BioPharma Must Innovate or Die
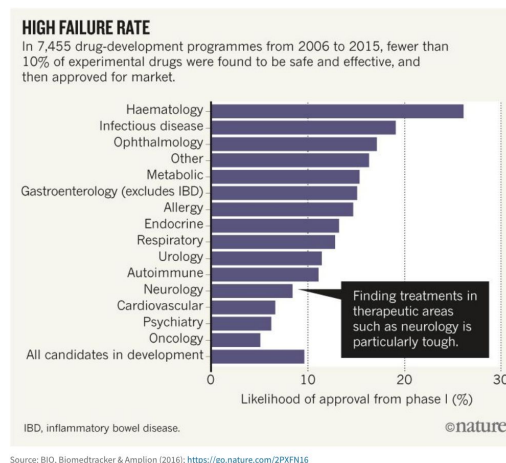
Although pharmaceutical companies spend over $172 billion on research and development annually, over 90% of molecules discovered using traditional techniques fail in human clinical trials. Moreover, 75% of newly approved drugs are unable to cover the cost of development and some analysts predict that ROI in R&D may hit zero by 2020.

In 2018 a robot scientist named Eve discovered that triclosan, an ingredient in toothpaste, could potentially treat drug-resistant malaria. AI systems like the one that powers Eve could become ubiquitous and transform BioPharma within 5-10 years. BioPharma companies capable of building strong AI divisions and acquiring the best AI startups will dominate the biopharma industry and see their market capitalizations skyrocket. Biopharma companies that fail to incorporate AI into their core R&D processes will most likely disappear.
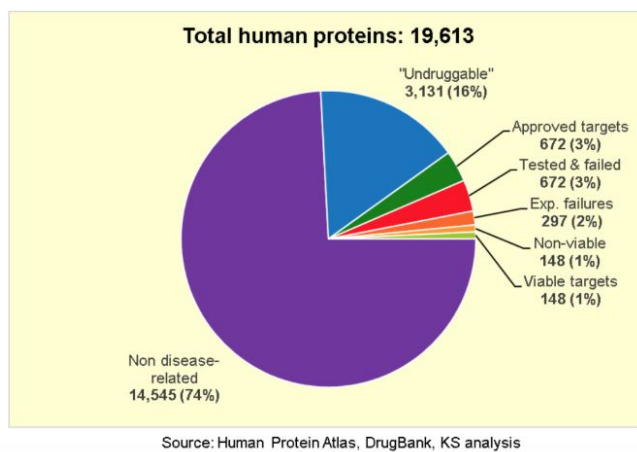

HIGH FAILURE RATE
In 7,455 drug-development programmes from 2006 to 2015, fewer than 10% of experimental drugs were found to be safe and effective, and then approved for market.

Finding treatments in therapeutic areas such as neurology is particularly tough.

IBD, inflammatory bowel disease.

©nature

Source: BIO, Biomedtracker & Amplion (2016); https://go.nature.com/2PXFN16

Taking into account the progress in AI for Drug Discovery over the last three years, it's reasonable to expect that really significant results could be achieved in the next three years, enabling a paradigm shift for the entire biotech industry. The major driver of change in drug discovery will most likely come from big technology companies such as Google, Amazon, Tencent and Alibaba rather than from BioPharma companies.

"As we learn more about what supercomputers can do, we gain confidence. Within three years, I want to go from a drug target to a molecule in twelve months. That takes five to six years now. That's what success looks like."

John Baldoni, PhD, Senior Vice President,
lnSilico Discovery, GSK Pharmaceuticals

Accelerating Discovery of New Compounds

The high cost of screening compounds drives up the cost of developing new drugs in traditional drug discovery. Commercial screening compounds can cost as much as $15 per milligram - over 10 times the price of gold. To screen an entire library of potential drugs, one would need to use these expensive compounds. AI helps reduce this cost.

Total human proteins: 19,613
"Undruggable" 3,131 (16%)
Approved targets 672 (3%)
Tested & failed 672 (3%)
Exp. failures 297 (2%)
Non-viable 148 (1%)
Viable targets 148 (1%)
Non disease-related 14,545 (74%)

Source: Human Protein Atlas, DrugBank, KS analysis

By using AI in drug development, it's possible to accurately predict which drugs will be safe and effective for specific patient subgroups. AI accelerates the drug development cycle by generating drug candidates for which we already have some evidence of effectiveness. Traditional pharmaceutical companies screen through a large number of candidates and test each one with the hope that one will work.

AI for Drug Discovery companies generate novel drugs with specific properties. Due to their specific molecular structures, compounds discovered using AI are more likely to be effective against specific disease targets.
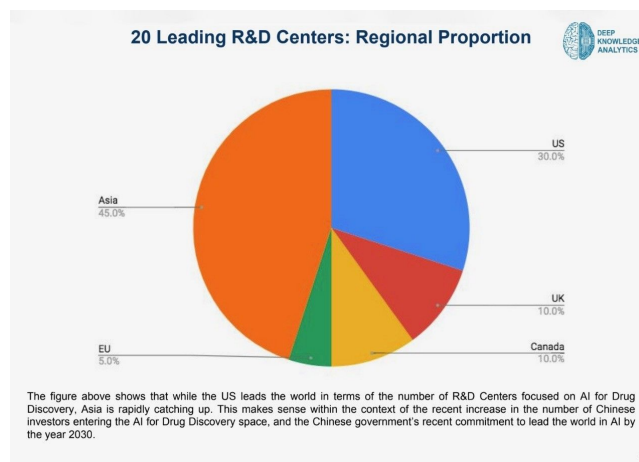
Some AI companies, such as [Insilico Medicine,](#) screen potential drug candidates by harnessing the power of generative adversarial networks (GANs). GANs create synthetic datasets that are indistinguishable from real datasets by having two neural networks compete against each other. One neural network generates the data and the other compares it to a real data set in iterative cycles so that the degree of error in the synthetic data set is gradually decreased. Rather than using trial and error when looking for molecular leads, requests are made to the network to generate specific leads and leads are generated on demand.

We don't know exactly how much time we can save using AI to successfully produce a drug because it's never been done. When an AI discovered drug candidate actually makes it through *in vitro* validation and through clinical evaluation, we'll have a better idea about how long the process takes. One thing we do know is that AI will help researchers leapfrog the most time-consuming and pain-staking part of drug discovery, which is finding molecular leads.
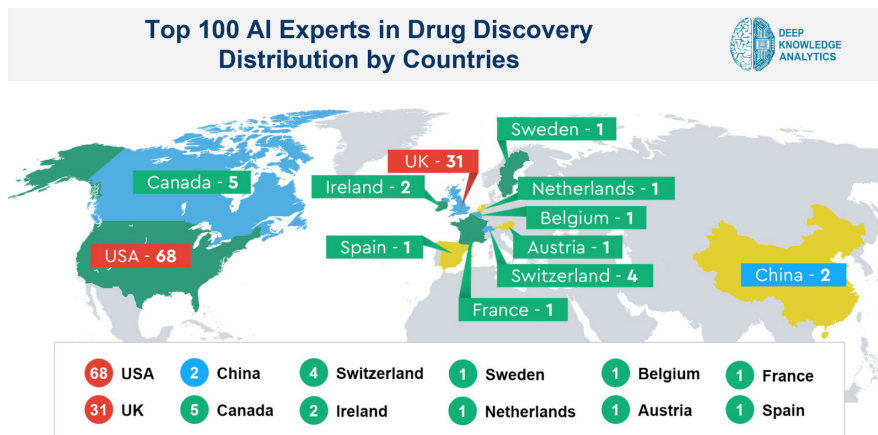
Progressive Technocratic Countries

In the next five to ten years, the number of compounds identified using AI will increase substantially and new drugs capable of treating very precise pathologies will become available. Accelerating this cycle will require progressive approaches to the methodology used in clinical trials including the use of AI. Progressive technocratically driven countries may reformulate their drug evaluation and approval processes to expedite the time it takes for drugs to reach patients.

20 Leading R&D Centers: Regional Proportion

The figure above shows that while the US leads the world in terms of the number of R&D Centers focused on AI for Drug Discovery, Asia is rapidly of catching up. This makes sense within the context of the recent increase in the number of Chinese investors entering the AI for Drug Discovery space, and the Chinese government's recent commitment to lead the world in AI by the year 2030.

The most advanced AI companies will move to these countries and regional biotech hubs will form. Today a number of countries are developing the best AI platforms in the FinTech space. These countries are attracting AI startups from all over the world. As a result, The UK and Singapore are quickly becoming global innovation hubs. In the next few years the most progressive countries will become regional biotech hubs for AI in healthcare in general and AI in Drug Discovery in particular. The most likely candidates to become regional biotech hubs include Singapore, Taiwan, South Korea, Hong Kong, Israel, and Switzerland.

> The AI for Drug Discovery market segment only accepts
> companies with the highest levels of expertise. Although
> there are more than 1000 AI in Healthcare companies
> globally, only 125 of them are capable of entering the AI
> for Drug Discovery sector, and only 20 of these companies
> are capable of actually delivering tangible results.

Global Landscape 3rd Edition

Deep Knowledge Analytics recently published AI for Drug Discovery, Biomarker Development, and Advanced R&D Landscape Overview, 3rd Edition. This report which includes Q3 2018, is the most comprehensive industry analytical report on this subject to date. The report provides in depth comparative and quantitative analysis of the entire AI for Drug Discovery landscape. It includes rankings of various AI for Drug Discovery companies according to their levels of scientific validation, clinical development, R&D, industry application diversification, and overall prospects for future growth. The report is well summarized in the recent Forbes articles An Insight of AI's Penetration In Drug Development Market and World's Top 20 AI Drug Development Companies.

Leading Companies
Advanced AI in Healthcare and Drug Discovery
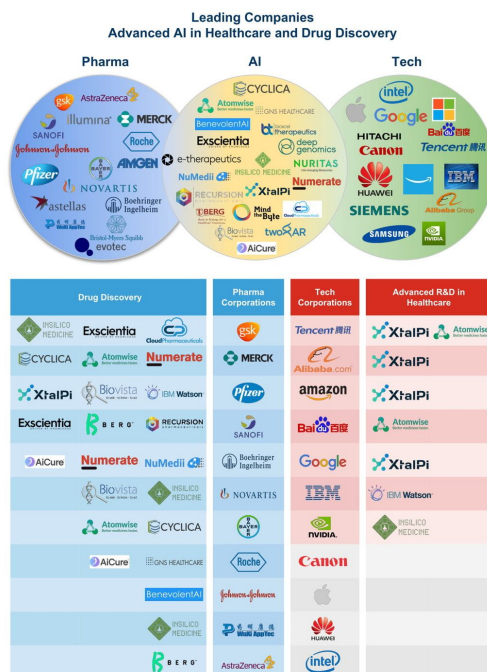
End to End Solutions

Although there are 125 AI companies working in the Drug Discovery space, very few of them are capable of building end to end solutions. To succeed in this space, companies must be able to hire and retain a good number of strong AI experts and biochemical specialists. They must also have significant financing and efficient administrative methods. Companies such as WuXi NextCODE, BenevolentAI, and Insilico Medicine are leaders in this area.

Insilico Medicine's drug discovery engine is involved in the drug discovery and in silico validation stages of the drug development cycle. The company focuses on the generation of novel drug candidates with specified molecular properties for precise disease targets. Traditional pharmaceutical companies screen through many possible leads, testing each one and hoping that one works. Insilico Medicine starts with molecular leads that have been specifically designed, in terms of their pharmacokinetic and pharmacodynamic properties, and therefore have a higher probability of being effective for specific disease targets.

END-TO-END DRUG DISCOVERY PIPELINE IN THE INDUSTRY UTILIZING NEXT-GENERATION ARTIFICIAL INTELLIGENCE
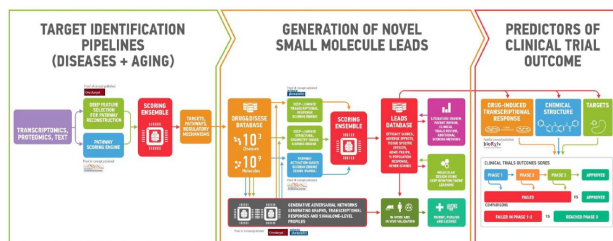
Major Disruption from New AI Techniques

There have been significant advances in the techniques used in specific AI domains. Every year these techniques evolve to produce next generation AI methods. Major disruption will come from biopharma companies that apply these next generation techniques in AI, Deep Learning, generative adversarial networks, and reinforcement learning to drug discovery, drug repurposing, and biomarker development.

> "Our AI-based biomarker discovery and compound generation engine allows for end-to-end learning from hypothesis generation, to target ID, to compound generation. We intend to utilize this system in a big way."
>
> Alex Zhavoronkov, PhD, CEO and Founder of Insilico Medicine.

Generative Adversarial Networks

Recently there's been a big increase in the number of papers published on GANs. Insilico Medicine was the first company to apply GANs to the generation of new molecular structures with specified parameters. The company has developed adversarial neural networks that compete with each other to generate and evaluate novel drug candidates with specific molecular properties, and through this established itself as a pioneer in advanced AI methods for drug discovery.

Insilico's drug discovery engine is trained on massive amounts of structural, functional, and phenotypic data in order to predict the biological activity of compounds. Insilico Medicine has published seminal papers in Oncotarget and Molecular Pharmaceutics. Another paper, published in Molecular Pharmaceutics in 2016, demonstrated the proof of concept of the application of deep neural networks for predicting the therapeutic class of the molecule using the transcriptional response data.

The MOSES Platform

When generative chemistry using GANs was first used in 2015, it was considered exotic and unproven technology. Today it is experimentally validated and the field is exploding with many groups joining and making meaningful contributions. It is important to develop a set of standards and benchmarks to help the community, and to accelerate the delivery of AI generated drugs to patients. Ongoing research in machine learning in general and deep learning in particular brings up the issues of reproducibility and fair comparison between different approaches. While there are multiple methods for generating novel molecular structures with machine learning models, there is no conventional way to run and evaluate the performance of these generative models.
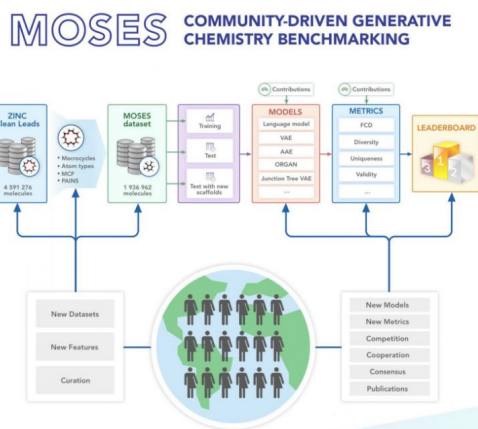
On November 30, 2018, AI researchers joined forces to develop the "ImageNet" of Generative Drug Discovery by launching a benchmarking platform that encompasses various machine learning techniques in order to compare them on a standard dataset. The MOSES (Molecular Sets) platform implements several popular molecular generation models and ranks them according to a predefined set of metrics. MOSES aims to increase the pace of drug discovery and facilitate the sharing and comparison of new models. MOSES is intended to boost AI powered drug discovery, just as ImageNet boosted deep learning for imaging data. The MOSES platform provides a standardized benchmarking dataset, a set of open-sourced models with unified implementation, and metrics to evaluate and assess the results of generation.

The launch of the MOSES benchmarking platform
NeuralPS2018 in Montreal on December 2, 2018.

Preventive Medicine and Longevity

In 2017 and 2018, a number of notable activities related to applying AI for Aging Research and Longevity emerged in rapid succession. Y-Combinator and the Buck Institute for Research on Aging in California are working on establishing AI for Longevity research hubs. Atomwise and BioAge are well known in the AI for Drug Discovery field, as well as in the field of aging research. Chinese iCarbonX backed by Tencent and Beijing Genomics Institute recently announced their interest in applying the most progressive precision medicine techniques and AI in particular to the problem of an aging population and healthy Longevity.

Current efforts closest to practical application are focused on geroprotectors derived from natural compounds and repurposing existing drugs toward new age-related disease targets. Insilico Medicine used AI to develop Ageless Cell, a longevity supplement containing natural geroprotectors that rank high in terms of their gene expression-level similarity to geroprotectors like metformin and rapamycin. Napa Therapeutics is a collaborative venture between the Buck Institute, Juvenescence and Insilico Medicine. It draws the best from three areas: great science from the Buck, funding and drug hunting and development expertise from Juvenescence and AI prowess and expertise in advanced bioinformatics from Insilico Medicine. Insilico Medicine and A2A Pharmaceuticals a biotechnology company focused on novel drug development for oncology, have collaborated to form a new company, Consortium.AI, which will apply advances in AI to discovery of novel small molecules for the treatment of Duchenne muscular dystrophy and other rare diseases.

A recent article in the Aging Research Reviews journal entitled Artificial Intelligence for Aging and Longevity Research: Recent Advances and Perspectives highlighted the following topics:

- Presentation of the most recent advances for the design of deep learning aging clocks
- Description of achievements in the development AI de novo molecular generators
- Strategies for developing AI based cross species aging studies
- Algorithms that are combined within a pipeline to optimize the drug discovery process
- Strategies to select and extract features relevant to aging research

Frost & Sullivan recently awarded Insilico Medicine the *North American AI for Aging Research & Drug Development Innovation Award* as part of their 2018 Best Practices Awards. The fact that a highly respected firm like Frost & Sullivan created a new award category for this specific area of research and development is indicative of the interest and support that AI in Drug Discovery is garnering from the drug development community.

Investment

Investments into the AI for Drug Discovery sector grew steadily from 2012 to 2017, and in 2018 the amount of investment and number of joint projects with pharmaceutical companies accelerated substantially. An inflection point of AI for Drug Discovery could happen as early as 2020. Investment in AI for Drug Discovery startups grew from $200 million in 2015, to $300 million in 2016, and has already exceeded $700 million in 2018. Currently, there are 260 investment funds investing into AI for Drug Discovery sector, including such leading investors as Soft Bank, Wuxi Apptec, Google Ventures, Andreessen Horowitz, Khosla Ventures, and Sequoia Ventures.

There is no consensus among analysts regarding the expected valuation of the AI for Drug Discovery industry projected for 2024. Conservative estimates predict a valuation of $5 billion by 2024, while others predict $10 billion and even up to $20 billion. It is absolutely clear that significant market capitalization growth of AI for Drug Discovery is inevitable. Only the dynamic of this growth may vary.

Only a select few of the most advanced 260 investment funds are capable of applying efficient due diligence to assess investment targets in this field. The reason is simple: an extremely high level of expertise is required to assess the most advanced AI for Drug Discovery companies and their technologies. The majority of those 260 investment funds are playing a type of roulette, while other investors, such as family offices and institutional investors do not consider investments in this field at all.

Pharma AI Index Hedge Fund

Deep Knowledge Ventures is currently developing a novel InvestTech solution which will be particularly relevant for the AI for Drug Discovery sector. The Pharma AI - Index Hedge Fund will use hybrid investment technologies combining the profitability of venture funds with the liquidity of hedge funds, significantly de-risking the interests of LP's and simultaneously providing the best and most promising AI companies with a relevant amounts of investment. Deep Knowledge Ventures is a leading investment fund focused on the synergistic convergence of DeepTech verticals, frontier technologies and technological mega-trends. Deep Knowledge Ventures is known for its use of sophisticated analytical systems for investment target identification and due-diligence. Major investment sectors include AI, Precision Medicine, Longevity, Blockchain and InvestTech. @DeepTech_VC
About Deep Knowledge Analytics

This article was written by Margaretta Colangelo and Dmitry Kaminskiy.

Margaretta Colangelo, Managing Partner at Deep Knowledge Ventures, is based in San Francisco. Margaretta serves on the Advisory Board of the AI Precision Health Institute at the University of Hawai'i Cancer Center.

Dmitry Kaminskiy, General Partner at Deep Knowledge Ventures, is based in London. Dmitry is Head of International Development of the Secretariat for the All Party Parliamentary Group for Longevity and Managing Trustee of the Biogerontology Research Foundation. @DeepTech_VC

The quote from John Baldoni was extracted from 6 Steps to AI Leadership in Pharma: An Interview with John Baldoni of GSK.