matured steadily over the past decades resulting in improved overall efficacy and safety profiles, and with several products on the market and many programs in advanced stages of clinical development.

"With more approvals in recent years and commercial success, big pharma now understands there is more to ASO technology than its application in classical genetic diseases. There are programs addressing major CNS diseases like Parkinson's and Alzheimer's, as well as in oncology, cardiovascular, fibrotic and kidney diseases," he pointed out. "Now in the next years the race is on for developing shuttle mechanisms that specifically deliver these compounds to the affected organ or cell types, resulting in further improved potency and less side effects."

"There's been a seismic shift in interest in mRNA as a therapeutic, and we'll continue to see this play out," declared Jason Downing, senior product manager at specialist contract development and manufacturing organization TriLink BioTechnologies. "In fact, 2024 needs to be a foundationally transformative year for mRNA as a modality to set us up for a strong 2025 and beyond. The pandemic cast a bright spotlight and drove up the number of mRNA-based programs in development in the US from 80 to more than 2,000. Over the course of the next year – with these programs in either Phase II or III – our industry will learn more about the effectiveness of these treatments, which

> *The journey toward unlocking the full capabilities of mRNA vaccines and therapeutics, in combination or alone, is an exciting one, and 2024 is poised to be a pivotal chapter for this promising biomedical modality.*
>
> **CHRISTOPHER PIRIE, HDT BIO**

span a variety of therapeutic areas, including oncology, cell and gene therapies, and infectious diseases. It's going to be an exciting time in biopharma, as the industry can now take a step back and strategically build the infrastructure necessary to not only realize mRNA's full potential, but to make this breakthrough modality accessible to all."

"In the past few years, we've seen ever increasing enthusiasm for mRNA as a new modality in the pharmaceutical toolkit. I'm excited to see that trend continue in 2024 as the industry continues to push the envelope in terms of what the modality is capable of, overcome remaining challenges in delivery, and address residual concerns related to safety," said Christopher Pirie, chief operating officer and co-founder of HDT Bio Corp., a developer of vaccines with a focus on creating products that harness the patient's immune system and are affordable even in low-income countries.

"From in vivo cell therapy, to enzyme replacement, and cancer and infectious disease vaccines, there's cause for that enthusiasm and hopefully we'll begin to see early-stage companies in the space read out critical clinical data next year," said Pirie. "The journey toward unlocking the full capabilities of mRNA vaccines and therapeutics, in combination or alone, is an exciting one, and 2024 is poised to be a pivotal chapter for this promising biomedical modality."

Yochi Slonim, CEO of Anima Biotech Inc., predicted that "In 2024, AI will continue reshaping drug and target discovery, notably in mRNA biology. High-throughput automation enables millions of biology experiments, unlocking insights into mRNA processes. Neural networks, adept at analyzing intricate image data, are key in unveiling disease mechanisms linked to dysregulated mRNA regulatory pathways. The vast data produced, such as images of specific mRNA life-cycle events, is managed effectively by knowledge graphs and LLMs. These technologies synthesize information, providing crucial contextual insights into mRNA biology. AI's interaction with biologists becomes seamless, with user interfaces like co-pilot translating natural language into knowledge graph searches. This enhances our understanding of disease biology and aids in planning, executing, and monitoring discovery activities. This shift not only streamlines the discovery process, reducing time and costs, but also leads to new and more effective treatments. AI's role in biotech, once theoretical, is now a dynamic force reshaping our fight against previously undruggable diseases."

Vaccines

Peter Jackson, CEO of UK-based Infex Therapeutics plc, flagged up developments in coronavirus vaccine approaches. "Biopharma is increasingly switching focus to novel prophylactic strategies against coronaviruses, particularly as greater evidence of resistance to current MPRO inhibitors emerges," he said. "This shift towards new mechanisms of action effective against a wide range of coronavirus strains is crucial. It signifies a proactive, rather than reactive, approach in our ongoing fight against viral threats with pandemic potential."

"Of the many lessons from the pandemic, COVID reiterated the importance of vaccines and how innovation in both proven and newer vaccine technologies is needed to protect us against serious illness and death," said Filip Dubovsky, president of R&D at Novavax, Inc. "Today's resurgence in vaccine research aims at furthering effectiveness and tolerability, new modes of administration, and understanding of the immune response across populations. This work will help protect us against acute infection as well as the durability and breadth of that protection."

Dubovsky went on: "Combination vaccines, like Novavax's COVID-19/influenza candidate, are among those that I expect to advance in 2024. We'll soon learn how far we can go to 'multiplex' vaccines to better protect people against multiple threats with a single effective – and convenient – shot."

Thomas Rademacher, CEO of Emergex Vaccines Holding Ltd., also flagged up durability, and pushed for the use of technology to improve on the latest synthetic vaccines so that they promote a longer-lasting response: "Historically, governments listed emerging flu pandemics as top-risk – but current 'flu jabs' potentiate the threat, attenuating natural birth-cohort immunity via childhood vaccinations. The same story plays out with 'COVID jabs.' In contrast, legacy vaccines provide single-injection lifetime protection against RNA viruses – polio, yellow fever, smallpox – uniquely perceived 'alive' by the immune system. Transformative technology thus aims to flag synthetic vaccines as 'alive.' Need we consult AI?"

Both Rademacher and Dubovsky highlighted the importance of public confidence in vaccines.

> *We'll soon learn how far we can go to 'multiplex' vaccines to better protect people against multiple threats with a single effective – and convenient – shot.*
>
> **FILIP DUBOVSKY, NOVAVAX**

"Whether due to fatigue or misinformation, only 17% of adults have chosen an updated COVID vaccine as of early December 2023, according to the CDC. Data show that when given options, people are more likely to choose to protect themselves. Therefore, combined with a clinical need for options, we must ensure availability of diverse platforms to help drive confidence, uptake and to save lives," said Dubovsky.

"The COVID-19 pandemic infectious disease (ID) arena highlighted widespread knowledge gaps in immunology, ID/virology and vaccines. Essential to public health management, vaccines rely on public trust of governments. Revolving doors between politicians, health stakeholders, and big pharma, unless

checked, will block transformative technologies from infiltrating the arena," warned Rademacher.

Jens Bjørheim, chief medical officer at Ultimovacs ASA, was optimistic about progress in cancer vaccines, meanwhile: "In recent years, there has been remarkable innovation and advances in the development of therapeutic cancer vaccines. New technologies are showing highly promising results in clinical studies. I believe this positive trend will continue throughout 2024 and in the years ahead. By training the immune system to target cancer-associated antigens and tumor antigens, we believe the vaccine approach could benefit more patients across tumor types. While many vaccines are tailor-made using neoantigens from the patient's tumor, a more universal approach is a complementary strategy in the emerging cancer vaccine landscape. Off-the-shelf vaccines that don't require sophisticated hospital infrastructure hold the potential to enhance applicability and impact a larger population of patients, including rural and underserved communities."

Antibody-Drug Conjugates

"Antibody-drug conjugates (ADCs) were the modality of the year, with a raft of new approvals accompanied by a frenzy of deals, and the current market of $9.7bn is expected to double in the next five years," highlighted Jason Gardner, CEO of Ampersand Biomedicines. "This is a clear recognition of the value of a medicine that specifically targets and delivers a payload to the site of disease while attempting to spare healthy cells. However, the 13 currently approved ADCs are used only in oncology against three cell types with three chemotherapy payloads.

"In 2024, I expect advances in technology and a growing understanding of human biology to provide an opportunity to expand upon the successes of ADCs. If we can broaden the targets to which we can deliver medicines and the types of therapeutic agents we can deliver, we can even go beyond oncology to create smarter medicines with even better specificity," concluded Gardner.

Tiffany Thorn, CEO of BiVictriX, also flagged up ADCs. "2023 was a pivotal year for the ADC sector, underscored by some of the largest M&A deals of the year, and the observed upswing in interest from big pharma will drive substantial and unprecedented growth in 2024," she said. "Expansion of the sector will be driven by the growing number of ADCs in clinical development, advancements in target specificity, payload technology and conjugation, and the heightened therapeutic potential for addressing secondary malignancies and solid tumours."

Thorn added: "We are now entering a transitional period for ADC technology, and developing a deeper understanding of efficacy and specificity drivers will be key to safely and efficiently developing these drugs for the people who need them."

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>
> **TIFFANY THORN, BIVICTRIX**

Better Targeting

"I believe we'll see a renaissance in small-molecule drug development driven by the convergence of several factors, including the emergence of promising therapeutic approaches like targeted protein degradation, patient preference for oral medicines, and technologies such as X-ray crystallography and cryogenic electron microscopy that are enabling us to better understand molecular structures and biological mechanisms and design better medicines," said Nello Mainolfi, CEO of targeted protein degradation specialist Kymera Therapeutics, Inc.

"Small-molecule drug development continues to undergo transformative shifts by notably focusing on proteins that have previously eluded traditional drug targeting or whose therapeutic potential remains largely untapped," said Rajesh Devraj, CEO of precision therapy developer Rectify Pharmaceuticals, Inc. "One such example is the ABC transporter 48-member superfamily that actively transports a range of substrates in a variety of tissues. Beyond the well-known example of CFTR therapeutics targeting ABCC7, there is a large opportunity to drug a number of ABC-transporters whose dysfunction drives a range of serious diseases. Recent advancements in sensitive and high-throughput assays to detect endogenous target protein-expression, cryo-electron microscopy, and the development of bespoke translational disease models enable our industry to discover novel small molecules that can restore and/or enhance protein function. Transformative technological advancements allow for the continued advancement of impactful first-in-class, disease-modifying drugs for serious diseases."

"The continued rise of targeted protein degradation therapeutics like PROTACs will undoubtably be a big part of 2024 for biopharma," predicted Benedict Cross, chief technology officer at Cambridge University drug discovery spinout PhoreMost Ltd. "Progress to and through the clinic was a major part of 2023, with countless R&D developments. As Phase III clinical data emerges, we'll see if the promise of this approach translates into patient benefit.

"With many bivalent degradation drugs in development, attention is shifting to smaller, less predictable, monovalent or molecular glue medicines, which have a radically different development path.

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>
> **RAJESH DEVRAJ, RECTIFY PHARMA**

With no technology available to systematically find these molecules, we anticipate breakthroughs in molecular glue design this year," Cross went on. "Building on the promise of pioneer molecules requires diversification from known liabilities of these drugs, principally into the new ligase space. Where most disclosed molecules depend on Cereblon, identification and exploitation of new E3 ligases will overcome toxicity and resistance concerns, enabling us to unleash the full potential of this exciting modality."

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Drug Delivery

"Heading into 2024, we can expect to see a continued rise of self-injected medications and transformative changes in drug delivery systems," said Jeff Hackman, CEO of Comera Life Sciences Inc., which specializes in developing subcutaneous versions of intravenous biologics to avoid the need for patients to attend infusion centers for dosing. "Patients are increasingly administering injectable drugs at home and the GLP-1 marketplace has driven this conversation even further in the last year," he said. "We are using excipients to transform monoclonal antibodies administered intravenously into subcutaneous forms and some of these could be available within the next five to seven years. Patient-centered care is the future of medicine and it will be driven by technological advancements, patient empowerment, and the need for more efficient health care delivery systems."

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