Rx Data News

Vol. 1

Issue 5

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
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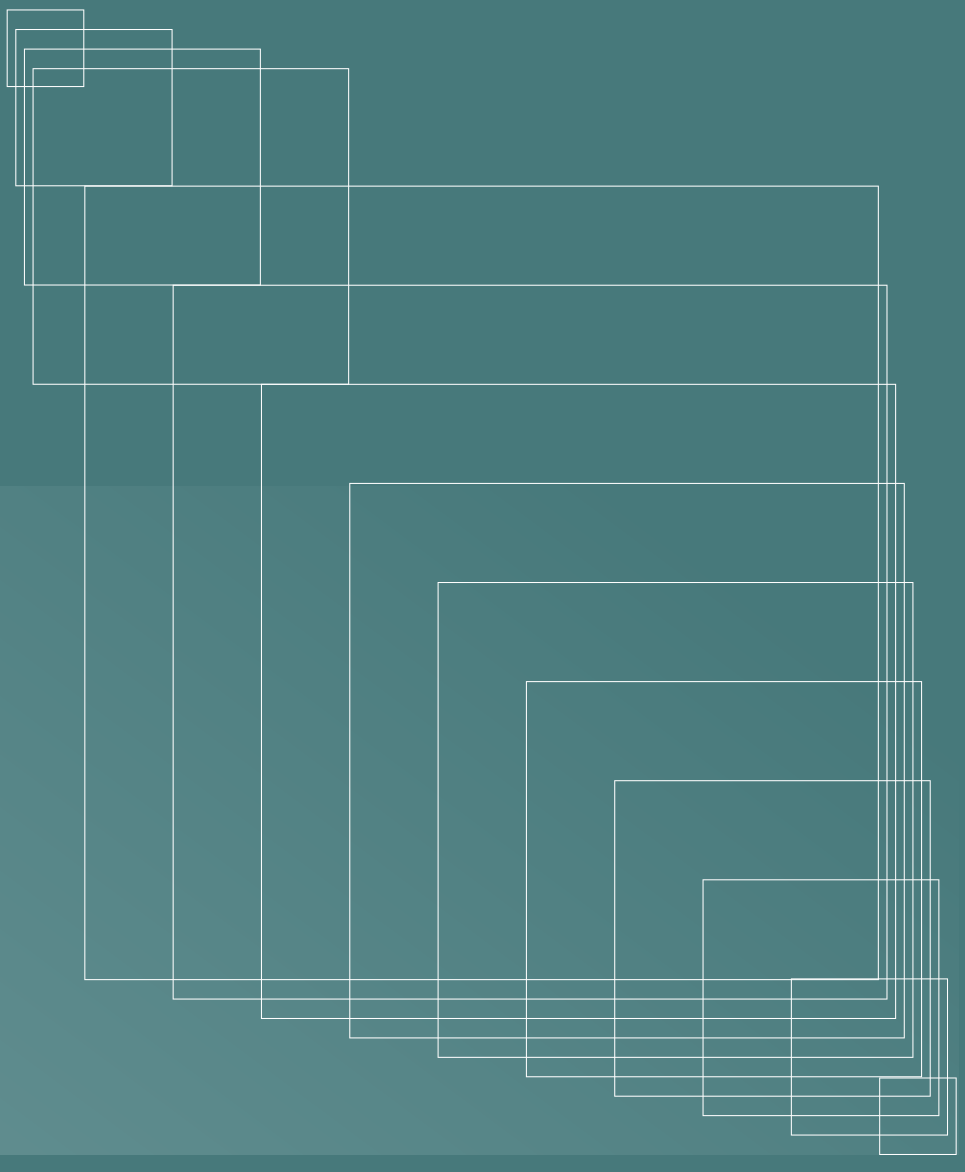
MONTHLY DEEP FOCUS:

What are the most important use cases for Blockchain in the Pharmaceutical Industry?



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News-In-Brief

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IBM is stopping development and sales of its tool that utilizes Watson AI to help pharmaceutical companies find new drugs, according to a STAT report. A source told STAT that the product, Watson for Drug Discovery, wasn't yielding large enough financial returns.

BenevolentAI has signed a long-term collaboration with AstraZeneca to use AI and machine learning for the discovery and development of new treatments for chronic kidney disease (CKD) and idiopathic pulmonary fibrosis (IPF).

Pfizer and AI-company Concerto HealthAI have entered a precision oncology collaboration. The partnership will develop new synthetic control arm and prospective study designs, for both pre- and post-approval research, based on real-world data outcomes for therapeutics.

Bristol-Myers Squibb has entered into a partnership with Boston-based Concerto HealthAI to use AI and real-world data to improve how it designs and conducts cancer drug studies.

UK-based Exscientia has delivered the first drug candidate to be found using its AI collaboration with GlaxoSmithKline, a potential therapy for chronic obstructive pulmonary disorder, or COPD.

Exscientia, an AI-driven drug discovery company, entered an AI drug discovery partnership with Celgene. The deal consists of a $25 million upfront payment and eligibility to receive significant milestones depending upon the clinical, regulatory and commercial success of the program.

The biotech industry is becoming the most active group for later-stage pipeline work, and while Big Pharma sees its R&D share drop, emerging life science companies are better prepared to go it alone. This is according to a new report by the IQVIA Institute for Human Data Science, "The Changing Landscape of Research and Development: Innovation, Drivers of Change, and Evolution of Clinical Trial Productivity."

The Consumer Technology Association launched an initiative to set standards for the use of artificial intelligence in healthcare, backed by more than 30 vendors and provider associations. The group will examine and advance AI technology in consumer health, fitness and wellness technology and recommend best practices — with major tech outfits like Blackberry, Google and IBM among the initial members.

Drug discovery startup Insitro has its first pharmaceutical partner. Gilead Sciences will work with Insitro to find medicines to treat a liver disease, nonalcoholic steatohepatitis (NASH), that is fast becoming a global epidemic fueled by poor diet and lack of exercise.

Innovation Endeavors, a fund backed by Google's Eric Schmidt, unveiled a new project called Deep Life, which intends to identify problems in the life sciences, and figure out how to use innovations in areas like machine learning to help fix them.

McKesson Corporation announced a technology collaboration with Google Cloud that will advance the development of next-generation applications and products, machine learning and AI technologies, and enhanced analytics to transform care delivery and drive profit.

Deep Lens, an AI-based startup developing a precision medicine software suite, announced that it's raised $14 million in series A funding led by Northpond Ventures, with participation from existing investors Rev1 Ventures, Sierra Ventures, and Tamarind-Hill Partners.

Life sciences digital transformation company Medidata, announced the launch of Acorn AI, a new company designed to provide actionable insights across the entire drug continuum – from R&D to commercialization.

Insilico Medicine, a biotech company developing the end-to-end drug discovery pipeline utilizing next-generation artificial intelligence, announced its partnership with Arctoris, the world's first fully automated cancer research laboratory providing robotic experimentation in the cloud, Science Entrepreneur Club, a life sciences network and Cluster Market, a leading online equipment sharing and booking platform enabling and accelerating science.

The American College of Radiology (ACR) Data Science Institute (DSI) just launched its ACR AI-LAB software platform and is collaborating with GE Healthcare. GE's Edison AI platform will integrate with ACR AI-LAB, giving ACR members and other industry professionals access to certain Edison-powered AI services.

Qulab, a pharma-chemical company, today announced Quleap, the first integrated artificial intelligence (AI)-based platform for small molecule drug design. Quleap is an integration of automated small molecule design, synthesis planning, and a cloud engine for simulating biomolecules. The first two are fundamental chemistry technologies that can be used for applications in the pharmaceutical and chemical industries.

Amazon's Alexa upgrade offers HIPAA-compliant skills, creating new opportunities for drugmakers that want to utilize the voice-activated AI platform. Express Scripts and Livongo have partnered with Amazon to offer apps that allow consumers to check on prescriptions, find urgent care and schedule visits, and log and track some health data.

NuvoAir, a digital therapeutics startup, has raised $3 million funding from a venture capital firm Industrifonden. NuvoAir aims to make respiratory diseases measurable and treatable. It uses cutting-edge technology so that patients, physicians and research companies take the right decisions. Its digital therapeutics software called Aira sends personalized care suggestions depending on the patient's condition.

Indegene, a leading partner to lifesciences industry, hopes to disrupt the traditional biopharma launch and commercialization model with the next generation AI-driven launch of Yosprala for secondary CAD and stroke prevention.

Deciphex, an Irish tech company which is using artificial intelligence (AI) to accelerate the delivery of pathology services, has raised €2.3 million in a new funding round. Among those participating in the round were Irish investors Irrus Investments and Act Venture Capital. Other participants included US-based Nextsteps Ventures, Inovata Personalised Health Accelerator and GI Partners.

South Korea CNS medicines specialist SK Biopharmaceuticals and twoXAR, a US artificial intelligence (AI)-driven biopharmaceutical company, announced an agreement to discover and develop therapeutics for non-small cell lung cancer. twoXAR will use its AI discovery technology to identify a set of initial candidates with the potential to treat lung cancer through novel biological mechanisms of action.

FEATURED INTERVIEW:

M. Khair ElZarrad PhD, MPH.

Deputy Director, Office of Medical Policy, Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Silver Spring, MD

Dr. ElZarrad is the Deputy Director of the Office of Medical Policy (OMP) at FDA's Center for Drug Evaluation and Research (CDER), where he leads the development, coordination, and implementation of medical policy programs and strategic initiatives. Prior to joining the FDA, he served as Acting Director of the Clinical and Healthcare Research Policy Division with the Office of Science Policy at the National Institutes of Health (NIH). At NIH he worked on policies related to human subject protections; the design, conduct, and oversight of clinical research; and enhancing quality assurance programs at pharmaceutical development and production facilities. Dr. ElZarrad currently leads multiple projects focused on exploring the potential utility of real-world evidence, innovative clinical trial designs, and the integration of technological advances in pharmaceutical development. He earned a doctoral degree in medical sciences with a focus on cancer metastases from the University of South Alabama, as well as a master's degree in public health from the Johns Hopkins Bloomberg School of Public Health.

"AI applications could be very useful to facilitate and guide therapeutic development, the monitoring of safety, and to potentially make regulatory operations more streamlined and efficient."

Rx Data News: What are the main elements of the FDA's real-world evidence program?

Dr. ElZarrad: As required by the 21st Century Cures Act (Cures), FDA established a comprehensive program to evaluate the potential use of real-world evidence (RWE) to help support approval of a new indication for a drug approved under section 505(c), and to help satisfy post-approval study requirements. This program is multifaceted and includes internal processes and functions to facilitate internal dialogue and to disseminate relevant knowledge regarding key areas related the potential utility of RWE. Of course, a major part of this program is guidance development efforts that are responsive to the needs of our stakeholders and to provide clarity on major issues relevant to exploring the utility of RWE. Stakeholder engagement is another important aspect of this program, we wanted to establish a robust mechanism for high-level exchange of ideas around the potential utility of RWE. CDER established a committee that includes top experts at the agency to participate in meetings with stakeholder to discuss real-world evidence projects. This will facilitate the exchange of high-level ideas and considerations that support mutual learning and the exploration of RWD utility. As you are well aware, the program is based on a framework that was published in December of 2018 and is available publicly online[1].
The published framework highlights three key regulatory consideration that must be considered when exploring the use of RWD. These are:

- Whether the RWD are fit for use
- Whether the trial or study design used to generate RWE can provide adequate scientific evidence to answer or help answer the regulatory question
- Whether the study conduct meets FDA regulatory requirements

It is important to note that data standards are a major overarching issue that needs to be addressed by all involved stakeholders. Our framework makes that point very clear because it is a prerequisite to enable the full consideration of RWD to develop RWE that is fit for purpose.

Rx Data News: Can you describe the emerging role of technological innovations in facilitating the use of real-world data? What issues does this raise from the FDA's perspective?

Dr. ElZarrad: There are many technologies that are currently available or are in development that may play a key role in facilitating the utility of RWD and the generation of RWE. The agency is fully aware of the promise of these technologies. When it comes to sources of RWD, we know that the discussion currently focuses on EHR and claims, but we believe that digital health innovations are very promising examples of tools that may help capture useful and relevant health data. Secure data transfer, storage, and management of electronic data, and the analytical tools needed to process such data are all important considerations to enable a robust therapeutic development and regulatory approaches. For example, the FDA developed MyStudies app[2] which is a flexible tool that can be used for capturing real-time data on medication use and other health information. The code for this app is available for free on GitHub[3]. Technological advancements such as mobile health tools and telemedicine platforms are also facilitating the development of innovative clinical trials such as decentralized clinical trial design that may enable the capture of health information direct-

ly from patients at home or other relevant locations. Such approach may also optimize the use of already established healthcare infrastructure and existing community care providers. We are hoping that capitalizing on technology to facilitate such innovative designs will serve to provide those in rural areas with the opportunity to participate in research, and to streamline real-world data capture and processing. Advance processing and statistical techniques may also provide us with key tools to help clean and make sense of real-world datasets. Of course, challenges do exist and can be variable depending on the technology being used. Just to name a few, the establishment of an audit trail throughout the data lifecycle, ensuring the validity of data collected from digital trackers and mobile systems, accounting for potential biases and confounders associated with different platforms, and understanding what endpoints could be captured reliably using such technological tools are all important considerations.

> **Rx Data News:** What are some examples of activities focused on the utilization of AI to support the development of therapeutics?

Dr. ElZarrad: AI applications could be very useful to facilitate and guide therapeutic development, the monitoring of safety, and to potentially make regulatory operations more streamlined and efficient. It is well known that FDA's Center for Devices and Radiological Health (CDRH) have already reviewed and cleared several AI algorithms[4]. CDRH is also leading the way by engaging with stakeholders by publishing and making its proposed regulatory framework for modifications to AI/ML-based software as medical devices[5] available for comments. On the drug side, there are many research programs that are exploring the utility for AI for drug discovery[6] and to aid in the diagnostic and therapeutic decision making[7],[8],[9].

FDA is committed to explore the utility of innovative technologies. The agency launched the Information Exchange and Data Transformation (INFORMED) initiative in collaboration with HHS's Innovation, Design, Entrepreneurship and Action (IDEA) Lab[10],[11]. This initiative aims at expanding the technical infrastructure to facilitate the management and analyses of big data and to explore innovative approaches to generate quality evidence that can be utilized to support regulatory decisions. INFORMED is a multifaceted initiative that will include exploring the use of RWD for clinical evidence generation and evaluating the potential used of digital tools, such as trackers and biosensors. The initiative is also focused on identifying opportunities for artificial intelligence to enhance research designs and analytical capabilities.

In December of 2018, the FDA published a detailed Framework for its real-world evidence program. As mentioned in the answer to question 2, technological innovations, including AI can be extremely helpful in exploring the utility of RWD. The Framework discusses certain needs and knowledge gaps that can be addressed using robust analytical and technological tools.

It is also important to note that as we explore the potential of AI and other innovative technologies, we need to recognize potential challenges. Although sophisticated, AI algorithms can imbed biases and may provide answers that do not take into account the complexity of the health care environment. We believe that a thorough

"It is important to note that data standards are a major overarching issue that needs to be addressed by all involved stakeholders. Our framework makes that point very clear because it is a prerequisite to enable the full consideration of RWD to develop RWE that is fit for purpose."

understanding of therapeutic development, disease complexity, patients' heterogeneity, and the specifics of clinical care should be key foundations for developing useful AI tools. Interdisciplinary teams that bridge all relevant expertise are most suited to develop relevant technological systems and tools.

> **Rx Data News:** What role do you see blockchain playing in the pharmaceutical industry in the coming years?

Dr. ElZarrad: FDA recognizes the potential uses and benefits of blockchain, for example, to help in securing the drug supply chain. The FDA in fact initiated a pilot program under the Drug Supply Chain Security Act (DSCSA) to explore the use of such technologies[12]. The scope and the approach were further outlined in an FDA press release in February of this year[13]. The promise of technologies, such as blockchain, to enable seamless tracing and robust verification is an important benefit. Furthermore, we are aware of multiple projects exploring the potential use of blockchain to track research and clinical data and to record and account for any data access and data manipulation. This could be an important area to ensure confidence in the way RWD is handled and processed to produce RWE. We are also aware of reports describing how blockchain technology can be used to protect the privacy of health data[14]. The INFORMED initiative mentioned above in the answer to question 3, also plans to explore the uses of technologies, such as blockchain.

> **Rx Data News:** What technologies do you believe will have the biggest impact on innovative clinical trial designs? What regulatory challenges will these innovations pose?

Dr. ElZarrad: At a time where we see a convergence of multiple powerful technological tools, it is difficult to single out a few technologies as having the most impact. We see therapeutic development and regulations as a continuum, and any technology that could hold promise to enhance any part of this continuum is something that is at least worth understanding and potentially exploring.

That said, the convergence of powerful processing capabilities along with the increased availability of large health datasets, thanks for example to the almost complete adoption of EHR, hold the promise of enabling us to streamline evidence generation and to enhance clinical trial designs. Digital tools hold the promise of providing us with data on patient experience on a more continuous basis, rather than through episodic interactions with the health care system. Such approaches may augment data collected in clinical trials and provide more comprehensive picture of therapeutic performance. New technologies may also help us clean and analyze real-world data and may provide us with the tools to ensure confidence in RWD along with helping in identifying and avoiding biases and confounders.

With the availability and continued refinement of these technologies, clinical trials can be designed more efficiently, and complex designs, data collection, and advanced analytical approaches can be increasingly utilized. For example, technologies may play a major part in facilitating FDA's pilot program "Complex Innovative Trial Designs Pilot Program."[15]

Finally, it is important to note that basic problems, such as failure to recruit continue to be a major hurdle and a primary cause for premature trial termination. Innovative technological tools can potentially be a game changer in enhancing clinical trial design and conduct to ensure that such trials recruit and succeed to provide us with the data needed to advance public health.

AI-Driven Operations Systems are Essential for Supply Chain Regulatory Compliance

WRITTEN BY: Frederick P. Dawson

Smaller pharmaceutical manufacturers are struggling to meet requirements set out in the US Drug Supply Chain Security Act (DSCS), according to a supplier of AI-driven manufacturing software.

The DSCS was brought in to provide greater traceability throughout the pharmaceutical supply chain. It is expected to better maintain integrity from producer of raw ingredient or medical component through to patient. The Act ensures records are kept of who touches the product, creates databases of key information and requires traceability elements such as scannable unique barcodes linked to relevant product data.

It has introduced a number of requirements for manufacturers in the pharmaceutical supply chain. This includes traceability elements such as a national drug code, lot number and serial number for each individual unit.

All of this requires a larger amount of tracking information for materials as they are transformed from raw ingredients all the way through to finished, repackaged products.

This has proven difficult to a wide range of supply chain stakeholders including manufacturers of prescription products such as skin creams and dental cleaners as well as re-packers of class on controlled substances, according to Dr Peter Green, president and chief technolo-

gy officer at BellHawk Systems – a provider of operations tracking and management software.

In order to generate these codes and identifying numbers, a significant amount of information has to be processed including items such as who worked on the ingredients used, where the ingredients were tested and where they were shipped in order to form a complete traceability report.

Large pharmaceutical companies usually already have a system in place that can provide this sort of detail, process as well as store it and then ensure it is linked to the right bar codes on the right products. But smaller manufacturers and re-packers – companies that, for example, take large consignments of drugs to be re-packaged into daily dosage packs for care homes and other facilities – are struggling to implement the necessary changes.

Currently the solution is to delay or to throw a large number of staff at the issue to capture and submit data.

At the moment, the US Food and Drug Administration (FDA) has not started cracking down on non-compliance, instead offering waivers to ensure steady supply of necessary pharmaceuticals, according to Green.

This must eventually change and additional requirements are expected to be added this November when the FDA ratchets up the minimum supply chain traceability specifications once again – in line with the guidance set out for the gradual implementation of the DSCS through to 2023. For 2019, manufacturers are expected to be able to produce product verification down to package level – though many are still working on sterilization compliance meant to have been fully introduced by 2018.

"It's going to get worse later this year and into next year when companies have got to supply more data into repositories and upstream as well as downstream data sources," Green said.

Meanwhile using additional staff resources is either a heavy cost or a detraction from other essential elements of the business. Staff capable of handling regulatory filings with the FDA can cost a company $70,000-$100,000 in loaded labor costs when items such as health insurance are taken into consideration, Green added.

Switching to an AI driven software could also mean fewer mistakes. A system could inform staff if something looks like a mistake or does not match the FDA guidelines as it is being entered, Green said.

"The real problem it solves is providing the ability to comply with material traceability and labeling without requiring a huge IT staff or spending a lot of money," he added.

Overall a more efficient way of dealing with the issues is through the use of an AI-driven management software tool. These can collect, store and allocate data as necessary to meet requirements but also can provide further potential uses to pharmaceutical companies. For example a system could enable a company to perform real-time tracking which would potentially mean it could increase logistics efficiencies by introducing lean inventory practices – ordering of materials only when absolutely necessary – cutting down on money spent on storage and warehousing costs as well as potentially spoilage risks in certain situations.

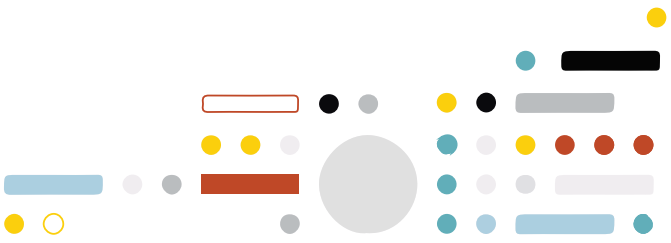
However, that is something still in the future, Greed explained. "What we see currently is less interest in [lean inventory advantages] in the pharmaceutical sector than in areas such as aerospace at this time," he added. "Most of the attention has been focused on meeting FDA drug requirements coming out as compliance is a requirement for doing business. If you can't ship product because you aren't in compliance then that makes any efficiencies in lean inventory moot. So compliance is everything at this point."

Further requirements are expected down the line as full implementation of the DSCS is brought in through to 2023. However details on this are still thin on the ground as the FDA itself is still working out issues such as format for future data repositories. The FDA has been running pilot programs and seeking feedback from stakeholders in order to determine the best path forward in areas such as this.

"On the surface it all looks organized but in reality the introduction of new requirements is more like a hodgepodge," Green explained. And for the smaller companies in the sector, digesting, applying and then ensuring continuing compliance with that hodgepodge can be a tall order.

Introducing AI systems could be a good step towards doing that – though they have to be scaled to the size of the company. A number of solutions currently on the market are geared towards the larger pharmaceutical entities in the market and are priced accordingly, Green warned.

But given the fact that companies would have to cease operations if they continued to be unable to comply – coupled with the potential future benefits from lean efficiency plus the use of the generated data in other applications – it would seem that AI driven operations systems are not only a necessary expense but could be viewed as a smart investment that will improve the bottom line in the future.



MONTHLY DEEP FOCUS:

What are the most important use cases for Blockchain in the Pharmaceutical Industry?

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The pharmaceutical industry today faces a set of significant challenges in which current approaches and technologies are failing to deliver needed solutions. These challenges include:

- **Booming Counterfeit Drug Trade:** The global counterfeit drug trade has become a fast growing mega-billion dollar business that reduces authentic branded medicine sales by 10-15% worldwide while creating a health threat for hundreds of thousands of people.
- **Inefficient and Expensive Clinical Trials:** The clinical trials required for government approval of new drugs have become very expensive to administer and yet may not be compliant with laws regulating informed consent, data collection, and data sharing.
- **'One Size Fits All' Rx:** The delivery of personalized medication is a goal for many healthcare organizations, however, the personal medical history and longitudinal datasets required to create and administer these medicines often do not exist.

Data issues sit at the heart of each of these cases. Data today is stored in systems that by their design create friction, increase costs, and reduce trust and accountability. More specifically, today's paper-based and centralized electronic systems are insecure, easily alterable, siloed, and contain a preponderance of poor quality data.

What is needed is an improved infrastructure that is secure, stores trusted data, enables safe data sharing, and integrates with high quality data sources. Blockchain technology delivers all of these capabilities, plus more, and as a result, pharma leaders are adopting blockchain to create powerful solutions. We discuss each use case in more detail below.

Fighting Counterfeit Drugs

Due to the rapid growth of the counterfeit drug trade, governments have passed laws requiring the pharmaceutical industry to create electronic systems capable of verifying authenticity and reducing fake drugs in circulation.

In the US, the Drug Supply Chain Security Act (DSCSA, 2013), directed by the FDA, gives a 2023 deadline for the pharmaceutical industry to provide electronic track and trace plus verification of the authenticity of prescription drugs. In Europe, the Falsified Medicines Directive (FMD, 2013) gave a deadline of February 2019 for all prescription medicines to be authenticated electronically and enclosed in tamper-evident packaging. The core idea for both laws is that a consumer should be able to scan a QR code on a drug package to confirm that the product is authentic.

Blockchain technology provides an immutable, shared source of truth and so, when combined with serialization and smart sensors, provides a perfect fit to establish compliance under these laws. As a result, there are now multiple blockchain-based technology platforms and consortia providing compliance with the DSCSA. These include the MediLedger consortium, which includes Pfizer, Genentech, McKesson, Amerisource Bergen, and Gilead, and SAP's Information Collaboration Hub for Life Sciences, co-developed with Merck, AmerisourceBergen, GSK, AMGEN, Boehringer Ingelheim, McKesson, and Novo Nordisk.

In Europe the EU Innovative Medicines Initiative (IMI), a public-private partnership between the EU and European pharmaceutical industry, has created the Blockchain Enabled Healthcare program. The scope of this program is to build a comprehensive solution that incorporates regulatory compliance but also extends to clinical trials, patient data sovereignty, and health data sharing. It includes 9 large pharma industry players plus key industry stakeholders.

Enhancing Clinical Trials

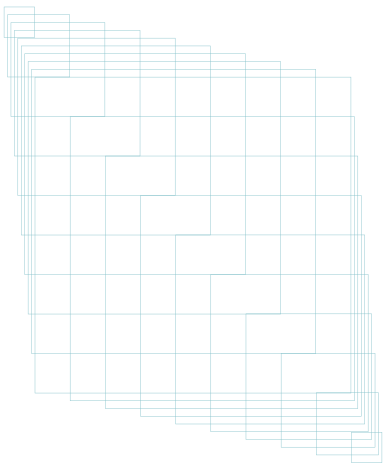
Many clinical trials use manual processes dominated by paper-based systems and centralized electronic databases. As a result, there are three major challenges which cost the industry billions of dollars annually: 1) inefficient and error-prone information and data collection, 2) inadequate coordination and data sharing across stakeholders, and 3) lack of patient centricity. Strict compliance with HIPAA, HITRUST, and other frameworks can further exacerbate siloing and lack of data transparency.

Blockchain-based systems address many of these shortcomings through a combination of digitization, ultra-secure encryption, and data transparency within a network. Process flows can also be mapped onto smart contracts that can ensure that key information, such as patient consent, is securely recorded prior to any clinical activities. Blockchain systems can also integrate tightly with smart device and Internet of Things (IoT) sensors to capture highly-quality data streams.

Clinical trials by their nature involve coordination across diverse stakeholders in the ecosystem. Unfortunately, today's clinical trials are rife with inadequate coordination and data sharing. Since blockchain is a 'team sport', it offers increased trust and transparency towards improved data sharing across stakeholders. Blockchain's single and immutable source of truth ensures that data integrity is maintained across the clinical trial process.

With median attrition rates across clinical trials running as high as 30%, it is becoming increasingly important to address better patient recruitment as well as patient empowerment. With blockchain's integration with sovereign PHR (personal health record), it is possible to acquire contextualized PHR to better qualify patients for the trials. Onerous schedules combined with a lack of transparency and data sharing can alienate patients. Blockchain systems, by contrast, can promote patient centricity by giving patients ownership of their data, by providing tokenized rewards, and by creating a more socially engaged experience.

Early blockchain applications in clinical trials are primarily focused on data issues and consent management. In February 2019 at HIMSS, Boehringer Ingelheim (Canada) Ltd. and IBM Canada announced that they are collaborating on a blockchain solution for clinical trials to provide data integrity, transparency and provenance as well as to automate trial processes including consent management.



Delivering Personalized Medication

The technology for delivering personalized prescription drugs via 3D printing already exists and is well documented. Importantly in 2017 the FDA released guidelines for the 3D printing of drugs at non-traditional locations like a hospital or doctor's office. However, to print useful personalized medicine, healthcare organizations must have access to a rich set of high-quality patient data, which often does not exist at any one location.

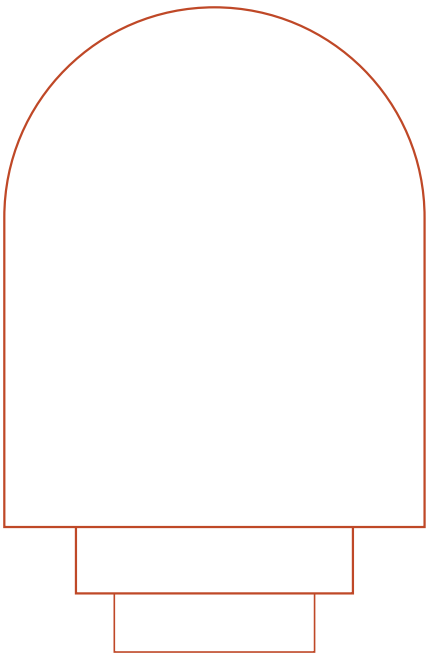
Due to data fragmentation and lack of data sharing across multiple disparate providers, the required information, especially -omics (i.e. genomics, epigenomics, proteomics, metabolomics) and allergy data, are not readily available. Also, importantly, longitudinal population health data is necessary, but often lacking, for determining active ingredient ratios based on a patient's genomic profile, demographics, and other risk factors.

With a blockchain-based framework, however, each patient's data can be owned by the patient and stored in a personal health record (PHR) keyed to a person's biometrics. In this way the patient's medical record becomes portable and remotely accessible, with consent, by care providers at any location. Such a system that gives patients control over their own data is undergoing testing at University Health Network (UHN), the largest medical research organization in Canada. Blockchain technology can also enable longitudinal population health data to be shared, creating useful datasets across different population pools.

This data foundation then makes it possible to leverage artificial intelligence (AI) and machine-learning (ML) based systems to quickly determine the most appropriate active ingredients and dosages personalized to a patient's specific needs. Integrating the AI/ML output with a 3D drug printer then enables the on-demand printing of personalized medication at a hospital or doctor's office.

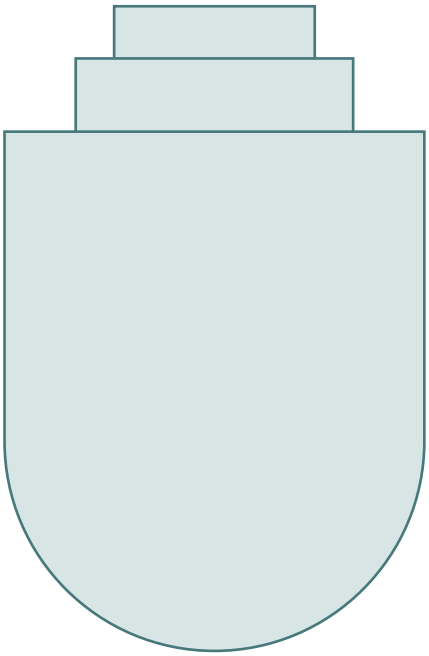
Conclusion

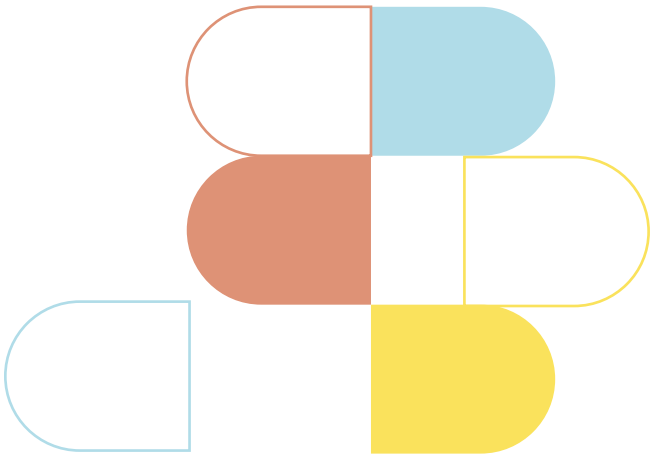
Blockchain technology is being used to safeguard the prescription drug supply chain and has the potential to reduce clinical trial costs and enable more widespread 3D printing of personalized medication. With such a transformative technology, earlier adopters will develop significant competitive advantage over those that follow.



IBM Ends Sales of Watson for Drug Discovery

WRITTEN BY: Peter Grant





Reports emerged in April that IBM will no longer be selling its Watson AI system as a tool for drug discovery. Pharma giants Sanofi, Johsnson & Johnson and Pfizer had established partnerships with the research tool. According to IBM officials, the companies currently using the software will continue to do so in the separate field of clinical development.

Watson relies on the modular system for drug discovery. In this system, a user identifies a specific gene, disease or pharmaceutical for targeted research and Watson then uses its powerful natural language processing (NLP) and machine learning capabilities to analyze reams of pharmaceutical literature and millions of academic publications and industry patents to highlight previously unidentified associations or relationships between them. According to IBM's website, the Drug Discovery program enables users to explore entities, receive post-translational modification summaries, identify co-occurrence, predict relationships, explore chemicals and networks, and conduct predictive analysis.

The retreat comes after a multiyear, aggressive marketing campaign promoting the capabilities of the AI system. The company maintains that sluggish sales are the reason why they pulled the plug, but others see signs of deeper problems. This is just the latest disappointment in a series of bumps in the road for the venerable technology company as it has attempted to make inroads into the healthcare and life sciences fields.

Watson's drug discovery program was first introduced in 2014. At that time, IBM invested $1 billion into the supercomputer in the hopes of building a $10 billion worldwide business within a decade. In the years that followed the company would face a series of high profile disappointments, leadership changes and internal lay-offs.

Transforming medicine through the use of artificial intelligence has been a core goal of IBM, often described by CEO Ginny Rometty as the company's 'moonshot'. On February 17th, 2011, only a day after Watson famously triumphed in the television game show Jeopardy, IBM issued a press release proclaiming their intent to, "explore, develop and commercialize the Watson computing system's advanced analytics capabilities in the healthcare industry."

These days, an increasingly large chorus of critics now criticize the company for taking a marketing first approach, before the system could produce they kind of results that could legitimate the hype. IBM promised that AI systems like Watson could optimize treatments, reduce diagnosis errors and help solve doctor shortages by enabling physicians to worker faster and more effectively. However, it isn't just an unrealistic marketing campaign that has come under criticism.

"When it comes to AI and drug discovery, the value is in talent, data, and turnkey solutions—not general purpose hardware and software," says Simon Smith, Chief Growth Officer at BenchSci. "This is because there's so much hardware, such as cloud GPUs, and software libraries, like TensorFlow, that anyone can get cheaply or free. What's scarce is talent, proprietary data, and solutions that use AI to impact business metrics immediately (rather than offering something vague, like the possibility of generating a new hypothesis). IBM Watson wasn't really offering much that was scarce. It used public data, for example".

"So rather than pay IBM," Smith continues, "Why wouldn't a pharmaceutical company invest in hiring talent to analyze its own proprietary data? Using available hardware and software libraries? And creating new models they can own? What we do see pharmaceutical companies investing in are turnkey solutions. For example, when a company has built its own datasets and models, used them to solve a pain point in drug discovery, and made the solution instantly available to a pharmaceutical company's researchers, with quantifiable impact, there's a huge appetite. But otherwise, when an offering is vague, or a pharmaceutical company would be better off doing the work in-house, it's not surprising if the offering isn't successful".

The trouble began with Watson for Oncology, a cloud-based supercomputer that digests vast data sets that include things like doctors notes, clinical guidelines, medical studies and more. However, the AI-system doesn't'

generate treatment recommendations itself but rather relies on training by humans who input information on how patients should be treated.

In September of 2017, STAT reported that Watson for Oncology was still struggling to identify and differentiate between different forms of cancer. At that point, only a few dozen hospitals had adopted the system. Physicians at foreign hospitals who used the system complained of bias towards American patients and methods of care.

The bad press was preceded by a high profile defection of one of Watson for Oncology's high profile users: MD Anderson Cancer Center. MD Anderson's prominent departure from the program provided fodder for critics who insisted that AI was simply not mature enough for practical applications in the complex environment of healthcare.

ment options to physicians, supported by evidence. Ultimately the treatment decision is always up to the doctor and patient. While a recent media report created the misimpression a potentially harmful treatment was recommended to a doctor in the field, the option cited was actually part of internal testing being done to improve Watson for Oncology, not a real patient. We also have an extensive quality management protocol through which we assess and address feedback and items that have been flagged by client, partners, and our own teams and systems."

A major part of IBM's problems comes down to the gulf between to company's rosy public statements regarding the capabilities of Watson and the actual situation on the ground. Speaking at 2017 conference for health IT professionals, IBM CEO Rometty claimed that AI, "is real, it's mainstream, it's here, and it can change almost everything about health care."

"The retreat comes after a multiyear, aggressive marketing campaign promoting the capabilities of the AI system. The company maintains that sluggish sales are the reason why they pulled the plug, but others see signs of deeper problems. This is just the latest disappointment in a series of bumps in the road for the venerable technology company as it has attempted to make inroads into the healthcare and life sciences fields."

In late July of last year, internal documents reviewed by journalists at STAT indicated that Watson for Oncology had recommended 'unsafe and incorrect' cancer treatments. The poor performance, it was suggested, was due to mistakes made by IBM engineers and Memorial Sloan Kettering Cancer Center. Instead of using real patient data, the system was trained using only a few hypothetical cancer cases.

The system's treatment recommendations were supposed to be informed by guidelines and evidence, instead they were overly reliant on the treatment recommendations of a small number of specialists. IBM had publicly proclaimed that Watson for Oncology used historical patient data, but this proved not to be the case.

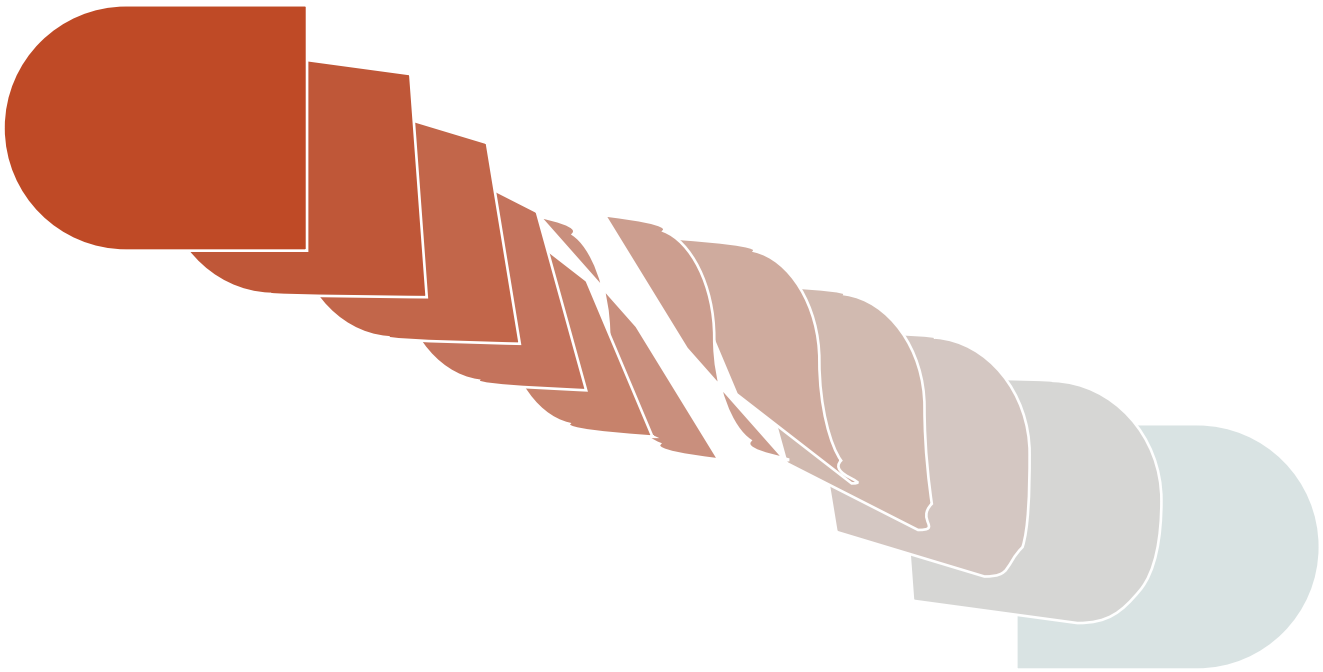
IBM has contested media reports related to its Oncology program, issuing the following statement on April 2nd:

"We are 100% focused on patient safety. It's important to remember this tool does not diagnose. It provides treat-

While few would dispute that AI holds great potential in areas such as diagnosis and drug discovery, Watson's current capabilities in these areas has proven incongruous with the expectations created by the IBM's aggressive marketing campaign. The company promoted Watson through a high profile commercials starring international celebrities such as Jon Hamm, Bob Dylan and Serena Williams.

As it stands today, regulators have approved only a few AI-based tools for actual use hospitals in doctors offices. Many of these products operate in the visual realm, utilizing computer vision to provide analysis on images such as retina scans and X-rays. When it comes to making sense of complex medical information, IBM's experience with Watson serves as a cautionary tale.

Watson's victory at Jeopardy was due to its relative mastery of natural language processing (NLP). Unlike a basic search engine which returns documents based on keywords, Watson utilizes hundreds of algorithms to map



complex entities within a sentence and identify relationships between them. This allows for a greater ability to understand the meaning of language, as opposed to simply recognizing patterns in words. The program developed this capability on its own through machine learning.

Health care data has long proved vexing for artificial intelligence and machine learning programs. Certain types of data, such as vital sign measurements and lab results, can be easily digested. However, the bulk of healthcare data, as much as 80% of a typical patients record, is unstructured in the form of doctors notes and discharge summaries. These narrative documents can often consist of subjective statements and shorthand.

IBM's experience with Watson would seem to indicate that AI programs today still have difficulty understanding and interpreting ambiguity and too often fail to pick up on subtleties that human physicians have little problem recognizing.

IBM's pivot to clinical development reflects its hope to alleviate a significant pain point in the drug delivery pipeline. The company hopes to use Watson to identify the best possible patients for clinical trials. In doing so, they hope to improve upon a process that for your average oncology drug could cost anywhere from $650 million to $2 billion and last on average up to seven years.

In a recent quarterly financial statement, IBM executives outlined a desire to redirect Watson Health towards data analytics applications. IBM has indicated for months that it desires to integrate its Watson AI tools with its cloud platform as organizations shift core business applications to multi-cloud platforms. IBM hopes that the new AI tool Watson Open Scale, designed to allow data scientists to monitor the quality of the machine learning models, including its accuracy or whether bias has been introduced into the model, will play a key role in this transition.

Despite the setbacks experienced by Watson, a whole host of well financed AI startups continue to explore ways to gain insights from unstructured data such as scientific research and clinical trials to improve drug discovery. Whether they will avoid the mistakes made by IBM remains to be seen.

IBM is far from out of the picture. It has a vast array of partnerships with influential players in the life science industry, companies like Pfizer and Novartis among others. However, the concept of an all-powerful, general AI that will discover miracle drugs has taken a hard blow. Instead, it seems more likely that AI and machine learning will have deeper impacts on a wider variety of narrow applications throughout the drug discovery and clinical trials process.

MONTHLY DEEP FOCUS:

What are the most important use cases for Blockchain in the Pharmaceutical Industry?

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As blockchain continues to receive praise for its applications in industries ranging from financial services to energy suppliers, the pharma industry is only beginning to actively explore a blockchain solution for its potential to resolve some of the long-standing issues facing the drug supply chain.

It is no secret that the supply chain has its weaknesses. Current visibility across the supply chain is often fragmented and incomplete, with limited control and traceability across the research materials, drug manufacturing and sales processes. Verifying where a drug product's ingredients were sourced, where it was manufactured and the distribution journey into the patient's hands has proved difficult- and yet is arguably becoming more scrutinized than ever as pharma is under increasing pressure and demand for greater transparency in the supply chain by regulators. With a number of medications not being labelled correctly and a growing counterfeit drugs market, the supply chain has become an issue for everyone.

The implementation of blockchain is by far one of the most promising solutions to many of these problems facing the drug supply chain today. Blockchain provides real-time access to data and visibility across the entire supply chain. It ensures there is always a single version of records, not two separate databases, preventing room for human error and other fraudulent activities. This means when you head to the pharmacy to collect your prescription, you will know if the medication contains the intended APIs and whether it was stored in the appropriate conditions, ensuring that it is of the highest quality standard. Once data is entered into the blockchain, it cannot be removed or deleted, and any changes are visible to all in the ledger, including who made the change, and at the specific date and time the change was made. Any lapses in integrity are easily detected.

Many companies are already investigating the use of blockchain within the supply chain, and the value it could add to different points across the supply chain, including drug safety, patient safety, and clinical trials management. A quick scan can pull up the entire history of a specific product within the supply chain, verifying its authenticity and integrity. This means that pharma will be better able to reduce the number of counterfeit drugs in the market, and significantly decrease the errors resulting in product recalls and associated deaths each year related to information gaps within the supply chain. Medical errors are estimated to be the third leading cause of death for Americans, and the use of a digital ledger could substantially decrease this figure.

Blockchain has the potential to help improve the efficiency of delivering a safe and effective medicine to patients and overall, develop a stronger foundation of trust in the pharma industry, who in recent years has been struggling to maintain its reputation with end-consumer patients.

MONTHLY DEEP FOCUS:

What are the most important use cases for Blockchain in the Pharmaceutical Industry?

Avani Desai
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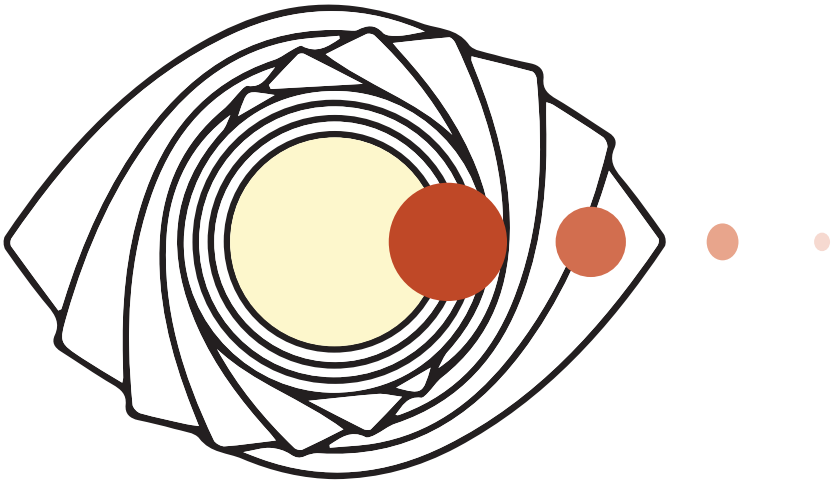
When you think of the value of blockchain, you immediately think transparency, integrity, security, and no controlling person, company, or government. So blockchain at the end of the day is just a digital distributed ledger

The opioid crisis has become an epidemic now and with the revolutionary technology of blockchain, I believe that it is the weapon that we need to combat this beast in the U.S. The National Institute of Drug Abuse has come out with some startling factors – 115 people in the U.S die daily for the use of opioids and the burden to the economy is over $78 billion for the mismanagement of opioid manufacturing and prescriptions.

When you think of the value of blockchain, you immediately think transparency, integrity, security, and no controlling person, company, or government. So blockchain at the end of the day is just a digital distributed ledger. When a transaction happens, the information is documented on the ledger and shared with every single computer node. This means one person or company cannot make a change, keeping the integrity.

So how can the blockchain help? The prescription drug supply chain process would no longer reside on multiple decentralized and disconnected systems – prescriptions would be put on the blockchain as well to increase the trust of prescriptions also information for the entire supply chain would reside there so the pills that are sent from the manufacturer to the pharmacy would be counted and quantities would be confirmed. Also, the doctor writing the prescription for the pills which are picked up at the pharmacy are documented on the blockchain for verification of integrity of the patient's prescription needs. Let's say pills are then found on school grounds, they will be able to use the identifier, see who the patient is, the prescribing physician, what pharmacy and where it came from. This also would help with authenticity – as we are seeing a wave of "counterfeit" opioids. T o go one step further, when you have this information on the blockchain, using predictive analysis can also help combat the problem by identifying where misuse may happen before it happen or identifying doctors that are overprescribing.



UK Competition Will Apply AI to the Search for Cancer Cures

WRITTEN BY: Frederick P. Dawson

> *The Arctoris laboratory is a fully automated cancer research laboratory providing robotic experimentation in the cloud. BioTarget candidates receive the equivalent of up to USD $100,000 worth of lab time to further assess the potential of their idea.*

A new competition is looking to use AI in the search for cancer cures. BioTarget is a new competition currently assessing its first intake of applicants following a submission period open through April.

The competition is looking for promising new molecules that could be used in the future treatment of cancer. It is open to anyone – though best fits small companies, start-ups or entities undertaking initial research, according to Martin-Immanuel Bittner, co-founder of Arctoris, one of the organizations behind the competition.

The eight most promising submissions to BioTarget will be taken to a pitching event in London, UK Initial submissions will be assessed by "an interdisciplinary group of experienced drug discovery researchers," according to Bittner. Criteria for assessment include:

- Quality of the scientific rationale
- Relevance of the approach for patients/ clinical need addressed
- Status so far (e.g. promising data, patents etc.) and convincing concept for the next steps

The ideas at the pitching event will then be further winnowed down by "A panel of industry-known thought leaders. These have not yet been announced, Bittner said. The ones awarded first through third by this panel will also receive use of Arctoris's cloud laboratory for experiments.

The Arctoris laboratory is a fully automated cancer research laboratory providing robotic experimentation in the cloud. BioTarget candidates receive the equivalent of up to USD $100,000 worth of lab time to further assess the potential of their idea.

The idea would be that researchers would be able to design and configure an experiment, upload it to the cloud laboratory where advanced robotics would conduct the necessary actions before delivering the data back to the researchers – eliminating the need for researchers to have access to expensive equipment as well as time restrictions on use of that equipment.

Support will also be provided by another of BioTarget's organizers – Clustermarket, a company providing access to specialist equipment for life sciences researchers. "Clustermarket is also keen to support the next generation of drug discovery researchers with their platform," said Bittner.

Altogether the aim of the competition is to further research while also creating publicity around these emerging research ideas in the hopes of driving greater interest and funding towards the projects, he added.

This will be done, in part, with one of the other partners in BioTarget – Science Entrepreneur Club, a life sciences network with extensive social media reach.

"The overall goal is twofold for applications: One is getting publicity and PR for fund raising by showcasing innovation," said Bittner." The other is the prize for one year experimentation. With this the researchers will then be able to take a big step forward."

The most promising products could then choose to enter into a collaboration with the third BioTarget organisation, Insilico Medicine, a biotech company developing the end-to-end drug discovery pipeline utilizing next-generation artificial intelligence.

Intellectual property remains solely in the hands of the researchers but a partnership with Insilico, if mutually agreeable, could drive the initial research much further down the road to becoming a viable product, according to Ola Popova, special projects manager for Insilico Medicine.

The BioTarget competition project also has support from Cancer Research UK, which claims to be the world's largest independent cancer research charity organization. It is a key backer for the project, according to Popova. With its involvement the competition remains much closer to the fighting end of the cancer research world – helping to better define and target the direction of investigations.

"When you're working with a non-profit, you're working with those as near to patients as possible," said Popova. "It means you're close to specialists and to the patients, which means you have great feedback."

Currently the organisers declined to comment on applications in detail until a full assessment could be made. However, they said they were pleased with the response both in terms of overall rate of applications and in terms of quality of pitches coming in.

It is the first such competition in the cancer research area, as far as the organisers are aware. "There have been similar competitions in other areas of pharmaceutical research but this is the first for cancer molecules," said Bittner.

Application remains free due to sponsorship from partners as well as support from Cancer Research UK – including the price of travel for the top eight selections. The partner organisations expected to send notifications about assessment of applications by the second week of May and plan to hold the London pitching event at the end of June.

The organisers intend for BioTarget to be an annual event going forward. If it is, it could prove to be an AI-driven boon to finding cancer cures.

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Featured Interview: M. Khair ElZarrad, PhD, MPH.

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