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Big Pharma Bets on AI to Accelerate Clinical Trials

(Source: An article by Natalie Grover & Martin Coulter for Reuters)

Major drugmakers are using artificial intelligence to find patients for clinical trials quickly, or to reduce the number of people needed to test medicines, both accelerating drug development and potentially saving millions of dollars.

Human studies are the most expensive and time-consuming part of drug development as it can take years to recruit patients and trial new medicines in a process that can cost over a billion dollars from the discovery of a drug to the finishing line.

Pharmaceutical companies have been experimenting with AI for years, hoping machines can discover the next blockbuster drug. A few compounds picked by AI are now in development, but those bets will take years to play out.

Companies such as Amgen, Bayer, and Novartis are training AI to scan billions of public health records, prescription data, medical insurance claims and their internal data to find trial patients - in some cases cutting the time it takes to sign them up by half.

The U.S. Food and Drug Administration (FDA) said it had received about 300 applications that incorporate AI or machine learning in drug development from 2016 through 2022. Over 90% of those applications came in the past two years and most were for the use of AI at some point in the clinical development stage.

Before AI, Amgen would spend months sending surveys to doctors from Johannesburg to Texas to ask whether a clinic or hospital had patients with relevant clinical and demographic characteristics to participate in a trial.

Existing relationships with facilities or doctors would often sway the decision on which trial sites are selected.

However, Deloitte estimates about 80% of studies miss their recruitment targets because clinics and hospitals overestimate the number of available patients, there are high dropout rates or patients don't adhere to trial protocols.

Amgen's AI tool, ATOMIC, scans troves of internal and public data to identify and rank clinics and doctors based on past performance in recruiting patients for trials.

Enrolling patients for a mid-stage trial could take up to 18 months, depending on the disease, but ATOMIC can cut that in half in the best-case scenario, according to Amgen officials. Amgen has used ATOMIC in a handful of trials testing drugs for conditions including cardiovascular disease and cancer, and aims to use it for most studies by 2024. The company said by 2030, it expects AI will have contributed to taking off two years of the decade, possibly more, that it typically takes to develop a drug.

The AI tool Novartis uses has also made enrolling patients in trials faster, cheaper and more efficient, said Badhri Srinivasan, its head of global development operations. However, he emphasized that AI in this context is only as good as the data it derives.

In general, less than 25% of health data is publicly available for research, according to Sameer Pujari, an AI expert at the World

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In Brief...

- Japanese pharma manufacturer **Eisai Co.'s** breakthrough Alzheimer's drug won clearance after the medicine was full cleared by the **U.S. Food and Drug Administration** in July. Japan's health ministry approved the use of *Leqembi* to suppress the progression of mild cognitive impairment and dementia following the backing of a panel's recommendation in August. Separately, Japan's new health minister, *Keizo Takemi* announced that he is resolved to "put public needs first" in approaching the drug pricing reform or 2024, while expressing his strong passion for fueling growth of the pharma industry.
- The **U.S. Food and Drug Administration (FDA)** has announced an extension on the enforcement of specific provisions under the *Drug Supply Chain Security Act (DSCSA)*. Initially set for November 27, 2023, the new enforcement date has been pushed to November 27, 2024. The goal of the delay is to grant additional time to trading partners and stakeholders (including manufacturers, wholesale distributors, dispensers, and repackagers) to adapt and ensure efficient implementation "electronic tracing at the package level, to achieve robust supply chain security under the DSCSA while helping ensure continued patient access to prescription drugs."
- In conjunction with **Johnson & Johnson's** release of its new logo and branding, the company has announced major changes, including that it will unite its medtech and pharmaceutical business so that they will be "more connected to the Johnson & Johnson brand." Over time, the company's **Janssen** brand will become **Johnson & Johnson Innovative Medicine** which the medical technology segment will continue to run with the

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U.S. IRA Price Negotiations Could Hit R&D Harder than Anticipated

(Source: An article by Nick Taylor for Fierce Biotech)

How hard will the U.S. Inflation Reduction Act (IRA) hit pharma R&D? Harder than the government expected, according to a study conducted by the University of Chicago that found lower R&D spending could result in 79 fewer new small-molecule drugs over the next 20 years.

The U.S. Congressional Budget Office (CBO) previously ran the numbers on the IRA, concluding that 15 out of 1,300 drugs would not come to market over the next 30 years. However, multiple analyses have called the CBO figures into question, with healthcare consulting firm Avalere, (and funded by Gilead Sciences) estimating that the IRA could cut pharma revenues by US$450 billion. Another analysis suggests between 24 and 49 currently available therapies wouldn't have reached the market if the pricing provisions took effect in 2014.

In the University of Chicago study, which was also partly funded by Gilead, researchers identified three ways in which the financial impact of the IRA may have been underestimated.

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AI in Clinical Trials (cont.)...

Health Organization.

German drugmaker Bayer said it used AI to cut the number of participants needed by several thousand for a late-stage trial for *asundexian*, an experimental drug designed to reduce the long-term risk of strokes in adults. It used AI to link the mid-stage trial results to real-world data from millions of patients in Finland and the United States to predict the long-term risks in a population similar to the trial.

Armed with the data, Bayer started the late-stage trial with fewer participants. Without AI, Bayer said it would have spent millions more, and taken up to nine months longer to recruit volunteers. Now the company wants to take it a step further.

For a study to test *asundexian* in children with the same condition, Bayer said it plans to use real-world patient data to generate a so-called external control arm, potentially eliminating the need for patients taking a placebo. That's because the condition is so rare in the age group it would be difficult to recruit patients and could raise concerns about whether it was ethical to give trial participants a placebo when there are no proven treatments available. Bayer said it hoped that would be enough to help discern how effective the drug is. Finding real-world patients by mining electronic patient data can be accelerated dramatically by using AI.

While not the normal process, external control arms have been used in the past instead of traditional randomized control arms where half the participants take a placebo - mainly for rare diseases where there are few patients or no existing treatments. Drugmakers typically seek prior approval from regulators to test a drug using an external control arm.

Some scientists, including the FDA's oncology chief, are worried drug companies will try to use AI to come up with external arms for a broader range of diseases.

Patients in trials tend to feel better than people in the real world because they believe they are getting an effective treatment and also get more medical attention, which could in turn overestimate the success of a drug.

This risk is one of the reasons regulators tend to insist on randomized trials as all patients believe they are getting the drug, even though half are on a placebo. Regulators, however, say that although AI has the potential to augment the clinical trial process, evidentiary standards for a drug's safety and effectiveness will not change.

"The main risks with AI are that we want to make sure we don't get the wrong answer to the question of whether a drug works," said John Concato, associate director for real-world evidence analytics in the Office of Medical Policy in the FDA's Center for Drug Evaluation and Research.

U.S. IRA Price Negotiations (cont.)

The effect of the legislation on the useful patent life of small molecules through negotiations was the first area of focus.

According to the researchers, the change could result in an up to 8% drop in overall industry revenue and a 12.3% reduction in R&D. The lower investment in R&D could translate into "79 fewer small molecule drugs or 188 indications, and 116.0 million life years lost over the next 20 years."

The researchers also argue that the impact of the IRA on classwide pricing has gone unrecognized. Once Medicare negotiations lower the price of one drug, "competitors are likely to reduce their prices owing to competitive pricing pressure of effective top-sellers being rebated," they predicted. The researchers found the "share of Medicare spending on small molecule drugs affected by negotiated drugs ranges between 35% to 86%."

Finally, the study looked at the impact of the IRA on the entry of generic copies of medicines with large Medicare market shares. "We find that 40% of FDA-defined drug classes have over 50% of their sales in Medicare. This market will be especially impacted by the IRA and made less profitable for generics to enter," the researchers wrote.

The data points factor into a fight that remains tense and unresolved. The first 10 drugs up for negotiation were named late last month but, with big pharma challenging the IRA in the courts, the situation will take a significant amount of time to resolve.

In Brief (cont.)

J&J MedTech name.

- Eleven U.S. Republican governors are demanding action from Congress to address the recent drug shortages plaguing the U.S. Citing shortfalls of critical medications like *albuterol*, *amoxicillin* and certain chemotherapies, the governors noted that shortages have sometimes lasted for years with "with no good explanation for why." The governors called on Congress to adopt new policy solutions to ensure adequate supplies, including transparency in the pharma manufacturing chain (ranging from the sourcing of raw materials to the finished product including country of origin labeling.) Additionally, the governors tasked Congress to encourage increased diversity in generic drug manufacturing regarding both raw materials and final manufacturing.
- **Novo Nordisk** is partnering with **Aspen Pharmacare** (South Africa) to shore up insulin supplies in Africa, which currently imports more than 80% of its medicine. The company has enlisted Aspen to make human insulin for the continent as part of an "expanded commitment" to reach more than 500,000 diabetes patients across sub-Saharan Africa. Aspen will produce vials from its existing sterile facility in Gqeberha, South Africa, which it's made about US$316 million in investments in recent years according to company officials.
- **Amazon** and **Anthropic** (an AI startup) are collaborating to bring their respective technology and expertise in safer generative artificial intelligence to accelerate the development of Anthropic's future foundation models and make them widely accessible to **AWS** customers. As part of the expanded collaboration, Anthropic will use *AWS Trainium* and *Inferentia* chips to build, train and deploy its future foundation models, benefitting from the price, performance, scale and security of AWS. The two companies also will collaborate in the development of future Trainium and Inferentia technology, and AWS will become Anthropic's primary cloud provider for mission critical workloads.

(Sources: Company Press Releases, Drug Store News, FiercePharma, FierceBiotech, Pharma Japan and World Pharma News)