Introduction:

Background and Fundamentals of AI in Drug Discovery

Introduction

The present chapter aims to give readers a basic background and fundamentals required to understand and effectively contextualize the more specialised chapters in this report.

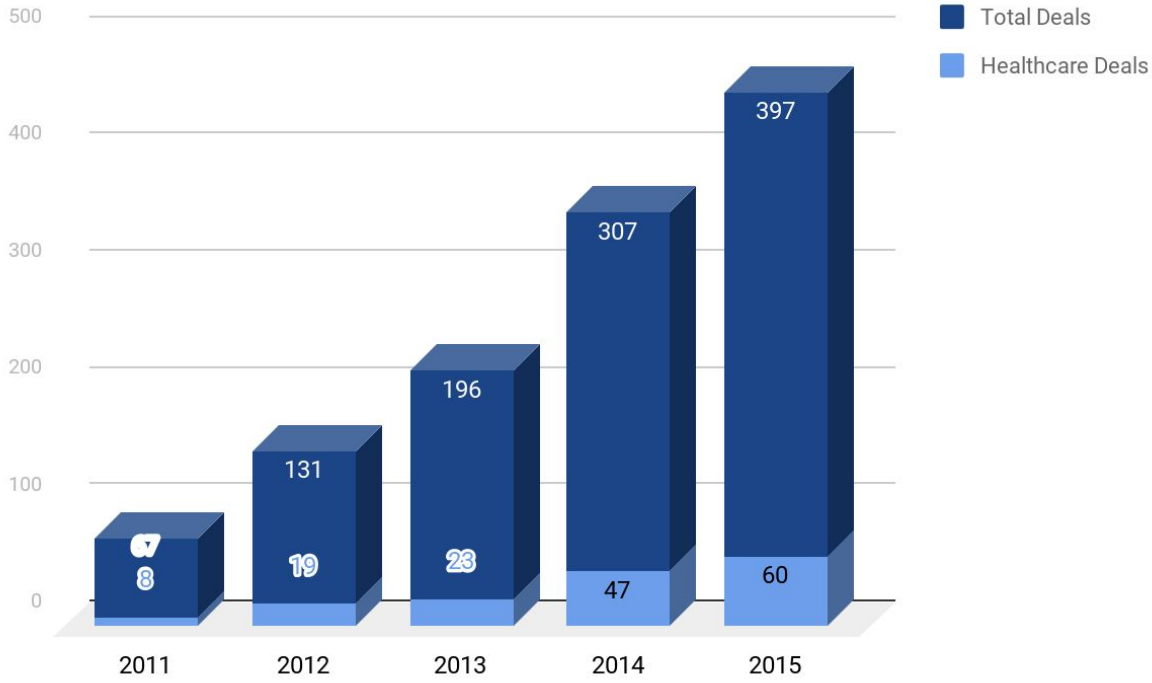
It offers a brief overview of:

- AI in Healthcare
- AI's Broader Role in the Healthcare Industry
- AI in Healthcare Applications & Use Cases
- AI for Drug Discovery, and how it fits into the broader AI in healthcare industry
- Roadblocks and barriers in the traditional BioPharma industry
- How the "broken business model of BioPharma" creates resistance to change and puts large BioPharma corporations unwilling to embrace and absorb technological innovations relevant to their industry at a disadvantage compared to IT and Tech corporations
- The various applications and use-cases for AI in Drug Discovery and Advanced R&D
- Emerging Trends in AI for Drug Discovery
- A brief look at the near future of AI for Drug Discovery

AI's Broader Role in the Healthcare Industry

Artificial intelligence is becoming an integral part of modern life. In recent years, machine learning scientists have made astonishing progress implementing AI in numerous industries in a short span of time. From stock trading to project management, AI is now a crucial part in the normal functioning of the world economy; a study conducted in Oxford shows that 47% of all existing jobs can be automated with artificial intelligence technologies. It is natural that AI is rapidly developing in a modern healthcare system. NPOs, government organizations, and enterprises alike include algorithms to enhance their therapies.

The number of healthcare deals occurring in the overall AI market is on the rise, up from just 8 large deals in 2011 to over 60 large deals in 2015. Similarly, the number of startups entering the healthcare AI space has increased in recent years, with over 50 companies raising their first investment rounds since January 2015. Deals to healthcare-focused AI startups went up from less than 20 in 2012 to nearly 70 in 2016.



Growing healthcare AI market compared to the overall AI market. Source: https://www.slideshare.net/galengrowthasia/cb-insights-ai-in-healthcare

Source: https://www.huffingtonpost.co.uk/2014/01/17/rise-of-the-machines-economist_n_4616931.html

AI in Healthcare Applications & Use Cases

Artificial intelligence will revolutionize the healthcare industry. Indeed healthcare will be leading the Fourth Industrial Revolution, and a major catalyst for change is going to be artificial intelligence (AI).

AI in health represents a collection of multiple technologies enabling machines to sense, comprehend, act and learn so they can perform administrative and clinical healthcare functions. Unlike legacy technologies that are only algorithms and tools that complement a human, health AI today can truly augment human activity.

AI has already found several areas in healthcare to revolutionize, starting from the design of treatment plans through the assistance in repetitive jobs to medication management or drug creation. And it is only the beginning.

The field of AI has been actively growing since 2015. But 2017 became year of the ‘cambrian explosion’ of AI in healthcare.

This market is primarily being driven by factors like the rise of personalized medicine in tests for clinical decision-making, big data in the healthcare industry, and the growing adoption of AI in genetics.

Also, AI created a real-time monitoring system, and wearables are playing a crucial role in digital healthcare monitoring.

AI in Healthcare:

- Drug Discovery
- Wearables
- Medical Imaging and Diagnostics
- Research
- Mental Health
- Lifestyle Management
- Digital Health Monitoring
- Patient Data and Risk Analytics
- Virtual Assistants
- Surgery
- Hospital Management

The Rise of AI in Healthcare

I believe that AI is a sleeping corporation for healthcare in general

Eric Horvitz,
director of Microsoft Research Labs
in Redmond, Washington

The number of startups entering the healthcare AI space has increased in recent years, with over 50 companies raising their first equity rounds since January 2015. Deals to healthcare-focused AI startups went up from less than 20 in 2012 to nearly 70 in 2016.

The field of AI for Healthcare has been actively growing since 2015. The market is primarily being driven by factors like the rise of personalized medicine in tests for clinical decision-making and big data in healthcare industry and the growing adoption of AI in genetics. Also, AI created real-time monitoring systems and healthcare wearables are playing a crucial role in digital healthcare monitoring.

A report published by The BMJ in 2016 noted that medical errors claim 250,000 lives each year, making it the third leading cause of death in the U.S. AI in healthcare and medicine could organize patient routes or treatment plans better, and also provide physicians with all the information they need to make a good decision.

“I have no doubt that sophisticated learning and AI algorithms will find a place in healthcare over the coming years,” Andy Schuetz, a senior data scientist at Sutter Health said. “I don’t know if it’s two years or ten — but it’s coming.”

Global Healthcare AI Market Growth Through 2024

Figure 6: Global Healthcare AI Market Growth Through 2024

Source: Markets and Markets; Global Market Insights, Inc.

The U.S. healthcare AI market exceeded $320 million in 2016, and is estimated to grow by more than a 38% CAGR through 2024 (Global Market Insights, "Healthcare AI Market Size, Competitive Market Share & Forecast, 2024").

The Global Healthcare AI market, among the AI industry's fastest growing sub-sectors, is expected to grow at a 39.4% CAGR to over $10 billion in worldwide revenue by 2024.

accenture

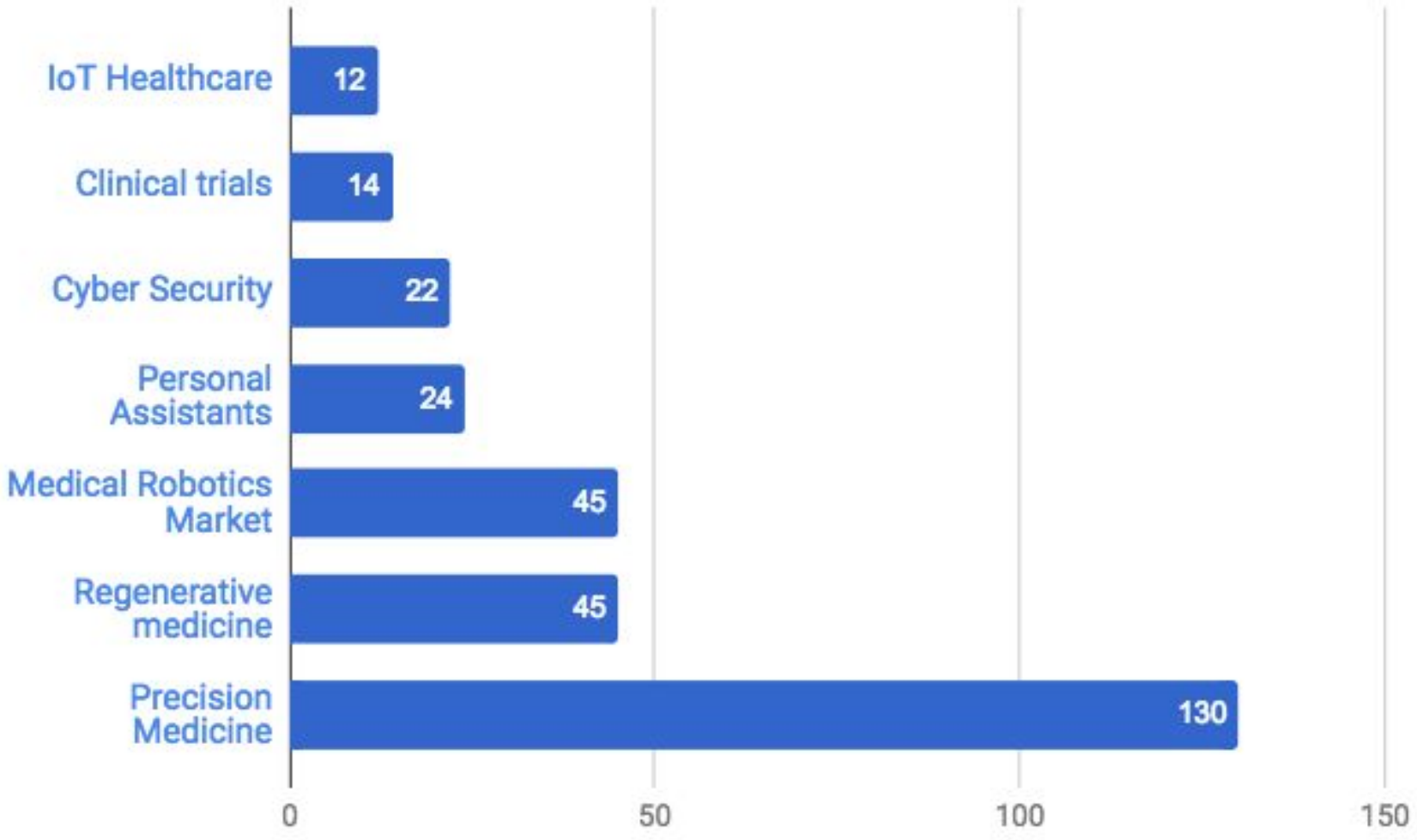
Top 10 AI Applications

APPLICATION	VALUE*
Robot-Assisted Surgery**	$40B
Virtual Nursing Assistants	$20B
Administrative Workflow Assistance	$18B
Fraud Detection	$17B
Dosage Error Reduction	$16B
Connected Machines	$14B
Clinical Trial Participant Identifier	$13B
Preliminary Diagnosis	$5B
Automated Image Diagnosis	$3B
Cybersecurity	$2B
TOTAL =	~$150B

Source: Accenture analysis
* "Value" is the estimated potential annual benefits for each application by 2026.
** Orthopedic surgery specific

Source: TM Capital "The Next Generation of Medicine: Artificial Intelligence and Machine Learning" Report

Global Healthcare AI Market Growth Through 2024 in $Billions



Source: Deep Knowledge Analytics

How AI in Drug Discovery Fits into the Broader AI in Healthcare Industry

The most disruptive impacts of AI will be on the business model of Advanced R&D, Biomarker Development and Drug Discovery.

Specific attention should be paid to those projects capable of applying Next Generation Artificial Intelligence techniques, Deep Learning and in particular GANs (Generative Adversarial Networks) and reinforcement learning for:

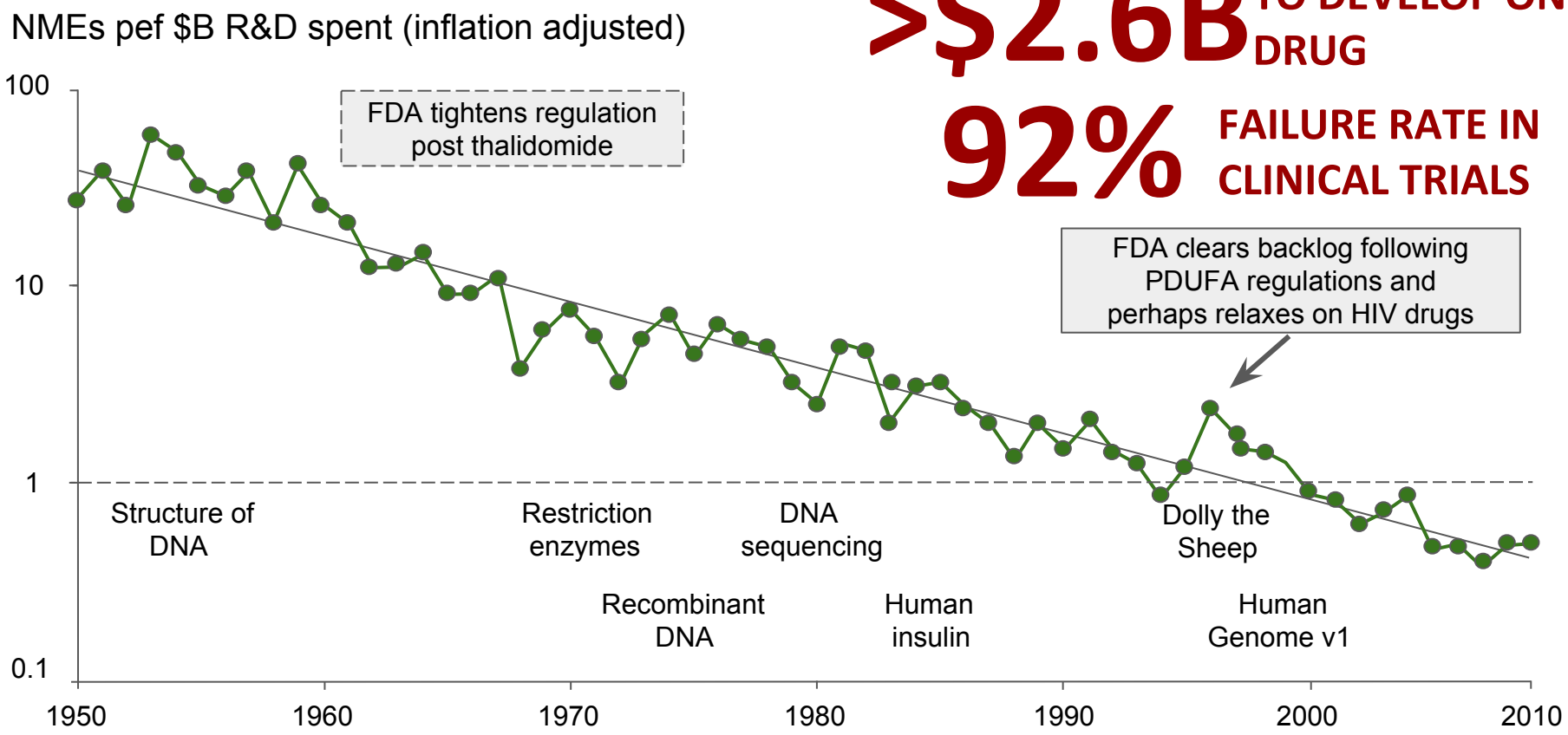
- Drug Discovery and Drug Repurposing
- Biomarker Development
- Clinical Trials Predictors
- Aging Research
- AI Solutions in convergence with Blockchain

The leading players in this specific niche will become game-changers for the entire market and significantly influence the capitalization of pharma companies.

The global healthcare AI market is highly fragmented and characterized by the presence of large number of industry players, while the AI for Drug Discovery segment has a comparatively lower level of competition because this market segment only accepts companies with very high levels of expertise. Even this, however, is beginning to change with the entry of large BioPharma corporations and IT/Tech corporations.

The breakthroughs in AI for Drug Discovery will change the R&D process of BioPharma, and will have a tremendous impact on the whole BioPharma industry. That is why the players from the AI for Drug Discovery market can become game changers and significantly influence the capitalization of the pharma industry.

Pharma Efficiency is Declining Steadily



>$2.6B TO DEVELOP ONE DRUG

92% FAILURE RATE IN CLINICAL TRIALS

Bernstein Research: The Long View - R&D Productivity, 2010

46 NEW DRUGS launched in 2014

Source: adapted from Insilico Medicine investor presentations, www.insilico.com

GLOBAL SALES:

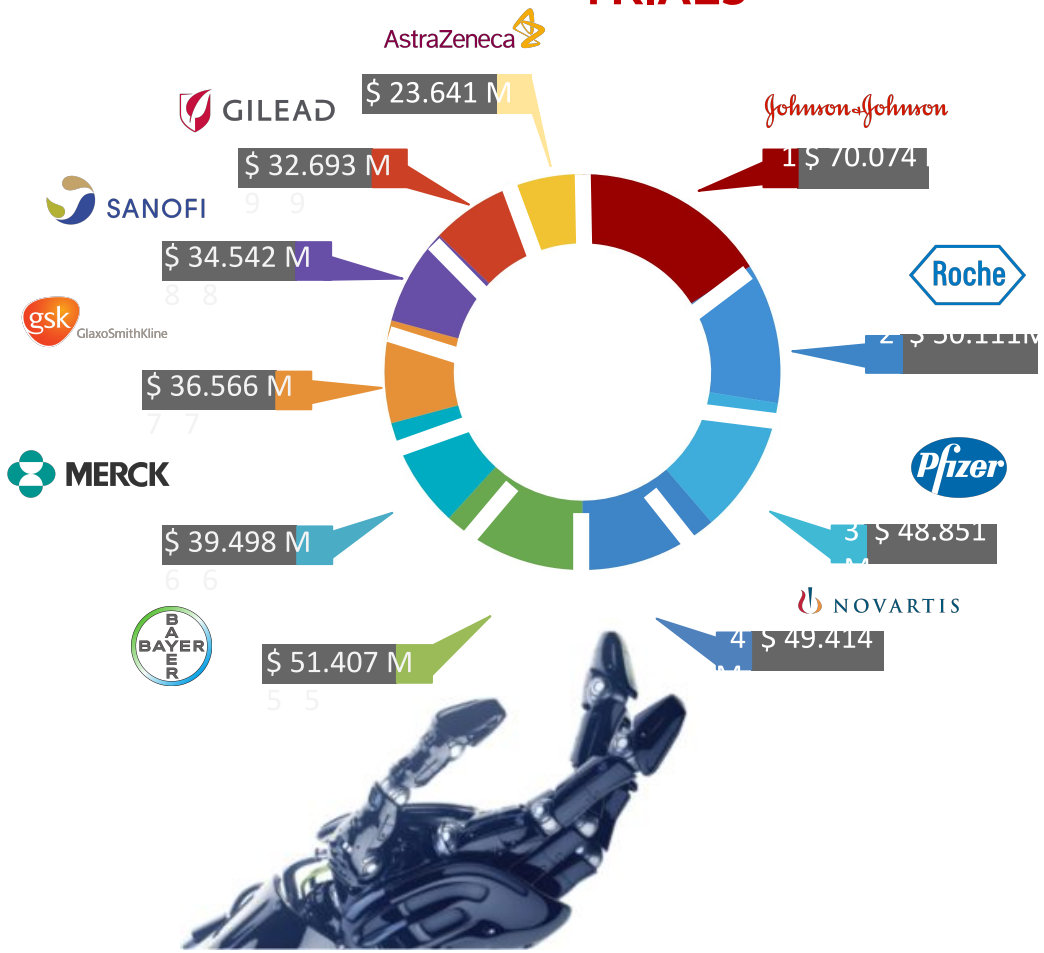
>$1 Trillion

GLOBAL R&D:

>$150 Billion

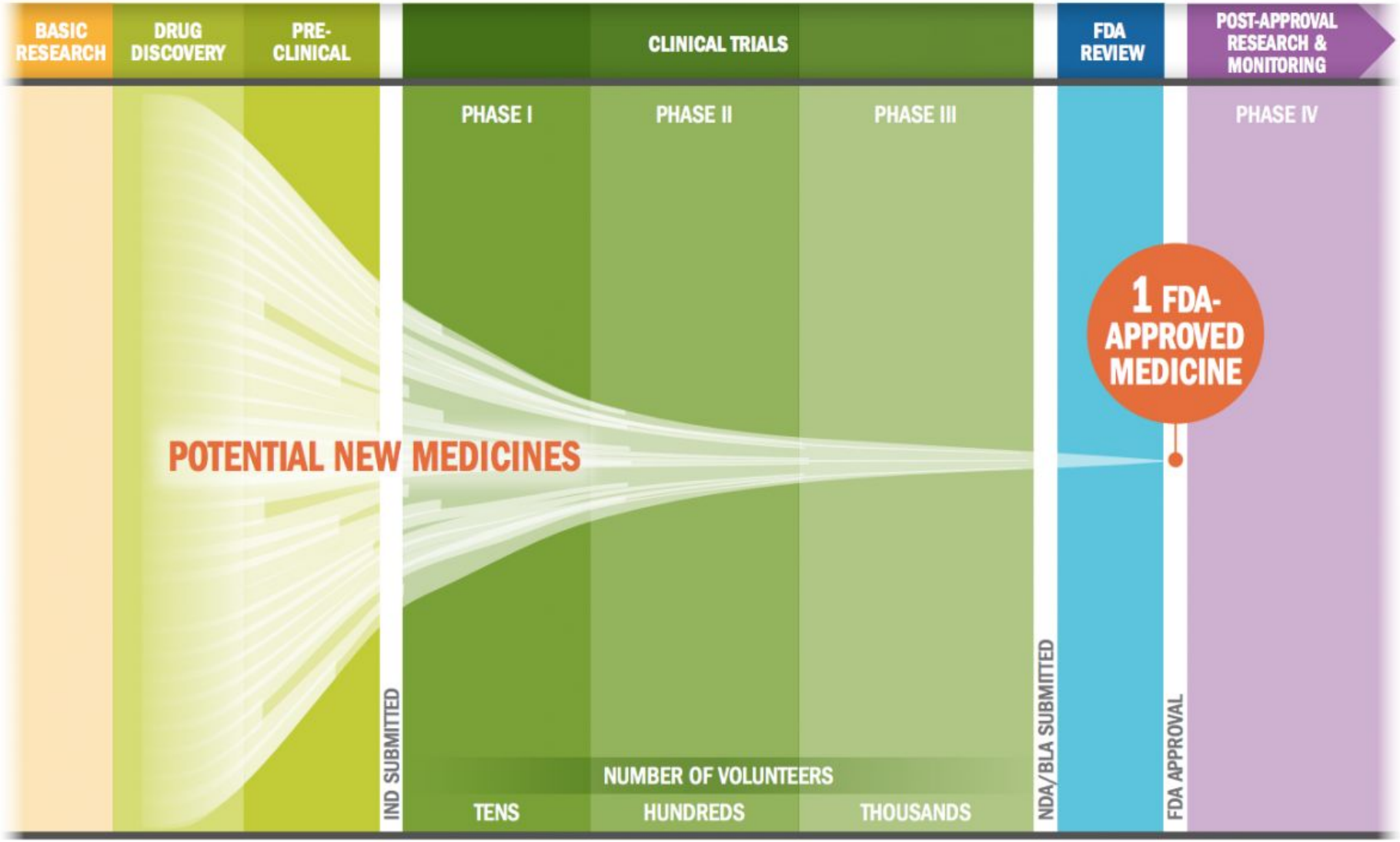
>$2.6B TO DEVELOP ONE DRUG

92% FAILURE RATE IN CLINICAL TRIALS



Source: adapted from Insilico Medicine investor presentations, www.insilico.com

THE BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT PROCESS



Source: Biopharmaceutical Research & Development, PRMA http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf

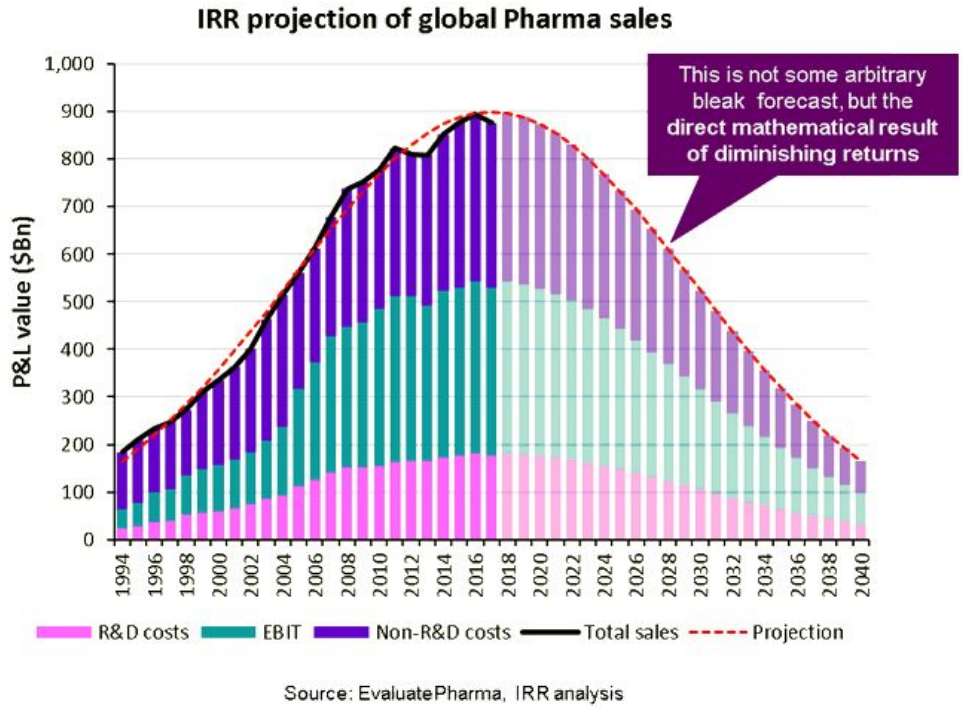
BioPharma's Source of Stagnation is Strategy, Not Capital

The pharmaceutical industry has accumulated vast amounts of capital but remains conservative, bureaucratic and risk-averse in its investment strategy**.** As government budgets become ever more constrained, it is increasingly urgent that the roadblocks to medical advancement be eliminated.

This may reflect the inefficiency of the organizations themselves and capital-intensive barriers to entry, more than the intrinsic intractability of complex biological systems - indeed, the most successful drugs historically have been discovered serendipitously.

In any case, the sector shows signs of sluggishness: twenty years ago, 20% of Swiss GDP was derived from pharmaceuticals — now it is down to 5.7% of GDP.

Banks and IT corporations are snapping up the best AI specialists and startups, and pharma will inevitably require the same scarce technology and talent.



Source: https://endpts.com/pharmas-broken-business-model-an-industry-on-the-brink-of-terminal-decline/

The Broken Business Model of BioPharma

The efficiency of research and development (R&D), defined as the number of successfully approved drugs given the budget allocated to new drug development, has declined for decades.

The cost of drug discovery and subsequent development is a massive challenge in the pharmaceutical industry.

A typical drug can cost upwards of $2.5 billion and a decade or more to identify and test a new drug candidate. Today, only about one in ten drugs that enter phase 1 clinical trials reaches patients.

Drug makers need to find a more efficient way of developing medicines. AI can speed up drug discovery, cut R&D costs, decrease failure rates in drug trials and eventually create better medicines.

What we have is an industry that is entering a vicious cycle of negative growth and terminal decline as its fundamental business model has run out of steam by the Law of Diminishing Returns: Diminishing R&D productivity and return on investment leads to diminishing growth in sales. Eventually, growth turns negative and sales start to contract. Decreasing sales then limits the amount of money available to invest back into R&D, which causes sales growth to decline even further. And so on, until the industry is gone altogether.

Pharma as we know it will shrink out of existence, and there is nothing we can do to stop it. The Pharma and Biopharma industries together will evolve into something quite different, most likely continuing the historic trend of increasing complexity towards more complex biological solutions to pressing healthcare problems, such as cell & gene therapy, tissue engineering and regenerative medicine.

Source: https://www.linkedin.com/pulse/pharmas-broken-business-model-industry-brink-terminal-kelvin-stott/
https://www.drugtargetreview.com/news/29432/new-2018-role-artificial-intelligence-drug-discovery/

Why AI? BioPharma's Outdated Business Model

The first practical results in AI for Drug Discovery will yield a number of domino effects, as BioPharma budgets are significantly related to spending on R&D and failures in clinical trials, meanwhile the breakthroughs in the use of AI for Drug Discovery will have dramatic impact on not just Biopharma companies but all biotech startups and biotech VC funds. All of them will be disrupted. The major progress in these technologies is coming not from the biotech side but from the IT side.

Due to the lack of AI specialists and promising AI & Drug Discovery startups, only a select few BioPharma players will emerge as the leaders of the AI race. Meanwhile others, even with substantial budgets and the will to succeed in this area, will fail if they are even one year late to the race, because all of the top AI specialists and AI in healthcare startups will have been acquired by then. The number of experts in the field of AI for Drug Discovery is insufficient to meet the demand of all big pharma companies, so only those few pharma companies and investors who will partner with the best AI for Drug Discovery companies in time will benefit from these collaborations and increase their capitalization accordingly.

Those BioPharma companies that create strong AI for R&D and Drug Discovery divisions and that will succeed to acquire the best AI startups will become the leaders of the field in as few as 3 to 5 years from now. *Consider the acquisition of DeepMind by Google for $0.5B in 2014*. Companies that invest heavily in AI for their drug discovery department will see their market capitalization skyrocket in coming years.

Bio Pharma companies that do not utilise AI will repeat the mistakes of Kodak. Once the leader of its industry, Kodak went bankrupt because it failed to embrace digital photography as the disruptive trend it was, despite the fact that the digital camera was invented inside Kodak labs. If Bio Pharma found the courage to spend 10% of their marketing budget on R&D in AI, they could blow IBM Watson out of the water, and by learning from their mistakes, reinvent themselves and come one step closer to halting the looming threat of the Silver Tsunami.

While our previous reports have put great emphasis on this big gap. However, as later chapters will show, this gap is already beginning to close, with significant displays of will and commitment through investments, M&As and even the launch of whole in-house AI for drg discovery departments being shown by pharma corporations.

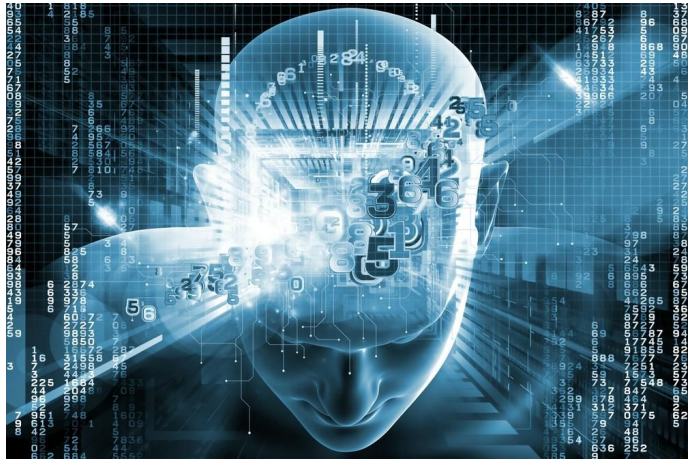
A Deeper Dive into AI for Drug Discovery

On average, it takes about a decade of research — and an expenditure of $2.6 billion — to shepherd an experimental drug from lab to market. And because of concerns over safety and effectiveness, only about 5 percent of experimental drugs make it to market at all.

But drug makers and tech companies are investing billions of dollars in artificial intelligence with the hope that AI will make the drug discovery process faster and cheaper.

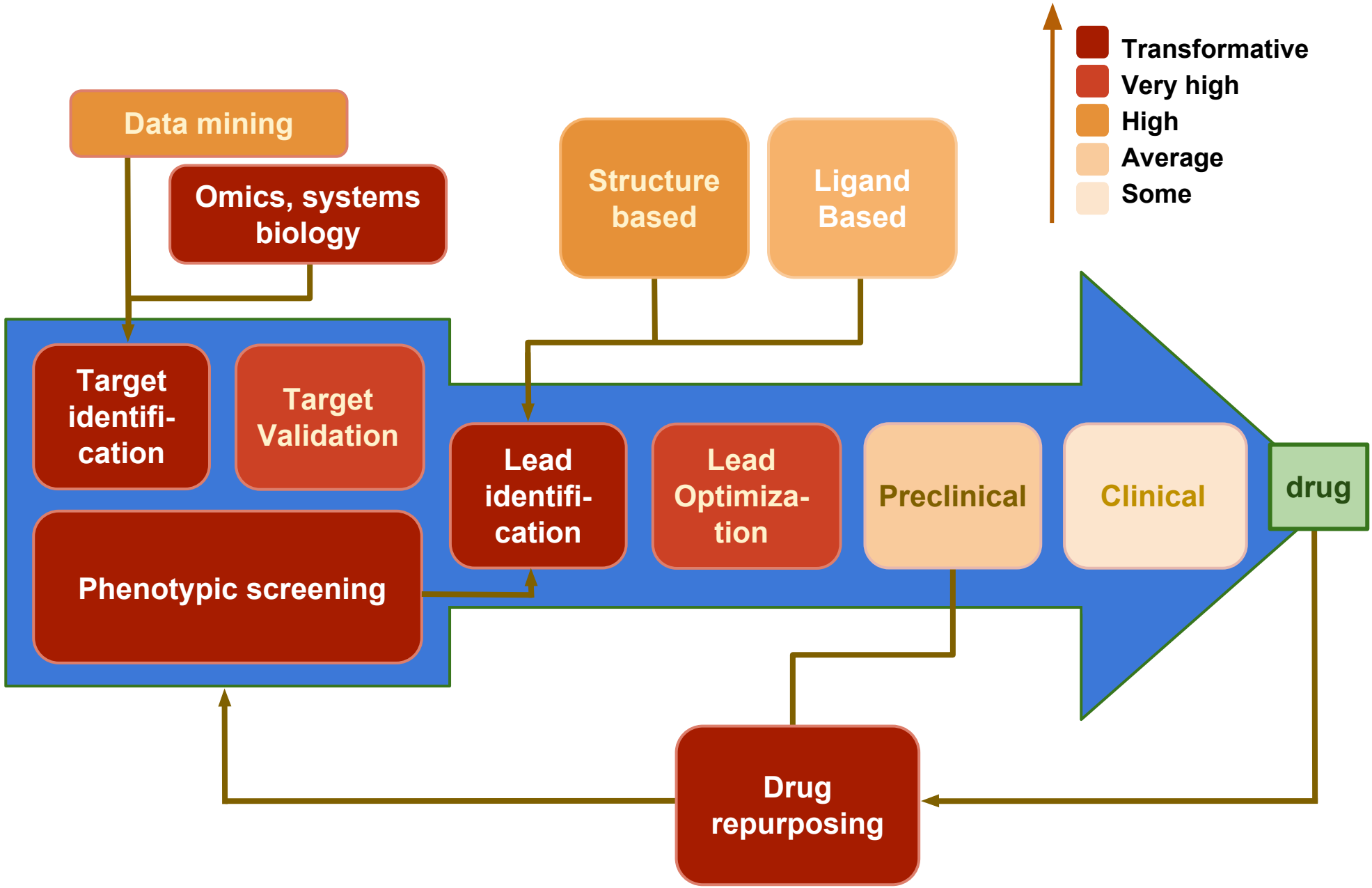
Microsoft Research Labs is investing in AI for drug design and pharmacology, which studies how drugs act in the body, and called the technology a “tremendous opportunity.” We have counted 10 pharmaceutical companies and 80 companies using AI for Drug Discovery. Benevolent.ai has used AI computer algorithms to explore new treatment options for amyotrophic lateral sclerosis, or ALS, a degenerative nervous system disease. AstraZeneca struck a partnership with BERG to use the latter’s A.I. platform to home in on promising biological targets and possible agents against neurological diseases such as Parkinson’s.

Healthcare will be the lead area of the Fourth Industrial Revolution and one of the major catalysts for change is going to be artificial intelligence (AI). AI in health represents a collection of multiple technologies enabling machines to sense, comprehend, act and learn so they can perform administrative and clinical healthcare functions. Unlike legacy technologies that are only algorithms/tools that complement a human, health AI today can truly augment human activity. AI has already found several areas in healthcare to revolutionize starting from the design of treatment plans through the assistance in repetitive jobs to medication management or drug creation. And it is only the beginning.



Source: http://medicalfuturist.com/top-artificial-intelligence-companies-in-healthcare/

The "heat map" of AI potential value for various R&D areas



The Application of AI for Advanced R&D

Generate Novel Drug Candidates

- Analyze data sets, form hypotheses and generate novel insights
- Identify novel drug candidates
- Analyze data from patient samples in both healthy and diseased states to generate novel biomarkers and therapeutic targets
- Predict binding affinity and other pharmacological properties of molecules
- Allow filtering for drug-like properties of molecules
- Reduce complexity in protein design

Aggregate and Synthesize Information

- Extract knowledge from literature
- Generate insights from thousands of unrelated data sources
- Improve decision-making
- Eliminate blind spots in research
- Identify competitive whitespace

Repurpose Existing Drugs

- Rapidly identify new indications for many known drugs
- Match existing drugs with rare diseases
- Conduct experimental biology at scale by testing 1000+ of compounds on 100+ of cellular disease models in parallel
- Generate novel biomarkers and therapeutic targets

Design and Run Preclinical Experiments

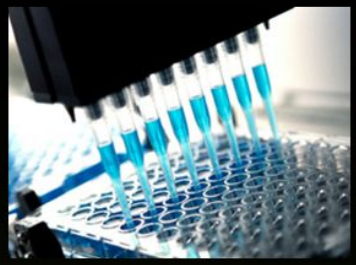
- Reduce time, money, and uncertainty in planning experiments
- Decode open- and closed-access data on reagents and get actionable insights
- Automate selection, manipulation, and analysis of cells
- Expedite development of cell lines and automate manufacturing of cellular therapeutics
- Automate sample analysis with a robotic cloud laboratory

Clinical Trials

- Optimize clinical trial study design
- Transform diverse streams of biomedical and healthcare data into computer models representative of individual patients
- Deliver personalized medicine at scale, by revealing optimal health interventions for individual patients
- Analyze medical records to find patients for clinical trials
- Automate matching cancer patients to clinical trials through personal medical history and genetic analysis
- Improve pathology analysis
- Identify patients that would benefit from novel therapies

Computation-based Drug Discovery

Millions of Compounds



1000s of Compounds

Clinical Trials FDA Approval Process

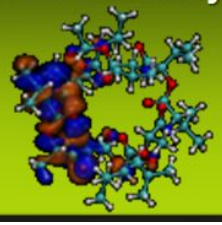
Synthesize new Chemical Compounds

Robot-assisted screening *High Throughput Screening*

Testing for Efficacy, Side Effects, Safety

Computational Chemistry

- Synthesize compounds based on similarity

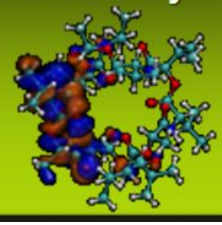


Virtual Screening

- Check if compounds bind to target proteins

Lead Optimization

- Modify chemicals to improve efficacy



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Source: https://blogs.nvidia.com/blog/2010/01/22/accelerating-the-pace-of-drug-discovery-using-gpus/

AI and Drug Discovery: Deeper Insights, Quicker Results

Drug discovery comes at a very high cost, but success brings significant benefits to mankind. A breakthrough drug can cure a critical disease for hundreds of thousands of patients across the globe and can earn the company making the drug billions of dollars in revenue.

That is why, just to bring one of the breakthrough drug to market, companies spend hundreds of millions of dollars on decades on a single avenue of research, not knowing where the research will bear fruit. This deep exploration of potential false avenues brings with it the potential for a tremendous amount of wasted time, money and effort.

But this research landscape is changing. Machine learning, unencumbered by human intuition and armed with vast quantities of data, can cut down on waste by prioritising research.The reliability of of AI-driven drug trials lies in the fact that hypotheses are generated not from occasional human epiphanies but from masses of cold hard data, yielding less wasteful hypotheses.

Drug companies have already been using artificial intelligence to decide in advance whether, for example, it is worth investigating whether a particular drug might bind to a particular protein. But there is trend toward ever more advanced estimates, such as how the same drug might subsequently affect a patient’s cells or tissues.

AI for Drug Discovery and Biomarker Development

- Applying AI for Advanced R&D, Biomarker Development and Drug Discovery will bring the most disruptive impact on the business model of the Pharma and entire Biotech industry.

- Specific attention should be paid to those projects capable of applying Next Generation Artificial Intelligence techniques, Deep Learning and in particular GAN's (generative adversarial networks) and reinforcement learning for:
  - Drug Discovery and Drug Repurposing
  - Biomarker Development
  - Clinical Trials Predictors
  - Aging Research
  - AI Solutions in convergence with Blockchain

- The leading players in this specific niche can become new game changers for entire market and significantly influence the capitalization of pharma companies.

Source: https://www.technologynetworks.com/drug-discovery/lists/4-toxicology-approaches-in-drug-discovery-294488

Emerging Trends in AI for Drug Discovery

- Today, drug discovery is a trial-and-error process that eats up enormous amounts of research time. AI can significantly narrow the focus of researchers by rapidly assimilating and analyzing the information in public and proprietary databases.

- Beyond scanning health records to help providers identify chronically ill individuals who may be at risk of an adverse episode, AI can help clinicians take a more comprehensive approach for disease management, better coordinate care plans and help patients to better manage and comply with their long-term treatment programmes.

- The use of AI is enabling review and translation of mammograms 30 times faster with 99% accuracy, reducing the need for unnecessary biopsies.

- Researcher Frost & Sullivan said artificial intelligence systems will generate $6.7 billion in global revenue from healthcare by 2021, compared with $811 million in 2015.

- In 2018, even more extreme challengers and disruptors will arrive with the convergence of next generation AI, blockchain and precision medicine.

- The global healthcare AI market is highly fragmented and is characterized by the presence of large number of industry players, while the AI for Drug Discovery segment has a comparatively lower level of competition because this market segment only accepts companies with very high levels of expertise. There are more than 300 AI in Healthcare companies, but only 30 of them are capable of entering the AI in Drug Discovery sector.

- The breakthroughs in AI for Drug Discovery will change the R&D process of Bio Pharma, and it will make tremendous impact on whole BioPharma industry.

- That is why the players from the AI for Drug Discovery market can become new game changers and significantly influence the capitalization of pharma companies.

Where is AI for Drug Discovery Heading?

The broad field of AI in Healthcare has already experienced a significant rise over the past several years, especially in the application of computer vision, text analysis and chatbot technologies. These techniques, first developed in the IT sector, have been effectively repurposed for the healthcare sector.

However, the use of AI in Advanced R&D is limited to companies and researchers with very high levels of expertise. This creates a specific scarcity for AI specialists in this niche.

2018 is expected to become the year in which AI will be recognized as the most powerful driver of progress in solving the crucial challenges of the most advanced sectors of science and R&D in the healthcare and Biotech industries.

The use of AI in Advanced R&D, Biomarker Development and Drug Discovery will make the most disruptive impact on the business model of the Pharma and entire Biotech industry. This is why the players in the AI for Drug Discovery market can become new game changers and significantly influence the capitalization of pharma corporations.

The efficiency of research and development (R&D), defined as the number of successfully approved drugs given the budget allocated to new drug development, has declined for decades. The cost of drug discovery and subsequent development is a massive challenge in the pharmaceutical industry.

A typical drug can cost upwards of $2.5 billion and can take a decade or more to identify and test a new drug candidate. Today, only about one in ten drugs that enter phase 1 clinical trials reaches patients. Drug makers need to find a more efficient way of developing medicines. AI can speed up drug discovery, cut R&D costs, decrease failure rates in drug trials and eventually create better medicines.