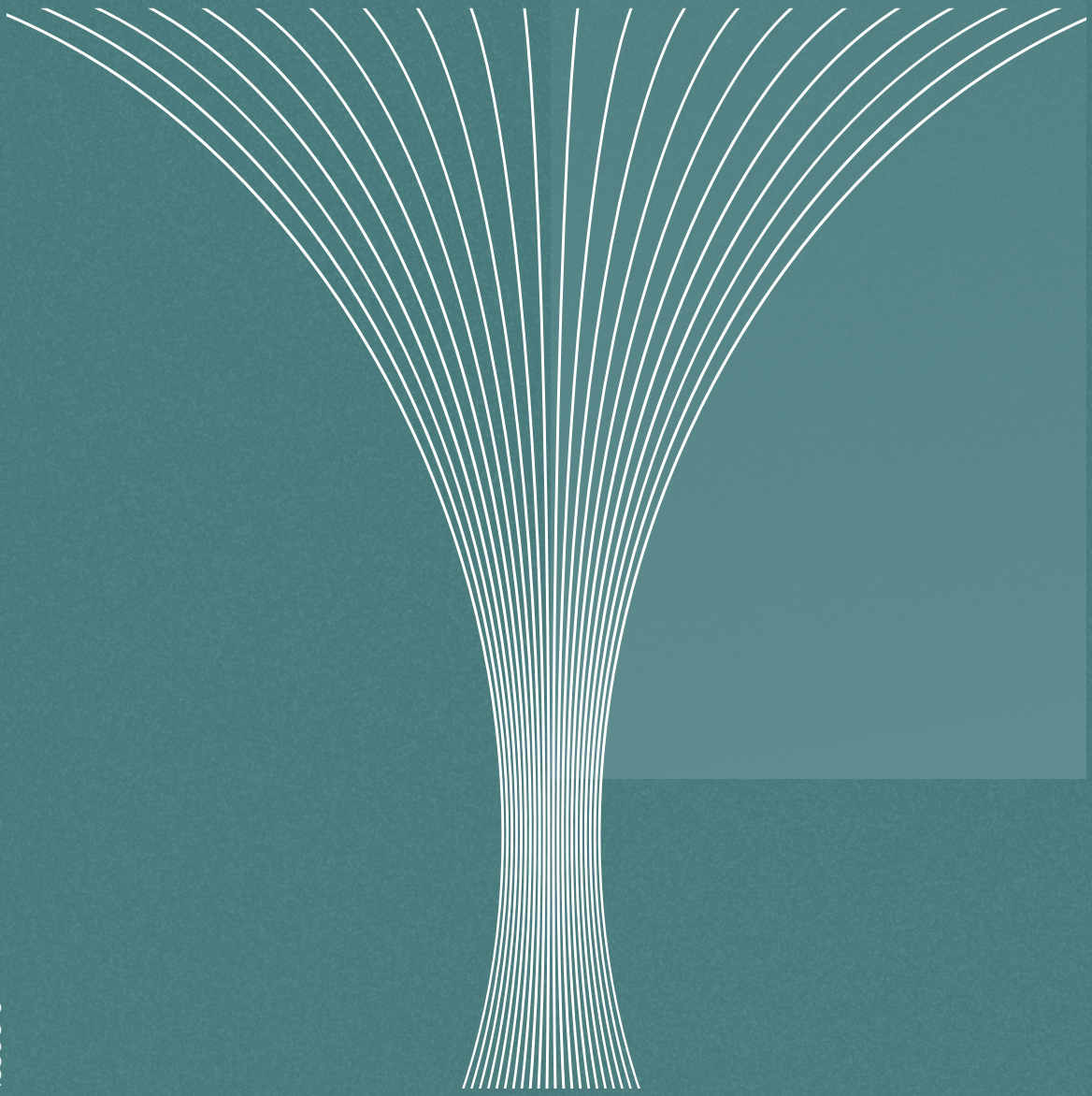
Rx Data News

Vol. 1



Issue 6

FOUNDER'S MESSAGE

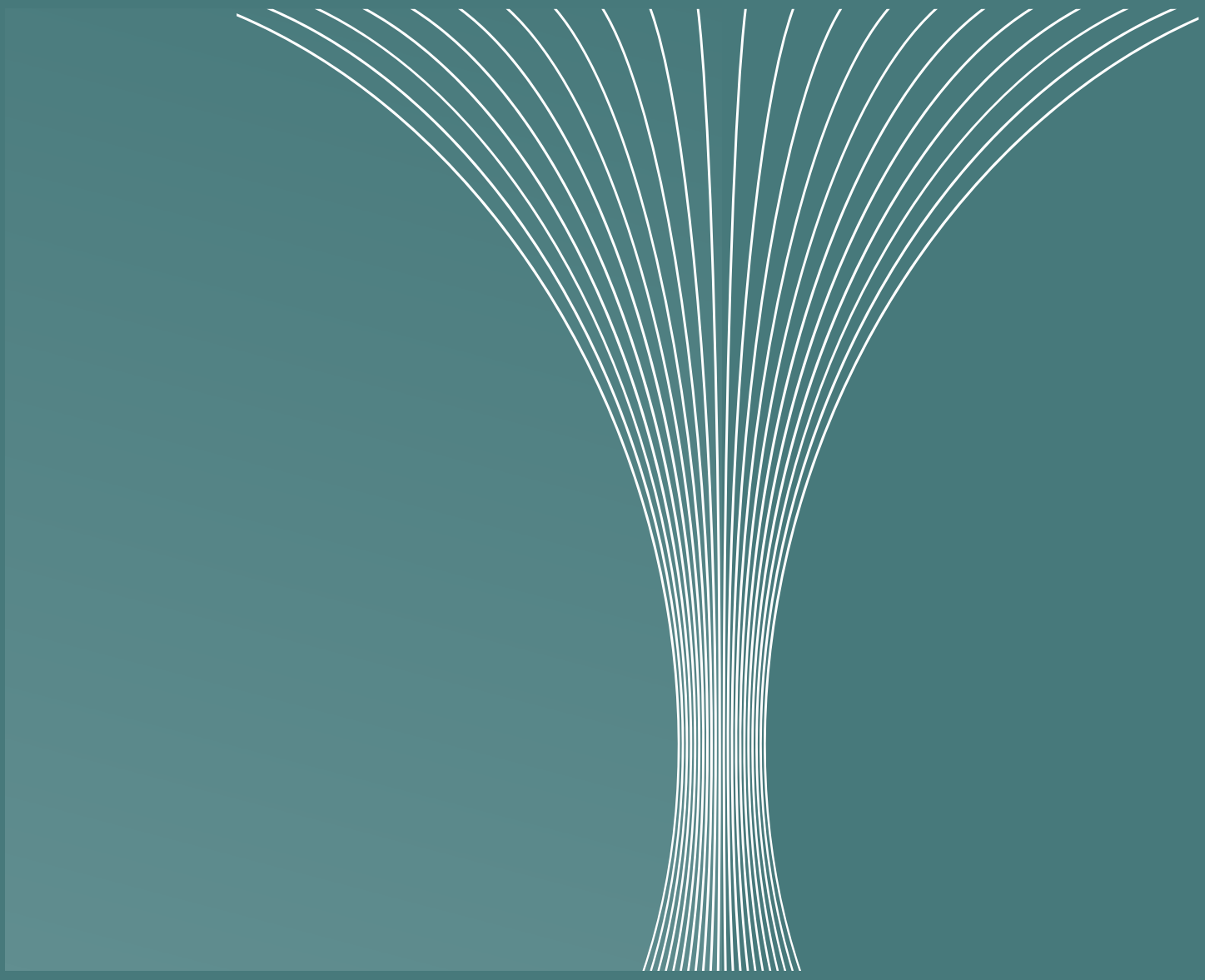
Greetings readers of Rx Data News! We would like to thank all of our subscribers for supporting this young publication. We are pleased to be bringing you quality content and deep insights from our original reporting and a combination of truly excellent thought leaders writing on a variety of salient topics. Thank you once again and please don't hesitate to reach out to me personally should you have any questions, comments or concerns.

Kind Regards,

Peter Grant
Editor, Rx Data News
peter@rxdatanews.com

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?



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News-In-Brief

ISSUE 6

verily

Verily, the health and life sciences company under Google parent-company Alphabet, announced partnerships with the pharmaceutical companies Novartis, Sanofi, Otsuka and Pfizer. The partnership aims to reach patients in new ways, make it easier to enroll and participate in trials, and aggregate data across a variety of sources, including the electronic medical record or health-tracking wearable devices.

BenevolentAI

BenevolentAI started an AI collaboration with AstraZeneca to accelerate drug discovery. The two organizations will begin collaboration between their respective teams to combine AstraZeneca's genomics, chemistry and clinical data with BenevolentAI's target identification platform and biomedical knowledge graph.

janssen

Iktos, a company specializing in AI applied to new drug design, announced a collaboration agreement with Janssen Pharmaceutica. Iktos virtual drug design technology will be applied to several Janssen small molecule drug discovery projects. Iktos will collaborate with Janssen to develop new applications, leveraging Iktos' deep generative models applied to chemistry and Janssen expertise in AI-enabled prediction of small molecule activities.

Microsoft

Vymo is collaborating with Microsoft to expand the presence of its intelligent personal assistant for sales. The partnership will focus on enabling organizations to strengthen their customer

relationship management (CRM) using AI capabilities and empower their sales function with predictive and actionable insights. Vymo is already powering an existing base of 85,000+ users in 50+ global businesses across Banking, Insurance, Financial Services and Pharma sectors.

MarkLogic announced a new version of its data integration platform expressly for the pharmaceutical industry. The MarkLogic Pharma Research Hub is designed to help researchers quickly and easily find, synthesize and share high-quality data – including, genetic, proteomic, drug, textual, binary and clinical trial data – within a single cloud service.

Chief.AI and Medicines Discovery Catapult have been awarded £370,000 of funding from Innovate UK to develop a searchable online platform that aims to make AI accessible to all drug discovery researchers.

Graphics card specialist NVIDIA and King's College London have announced they are partnering to build an AI platform that could allow specialists in the NHS to train computers to automate the most time-consuming part of radiology interpretation.

Salt Lake City-based biotech company Recursion Pharmaceuticals released a dataset of genetically altered cell images on May 6 that can be downloaded at no cost and aims to improve the use of artificial intelligence in drug discovery, STAT reports.

Y Combinator, the high-profile startup accelerator based in Mountain View, California, announced in a blog post that it will prioritize applicants that are using Atomwise's artificial intelligence software for drug discovery.

AI-enabled monitoring and decision support platform Biofourmis announced a $35 million Series B raise. The round was led by Sequoia India and MassMutual Ventures with participation from EDBI, Jianke and existing investors Openspace Ventures, Aviva Ventures and SGInnovate. The Singaporean company will be moving its headquarters to Boston, where it has a 10-person team.

Founded in 2016 by scientists and researchers from the Technion and Stanford, Cytoreason has built a machine learning platform that can quantify a person's immune system at a cellular level in order to better understand disease responses and treatments, and facilitate the discovery and development of more effective drugs. The simulations are applicable to cancer immunotherapy, and autoimmune, neurodegenerative and infectious disease research.

Ping An Technology has completed a clinical trial of the world's first intelligent optical coherence tomography retinal disease screening system. The technology arm of China's Ping An Insurance Group is developing the system jointly with US-based Optovue.

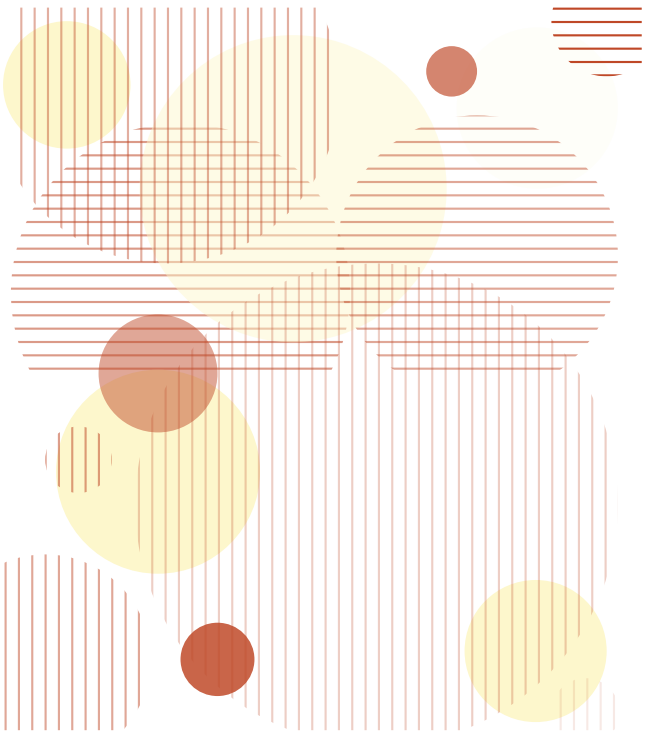
Leuven, Belgium-based icometrix has secured $18 million in funding from Forestay Capital, Optum Ventures and prior backer Capricorn Venture Partners. The company claims its technology has the potential to transform care for patients with brain injuries and disorders, by extracting clinically meaningful information from brain MRI and CT scans of patients.

FEATURED INTERVIEW:

Brandon Allgood, PhD

Chief Technical Officer and Cofounder, Numerate
San Francisco, CA

Brandon Allgood manages the development and application of Numerate's AI platform and is responsible for Numerate's technological vision. Brandon has also served as Director of Computational Science at Numerate and as a Research Scientist at Pharmix. He received a B.S. in Physics from the University of Washington, Seattle, and a Ph.D. in Computational Physics from the University of California, Santa Cruz. Brandon has authored scientific publications in astrophysics, solid-state physics, and computational biology and has 15 years of experience in large scale cloud and distributed computing, AI, and mathematical modeling. He is a member of the Forbes Technology Council and is a UCSC Foundation Trustee.



Rx Data News: What kind of cultural shift does the pharmaceutical industry need to make to most fully realize the benefits of data science?

Dr. Allgood: The first is a shift to the understanding that the industrialized process that the sector has built and relied on is ill equipped to handle the non-blockbuster future. No longer can we develop a drug that inhibits an enzyme lowering cholesterol and make billions of dollars. We are now faced with far more complex biology.

This is not only true in unaddressed disease areas, such as, neurodegeneration and oncology, but also in areas where the standard of care is lacking, such as, cardio-vascular disease. We are also faced with the long-tail of disease that only affect small and/or poor patient populations. Recognizing these facts and how AI/ML will help to unlock the complex biology and reduce the cost of developing a drug is a much needed shift.

The second is a shift to educate all scientists and decision makers in pharma about data science and AI/ML. This education has to also be coupled with the restructuring of research and development teams. Historically, the industry has been good at generating data, but poor at fully utilizing all data. This is not a shortcoming of the researchers themselves, but of their limits as humans given the tools that they had. We have long relied on human intuition, which is limited in its ability to take in all of the data available and in its ability to build complex models of the high dimensional problems we are trying to solve in pharma. Now, with modern AI/ML, the proper datasets, and empowered data scientists working directly with their drug-hunter and clinician peers many of the benefits can be realized. But, this can only be done by leveraging the best of both the AI/ML and the individual team members. In order to do this, everyone must understand at some level what the AI/ML can do and what its limitations are.

Finally, there needs to be a shift in the way we think about data. Data wants to be free and if we want to really solve the healthcare problems of the 21st century we need to share data. I don't mean that we need to give away our crown jewels, but what about all of the other data we collect? In particular, the data around attrition (ADME, toxicity and clinical) needs to be shared so those that are building the algorithms can get access to it. If we learn to share historical data and build collective capabilities, we will be able to tackle many of the big problems in healthcare.

Rx Data News: What are some ways in which artificial intelligence and machine learning are impacting drug development right now?

Dr. Allgood: AI/ML are impacting all areas of drug discovery and development, just not at the same level along the pipeline and not at all levels within the same company. Most large pharmaceutical companies have deployed some level of AI/ML, either in partnership or internally. BenchSci has a very good list of things* that the large pharmaceutical companies have announced publicly, but I know that there are even more efforts going on that are not being discussed publicly.

On the small company side there is, as much, if not more, going on. We at Numerate have developed an AI platform that can provide AI driven answers along the entire small molecule drug discovery pipeline from hit ID to IND filing, including ADME and toxicity. Using these tools we have shown that we can not only increase the speed and reduce the cost of discovery, but unlock emerging biology and design compounds with a lower likelihood of clini-

*https://blog.benchsci.com/pharma-companies-using-artificial-intelligence-in-drug-discovery

cal failure. Nuritas has a platform technology for doing similar things in the larger peptidic drug space. Recursion and In Sitro are using cellular image analysis to perform novel target discovery and repurposing. DEEP6 is using NPL and other AI techniques to analyze EMRs to develop patient cohorts and enable recruitment for clinical trials. Brite Health is using AI to improve patient engagement and retention in clinical trials. Finally, companies like Genpact are offering AI solutions for pharmacovigilance. A list of some of the more cutting edge companies in the AI healthcare space can be found on the Alliance for Artificial Intelligence's website (www.theaaih.org). These are but a few examples of where AI is having an impact today and the number increases almost daily.

"The inability to extract value from historical data has led to our inability to improve on compound attrition rates. The numbers in the PhRMA funnel diagram have not changed in over 10 years. This is a direct indication that we as an industry have not learned to leverage the data we have collected to avoid the mistakes of the past."

> **Rx Data News:** The pharmaceutical industry has historically been data rich and algorithm poor. What have been the consequences of this and how can it be remedied?

Dr. Allgood: One consequence of this has been a slow understanding and adoption of how modern AI/ML can help pharma drive innovation and reduce the sky-rocketing cost of developing drugs. This has led to most pharmaceutical companies being late to the market in understanding, hiring, and properly compensating the expert data scientists that they need.

A second consequence is that the state of the data that has been collected is almost always far from model ready. The data is often in multiple databases with inconsistent permissions and access rules making much of it undiscoverable. In a lot of cases, the proper metadata and relevant parameters were not recorded and cannot be recovered.

Finally, the inability to extract value from historical data has led to our inability to improve on compound attrition rates. The numbers in the PhRMA funnel diagram have not changed in over 10 years. This is a direct indication that we as an industry have not learned to leverage the data we have collected to avoid the mistakes of the past.

These issues are, however, not totally unique to the pharma industry and the situation is changing with many pharmaceutical companies beginning the process of confronting them. One way in which these can be addressed in the immediate future is through data and asset based partnerships between large pharma and smaller AI driven companies, such as Numerate, where the value that the smaller company delivers is recognized, aligning incentives. Larger pharmaceutical companies need to also begin to deploy more capital toward broader AI initiatives, including hiring more data scientists and training all research staff in AI.

> **Rx Data News:** How do you think artificial intelligence and machine learning will impact drug development in the future?

Dr. Allgood: Currently, the IRR (internal rate of return) in discovery is approaching 0%. We are already below the cost of capital as an industry. On top of that, the US alone spent $3.67tr on healthcare and that is increasing year over year at an alarming rate. While prescription drugs are only 10% of that the deployment of those drugs is a much larger fraction. I think that AI/ML is a major part of the solution to turning this around, but we must be willing to dedicate the capital needed now to do this. Those that don't will lose and likely end up in bankruptcy or on the wrong end of an acquisition.

Overall, AI/ML will lead to lower R&D costs, to the unlocking of new drug targets and complex diseases, to getting into the clinic more often, and to a reduction in clinical failures. We will also be able to achieve higher returns by going after the largest areas of unmet need, which are held back by our inability to model complexities in areas,

"Data wants to be free and if we want to really solve the healthcare problems of the 21st century we need to share data. I don't mean that we need to give away our crown jewels, but what about all of the other data we collect? In particular, the data around attrition (ADME, toxicity and clinical) needs to be shared so those that are building the algorithms can get access to it."

such as, neurodegeneration and cardiovascular medicine. This will not lead to job losses, but to a change in required skill sets.

Rx Data News: This is a field that is occasionally accused of being overhyped. How do you distinguish between practical and more fanciful applications?

Dr. Allgood: Artificial Intelligence is the perfect hype term. Experts don't agree on exactly how to define it and it involves a large amount of math. So it is not surprising that it seems overhyped. The way that I distinguish between the practical and fanciful or false is through diligent examination. First, one must ask, is there enough data in the case of an ML system or expert knowledge that can be encoded in the case of an informed system to support the claims? Second, always insist on independent prospective proof of a claim. But, make sure you are listening to the developers of the system so that you don't come to a false conclusion based on a bad experimental set-up. Third, most solutions have sample dependent accuracy. This is reflected in the first and second points above, but I point it out specifically, because one should always be aware that a tool my work very well in one area of a problem, but that is not always indicative of performance in another area.

Rx Data News: What is unique about Numerate's AI Platform and what plans do you have for the future?

Dr. Allgood: We have been around since before AI was hype. We founded Numerate in 2007 before one could get a deal based on just the promise of AI. We were forced to put compounds where our mouth was. Now, we are the only company in this field that can say that we have worked on and delivered solutions for 30+ drug discovery programs both independently and with large pharma partners. We are also the only AI driven company that has out licensed drug programs that were started in house. One thing that we learned early on that has led to much of our success is that AI is only half of the solution. We also needed internal chemists and biologists that understood how to leverage the tools we were building.

Unlike most of the smaller companies in this space that are focused on the biology, Numerate is hyper-focused on the chemistry. We believe that there is a wealth of information in the compounds and the data related to the compounds and that it is currently underutilized and overlooked in most companies. Because of our longevity, we have been able to develop a platform that can address all aspects of chemical design in drug discovery, from hit ID to IND. And because of our experience we are able to continue to stay ahead of the competition through the development of a large set of proprietary AI backed tools that our internal drug hunter team uses to execute on both our internal and external drug programs.

Until now, we have largely worked in the pre-clinical space, licensing our programs out to in the discovery phase, but we are now working on a number of internal programs in neural and cardiovascular medicine that we plan to take into the clinic ourselves. In addition to that we are investing in bringing in more biological insight into our platform to enhance and augment our chemical design capabilities.

Using AI to Repurpose Underutilized Drugs

WRITTEN BY: Frederick P. Dawson

"The project uses Benevolent AI platform to review millions of scientific papers, clinical trials and additional data sets relating to age-related macular degeneration (AMD) with a view to finding potential gene targets and treatments."

A new AI project looking at other uses for drugs has delivered some promising initial results. The AI project from UK company, BenevolentAI along with charity research partners, Action Against AMD (Age-related Macular Degeneration) looked at a vast array of scientific studies governing existing drugs to see whether they may also be beneficial in the treatment of forms of macular degeneration.

The project uses Benevolent AI platform to review millions of scientific papers, clinical trials and additional data sets relating to age-related macular degeneration (AMD) with a view to finding potential gene targets and treatments.

It has identified seven potential drugs – either already being used to treat other diseases – or in some form of development – that might be repurposed to treat AMD.

"It's really promising that we have identified current drugs that may have a positive effect on macular degeneration," said Dr Wen Hwa Lee, chief executive for Action Against AMD. "Our next step will be to confirm which of these drugs have the potential to slow progression of the disease and reduce sight loss for people with this condition."

However a spokesperson for Fight For Sight, one of the charities forming Action Against AMD, declined to

specifically name the seven drugs.

The spokesperson told Rx Data News: "At this stage we can't reveal the specific drugs as we'd like to conduct additional experimental validation work before sharing the information with the research community. However, we will keep the community updated on any significant progresses coming from our validation work."

The number of drugs that could be repurposed for macular degeneration could in fact be even higher. The study limited itself to focusing on early AMD. As a result it only looked at drugs that were well-tolerated, convenient to be dosed (avoiding injections or intravitreal delivery) and potentially affordable.

"We have prioritized strategies and pathways which are different from the established lines of enquiry – thus avoiding anti-VEGF and other anti-angiogenic strategies, as well as the Complement system," the spokesperson said. "As we explore the biological pathways implicated in early AMD, we hope these will be able to address both late dry and wet forms of AMD."

In addition the analysis identified new genes targets for further investigation, Benevolent AI said.

The partnership to do this was established with Benevolent AI because Action Against AMD thought the AI company's platform could quickly work through the large data set. It is open to working with Benevolent AI on the project to a further degree. However it has not eliminated other potential opportunities.

"We will definitely be exploring future opportunities to work with BenevolentAI, but we are also open to discuss partnerships with other groups – in academia and industry alike – which might bring the necessary expertise, as we move the validation work forward," the spokesperson said.

"It has been a very productive partnership with Action Against AMD and we are delighted to have contributed some promising new research in age related macular degeneration," said Dr Jackie Hunter, board director at BenevolentAI. "I very much look forward to seeing the results of this research as it is developed further by Action Against AMD."

Action Against AMD consists of the aforementioned Fight For Sight along with Blind Veterans UK, The Macular Society, and Scottish War Blinded. The project was funded by the Macular Society with donations from the Clothworkers' Foundation – the grant giving arm of the Clothworker's Company, an ancient British livery company founded as a guild for clothworkers but now mostly getting its assets from investments and property – and another anonymous donor.

It said that AMD is the leading cause of sight loss and has an estimated prevalence of 196m people worldwide. There are currently no approved treatments for the 95% of patients with early and "Dry AMD" – although there are treatments for the 5% of patients with "Wet AMD", caused by new blood vessel growth, if it is caught early enough.

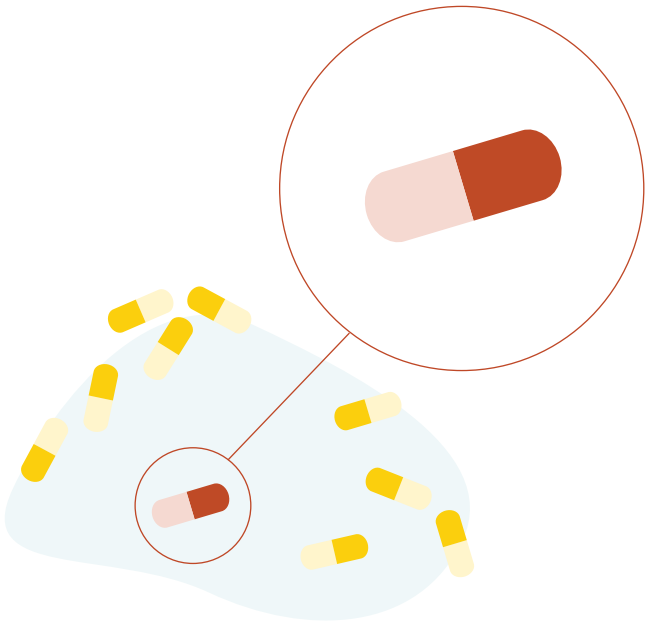
Utilizing AI to assess the viability of using existing drugs for new purposes offers significant potential for both patients and pharmaceutical companies. It automatically takes a large portion of the risk and cost inherent in starting the drug discovery process from scratch out of the equation.

It's often been pointed out that it costs more than $2bn to develop a new treatment from scratch and that around 90% of treatments never even make it all the way to the point where they would be eligible for regulatory approval.

And repurposing of drugs has been performed for longer than AI has been present in the pharmaceutical industry. For example, aspirin went from pain killer to something that could be used for blood pressure while Viagra went from a hypertension drug to one for impotency.

AI has also had other successes in this area too. One study has found promising candidates to tackle motor neuron disease, also known as Lou Gehrig's disease. Another project took a short-cut to finding an inhibitor for Ebola. It found phase II drugs that may be able to block the Ebola virus from entering healthy cells. That meant the potential treatment could skip straight to later trial phases and potentially could be available for use significantly earlier than a drug discovered through traditional methodology.

Altogether the research of existing drugs and compounds for alternative uses is full of promise. However there is still a while to go before we see the first cross-purpose AI discovered drug approved for use and available on the market.



MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Andy Greenberg
Managing Director, North America Connected Health Lead, Accenture
Philadelphia, PA

Andy Greenberg is an expert in launching technology-based products in the life sciences, healthcare, and wellness spaces. With 15+ years leading and developing companies in start-up environments, to 4+ years as a consultant supporting digital strategies for pharmaceutical companies around the world, Andy brings an in-depth knowledge of behavioral research and the latest in AI, sensor, and mobile advancements, to help organizations accelerate their success.

Despite the potential Artificial Intelligence (AI) holds to all but revolutionize healthcare, pharma companies can be reticent to embrace the technology. This hesitancy is understandable given AI's nascence, the high risks of potentially costly (and even deadly) errors, and historic reluctance of regulatory agencies surrounding new technologies. However, pharma companies that don't begin incorporating AI into their clinical trials will miss opportunities to reduce costs, glean new insights, produce new therapies, and move to market more quickly, among other benefits. Indeed, from discovering new molecules to improving the quality of life for patients on therapy, AI stands to increase the broader medical industry's value by about $150 billion over the next seven years.*

In a somewhat paradoxical twist, the traditional barriers to adopting new technologies in clinical trials – namely, regulatory roadblocks – are not the things delaying pharma companies' entry into AI-enabled clinical trials. Instead, it can sometimes be the conservative approaches of their own internal regulatory teams that can block the path to the adoption of disruptive technology. Put another way, to a large extent, big pharma companies sometimes stand in their own way when it comes to utilizing AI.

In fact, the U.S. Food and Drug Administration (FDA) recently issued a proposal seeking input on how to best incorporate emerging technologies such as AI into drug manufacturing and medical discovery. The FDA said it is "considering a total product lifecycle-based regulatory framework for these technologies that would allow for modifications to be made from real-world learning and adaptation, while still ensuring that the safety and effectiveness of the software as a medical device is maintained."

What's at stake

Beyond missing out on the benefits of faster and more efficient drug discoveries and speed to market, pharma companies slow to adopt AI can risk losing market share to more nimble startups. The FDA's recent announcement that it has not yet taken a position on newer technologies is further proof that the market is ripe for disruption. At a minimum, big pharma should consider partnering with smaller, more tech-savvy startups to get the AI ball rolling.

"Beyond missing out on the benefits of faster and more efficient drug discoveries and speed to market, pharma companies slow to adopt AI can risk losing market share to more nimble startups."

For example, last year, Roche announced its acquisition of Flatiron Health, a healthcare technology and services company focused on accelerating cancer research and improving patient care. Founded in 2012, part of Flatiron's mission is to break down the silos across health systems. Specifically, the company's aim is to collect, synthesize and utilize the unstructured data "stored across thousands of disconnected community clinics, medical centers and hospitals." Startups such as Flatiron are part of the industry dynamic that Accenture calls New Science —an evolving, unique combination of the best in science and health technology (e.g., genomics, biomarkers, companion technologies, delivery methods, etc.) that is filling an unmet need and raising the standard of care.

Another example is BenevolentAI, a 250-person company founded in 2013 that pores over massive quantities of scientific data to significantly increase the speed at which drugs are developed for rare diseases. The company recently announced a deal with Parkinson's UK and the Cure Parkinson's Trust to utilize BenevolentAI's "healthcare knowledge graph," which comprises more than 1.3bn bioscience relationships and is likely to lead to breakthrough treatments.

Embracing AI

Today, most big pharma companies lack the agility of health startups such as Flatiron and BenevolentAI. But partnering with these – and other – companies is one way for industry stalwarts to make inroads toward greater outcomes through technology. At a minimum, they can start demonstrating the value of AI in areas viewed as lower risk to the organization because they don't directly "touch" the patient. These can include the application of Natural Language Processing (NLP) in search within the company's own data or conversational AI for improving the site investigator experience. Pharma companies need to understand that as AI increasingly reaches new levels of sophistication, AI will become virtually indispensable, far beyond its function of processing massive amounts of data.

For an industry as highly regulated as life sciences, AI offers new opportunities to address crucial life-and-death issues more quickly and cost-effectively. Companies already seizing the AI moment and looking over the horizon toward new and potential use cases face less risk in the long-run and won't struggle like slow adopters to catch up with new regulations and patient expectations.

* "Value" is the estimated potential annual benefits for each application by 2026.
** https://www.accenture.com/_acnmedia/PDF-49/Accenture-Health-Artificial-Intelligence.pdf

New facility will employ AI in "Darwinian" cancer research

WRITTEN BY: Frederick P. Dawson

A new cancer research center in the UK will look to use AI and machine learning to discover "Darwinian" cancer drugs.

The center by the Institute of Cancer Research (ICR), a charity and research college of the University of London, is to cost around £90m all told. It will focus on a new approach to drug discovery. By using AI and advanced mathematics to forecast how cancers will react and evolve when faced with new treatments, scientists at the center expect to be able to control cancerous cell growth and change.

"Artificial intelligence and mathematical predictive methods have huge potential to get inside cancer's head and predict what it is going to do next and how it will respond to new treatments," said Dr Andrea Sottoriva, expected future deputy director of cancer evolution in the new Center for Cancer Drug Discovery, once it is opened.

"We will create exciting new ways of meeting the challenge of cancer evolution head on, by blocking the entire process of evolutionary diversity, using AI and mathematics to herd cancer into more treatable forms, and tackling cancer with multi-drug combinations as used successfully against HIV and tuberculosis," said Professor Paul Workman, chief executive of the ICR.

Currently cancer cells are well adept at adapting to treatments and becoming drug resistant. A series of projects will simultaneously look at different methods to either control this or turn it against tumours.

One project will use AI and mathematics to predict how cancer cells will evolve when faced with treatments. This means that the system should be able to predict how a cancer will develop weaknesses against certain treatments when it evolves to counter another one.

"By selecting an initial drug treatment, they have found they can force cancer cells to adapt in a way that makes them highly susceptible to a second drug or pushes them into an evolutionary dead end," the ICR said.

Another project will look to create a family of "anti-evolution" cancer drugs in order to slow down cancer's ability to evolve and thus delay its resistance to treatment. These drugs will target a molecule called APOBEC. By halting its action, they would reduce the rate of mutation in cancer cells – slowing down evolution and delaying drug resistance.

"More and more cancer patients are living longer and with many fewer side effects through new targeted cancer treatments. But unfortunately, we're also seeing that cancer can become resistant very quickly to new drugs – and this is the greatest challenge we face," said Dr Olivia Rossanese, planned future head of biology in the new Center for Cancer Drug Discovery once it is opened.

This family of drugs could also increase the effectiveness of new types of treatment. For example, they could slow cancer responses to viruses – increasing the effectiveness of a series of treatments that use them as a form of immunotherapy to attack tumors.

"APOBEC protein molecules are crucial to the ability of the immune system to adapt to different infectious diseases – but are also hijacked in over half of cancer types to speed up evolution of drug resistance," the IRC said. "Researchers hope that a new class of APOBEC inhibitors could be given alongside a targeted cancer treatment to ensure it can keep cancer at bay for much longer."

"We're especially excited by the potential of APOBEC inhibitors to slow down evolutionary diversity and drug resistance, and ensure our existing cancer drugs work for patients for much longer, Dr Rossanese added. "We believe this will be the first treatment in the world that rather than dealing with the consequences of cancer's evolution and resistance, aims to directly confront the disease's ability to adapt and evolve in the first place."

A third project will look to combine knowledge and expertise from drug discovery as well as evolutionary scientists. It will essentially attempt to overwhelm cancer but in a more precise and targeted way compared to current chemotherapy treatments – the equivalent of the use of precision munitions compared to carpet bombing tactics.

This project has already seen some promising signs – with bowel cancer cells responding promisingly to combinations of three treatments in laboratory testing. The cells could evolve resistance in response to two treatments but would be overcome by the third.

"Scientists at the ICR believe approaches like this could be a highly successful way of managing cancer and its spread to ensure good quality of life for longer – or to achieve cures through combination with exciting new immunotherapies and viral treatments," the ICR said.

However the center is currently experiencing a £15m shortfall in funding which means it is incomplete and unequipped at this time. The ICR is seeking a further £15m from philanthropic donations to complete the new building and equip it with the requisite instruments, devices and technologies.

"If we can raise a further £15m to deliver our new Center for Cancer Drug Discovery, we can bring together under one roof experts in cancer therapeutics alongside others studying evolution in animals, cells and individual patients, to create a new generation of cancer treatments," said Professor Workman.

"Within the Center for Cancer Drug Discovery, we plan to deliver a drug discovery program that is wholly focused on meeting the challenge of cancer evolution and drug resistance through completely new ways of attacking the disease," said Dr Rossanese. "This 'Darwinian' approach to drug discovery gives us the best chance yet of defeating cancer, because we will be able to predict what cancer is going to do next and get one step ahead."

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Timothy Hare
VP, Head of Data Science, 81qd
New York, NY

Artificial intelligence (AI) will have a direct and marked impact on the future of clinical trials by increased incorporation into the clinical trial process itself, as well as an indirect impact via improvements in the preclinical drug discovery process, including the target identification (TID), lead identification (LID), and lead optimization (LO) processes that supply the pool of preclinical candidates (PCCs) for clinical trials.

The most discernible direct impact of AI on the evolution of clinical trials will likely be seen in recruitment, participation, and data collection, as well as the emergence of new clinical biomarkers (indicators of the severity or presence of some disease state) and surrogate end points (observed effects of treatment that may correlate with a clinical end point).

The US Food and Drug Administration (FDA) now supports the use of AI to improve patient diagnosis and prognosis, identify early response to treatment, and develop novel imaging biomarkers that can be used to categorize and triage patients. Integrated understanding across a broad range of complex patient data types (imaging, ECG, genomics, proteomics, human biome genetics) is increasingly facilitated by AI as part of biomedical investigations into human health and disease, all of which sets the stage for more efficient and effective clinical trials.

AI is increasingly facilitating better real-time data capture for more desirable and demographically diverse clinical trial enrollment. Patients are increasingly comfortable with AI as part of the health care ecosystem, as seen in a recent survey that indicated 42% of respondents are comfortable with doctors using AI to make decisions about their care and treatment. Increasing integration of social media data, the Internet of Things data, laboratory data, and electronic medical records will enhance AI effectiveness in this regard.

Additionally, there is the prospect of virtualization of parts of the clinical trial process, allowing patients to participate more easily and irrespective of their geographic region. This is helpful since approximately 70% of potential participants live more than two hours from a clinical trial site and traveling is considered a significant burden. Clinical trials will increasingly utilize social media, telemedicine, and biosensors as part of the clinical trial process, facilitating recruitment and simplified real-time data collection.

In late-stage clinical trials, with the majority of recruitment sites having difficulty meeting minimum and demographically diverse enrollment levels, AI supports increased levels and diversity of patient recruitment by shortening the time to diagnosis for patients who have been misdiagnosed or are under-diagnosed – expanding the pool of candidate clinical trial patients. AI is able to predict the risk of non-adherence, so that clinical trial patient selection can be refined to reduce the risk of falling below enrollment levels needed to achieve statistically significant results.

AI will improve clinical trial patient qualification and monitoring by being able to identify more prognostic surrogate end points and by discovering new biomarkers for disease type, state, and potential for progression to different outcomes. This will allow more nuanced and earlier detection of efficacy, as well as better constellations of assay readouts indicative of emergent toxicity.

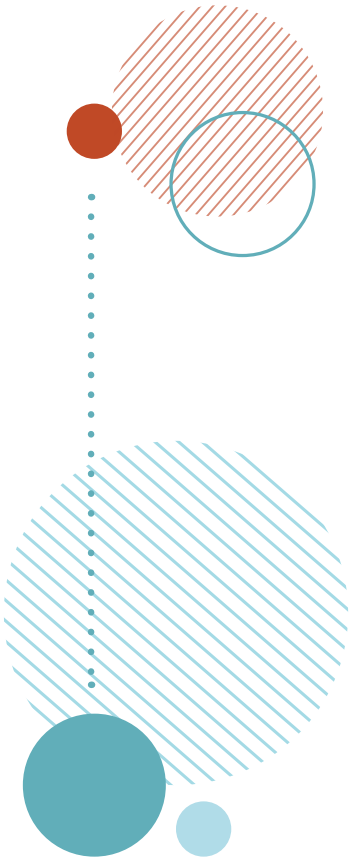
"Clinical trial designers are increasingly positioned to make use of all of this information, leading to better-informed strategic decisions about clinical trial structure and feasibility."

In addition to the marked improvements that AI will undoubtedly directly effect on the clinical trial landscape, there are a number of indirect impacts that will also contribute to reshaping research and development. This is an AI high-leverage point for clinical trial impact. Better preclinical decisions will result in safer and more efficacious PCCs, reducing the escalating costs of bringing new drugs to market, and allowing drug development in formerly refractory therapeutic areas.

AI will improve our knowledge of TID networks (maps identifying biological pathways for a given therapeutic area), improving preclinical research and development's (R&D's) ability to focus efforts on more efficacious points of therapeutic intervention. AI will reduce error rates in LID that would otherwise inflate R&D costs and introduce unacceptably high late-stage clinical trial risks.

AI will also improve the complex drug candidate structure-activity relationship (SAR) maps that medicinal chemists rely on for reducing toxicity, enhancing potency, increasing target specificity to avoid side effects, increasing oral bioavailability (the fraction of drug in circulation after oral dosing), and optimizing the half-life in circulation of drug candidates, as part of the synthesis of chemical variations on a theme during LO. LO is the stage where medicinal chemists begin borrowing information from different parts of the SAR map, across the full-range of active molecules coming out of LID, to produce improved PCCs.

Drug discovery assays (laboratory biochemistry that attempts to mimic a particular therapeutic area of human biology in a meaningful way) often test millions of candidate molecules, all of which need to be assessed in a fully automated and cost-effective manner. The increasingly complex processes that support this goal produces a subset of false-positive (FP) and false-negative (FN) results that inflate follow-up costs in the first instance by sending too many candidates into expensive (materials, time, labor) secondary confirmatory assays, and also degrade the body of information (the SAR map) needed by medicinal chemists for effective LO in the second instance. This puts clinical trials at a severe risk of bringing suboptimal drugs to market and also an unacceptable risk of program failure, where the clinical trial fails to support bringing the new drug to market, and the program is subsequently cancelled.



In this context, AI will enhance our understanding of biological networks and help identify the subset of truly viable drug targets they contain. This TID network knowledge map is essential to evaluate all PCC on-target effects (the effect on the intended target and known biological pathways), and also off-target effects (the effects on unintended targets and associated biological pathways, known and unknown), as the latter can lead to side effects that put clinical trials at risk of failure for lack of efficacy and/or toxicity. AI will help biopharmaceutical companies to realize the holy grail of "fail early" in the preclinical drug development pipeline.

Failing early is good as it minimizes R&D investment in the wrong PCCs destined to fail late, otherwise inflating the cost of preclinical development and/or late-stage clinical trials. Late-stage clinical trial failure is of particular concern as it has a larger adverse impact on the average cost of bringing drugs to market, which has been steadily rising for decades. R&D costs need to be recovered. Without AI, the only option is to continue to increase the selling price of the drugs that get approved, in order to recoup the losses for all of the failed R&D programs.

AI-based virtual screening, the process of searching for new drugs via computer simulation (eg, without actually running physical assays in the laboratory), can predict which candidate drugs are good leads, reducing LID error rates that otherwise inflate R&D costs, or increase the probability of late-stage clinical trial failure. Often physical assays are run and compared with AI predicted values, such that bad assay results (assays have artifacts, they are not perfect) that would have incorrectly eliminated a PCC that would have otherwise contributed information to the SAR map or even been a clinical trial success on its own (FN) are flagged and rescued during follow-up testing. Thus, reducing FNs reduces program risk.

As well, those candidate drugs that are truly inactive and would otherwise have made it farther along in the process (FP) can also be eliminated. Allowing FPs to linger in the R&D development pipeline raises costs, increases development time, and contaminates the SAR map that medicinal chemists rely on to make improvements to PCCs. Thus, reducing FPs reduces program costs.

Overall, this process of winnowing out FNs and FPs earlier improves the efficiency and effectiveness of the R&D process.

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Timothy Hare
VP, Head of Data Science, 81qd
New York, NY

A purely AI-driven design of drug candidates is coming into its own, as scientists discover better AI model inputs for drug candidate features (molecular "feature encodings" that AI consumes), as well as improved physical molecular library design. Molecular library design involves the purchase and/or chemical synthesis of a broad range of molecular structures. This inventory is then stored in very large automated warehouses for testing across all future drug programs.

Strategies coming from AI recommendations, where AI designs truly novel drug candidates that medicinal chemists might not otherwise have created, represents a strategic and tactical paradigm shift. Participation of AI in this way will provide higher quality candidate drugs for validation, as well as expand diversity in the molecular libraries used for other therapeutic area opportunities.

Preclinical LID assay development has been made more robust by AI, which is able to interpret a broad array of complex data. Large, complex mixtures of data such as candidate drug biophysical attributes (solubility, size, etc.) as well as protein and gene network expression data are increasingly fed into AI to provide a richer constellation of information to model.

Also, live cell assays where the size, shape, and health of the cell are observed after exposure to candidate drugs, can be interpreted by AI. The capacity to quickly process this vast and diverse body of information means that AI is now able to contribute new information in areas like drug-target interaction theory, rational drug design, biological pathway analysis, and the planning that goes into new drug synthesis by medicinal chemists.

AI is also being used to improve early warning of diminished LID assay quality by monitoring the inputs, the outputs, the robotics, and the influence of uncontrolled factors in the environment in which these complex automated processes run. The cost of complexity can be instability, and complex systems are prone to failure in ways that can't be anticipated by humans, but can easily be predicted by AI. Round-the-clock system monitoring can dramatically reduce the cost of R&D attributable to materials waste, the challenge of scheduling the use of limited fixed resources such as shared robotic platforms, and the cost of rework when systems degrade and the product becomes unacceptable.

With the advent of new FDA standards and guidelines, the direct impact of AI on clinical trials will be manifested by the increased diffusion of innovative therapies into the design and execution of clinical trials. In addition to the marked improvements that AI will undoubtedly directly effect on the clinical trial landscape, there are a number of indirect impacts that will also contribute to reshaping R&D.

When you consider the fact that only about one out of eight PCCs will ultimately make it to market, the total R&D burden in modern biopharmaceutical drug discovery becomes clear. Studies estimate that the full life cycle development cost of bringing a single new drug to market may average almost $3bn. This is up from $802m in 2003 or approximately 275% in 15 years, unadjusted for inflation.

Studies also focus on industry productivity and profitability. Productivity and profitability in the biopharmaceutical industry have been declining as well, and some studies indicate that the industry may soon reach a crisis point if this trend is not reversed. A recent study indicates that R&D returns in drug development currently stand at 3.2% and could reach 0 in 2020, meaning that a dollar would return a dollar— ie, no profit.

AI will be the catalyst to slow down and eventually reverse this trend in the biopharmaceutical industry. AI has the potential to dramatically improve clinical trial efficiency and effectiveness, directly and indirectly, ensuring that the volume of new drugs for unmet medical needs coming to market continues and even accelerates.

Evaluating Value: Using RWE to Determine a Product's Worth

WRITTEN BY:
Nancy Dreyer, Chief Scientific Officer, IQVIA

Every healthcare stakeholder group has different inherent risks they're willing to accommodate when making decisions about a product. There's a need to quantify stakeholder value to ensure a product's cost is commensurate with the value it creates for each stakeholder. Embracing strategies that optimize value for everyone is a collective effort that can benefit all healthcare stakeholders and drive long-term success for the healthcare industry.

The conditions that influence the value of a drug throughout its lifecycle are dynamic and continuous, and industry leaders are increasingly looking to real-world data and evidence to identify key value attributes that drive adoption of a drug in a given therapeutic area.

Real-world data (RWD)[1], information about patient health status and/or the delivery of healthcare that is routinely collected from a variety of sources, is a critical component central to fostering optimal performance within the healthcare ecosystem.

RWD is gaining new respect due in part to work like a pilot study[2] led by Friends of Cancer Research and released in July 2018. All participants in this voluntary collaboration followed a broad protocol outline to match the inclusion and exclusion criteria used in a randomized controlled trial of a treatment with approved immune checkpoint inhibitors for advanced non-small-cell lung cancer. The study was a retrospective observational analysis of data derived from electronic health records and claims data, and it demonstrated that several extractable endpoints from EHR and claims data correlate with overall survival.

Regulators, patients, and payers are now demanding evidence about how treatments work in real-world settings. The FDA has come to understand that many of the quality concerns about real-world data can be addressed through careful design and analysis, as evident in the Framework for FDA's Real-World Evidence Program[3], which was released in December 2018.

The FDA defines real-world evidence[4] (RWE) as the clinical evidence regarding the use and potential benefits or risks of a medical product derived from analysis of RWD. It is essential for establishing price premiums that match stakeholder value. Therefore, standardizing the use of RWE is the key to informing evidence-based valuation methods that can accelerate the drug development pipeline and offer healthcare consumers better access to more affordable and effective treatment options.

Healthcare companies that embrace the idea of creating shared value by utilizing RWE will strengthen their businesses by expanding markets and differentiating themselves. With the availability of RWE, its generation and use occur across the entire healthcare continuum, where all stakeholders collaboratively create, analyze, and share results for better individual and population health outcomes.

Creating shared value by utilizing RWE can be a difficult concept for an industry built on a foundation of privacy and intellectual property. Companies may want to wait for a framework for RWE to be fully fleshed out. Or stakeholders can choose to embrace a new value model of data sharing across the healthcare ecosystem, one that will generate more and better data, which will steadily increase its value and impact over time and, most importantly, help the industry to ultimately improve public health.

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Alif Saleh
Chief Executive Officer, Scipher Medicine
Boston, MA

There are more than 300,000 clinical trials going on globally right now. However, the traditional phase approach to clinical trials has not changed since 1963 – this was the pharmaceutical industry's winning model for drug discovery and commercialization for decades: develop a drug for the average patient and get as many people on their respective medicines as possible for the highest margins. Now that precision medicine is continuing to grow and change treatment approaches, that model begins to make less and less sense. Industry and researchers need to first study an individual's disease to create sub-groups of patients with similar disease signatures, not an "average" patient, before creating treatments personalized to each group.

Using artificial intelligence (AI) to hone precision medicine can be a powerful tool in getting patients the right medicine that will successfully treat their individual disease and holds the promise to transform the traditional clinical trial format that has been left unchanged for the past six decades. However, as we heard at conferences like J.P. Morgan this past January, there is still much debate around whether AI is more than just a buzzword when it comes to health care, since the idea has been around since 1955.

In order to maximize the use of AI and precision medicine in drug discovery and make the technology a reality, there first must be the data and it is up to the industry to generate it. Many companies are in a race to generate quality data to be able to unlock the return on investment that AI in drug discovery promises by applying the technology to large datasets in order to tailor treatments to each individual patient's disease biology.

Biotechnology companies have collected large pools of data in order to explore currently unknown human biology and understand what makes patients either a responder or non-responder to a certain targeted therapy. This could help improve patient stratification and ultimately find tailored treatments for each patient sub-group by applying AI. Using this technique can help get safe, approved drugs into the hands of only the patients who will benefit and allows the creation of treatments based on data analysis – improving response rates to drugs and helping patients successfully reach treatment goals.

Specifically, applying network science approaches to build a human interactome, a database of information around the protein–protein interactions that occur in human cells, in order to understand specific disease modules – such as cardiovascular disease, rheumatoid arthritis, and ulcerative colitis – can help determine which patients will respond to which targeted drugs. This information can ultimately be used to build diagnostic tests that help identify a "responder" and "non-responder," which would therefore improve the chances of a successful clinical trial by personalizing the potential drug to a sub-group of patients based on their similar disease biology.

By understanding how those drugs work on each disease module, companies like Scipher Medicine, which analyzes RNA data to advance its understanding of autoimmune diseases and treatment response, are able to identify new targets for pharmaceutical companies and alternative indications for currently approved or prior failed drugs – propelling precision medicine forward in health care. AI technology helps with this understanding of the disease both at a general patient population and individual level. This insight is crucial to finding those who do not respond to drugs available today and then helping to discover new drug targets for these patients to jumpstart the clinical trial process of bringing the new, successful drug to market.

AI can advance precision medicine to uproot the traditional phase approach of clinical trials by identifying the exact type of patient the treatment will help before the trials for safety and efficacy even start. Collecting population data to understand where the need is for treatments of both widespread and rare diseases, and then interpreting it with AI methodologies to bring greater treatment success and more precise medicine, allows both patients and pharma to thrive. With technologies like these becoming a reality, health care and pharma are being catapulted into the age of the individual through precision medicine and refreshed models of traditional processes.

Impact of Advanced Data Technologies on Pharma R&D

WRITTEN BY: Jane Z. Reed, PhD

Jane Z. Reed, Ph.D, is the Linguamatics' head of life science strategy and responsible for developing the strategic vision for Linguamatics' growing product portfolio and business development in the life science market.

In his 2017 book "The Fourth Industrial Revolution," Klaus Schwab describes how the fourth revolution is fundamentally different from the previous three. Each previous Industrial Revolution (IR) was characterised by advances in technology: iron and textile industries for the first, electricity-fuelled innovations for the second, digital technology for the third. 4IR builds on the digital revolution, embedding technology more deeply in society.

Schwab reasons that the underlying basis for 4IR is advances in connectivity and communication - and these advances are having significant impact on all industries, including pharma and healthcare. Access to huge amounts of varied data and the ability to connect, integrate, query and analyse these vast volumes is enabling radical changes in how we envisage drug discovery and delivery in the clinic.

If we take a step back and reflect, the pace of change we are seeing is amazing. For example, our understanding of the human genome has grown immensely over the past few decades. The first human chromosome was sequenced in 1999; the human genome published in draft in 2001.

Now across the globe there are national genome projects, such as the UK 100k Genomes project, the China 100k Genomes Project, the US "All of Us" research program, and more. These are all sequencing large numbers of whole genomes, aiming to connect the genomic data to other data types - clinical, wearable, scientific - in order to fuel innovations around health, wellness, and precision medicine.

Key components for these innovations include data integration and data analysis. In order to develop new therapeutics for the revolution promised by precision medicine, pharma companies need to be able to join up genomic data with clinical information, plus the landscape of knowledge around the natural history of a particular disease from scientific papers.

Tools and processes for data interoperability are critical; examples include use of standard ontologies to map data to suitable identifiers, the FAIR principles (https://www.go-fair.org/fair-principles/), and the increased adoption of cloud-based technologies, enabling research groups to access the most relevant and efficient technology.

As well as data integration, advanced analytics technologies are impacting R&D. We now have more data than the human brain could interpret in a lifetime, and are turning to AI technologies, applying algorithms and machine learning models to search for patterns and significant links. AI in early research isn't new. Algorithms for sequence manipulation (BLAST, Clustal), methods in computational chemistry and QSAR, these have all been used for years.

But with the increase in genomic and clinical data, researchers can now start to develop models to investigate genotype-phenotype associations, cluster symptoms to understand rare disease, and correlate sequence and clinical data to pinpoint small patient populations where specific focused treatments will be effective.

It's important to remember that each significant leap forward is actually composed of many tiny steps rather than a single major revolution. Using specific technologies to bring benefits in particular areas can move a particular drug project forward, or make an organization more efficient in work processes. Natural language processing (NLP) can assist in extracting the key data from unstructured text, and thus provide critical decision support. Within development (e.g., clinical, regulatory or safety), robotic process automation (RPA) can integrate into the daily lives of employees, reducing the burden of repetitive tasks, such as receiving, checking and filing case forms. So, connecting the data, communicating across teams, tailoring the analytics to the problem in hand, and taking small, but significant, steps in the right direction are all essential to ensure pharma can really benefit from 4IR.

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Brian D'alessandro, MBA
Director of Data Science,
SparkBeyond
New Rochelle, NY

Artificial intelligence (AI) is gaining attraction across most industries these days. And one of the most interesting areas of impact is its role in clinical drug trials. Clinical drug trial management is both big business, as well as critically important for society and AI is driving improvements in both. Specifically, AI helps drug trial managers create operational efficiency and drive more complete studies, faster. It also helps clinicians better analyze and collect outcomes, creating more evidence to make very important approval decisions.

Two key challenges in clinical trial management are recruiting and retaining enough participants to provide sufficient evidence to satisfy trial requirements. AI can help managers remove frictions that result in too few or lost participants. For instance, individual trial sites have local properties (i.e, location, doctors present, areas of specialty and past performance on previous studies) that lead to higher engagement and retention. When operators take a global view, they can compare successful from unsuccessful studies, and use AI to discover differentiators of success, as well as build predictive systems to select future sites that have a high likelihood of positive outcomes. On a patient level, if recruitment processes are collecting the right data, they can use AI to target the best candidates in their direct-to-patient outreach.

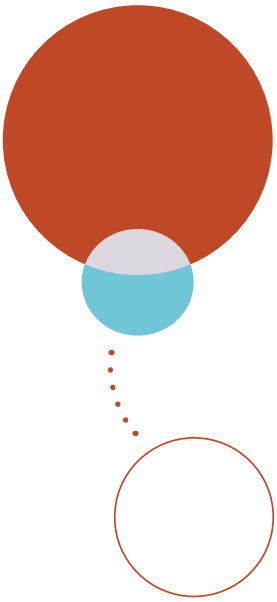
A big risk factor in clinical trial management is patient drop-out due to long study durations or adverse drug reactions. AI systems can provide predictive analysis on the likelihood of both drivers of patient churn during the process and assist clinical trial operators by both flagging who is at risk as well as giving insight into the nature of the risk. This can enable them to proactively address issues before they arise, enabling more efficient and conclusive studies.

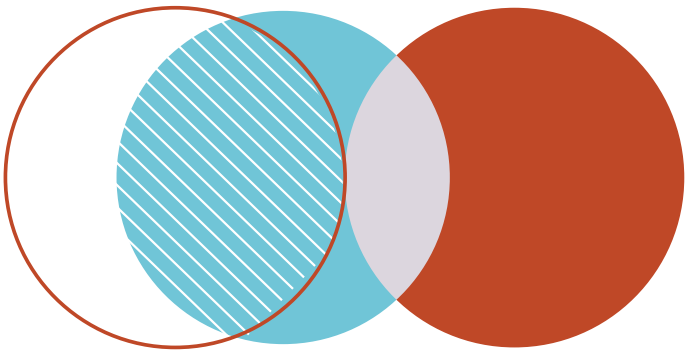
Overall, while AI can reduce costly operational risks, this comes with potentially introducing new inclusion/exclusion criteria. This could result in changing the underlying patient populations under study, which has implications on the applicability of the results to target patient populations. Operators will have to balance the use of AI tools with explicit regulatory requirements to avoid unanticipated population biases that could result in rejected study results.

AI and evidence

Artificial intelligence systems also have applications in observing various trial outcomes that could be considered an adverse drug reaction (ADR). Two questions coming from these observations include: Is the ADR by chance (or more precisely, different from baseline levels)? And if it's not, what are the biological mechanisms causing the ADR?

Classical statistics within a randomized control trial can answer the first question, but AI can augment classical statistics through more powerful and personalized modeling. With sufficient data and the right AI tools, clinicians can understand who may be at higher risk for certain ADRs, and can even use knowledge of similar drug compounds to anticipate ADRs that have yet to be observed. Access to





"A big risk factor in clinical trial management is patient drop-out due to long study durations or adverse drug reactions. AI systems can provide predictive analysis on the likelihood of both drivers of patient churn during the process and assist clinical trial operators by both flagging who is at risk as well as giving insight into the nature of the risk. This can enable them to proactively address issues before they arise, enabling more efficient and conclusive studies."

electronic health records (EHR) would enable this process to be more personalized and even allows researchers to pool data across studies (and even other observational mechanisms, such as hospital records). AI technologies like Recurrent Neural Networks can enhance the ability to use EHR to make these predictions because the tech is well suited to model the longitudinal complexity of human biology.

When it's possible to rule that an ADR isn't driven by chance, an AI system can help better understand the underlying mechanisms specifically by discovering how a certain compound might interact with a set of target proteins within an individual's genomic make-up. This complex analysis is difficult to unravel with classical statistical methods. Graph databases are an emerging technology that enables researchers to represent different aspects of drug behavior, that when coupled with AI prediction technology, can help researchers identify ADRs for both new and released drug compounds, as well as identify candidates for drug repurposing efforts.

Aside from simply analyzing the data, AI can also help collect more objective evidence during trials, particularly through new instrumentation techniques such as using wearable technologies and mobile phones to collect physiological diagnostics, mobility, sleep patterns and emotional state.

There are some caveats to consider when adopting AI for understanding personalized ADRs because the AI tools require orders of magnitude more data than typically needed in an RCT. And, while the methods are centered on prediction tasks, the real goal behind using AI in clinical trials to assist researchers in understanding the cause and effect of observed outcomes. This might mean researchers will have to employ more interpretable glass box methods rather than standard AI techniques.

FEATURED INTERVIEW:

Frank DeFalco

Director, Epidemiology Analytics,
Janssen Research & Development
Bridgewater, NJ

Frank DeFalco is an associate director of Epidemiology Analytics at Janssen Research and Development where he architects software solutions and data platforms for the analysis and application of observational data sources. Prior to joining Janssen Research and Development, Frank held the position of senior principal and director of collaboration and analytics at British Telecom where he was a strategic advisor for multiple Fortune 100 companies across sectors including consumer products, telecommunications and pharmaceuticals. Frank received his undergraduate degrees in Computer Science and Psychology at Rutgers University.

Rx Data News: What are some ways that Janssen, in particular – and the pharmaceutical industry in general – are facilitating the sharing of code and standards, while at the same time protecting proprietary data?

Dr. DeFalco: There are two initiatives I would highlight as opportunities for organizations to adopt standards and facilitate the sharing of software and data.

The first initiative is Janssen parent company, Johnson & Johnson's partnership with the Yale University Open Data Access (YODA) Project. Through the YODA Project, Johnson & Johnson shares clinical trial data from across the enterprise with external researchers. Partnering with the YODA Project, enables a fair and unbiased approach for assessing external research proposals requiring the use of clinical trial data from our pharmaceutical, medical devices or consumer products groups. We grant the YODA Project full decision rights regarding the release of our clinical trial data.

By responsibly sharing our data, we aim to pave the way for better healthcare data sharing practices for greater discovery and to improve health outcomes for the greatest number of people.

The second initiative is through Johnson and Johnson's work with Observational Health Data Sciences and Informatics (OHDSI) initiative. OHDSI is a multi-stakeholder, interdisciplinary collaborative to bring out the value of health data through large-scale analytics. OHDSI leverages the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) and then builds on it by developing tools and analytics for all organizations that have adopted the CDM standard to share software and analytics to generate evidence using standard vocabularies, tools, and reporting systems.

It gives members unprecedented access to 60+ databases representing more than 1.2bn patients in 20+ countries and developed several open-source data tools. All findings, methodologies, analysis code and related software tools are shared publicly and published with free access to advance public health. Specifically, OHDSI shares all of its projects as open source software under the Apache 2.0 license with over 100 repositories on Github (www.github.com/ohdsi) including data standards, R libraries, web applications, and service layers to enable integration.

> **Rx Data News:** In addition to your role at Janssen, you are currently leading the OHDSI open source architecture working group. Can you describe what the goals and activities of the working group encompass?

Dr. DeFalco: I have led the OHDSI architecture working group starting in 2014. The role of the working group was to establish a data and software architecture to facilitate the generation of evidence from patient-level data converted to the OMOP Common Data Model. The working group has seen contributions from dozens of organizations and individuals over the past five years and has delivered multiple open-source tools to facilitate observational research. One such tool is ATLAS, a web application that allows users to explore medical terminologies and define sets of codes that represent medical concepts, define cohort phenotypes, characterize populations and design population-level effect estimation and patient level prediction studies.

> **Rx Data News:** What are some important things to know about architecture and common data model vocabulary as relates to the pharmaceutical industry?

Dr. DeFalco: I think the focus should remain on producing meaningful, reliable, and reproducible evidence for patients, their families, and providers. Architecture, common data models, vocabularies and standard analytics will all help facilitate evidence generation. Making real progress in generating evidence requires cross-functional teams that include robust and scalable data platforms, data scientists, clinicians, epidemiologists, mathematicians, statisticians and a lot of coffee.
It is important to have an open dialog across these functions and try and prevent too many initiatives in silos that prevent the collaboration necessary to advance the science. Openly sharing architectures, data models and standards will allow us to make meaningful contributions to our individual organizations, the industry, and ultimately patients.

> **Rx Data News:** Looking towards the future, how do you see data sharing practices in the pharmaceutical industry evolving in the coming years?

Dr. DeFalco: I anticipate unsteady progress regarding data sharing practices. We will see some organizations share more data but others that share less. Concerns about patient privacy will need to remain a major focus that underlies research. Data ownership will need to be clarified, everywhere from data generated by our personal devices, to data collected in clinical trials, to data generated as the exhaust from the healthcare system and insurance industry. I do not anticipate data sharing within the industry to define the coming years but rather our ability to share standard data models and analytical methods. Those standards will facilitate distributed research and evidence sharing and help enable a learning healthcare system.

MONTHLY DEEP FOCUS:

What Impact Will Artificial Intelligence (AI) Have on Clinical Trials?

Tod Northman
Partner, Tucker Ellis LLP
Cleveland, OH

The increasing complexity of clinical drug trials in the United States has resulted in the cost and time to commercialize a drug to skyrocket. In this context, artificial intelligence appears perfectly timed to help reduce the costs and time for clinical trials while potentially providing better results. Some of the most promising changes in the conduct of trials are directly facilitated by AI: monitoring through wearables (which also enables site-less or virtual trials), centralized trial monitoring, drug-adherence monitoring, and pre-emptive in-trial risk-monitoring.

AI will depend on collecting and sifting through enormous pools of data. While simultaneously improving and expanding data collection methods and data quality, AI could shrink trial periods and reduce costs. The sum is that AI has the potential to help bring therapies and drugs to market quicker, with more reliability, and at a reduced cost.

The promise is clear. However, there are formidable challenges. The foremost challenge is the limited availability of talented AI professionals, as nearly every endeavor seeks to deploy artificial intelligence. Those AI experts who can be wooed to pharmaceuticals are unlikely to have the desired background. Ordinarily, I would consider regulatory approval to be a barrier, but the FDA's implementation of the 21st Century Cures Act supports hope that the FDA will support the use of AI in clinical trials.

Heather Logrippo
Cofounder and Chief Wish Officer, United States Chief Healthcare Advocacy Group
Shrewsbury, MA

After about 18 months of healthcare data being overlaid into a Deep Learning AI system, the AI will be able to not only give predictive insights into the data for millions of patients based off of the collective data, but able to find trends, relationships between medications and their efficacy that are not easily evident to singular healthcare providers, along with data that would present a strong case for a clinical trial.

What this means is that clinical trials may increase at a very fast pace once the AI makes correlations based on immense amount of data. It could also mean that clinical trials could be proven and sped up through the AI data. For instance, if the AI picks up that a group currently on medicine A, has a side effect that solves a different medical issue, that data will come forth more quickly than it does today due to the massive processing power and deep thinking that mimics the frontal cortex of the human brain. In other words, the AI, because of its ability to process more data than any human, will find case uses and studies before humans do.

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