Sujet traité : La révolution biotechnologique : l'innovation à l'oeuvre! / The Biotech Revolution : Innovation Unleashed! (Part 1)

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INNOVATION THEMES & STRATEGY

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The Biotech Revolution: Innovation Unleashed! (Part I)

In This Report

The biotech sector is emerging as a hub of innovation primed to disrupt the $12 trillion healthcare industry. Biotech holds immense potential to revolutionize clinical care, pharmaceutical development, diagnostic accuracy, and improve overall healthcare efficiency. Yet, biotech's most transformative impact will be equipping healthcare professionals with new "tools" to prevent diseases rather than just treating them. This is a monumental paradigm shift in clinical practice that is beginning to make enhancing human longevity attainable. Medicine is on the brink of its most significant transformation in modern history.

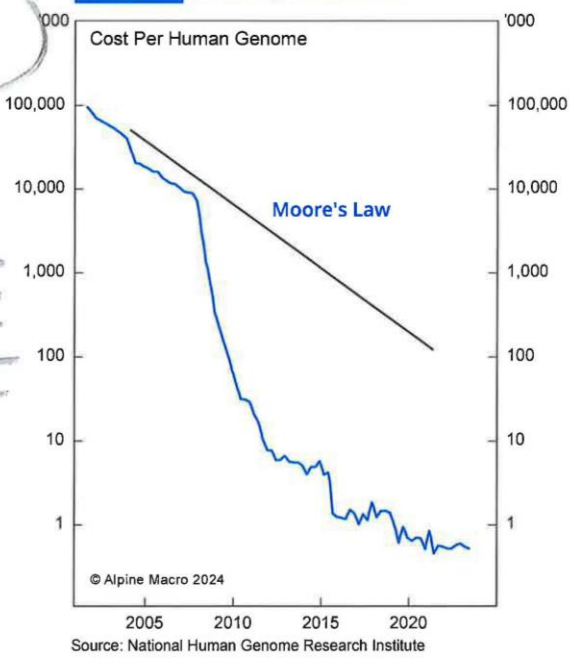
"Today, by some estimates, science is adding about three months to your lifespan every year. In the near future, additional scientific breakthroughs will extend your lifespan by more than a year for every year you remain alive."

- Ray Kurzweil, Co-Founder of Singularity University and Futurist at Google

Analogous to all emerging exponential technologies, biotech is successfully achieving milestones as it accelerates down the demonetization and democratization curves. The cost of sequencing a complete human genome exemplifies this perfectly. Since 2002, the cost has exponentially declined 3x faster than Moore's Law; from costing $2.7 billion (Human Genome Project) to less than $500 today (Sanger Institute) (**Chart 1**). Soon, every human's genome could be affordably sequenced at birth.

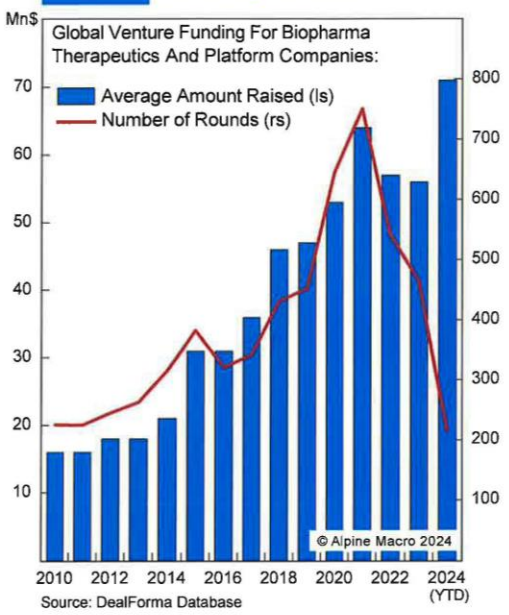
We are initiating a two-part series covering biotech's disruptive potential. Today's report will cover the key drivers for the biotech revolution and will focus on

Chart 1 Decoding The Genome



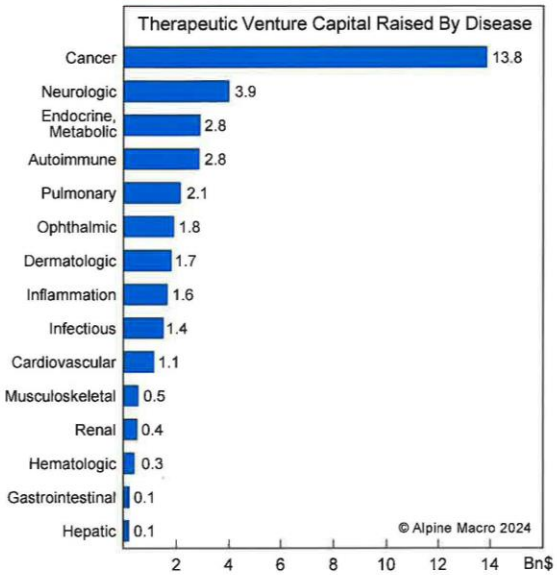
Source: National Human Genome Research Institute

Chart 2 VC Funding Rebound



Source: DealForma Database

Chart 3 VC Funding Allocation By Type Of Disease



Source: DealForma Database

emerging AI-powered technologies leading biotech innovation. Key AI-enabled technologies include next-generation diagnostic screening, predictive analytics, robotic surgery, and AI-powered drug discovery/development.

Next week, part two will examine genomics across targeted therapeutic formulation, novel delivery mechanisms, and regenerative medicine. Part two will conclude with our key investment considerations on the biotech sector.

While nascent and subjected to above average volatility, biotech provides long term risk-tolerant investors unparalleled access to disruptive investment opportunities. We believe that in the intermediate to long run, small-cap biotech companies will benefit from equity leadership "broadening out" and the "soft landing" outlined in our Equity Strategy reports.[1] Biotech companies positioned at the cutting edge are profoundly changing healthcare and have the potential to become some of the most transformative companies in the world.

Biotech's Comeback Story

After a challenging couple of years following the pandemic boom, biotech began showing signs of life again last year despite volatile equity performance. For example, the FDA approved a record 73 new therapies – proof of accelerating innovation in the sector. M&A activity also steadily rebounded from post-pandemic lows, with 22 deals valued at $1 billion or more – 2x the number in 2022.

1 Alpine Macro *Equity Strategy* "The most Misunderstood Bull Market" (July 3, 2024) and Alpine Macro *Equity Strategy* "How to Make Money in Small Caps" (June 26, 2024).

Chart 4 Healthcare Wages Resistant

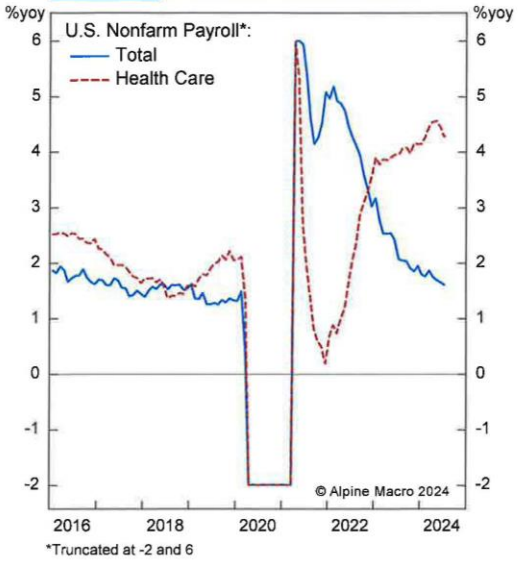
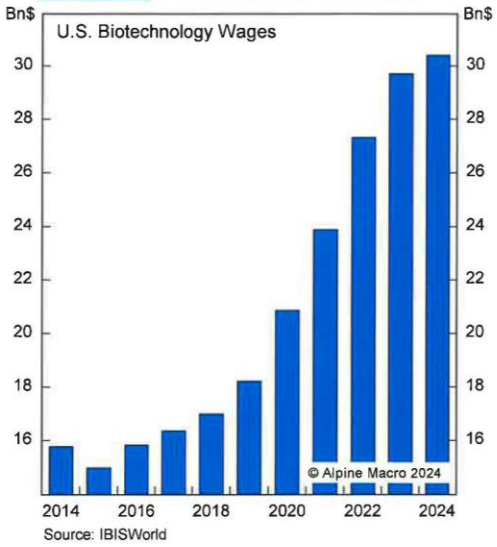


Chart 5 Biotech Salaries Increasing



We believe that continued positive momentum in the first half of this year indicates biotech is at an inflection point. Compelling evidence includes:

- Biotech venture funding is surging. In the first half of 2024, average biotech venture funding round sizes reached an all-time high (**Chart 2**). Specifically, 25% of all series A rounds topped $100 million while the average series A round totaled $80 million – more than double the average five years ago (**Chart 3**).

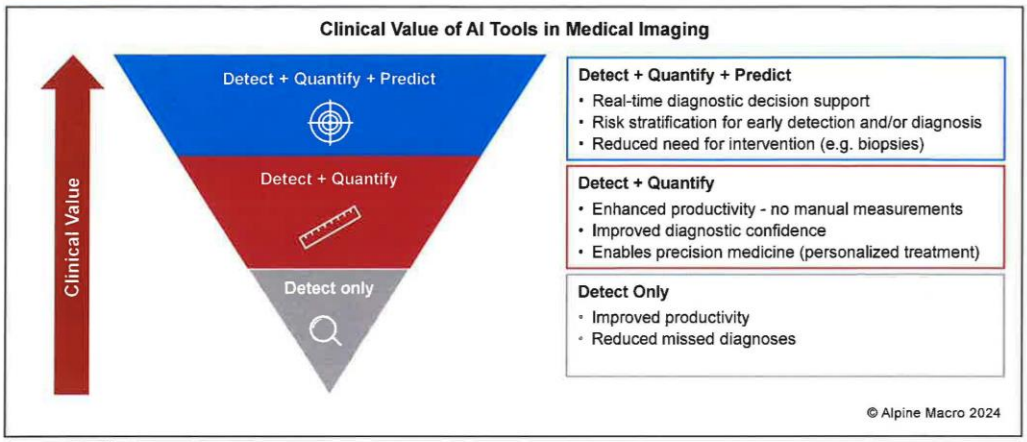
- The prospect of the Fed dropping interest rates is a huge tailwind. Indeed, a recent KPMG survey of healthcare and life sciences leaders highlighted that high interest rates have been the largest inhibitor of M&A activity in the healthcare space. Historically, large-cap pharmaceutical companies have been reluctant to engage in small-cap biotech M&A when interest rates are high.

- Big pharma has record "dry powder" ready to be deployed. A recent EY report outlined that big pharma companies have about $1 trillion to spend.

- The public biotech market is rebounding. Capital raised via the eleven biotech IPOs in the first half of 2024 has already surpassed both 2022 and 2023 totals.

- The healthcare sector in general is also displaying signs of economic resiliency. Health services payrolls remain robust and are growing at a faster rate than the rest of the economy (**Chart 4**). Biotech payrolls are also on an upward trajectory, increasing 10.7% per year on average since 2019 (**Chart 5**).

Chart 6 AI's Value In Diagnostics



Source: Signify Research

AI Is Driving Biotech

Biotech is emerging as a contrarian AI play. While the "AI hype" seems glued to almost everything in today's market, we strongly believe that AI will have a disproportionately positive impact on biotech compared to other sectors. Investors see the potential, as approximately 200 "AI-first" biotechs have secured more than $18bn in funding in the last decade, according to consultant BCG. Many of AI's most immediate and tangible effects are emerging in the healthcare sector.

In 2023, ChatGPT passed all three parts of the U.S. Medical Licensing Exam. This accomplishment was a defining moment for AI's role in healthcare, as it proved that a general-purpose AI model could demonstrate human-level complex medical reasoning.

The growing aggregation of holistic health data is an AI development treasure trove. Aside from general purpose AI development, access to niche healthcare data allows researchers to create specialized AI models trained on focused data sets. These models are playing a key role in accelerating biotech breakthroughs, driving biotech cost declines, improving diagnosis accuracy, and facilitating intelligent therapeutic targeting.

We believe AI's four largest impact areas in biotech are next-generation medical diagnostics, predictive analytics, robotic surgery, and drug development.

Next-Generation Medical Diagnostics

Leveraging AI to analyze data from innovative imaging techniques, tests, blood assays, and sensors is transforming medical diagnostic capabilities. First and foremost, AI is improving disease detection accuracy by reducing human error while also accelerating diagnosis speed and increasing screening accessibility. Most importantly, AI-powered screening is beginning to unlock disease detection prior to symptom expression (Chart 6). This is critical, as many

diseases are currently "falling through" screening cracks, preventing timely disease treatment at early stages. For cancer patients, most symptoms arise in stage-3 or stage-4, when the chances of full remission are vastly reduced. Early detection is key to transitioning healthcare from reactive to proactive treatment approaches.

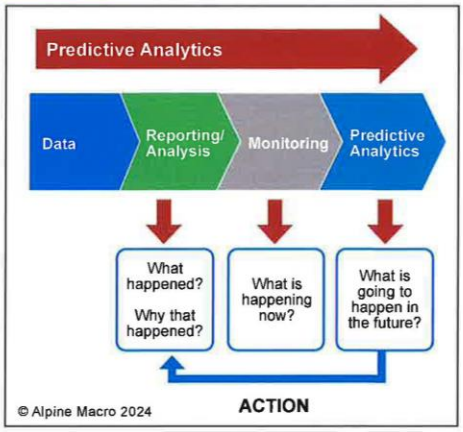
Equally as important, specialized AI detection models coupled with next-generation data is increasing medical bandwidth to test for more diseases – many of which currently fly under the radar or have no developed test at all. Take cancer for example, currently 70% of all cancer types that are fatal are not routinely tested for using today's approaches.

AI's impact on diagnostics is wide-ranging. Several compelling examples include:

- Startup PathAI is using AI in pathology to improve diagnostic development. The company has a range of specialized AI-powered tools including solutions in oncology, liver diseases, and inflammatory bowel disease. PathAI's machine learning and computer vision technologies enhance diagnostic accuracy by 20% and cut errors by 25% compared to conventional methods.

- Medtronic has created an FDA cleared AI-powered computer-aided detection system to identify pre-cancerous and cancerous colorectal polyps during a colonoscopy. Dubbed GI Genius, it improves polyp detection by catching small, flat polyps that can easily go undetected by the human eye in real time. GI Genius' trial results reduced missed colorectal polyps by 50% compared to a standard colonoscopy.

Chart 7 Predictive Analysis Flow Chart



- Radiology is another area being disrupted by AI. According to the American College Of Surgeons, "research shows that scan interpretation from AI is more robust and accurate than those from radiologists, often picking up small, rare spots in the images." A Swedish study of 80,000 women found a single radiologist utilizing AI identified 20% more cancer cells than two radiologists using traditional methods. In another example, Aidoc's FDA-cleared AI radiology platform reduces the time of diagnosis by up to 50%, while boasting a 95% sensitivity rate for flagged findings.

Predictive Analytics

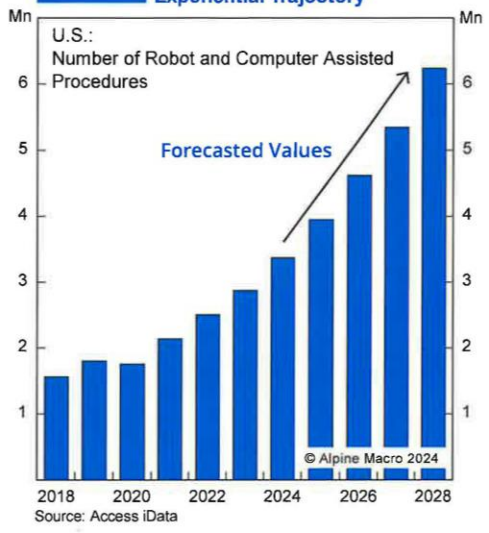
Predictive analytics evaluates historical and real-time data to make predictions about the future. In the healthcare sector, predictive analytics can be highly accurate due to the quality and volume of available data. Data including electronic medical records, health claims data, radiology images, lab results, and patient wearables are driving more accurate predictive analytics by the day (Chart 7).

A range of healthcare applications are set to benefit including preventative care, management of chronic conditions, public health strategies, and healthcare resource allocation. Importantly, predictive analytics is primed to be a key driver to reduce healthcare costs by improving patient treatment, reducing hospital length of stay and readmission rates.

Examples of predictive analytics being leveraged include:

- Unity Health is developing a data environment encompassing clinical, medical imaging, and waveform data from monitors and ventilators to power a predictive analytics platform. The project aims to constantly ingest data in real time to predict when a patient could begin to show symptoms. For example, predictive analytics from ventilator data could flag when a patient could have trouble breathing in the near future. In another example, Sharp HealthCare's predictive clinical analytics model identifies patients at risk of needing an intervention from the rapid response team in the next hour with an 80% accuracy.
- Penn Medicine has developed a collaborative data platform to help predict and prevent sepsis and heart failure – two of the most common and costly issues for hospitals. The model identifies about 85% of sepsis cases as early as 30 hours before the onset of a septic shock (as opposed to two hours using traditional methods). For heart failure, the model identifies between 20-30% of heart failure patients who have not been properly identified.
- Hospitals are using predicting analysis to improve resource allocation and cut costs. For example, a big data predictive analysis platform helped a large hospital group save $120 million in annual costs (about $12,000 per patient) while boosting facility utilization by 5%. Another large hospital has reduced readmission occurrences by 6,000 cases through identifying patients with a high readmission risk at the time of diagnosis.

Chart 8 **Robotic Surgery Adoption On Exponential Trajectory**



Robotic Surgery

While robotic surgery feels like science-fiction, it is one of the most advanced applications of automation in healthcare. Robots have been used in surgery for over 20 years. That said, recent advancements in sensors, advanced materials, and vision systems have brought robotic surgery to the inflection point of widespread surgical integration (**Chart 8**). Already, a wide range of solutions exist from robots capable of performing surgical subtasks to even entire surgical procedures.

Advancements in robotic surgery technology now allow surgeons to feel as though they are operating with their own fingers while increasing surgical precision and reducing human error. The result is often a quicker, less invasive procedure. For example, for an open kidney transplant, patients can return to work and normal activities within a few weeks rather than over eight weeks from traditional surgical methods.

Examples of advanced robotic surgery include:

- Intuitive Surgical's (ISRG) da Vinci robot enables skilled surgeons to operate remotely. da Vinci has directly been involved in over 10 million procedures to date. Recently launched da Vinci 5 has a computing power 10,000 times greater than its predecessor and boasts sensitive feedback controllers that reduced tissue force by 43% in preclinical trials.

- Medical Microinstruments' novel robotic Symani Surgical System has created the world's smallest wristed medical microinstruments for open surgery. The system can reconnect blood vessels as small as 0.3mm and remains the only commercially available system in the U.S. for reconstructive microsurgery. Symani is uniquely positioned to perform highly intricate procedures – an area of great need due to the looming shortage of specialized surgeons.

AI-assisted robotic surgery is positioned to take robotic surgery to the next level. AI is beginning to impact surgical approaches by improving precision, reducing invasiveness, and shortening patient recovery timelines. Importantly, AI-robotic platforms could learn exponentially from continuously performing surgery and studying data, expediting the autonomous surgery learning curve. Autonomous robotic surgery can also leverage infrared and ultraviolet imaging capabilities to guide highly accurate surgical movements.

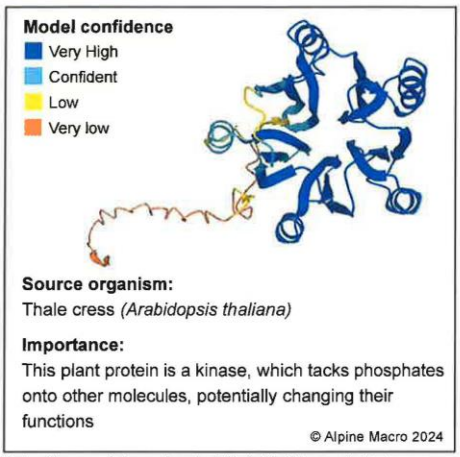
While use cases remain limited, the AI-robotic surgery synergy is beginning to show promise. Recently, the startup Perceptive performed the first fully autonomous dental procedure using their AI-powered robotic system. Perceptive combines 3D imaging, AI, and robotics into a specialized surgical package to complete crown placements in just 15 minutes, eight times faster than a human dentist can.

AI-Powered Drug Development

AI's most disruptive impact on healthcare could come from turbocharging drug discovery and development. The current approach to pharmaceutical development is vastly outdated and extremely costly. Currently, it can cost more than $2.5 billion (sometimes up to $12 billion) and take over 10 years to bring a new drug to market. Failure rates are extremely high, as over 9 out of 10 drugs entering Phase I clinical trials will never actually reach patients.

We are in the early stages of a major pharmaceutical transformation. An era is emerging where AI-powered drug discovery will make developing new therapeutics quicker, cheaper, and more effective. Although no AI-derived compound has been approved for human use thus far, at least 73 compounds are under development, according to the WHO.

Chart 9 AlphaFold Protein Model



Note: The confidence level of AlphaFold's predictions vary within each protein. Dark blue and light blue regions on a predicted structure mean the algorithm is relatively sure. Less certain predictions are colored yellow and orange.

The foundational tools for AI-powered drug discovery began to take shape in 2018 when DeepMind released AlphaFold (known as the ChatGPT moment for biology). AlphaFold is an AI algorithm that predicts protein structures (a scientific feat often compared to mapping the human genome). In May of this year, AlphaFold-3 was released, improving prediction accuracy by at least 50% compared to previous iterations and expanding capabilities past proteins to the complex world of DNA, RNA, and biomolecules (**Chart 9**). AlphaFold is the bedrock of AI therapeutic development, as it allows researchers to dynamically model molecular interactions. Specifically, it can forecast how proteins alter their shape when interacting with other molecules, which is essential for drug design. This is already providing priceless information to accelerating treatment development for the most challenging illnesses. This could save trillions in failed drug development and accelerate clinical use.

Drug development is being revolutionized from the ground up. Exciting examples include:

- Insilico Medicine developed the first drug fully generated by artificial intelligence to enter human clinical trials. The drug, INS018_055, treats a chronic disease that causes scarring in the lungs, affects about 100,000 people in the U.S. and can lead to death within two to five years. Insilico's leading generative AI drug discovery platform uses Generative Adversarial Networks (GANs). GANs consist of two parts: a generator that creates new data (like new molecules) and a discriminator that evaluates and test them.

- Verge Genomics is focusing on using and creating AI-Developed drugs to treat neurodegenerative diseases. Verge's platform maps disease mechanisms and discovers new therapeutic targets. Results have reduced drug candidate identification time by 50%. The company is a global leader in the formulation of treatments for complex neurological conditions and has several compounds in preclinical development.

Stay tuned for part two of our biotech series that will be published next week under our ITS banner. Part two will cover genomics, regenerative medicine, and our long-term investment considerations for the biotech sector.

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