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Guggenheim Grand Rounds - Dx/Tools Series: AI-Driven Drug Discovery, Development & the Outlook for Life Sciences Tools

Key Message: Earlier this week, we hosted a KOL in AI driven drug discovery and development to talk about where the use of AI for these initiatives stands today and her outlook for the space going forward. Our key takeaway for life sciences tools is that there is still an unmet need in the biological data that has been generated to date that necessitates ongoing wet lab experiments to support the use of AI longer term. For diagnostics companies that have data licensing businesses, our key takeaway is that there is a definitive advantage to real-world data over synthetic or matched data in terms of the value it brings to supporting AI model training.

Key Takeaways

1. **The most valuable application of AI in the drug discovery, development, and manufacturing process would be in the clinical trial stage, given this is where the process is the most costly.** The KOL showed us data that sized the cost of each stage of development, and noted that while most of the excitement is in the area of early stage discovery, the biggest cost and time saving opportunities are actually in the clinical trial stages because this is the most expensive step of the process and many drugs still fail in later stages of clinical development.
2. **While biotech & pharma companies' application of AI to existing pipeline structures is nearly ubiquitous, the KOL looks forward to a more transformative application in the future which completely re-imagines the process.** Our KOL explained that applying AI to existing drug pipelines is able to save time and money, but to date, she has not seen this lead to a novel drug class, modality, etc. that was discovered or driven by AI specifically.
3. **Life sciences tools remain necessary to generate biological data that we do not yet have, which feeds into AI models.** The KOL did not have a definitive answer whether AI's application to drug discovery & development will be a headwind or a tailwind for life sciences tools long term; however, she explained that at present, there is still a large gap in the biological data required to train these models. Building the necessary data sets won't happen overnight, and will require more wet lab experiments and life sciences tools to get there for the foreseeable future.
4. **In terms of life sciences data sets for training AI models, the KOL firmly believes that real world data is necessary, and cannot be substituted by synthetic or matched data.** The provider of massive multi-modal (genomic, clinical, pathology, etc.) data sets from real-world patients across indications would be best suited for building foundation models.

KOL Background

Our KOL is a distinguished professor in AI & Health in the Department of Computer Science at a prestigious university in the Northeast. She develops machine learning methods for drug discovery and clinical AI, and in the past, she worked on natural language processing. Her research has been recognized with the MacArthur Fellowship, an NSF Career Award, and the AAAI Squirrel AI Award for Artificial Intelligence for the Benefit of Humanity. She is a member of the National Academy of Engineering, American Academy of Arts and Sciences, and the National Academy of Medicine.

KOL Presentation Summary

Challenges in Drug Discovery Today

- In drug development, our KOL showed data that found that almost 9 out of 10 drugs in development still ultimately fail today, usually due to sub-par efficacy. This is often not determined until a Phase 3 trial, which is when the cost of development is the highest and after many years of development time have been wasted.

AI Use in Drug Discovery & Development Today

- While the number of drug candidates discovered using AI has continued to grow each year, few are actually commercially available on the market. Additionally, the KOL noted that drugs designed using AI today have similar clinical trial success rates as the industry average. Instead, the place today where she sees AI adding value in this process is in speeding up the timeline overall. More specifically, in the KOL's view, a basic understanding of the biology of the target and disease state are required, prior to implementing AI, so that one knows what they are drugging. From there, AI can be leveraged to design optimal binding to that target (aka the chemistry component). The chemistry is more predictable and many models across modalities exist to optimize drug candidate molecules in silico. Generally though, one still needs the biological information as to what they are targeting. The KOL discussed how AI driven cell models have fallen short of delivering on druggable targets at present, in her view, due to the complexity of biology and the amount that we don't understand yet under the disease biology umbrella.
- She also emphasized that where the excitement about applying AI to drug discovery lies today, in the earlier discovery stages, is actually not where the greatest cost of the broader drug development process lies. However, there have started to be more applications in clinical trial matching and enrollment, which she said is a newer offering, but that has seen rapid adoption due to the ease and benefit of implementation. She was also optimistic about AI applications that can support the push from the FDA/NIH level to decrease the use of animal testing and replace it with AI driven modalities (though noting, as stated above, that a lot of cell models today have fallen short and this is an area for further investment and development).

AI Use in Drug Manufacturing

- Across therapeutic modalities, the KOL noted there are various ways AI is being applied in these processes to drive efficiency. For small molecules there are some commercial solutions available to drive efficiency in synthesis, and in biologics some may be commercial and others are developed in house. Regardless, the KOL noted that she is certain that all the major biotech and pharma companies are using these tools to drive more efficient drug product synthesis as it is in the best interest of their cost efficiency.
- Another opportunity to apply AI in manufacturing is within the arena of the various tests the FDA requires in later stages of filing to support which conditions the drug can safely be manufactured in. Here, AI can be used to reduce the number of experiments needed to determine the optimal range. AI can also be used to monitor visual tools for possible issues in manufacturing processes, and potentially for toxicity testing applications.

Select KOL Q&A

How has pharma & biotech AI usage changed over time?

- Our KOL started in this field around 2017, and at that time bigger pharma companies were just starting to move into the space of applying AI for drug discovery & development. The open source availability of AlphaFold was a big catalyst that drove more molecule design/discovery driven by AI, as well as her laboratory's Boltz & BoltzGen models. Today, AI is used throughout the drug discovery and development workflow.
- In terms of how these companies learn to use AI and who executes its usage, this can be a pain point, as changing the habits of leadership folks in these companies can take time. In her view, the most common way that AI is implemented is when the data science group of a pharma company evaluates an externally developed platform or interface, structures or combines the internal data, and then advises chemistry/biology teams as to how and what to use.

Are any companies at more or less of an advantage in terms of AI positioning?

- In terms of who is ahead or behind on this curve, she explained that while AI/tech companies may have a leg up on the AI/ML component, the pharma companies have a key advantage: they own massive, proprietary data sets that are not able to be purchased or generated elsewhere. Specifically, all the failed trial data is extremely valuable: it is just, if not more, valuable to know what didn't work and why than what did work. This positions pharma companies to have an advantage when implementing whichever AI platform their data science team recommends.

What makes for a successful AI training data set?

- Reiterating some of the above comments, the KOL emphasized the importance of the vast amounts of unpublished data within pharma companies' electronic laboratory notebooks. Data on failures is very valuable (just as valuable, if not more valuable, than successful, published data) and can be used to internally retrain and fine tune AI models. That said, in the KOL's view, no one company would have enough internal-only data to train its own full foundation model, but they do have enough to utilize models for their more narrow areas of interest. Biological target discovery is one of the areas where the KOL thinks it is especially a challenge to generate enough data for an AI model to be helpful and accurate. The KOL was not bullish on single cell Perturb-seq because, in her personal opinion, she has not yet seen this add value to new disease models or new drugs. She noted that others in the research community must have a different view, given the dollars that are funneled to these projects at present. In her personal experience, she saw first hand in one of her projects that a Perturb-seq trained foundation model was not able to outperform a simple variable genetic screen in terms of predicting patient therapy response. Additionally, in some indications it can be difficult to train a model because the data that is required for actual disease prevention is not available. For example, in the neurodegenerative disease space, the data required to develop preventative

interventions would need to be collected long before patients become symptomatic, but we don't have that collection mechanism in process until they already have become sick.

- The KOL also had a strong opinion that there is no reason to use synthetic data (which she described similarly to matched clinical + genomic data) when real-world data all from the same real patient does exist. She noted TEM as an example of a company she knows offers combined genomic, clinical, pathologic, and other data sets together in bulk for the same patients. Given current AI models are still often wrong based on this real-world data, the KOL explained that it would be moving in the wrong direction to introduce synthetically generated data sets.

Is increasing use of AI in drug discovery & development a tailwind or headwind to life sciences tools companies?

- First, AI allows for a research team to screen many more promising molecules on the same budget. Or, depending on the application of the AI, the research team can screen for the same amount of molecules or amount of time, but in a more targeted, higher likelihood of success, area. Another change is that for these models to work properly, more training data on the biology needs to be generated, and this still requires wet lab assays. For example, in some modalities, like RNA, there is not yet enough data to train an AI model properly for accurate output.
- Ultimately, while the KOL took a "never say never" attitude to whether or not AI/in silico research could fully replace wet lab research, she noted that we are far from it, citing the mistakes these models still make today. Ultimately she doesn't see a way that wet lab validation would not still be necessary.
- A key point the KOL made on this topic is the lack of biological data available. While large language models (LLMs) for reading and writing purposes are being fed what seems like nearly infinite data inputs, this is because we, as a population, are *constantly* generating written language, at little to no cost, for these models to train on. In comparison, biological data is not being generated at nearly the breadth, depth, nor speed, and it has a significantly higher cost. Investments will still need to be made in life sciences tools and wet lab research to generate the biological data to train these models for the foreseeable future.

What are some of your expectations for AI applications in this field in the coming years?

- While biotech and pharma companies are broadly using AI today, the KOL noted that AI has been applied ultimately to the existing pipeline structure to save cost and time. What hasn't happened yet, and she thinks could come in the future, is applying AI to rethink the whole pipeline (both in content and structure). Additionally, she envisioned a future where more challenging indications where we still do not have first in class drug solutions would become more addressable.
- Another key opportunity, looking forward, to this KOL is better therapy selection and risk stratification of cancer patients, supported by AI. She noted her involvement in the ARPA-H ADAPT program, which aims to select better precision therapies for cancer patients leveraging AI/ML.

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