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Learning Curve: Absci, NVIDIA Partner on Antibody Design

Companies to apply Absci-developed machine learning models that predict target affinity, naturalness of sequence variants and other mAbs of interest

Absci has recently found a partner in its quest to develop machine learning models for designing and refining novel therapeutic antibodies. NVIDIA—the Silicon Valley microprocessing giant that revolutionized computer graphics when it invented the graphics processing unit (GPU) more than two decades ago—recently partnered with Absci to develop ML models for designing and refining novel therapeutic antibodies. [Absci]

Alex Philippidis

It's a fun piece of science trivia: there are more sequence variants among monoclonal antibodies (approximately 20^{62}) than there are atoms in the universe (about 10^{80}), as Absci's founder and CEO Sean McClain likes to say.

Within all those antibodies, McClain and his company reason, is an equally near-infinite number of possibilities for designing new treatments exclusively in silico using the artificial intelligence (AI) application of machine learning (ML), as well as synthetic biology.

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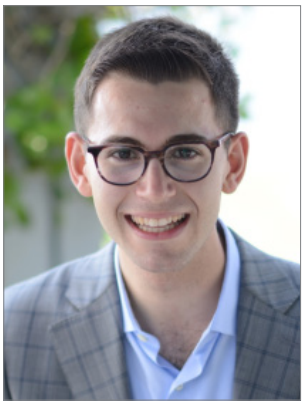
During a presentation at the recent NVIDIA GTC global AI conference, Absci's Lead AI Scientist Joshua Meier announced the company's partnership with NVIDIA, detailing two of the company's drug discovery ML breakthroughs, and presented validation of Absci's in-silico lead optimization models.

Sean McClain, Absci founder and CEO

Absci's first breakthrough is an ML model for quantitative prediction of antibody target affinity, enabling computational predictions of binding strength. Meier showed how the model could accurately predict affinity across four orders of magnitude for previously unseen variants of Herceptin® (trastuzumab), the HER-2 positive breast cancer blockbuster drug marketed by Roche and its Genentech subsidiary.

Meier also showed how the model could accurately predict variants that had better target affinities than wild-type trastu-



Joshua Meier,
Absci Lead AI Scientist

zumab. The goal is to ask whether a particular drug candidate binds to a specific protein or not?

"What we showed in the presentation is examples of that binding to one protein," Meier said. "But you can just do the same thing for multiple proteins. You can say, I want something that doesn't just have high affinity to HER-2. I want something that has high affinity to other proteins as well."

Absci's second breakthrough is an ML model designed to score the 'naturalness' of antibody variants—a parameter that the company says is linked to multiple developability characteristics. Antibodies with better developability are more likely to show success as drug candidates in preclinical testing and clinical trials.

Absci defines naturalness as characteristics that define what an antibody looks like, drawing on models that have seen examples of hundreds of millions of naturally occurring antibodies. Based on those, the model predicts the naturalness of antibodies of interest, such as sequence variants.

Does this look like an antibody?

Meier and Absci showed the value of the model using an example of polygons—a four-sided square shows a natural polygon, but not a three-sided square.

"I can train the model on Internet text. I can say, 'Does this look like real English? Are there spelling mistakes, or things like that?'" Meier said. "We're doing the same thing in the antibody space. We trained models on hundreds of millions of these antibody sequences, and now, when the model is designing things, the model tells us, 'Does this look like an antibody that I'd expect to see in nature?'"

"We show some data that [suggests] this correlates nicely with developability properties like whether an antibody could be developed in the clinic, or whether the antibody is immunogenic, if the body is going to have immune response against that antibody," Meier added.

Absci says its ML models can also be extended to assess other properties of antibodies.

"The more properties you look at, the harder the drug discovery campaign becomes, and you get to the point where you just won't find anything and use a traditional a drug discovery method," Meier said. "But when you do it on the computer, you just look through so many more proteins in silico that it becomes a lot more tractable.

According to Absci, in silico creation of antibodies enables discovery of novel targets from patient samples, as well as novel drugs targeted to epitopes. McClain cited the spike protein of SARS-CoV-2, which has evolved over time as new epitopes have emerged.

"What if you could design an antibody that could bind to all of those potential epitopes that would evolve over time, allowing you to design an antibody that doesn't out-evolve or doesn't get out-evolved by the virus," McClain said. "These are really novel applications that that we can now do because of the AI technology we've developed, which is really exciting."

Added McClain: "Why does this matter? It matters because we can now use AI to design and create antibodies or biologics that previously haven't been able to be designed before."

"This is going to allow us to increase overall probability of success throughout the clinic, create more efficacious drugs, and get those to patients a lot faster," McClain added.

Growing market and company

Among drug developers tapping into Absci's technology is Merck & Co. The companies inked an up-to-$610 million collaboration in January, through which Absci agreed to deploy its Bionic Protein™ non-standard amino acid technology to produce enzymes tailored to Merck's biomanufacturing applications. Merck has the option to nominate up to three targets and enter into a drug discovery collaboration agreement with Absci.

Absci has also launched partnerships of undisclosed value with EQRx, which aims to develop new drugs at far lower cost than conventional therapies; and Xyphos Biosciences, an Astellas Company. The companies agreed to apply Absci's Protein Printing™ technology toward selecting an optimal variant of Xyphos' MicAbody™ lead candidate, and a custom E. coli SoluPro® production strain for further development and cGMP manufacturing.

Absci is among companies focused on harnessing ML to design new drugs. The global market for applying AI to drug discovery is expected to expand at a combined annual growth rate (CAGR) of 38%, from $470 million last year to $1.69 billion in 2025, ResearchAndMarkets projected in a report issued in December 2021.

Hoping to tap into that growth is Absci, which went public last July through an initial public offering that generated approximately $210 million in net proceeds. Three months later in October 2021, Absci opened a new 85,000-square-foot headquarters in Vancouver, WA, where the company has been based since 2016. McClain founded Absci in 2011 from a tiny basement lab where he began pursuing a vision of revolutionizing the development of protein-based drugs by using DNA to program E. coli bacteria.

Absci finished 2021 with a net loss of $100.96 million, seven times its 2020 net loss of $14.35 million, largely due to a four-fold jump in R&D expenses (to $44.58 million last year) and a five-fold leap in selling, general, and administrative (SG&A) expenses (to $28.78 million). The company's total 2021 revenues stayed flat at $4.782 million, up $2,000 from a year earlier.

Among other AI drug discovery platform companies:

- Cyclica last month expanded a two-year-old partnership with Arctoris to advance drug discovery in Alzheimer's, a condition that has seen years of drug development failures—as well as partnerships with 10 academic institutions, including Brown University, the Fred Hutchinson Cancer Research Center, Rutgers University, and University of California, San Francisco (UCSF).
- Exscientia announced in April 2021 a $225 million Series D financing and $300 million equity commitment it can draw on at its discretion, toward developing its Centaur Chemist AI design platform.
- A month earlier, Insitro completed a $400 million Series C financing, on top of a $200 million Series B raised in 2020. The company—whose name is a portmanteau of in silico and in vitro—combines ML of datasets consisting of genetic, phenotypic, and clinical data with predictive cell-based disease models.

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Also last year, NVIDIA joined with Schrödinger to further expand the speed and accuracy of its computational platform, which integrates predictive physics-based methods with ML techniques to accelerate drug discovery, in order to accelerate evaluation and optimization of chemical matter in silico ahead of synthesis and assay.

All those companies, McClain notes, have targeted their ML drug discovery platforms to identifying small molecules, a small universe of potential candidates than the antibodies Absci looks for: "Where our synbio technology comes into play is being able to generate as many as 10^{10} protein-based biologics. And in a given week we can add functionality and manufacturability versus current industry standard of 10^3."

Proteins are also the focus of another ML discovery platform developer, Nuritas, which applies its technology toward finding plant-based "bioactive" peptides with beneficial effects on the body and human health, for use in foods and skin products. The company has partnerships with BASF, food giants Nestle and Mars, and one drug developer, Sumitomo Pharma.

Probability of success

McClain said Absci's ML models could address a disappointing statistic cited in the literature (a 2010 study published in *Nature Reviews Drug Discovery*), which stays that only 4% of conventional drugs advance all the way from discovery to market launch.

Through its partnership with NVIDIA, Absci aims to accelerate and scale its in-silico ML pipeline using NVIDIA expertise as well as optimized graph- and transformer kernels on NVIDIA's A100 Tensor Core GPUs.

"We are evaluating and implementing NVIDIA optimized GNN [Graph Neural Networks] architectures, such as those in the announced DGL [Deep Graph Library] container, in addition to optimizations that lower both the total compute cost and memory consumption of SE(3) transformer kernels," Kimberly Powell, Vice President of Healthcare, told GEN Edge.

"These are critical bottlenecks in Absci's de novo protein assembly architecture. Accelerating the fundamental architecture that comprises Absci's in silico platform is key to efficiently scaling the architecture to achieve the best possible performance in their end-to-end drug design platform."

That acceleration, she said, will ultimately enable Absci to build much larger AI models and take advantage of additional computing scale, such as on DGX Foundry—NVIDIA's infrastructure solution for businesses seeking premium AI development without having to deploy and manage it themselves.

"With NVIDIA's expertise, Absci will continue to synthesize and test the predictions from the models in its proprietary ultra-throughput assays to further validate, iteratively train, and refine the AI performance," Powell added.

DGL is a framework-neutral and scalable Python library designed for easy use and intended for implementing and training GNNs, a class of deep learning methods designed to perform inference on data described by graphs.

"Nvidia wants to sell more GPUs. If I'm a biopharma company, why should I go out and buy a GPU?" Meier recalled asking NVIDIA representatives.

When they asserted that a GPU would make a difference in drug discovery, Meier said, Absci and NVIDIA entertained another conversation

'When we pitched them on some of this stuff that we're doing, they were blown away, impressed by this, and wanted to work together," Meier recalled. "Absci is a potential player to activate this ecosystem, so we started exploring different ideas together, giving them a taste of what we work on."

"We really found common ground on problems where we would benefit a lot from the scale of compute and engineering expertise of NVIDIA. They wanted to see examples of this stuff actually playing out in the real world. So it's a really nice collaboration," Meier added. "This is really exciting for us to work with the leader in the AI space here, and really think together about what does the future of AI and healthcare look like."

Expanding healthcare presence

For NVIDIA, the Absci collaboration is among its latest moves toward expanding its presence in AI-based drug discovery.

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"Our collaboration with Absci is aimed at enabling the most advanced AI paradigms and accelerating protein design," Powell said. "Absci's powerful data generation and AI protein engineering platform is already helping the drug discovery industry, and NVIDIA is excited to help power and scale Absci's in silico technologies to achieve the best positive impact.

"We're also impressed with Absci's differentiated synthetic biology platform and breakthrough assays to advance the field and enable the development of better medicines," Powell added.

Absci is among members of NVIDIA Inception, an accelerator program whose member startups receive access to NVIDIA technology and expertise, as well as connections with venture capitalists and co-marketing support.

In addition to the Absci collaboration, NVIDIA also announced at GTC that four other NVIDIA Inception member startups were the first cohort to be granted access to the company's Cambridge-1, the U.K.'s most powerful supercomputer. Cambridge-1 is designed to deliver more than 400 petaflops of AI performance and 8 petaflops of Linpack performance.

Officially launched in July 2021, Cambridge-1 is an NVIDIA DGX SuperPOD cluster powered by NVIDIA DGX A100 systems, BlueField-2 DPUs and NVIDIA InfiniBand networking.

Also during GTC, Johnson & Johnson's Janssen Pharmaceutical shared how it has applied natural language processing models in pharmacovigilance applications—namely scanning medical literature in search of reports about patients who may have experienced possible side effects.

Janssen is applying an AI platform that features a customized version of BioMegatron, an adaptation of NVIDIA's Megatron language model using the NVIDIA NeMo framework, and pretrained on uncased data from the PubMed dataset. PubMed consists of more than 33 million citations for biomedical literature from MEDLINE, life science journals, and online books. The customized BioMegatron was set up in late 2021 to help accelerate the shortlisting of medical literature for human review to analyze drug safety.

Janssen has credited BioMegatron with a 12% improvement in the overall accuracy of its model. Janssen also uses NVIDIA TensorRT and NVIDIA Triton to optimize its AI models for inference, technologies the drug developer said has doubled its compute throughput and efficiency. GEN