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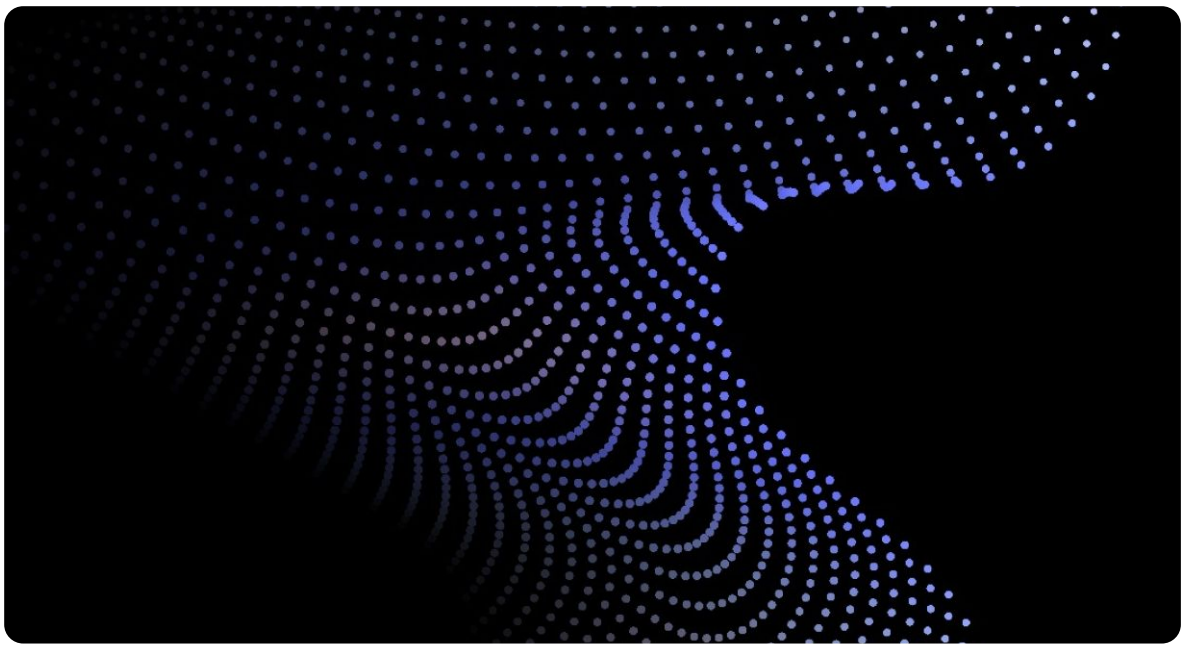

Use Cases for Artificial Intelligence and Machine Learning in Late-Stage Life Sciences

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White Paper

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EXECUTIVE SUMMARY

We are living through one of the most transformative eras in our lifetime. The rise of working, usable artificial intelligence (AI) coupled with machine learning (ML) is transforming so many things in our day-to-day lives that soon, we will wonder how life before AI was possible. The development of new medications and therapies is one of the areas that is poised to change more dramatically than most, thanks to these new technologies. AI and ML have immense potential in various aspects of life sciences, including clinical trials. In Stage 3 clinical trials involving large-scale testing of a potential drug or treatment, AI and ML can be crucial in optimizing processes, improving efficiency, and enhancing decision-making. This paper will discuss ten of the most transformative use cases in the late-stage drug development pipeline, including Stage III clinical trials, Medical Affairs, Safety, and Regulatory Affairs. Here are ten prominent use cases for AI and ML in late-stage clinical development:

Patient Recruitment & Eligibility Screening	Biomarker Discovery in Support of Personalized Medicine
Clinical Trial Design Optimization	Adverse Event Detection and Pharmacovigilance
Clinical Trial Monitoring	Data Quality Control and Validation
Clinical Trial Data Analysis	Drug Repurposing and Novel Combination Therapies
Predictive Modeling and Simulation	Regulatory Compliance and Risk Assessment & Management

PATIENT RECRUITMENT & ELIGIBILITY SCREENING

Phase III clinical development is among the most expensive phases of drug development. These trials require hundreds to thousands of patients in interventional and control arms. Finding patients who fit the eligibility criteria for inclusion in clinical trials can, at times, be a daunting task. Not only do you need to identify eligible patients, you also need to establish contact, validate interest on behalf of the patient, and obtain informed consent to allow the patient to participate in the study. In the case of rare diseases, finding these patients can be exceptionally difficult. One area where AI and ML can impact this is to help screen for patients in electronic health record (EHR) data sets. In many hospitals today, there are opt-out programs where patients' information can be queried for clinical trial inclusion (and contacting) unless they opt out. However, even with permission to review the data and contact these patients, finding eligible patients remains challenging. AI and ML algorithms can dramatically speed the screening process and serve up qualified lists of eligible patients far faster and with greater accuracy than current methods. Ensuring that trials can find enough eligible patients will lower the time needed to fill trials and conduct the needed studies.

CLINICAL TRIAL DESIGN OPTIMIZATION

Another challenge for clinical trial work includes creating trials that have not only sufficient statistical power but also craft the trial in such a way as to optimize the chances that one or more observations will be statically significant. This has, in the past, been the domain of biostatisticians. Complex power calculations need to be performed and predictive models created to find create predictive models that could help to optimize the trial design. In addition, being able to run "what if" scenarios were needed to optimize for trial inclusion/exclusion criteria.

AI and ML can automate much of this process, identifying patterns and providing predictions faster than humans can, thus increasing efficiency and productivity. For instance, AI can analyze massive volumes of data from previous trials to help design trial protocols that are more likely to succeed. This could involve optimizing the choice of endpoints, dosage levels, or patient inclusion and exclusion criteria, to name just a few.

Secondly, AI and ML can optimize patient selection and recruitment, one of the most challenging aspects of clinical trial design. Predictive models can be used to analyze EHRs and other data sources to identify patients who are likely to meet the trial's eligibility criteria and are at a high probability of adhering to the protocol. By identifying the right patients for the trial, AI and ML can reduce the likelihood of participant dropout, thereby improving trial efficiency and reducing costs. These technologies can also be used to predict how well a patient might respond to a particular treatment, enabling a more personalized approach to treatment.

REAL-TIME MONITORING AND DATA ANALYSIS

AI can also be used in real-time monitoring to detect protocol deviations, safety signals, or anomalies in patient or clinician actions and allow for immediate corrective action. This real-time monitoring can significantly improve the accuracy of results and expedite the overall trial process, accelerating the development of effective treatments. In summary, AI and ML are promising for clinical trial design optimization, enhancing efficiency, reducing costs, and ultimately accelerating the path to new treatments.

ML models can help identify patterns in patient responses (whether they are related to the dosage of a compound or even a series of patient-reported outcome responses), potentially predicting trial outcomes much earlier than traditional methods. These insights could enable trial designers to make adjustments during the trial, increasing its chance of success. In fact, by treating different data sets as a multimodal set on a given patient, ML algorithms can create novel approaches to clustering to allow for more non-obvious insights concerning adverse events (AEs) and severe adverse events (SAEs).

PREDICTIVE MODELING AND SIMULATION

One of the things that AI can do at scale is to create and run various predictive models. This kind of interactive approach can be long and tedious if performed by hand, or even via computer-assisted algorithms. Not only can AI recommend predictive models, it can also serve to analyze the results and run far more iterations on the data sets than can be done today. The more iterations, the more modeling can be accomplished and the more subtle the insights that no human could ever hope to identify may be surfaced due to the number of iterations possible using these techniques. And the more data sets you can add into the mix (aligned to the same patient), the more likely that new insights will be identified.

BIOMARKER DISCOVERY IN SUPPORT OF PERSONALIZED MEDICINE

Biomarkers play a critical role in late-stage clinical development, serving as valuable indicators of the physiological response to a therapeutic intervention. The discovery and validation of such biomarkers, however, remain challenging tasks. For example, while working at a top-tier life sciences company in the early 2010s, the organization had a goal of having 50% of it's molecules under development having an identified biomarker. These biomarkers can help determine which patients will respond to a drug, which may experience an AE, or which should have the best expectation of some other outcome. AI and algorithms provide powerful tools to expedite this process, allowing researchers to sift through large volumes of complex data to pinpoint meaningful biomarkers. A key approach uses ML algorithms to analyze multivariate data from clinical trials or electronic medical records, including genomic, proteomic, and metabolomic data. These algorithms can identify patterns and correlations in these data that may be indicative of potential biomarkers. For example, specific gene expression profiles, protein levels, or metabolic changes can be linked to disease progression or response to treatment.

In addition to pattern recognition, AI and ML can also be used to predict the relevance and validity of potential biomarkers. A given biomarker's effectiveness is determined not only by its presence but also by its predictive value in indicating disease progression or response to therapy. Using supervised learning algorithms, researchers can train AI models on known biomarker data and then apply these models to new, unclassified data. In doing so, the AI system can predict whether a certain biomarker is likely to be significant in a specific clinical context. For instance, an AI model might predict the effectiveness of a biomarker in forecasting a patient's response to a novel treatment based on patterns seen in previous clinical trials.

AI and ML also have potential in the integration and analysis of real-world data (RWD) and real-world evidence (RWE) for biomarker discovery. In late-stage clinical development, RWD and RWE provide crucial insights into a treatment's effectiveness and side effects in a broader population. AI and ML algorithms can integrate and analyze RWD from a variety of sources, such as EHRs, insurance claims data, and patient-generated data. By analyzing this data, these algorithms can help identify new biomarkers or surrogate biomarkers that might not be evident in controlled clinical trial settings. These biomarkers can then be used to tailor treatments more effectively to individuals, advancing precision medicine.

ADVERSE EVENT DETECTION AND PHARMACOVIGILANCE

Given the vast amount of data generated during late-stage trials as well as when a drug is approved and in use in the general population, manual review and analysis of potential adverse events (AEs) is both time-consuming and resource-intensive. And to add pressure into the mix, as soon as an AE is identified, it must be reported to the FDA in 15 business days. AI and ML can automate this process, improving speed, accuracy, and comprehensiveness of reviewing data to identify AEs and SAEs. ML algorithms can be trained to review clinical notes, patient feedback, and other forms of unstructured data to identify instances of AEs. This can be either in hypothesis generation mode or in actual clinically identified AE. These algorithms can process the vast amounts of information faster than humans can. Machine learning algorithms can also improve their accuracy over time as they 'learn' from more data. Furthermore, AI can use natural language processing to interpret free-text descriptions of AEs, increasing the volume and types of data that can be analyzed.

In the second stage of clinical trials and the post-marketing phase, AI and ML can aid in the detection of rare or unexpected AEs. Traditional methods might miss these events due to their low frequency or because they occur in patient populations not adequately represented in clinical trials. ML algorithms, particularly those using unsupervised learning, can identify patterns and associations that would otherwise go unnoticed in large data sets. For example, AI can analyze RWD from EHRs or social media to detect AEs not identified during clinical trials simply by virtue of having the opportunity to analyze more streams of data in the real world. These technologies can therefore provide an early warning of potential safety issues once a drug is on the market.

Furthermore, AI and ML can assist in causality assessment, which is the determination of whether a drug caused a particular AE. AI can analyze a patient's medical history, genetic information, and exposure to other medications to assess the likelihood that a specific drug caused an AE. This could also involve comparative analyses with similar patients who did not experience the AE. By making this process more accurate and efficient, AI and ML can greatly enhance the safety of drugs in clinical trials and post-market.

DATA QUALITY CONTROL AND VALIDATION

One area that is currently very human-intensive is the task of data quality control. Ensuring that data is not only collected properly but that it is entered into systems correctly without error as well. If this is not done properly, the quality of the downstream analysis can be called into question. AI and ML can automate these processes, increasing their speed and accuracy. For instance, ML algorithms can review clinical data in real-time, identifying inconsistencies, missing data, or outliers that may indicate data errors. Such an approach allows for prompt identification and rectification of issues, thus ensuring the integrity of the data throughout the trial. Moreover, because AI models are beginning to leverage natural language processing, they can also be used to validate unstructured data, like clinical notes, enhancing the breadth of data that can be validated.

AI and ML can also improve data quality by predicting and preventing potential data quality issues before they occur. By analyzing historical data from past clinical trials, ML algorithms can identify patterns that may signal potential data quality problems in the future. This predictive ability allows for a proactive approach to data quality control, as potential issues can be addressed before they impact the trial. For example, if an AI system predicts a high likelihood of missing data in certain fields based on past trials, extra checks or reminders can be implemented to ensure complete data collection.

DRUG REPURPOSING AND NOVEL COMBINATION THERAPIES

One thing that a computational model can do that humans cannot do (not easily, at least) is to create and test hypotheses around drug combinations. This is generally a very labor-intensive process. This is generally done by empirical testing during early-stage drug development. However, by ingesting large volumes of data in multiple domains, a multimodal analysis can create hypotheses around what drugs, and in what combinations may have a higher degree of likely success. A formalized clinical trial may be necessary to test these hypotheses.

AI and ML technologies hold immense potential in drug repurposing and discovery of novel drug combinations. Drug repurposing, or the identification of new uses for approved or investigational drugs that are outside the scope of the original medical indication, is a strategic approach in drug development. AI and ML can streamline this process by analyzing large and diverse sets of biological, pharmacological, and clinical data to identify potential new drug-disease associations. For example, ML algorithms can analyze 'omics' data (such as genomics, proteomics, or metabolomics) to identify patterns suggesting that a drug used for one disease might be effective for another (where a given enzyme or genomic marker may be common to both diseases). Additionally, AI can analyze text from scientific literature and clinical trial databases to identify potential new indications for existing drugs.

Combinatorial drug therapy, where two or more drugs are used together, is common in the treatment of complex diseases such as cancer or infectious diseases. However, the experimental exploration of potential drug combinations is vast and requires an infeasible number of tests. AI and ML algorithms can analyze data from previous studies on individual drugs, predicting how different drugs might interact when used in combination. This can help identify promising drug combinations that are likely to have synergistic effects or combinations that might lead to adverse interactions. Though clinical trials may still be needed to test these combinations, the identification of such possible combinations can shave years off of the development cycle, saving time, money, and, eventually lives.

Furthermore, AI and ML can support the design and execution of clinical trials to test repurposed drugs or novel drug combinations. These technologies can predict patient populations likely to respond well to the repurposed drug or combination therapy, aiding in patient selection and recruitment. They can also forecast the outcomes of these trials, guiding modifications to trial design and increasing their likelihood of success. In conclusion, AI and ML can revolutionize drug repurposing and the discovery of novel drug combinations, making these processes more efficient and successful, ultimately accelerating the development of new therapeutic strategies.

REGULATORY COMPLIANCE AND RISK MANAGEMENT

Regulatory compliance is a complex, multifaceted process that includes ensuring adherence to regulations and standards, tracking changes in legislation, and maintaining proper documentation. Traditional methods of managing these tasks can be laborious and prone to human error. Ensuring that a development program's submission to the FDA or other regulatory body is complete and covers all domains of exploration can be a human-intensive process. However, AI and ML can automate these processes, enhancing efficiency and reducing the potential for errors. For instance, AI algorithms can monitor regulatory changes in real-time, notify relevant stakeholders of updates in regulations and laws, and automatically apply necessary changes to compliance protocols. ML algorithms can analyze previous compliance issues and predict future risks, enabling proactive risk management.

AI and ML can also assist in managing risk by identifying and addressing potential issues before they occur. In the life science industry, risks can arise in a variety of areas, such as clinical trials, drug manufacturing, and post-market surveillance. AI can monitor data from manufacturing processes in real-time, identifying deviations from quality standards and enabling immediate corrective actions. In post-market surveillance, AI can analyze RWD, such as EHRs and social media, to identify potential safety issues with marketed drugs. And, if additional matched data is available, such as genomics or proteomics, those data can be added to the analysis to help gain more precise and accurate results.

In addition to these practical applications, AI and ML can also provide a comprehensive overview of risk and compliance issues, allowing for more informed decision-making. By integrating and analyzing data from various sources, these technologies can generate a holistic view of risk across different areas of the organization. This includes, for example, identifying areas of high risk, predicting the impact of potential risks, and assessing the effectiveness of risk mitigation strategies.

LOOKING FORWARD

While you might think that the use cases listed above are in the domain of science fiction, Quantori engineers are working today with top-tier life science organizations around the world to exploit the promise of AI and ML to produce novel approaches to the late-stage R&D process. From an artificial vision system that was used during the pandemic to grade and read chest X-rays, to using multimodal ML to generate new hypotheses for drug targets in neuroscience drug development, Quantori scientists, engineers, and clinicians are creating solutions that are bringing these use cases from the pages of science fiction to real-world solutions today.

Our focus is on Life Sciences. Our teams are comprised of Ph.D. and Master-level scientists. Our engineers are well-versed in how to leverage all that cloud computing has to offer to bring these AI use cases to life. We are at the core of helping some of the largest and most forward-thinking organizations bring these technologies and solutions to life to advance new drug discovery, finding new targets, leveraging multi-modal data, and even the gut microbiome to help our clients advance their goals.

If your organization is considering bringing AI to life to solve some or all of these challenges, please contact us. We can give specific use case examples of our scientists solving these problems today and accelerating the R&D process to advance pipelines for our Life Science customers.

We develop cutting-edge technology systems, applications, and infrastructures for biotech, pharmaceutical, and healthcare companies that accelerate drug discovery and improve patient outcomes. Our innovative approach harnesses the power of data engineering and informatics, machine learning, emerging technologies, and cloud expertise to advance research and development and ultimately bridge the gap between meaningful data and patient success.

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