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Q&A With Luba Greenwood on Healthcare Innovation

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At Global X ETFs, we believe a chart is worth a thousand words, and then some, when it comes to our changing world. Charting Disruption, our annual thematic research project, depicts the disruptive themes changing our world through charts, graphics, and much more. While the topics of the four main sections, including Personalized Medicine, A Greener Economy, Experiential Technologies, and FinTech, Blockchain, & Web3 are each unique, they are connected by innovation and the ability to transform the world.

To explore the depth of these changes, Global X ETFs' Research Team partnered with handpicked experts from academia, consulting, and investing. Below, we discuss driving forces behind healthcare innovation with Luba Greenwood. Luba is a veteran biotech and pharmaceutical executive – the CEO of Kojin Therapeutics, Managing Partner of Binney Street Capital, Dana-Farber Cancer Institute's Venture Capital Fund, and a Harvard lecturer in the School of Engineering and Applied Sciences. Luba also previously held leadership roles at Google Life Sciences (Verily) and Roche.

The medical industry has made great strides in improving patient care, though an estimated 350 million individuals worldwide have an undiagnosed disease, and we still fall short in effectively treating a wide variety of illnesses.[1] Recent developments are encouraging rapid innovation and play a key role in the transformation of the healthcare industry as we know it.

1. We saw a significant push towards rapid response for COVID-19, where the public got a very in-depth view of genomics and drug development. Where are we in healthcare now?

Biotech is in a transformational period where innovation has no bounds. We're developing novel tools, collecting data in new ways, and discovering new insights that guide us on where and how to accelerate innovation moving forward. We are now beginning to crack the code on human biology, which is quickly changing the way we think about clinical development of medicines. The global pandemic was an excellent example of how the industry can rapidly leverage genomic insights and novel technologies to develop impactful vaccines and drugs.

The previous mindset of treating illnesses has been largely ineffective. For example, we still don't know what causes Alzheimer's and only 8% of cancer patients can be treated with mutation-specific therapies.[2] Through the advent of new genomic technologies, that is beginning to change. Companies are rushing to understand causes of diseases and formulating highly targeted treatments across a variety of disease areas.

Data interoperability and leveraging artificial intelligence (AI) and machine learning (ML) capabilities adds an additional layer of opportunity in the industry. This shift is enabling healthcare to develop therapies faster with a 20-40% reduction in costs for clinical development of biotechnology drugs.[3]

2. The Human Genome Project started in 1990 with the goal of mapping all the genes in the human genome. The project concluded in 2003 with about 92% of total human genome sequenced. Only in 2022 were scientists able to use new

technology to decode the remaining 8%. What's the next frontier in biotech and life sciences as a whole?

The next frontier, and where innovation will come from for the next 10 years, is unlocking new biology. The developments that human genome sequencing have granted, will now allow the industry to start making a new host of medicines that go after the cause of illnesses rather than its symptoms.

We've already seen developments in the tools, like CRIPSR, to address genetic mutations. We've found new delivery methods, including mRNA, which we saw with the COVID-19 vaccines. We've also discovered new modalities, as with cell and gene therapies.

Applying these insights and tools to find new biology that plays a key role in how illnesses progress will be another major step forward. That's our goal at Kojin Therapeutics. Until recently, we thought that cells die by only one mechanism, apoptosis. This is when cells die as a normal part of an organism's development. Our scientists discovered that they can also die by ferroptosis, a cell death where a large amount of iron is unleashed allowing for lipid peroxidation to occur. We have also cracked the code on how to induce and prevent that ferroptosis, which is relevant for chronic diseases like Alzheimer's in which neuronal cell death causes dementia.

In cancer, scientists have harnessed our understanding of cell death to kill cancerous cells. Historically, they've relied on apoptosis, but we've found cells build up resistance to this type of death and many patients become resistant to current treatments. More effective, alternative methods of inducing cell death to treat cancer offers a viable treatment option for the oncology community, particularly patients who are not good candidates for mutation-specific therapies.

The discovery of ferroptosis has potential far beyond oncology. At Kojin, we have invested deeply into our platform capabilities and now can effectively modulate ferroptosis in a variety of therapeutic areas. Ferroptotic induction is key in cancer, inflammation, immunology, and autoimmune diseases while prevention of cell death plays a central role in neurodegeneration. We can leverage these insights to generate transformative therapies for patients.

3. What are the key challenges in the life sciences, and how is the industry adapting to overcome these challenges?

A longstanding challenge in therapeutics is achieving stronger translation of AI/ML tools, data sources, and preclinical models into successful and efficacious therapies in the clinic. Currently, AI is only scratching the surface to generate actionable insights in the medical community. As we continue to feed greater amounts of biological data into these AI models, we'll achieve higher quality insights that will unlock the underlying cause of disease and ways to intervene to improve patient outcomes.

Another challenge in therapeutics is that although we call biotech a risk-taking business and investment, a lot of healthcare companies still go after the same pathways or repurpose generics or marketed drugs. Only innovative approaches will make a real difference to patients. The companies that take risks to discover something truly revolutionary will be the players that win out.

In diagnostics, we've seen exciting developments in the early detection of cancer via liquid biopsy. It's great to see healthcare embracing home tests and different delivery models. But with cancer, most patients still find out too late, at Stage III and beyond, where the cancer has grown and spread. Liquid biopsy offers significant promise in addressing these issues. Instead of performing an invasive biopsy and removing tissue, blood samples collected non-invasively can enable earlier detection. This is the sort of paradigm shift that we look to achieve in the treatment space, which disrupts the standard landscape while having enormous value to patients.

4. How has macroeconomic environment, including inflation, rising interest rates, and stock market volatility performance, affected fundraising in life sciences? How are firms adapting to a changing economic environment?

This year will go down as a difficult year for fundraising in biotech. Theories as to why run the gamut—the economy, inflation, the Federal Reserve, short sellers, high valuations, the sheer number of IPOs (Initial Public Offerings), or some combination thereof. As a result, some investors lost appetite for risky early-stage assets in favor of clinical-stage companies. Others shifted focus from cross-over and later-stage investments in favor of Private Seed and Series A and Bs.

The good news is that these factors should only have short-term impact. I expect high quality novel science, regardless of stage of development, will still find funding and be successful. Healthcare spending as a percentage of GDP keeps climbing, and patients with chronic diseases are living longer. We are only at the beginning of unlocking human biology, so I am bullish on the life sciences sector in the long run.

5. M&A activity was high in 2020, and it held steady in 2021. In 2022, M&A slowed. How do you expect the M&A strategies to evolve for large pharma?

The slowdown in M&A is only temporary, in my view. Appetite for acquisitions in the industry remains strong, and low valuations and fewer financing options for public and private companies suggest that a pickup is likely. Also, we know that large pharma relies on small biotechs to drive innovation, whether through outright acquisitions, research and development (R&D) collaborations, or licensing deals.

External R&D makes sense for large pharma. The ideas mostly come from leading academic centers, spun out of labs into start-ups where whole teams are built around one novel scientific idea. Only one in 10 ideas succeed, but that one has all the ingredients for success, including the right science, team, and focus.[4] Funding for smaller biotechnology startups also plays a key role, with significant investment dollars in R&D for startups.

A combined 66% of drugs sold by large pharma are sourced via external R&D, though they do rely on multiple business development strategies to collaborate with small biotech firms and academic centers.[5] Product and corporate acquisitions will continue to be popular, though I expect large pharma to rely on R&D collaborations less given the current economic background and resulting large up-front payments.

Though business development deals across the board should pick up in 2023, deals with lower upfront payments and earlier-stage firms will be particularly popular. In particular, certain therapeutic areas, such as immunology and autoimmune will be an area to watch for deal activity.

6. What needs to happen to lower the cost of making medicine?

In short, better R&D efficiency. It's a simple answer to a complex question, but it's proved elusive for too long. To achieve this goal, a multipronged approach is required: increasing availability and utilization of digital tools; employing more and better data; widely using modeling and computational analysis to identify new targets and predict efficacy and toxicity; using biomarkers to identify patients who would benefit from targeted medicines; and using a focused approach to enroll patients into clinical trials faster.

Digitization, real-world evidence (RWE), AI, even synthetic arms have been talked about as cost controls measures for many years. And there's no shortage of players in the space, both big and small, to make it happen. And yet, R&D is still not run as efficiently as it should.

To truly drive down costs of novel therapies, the healthcare industry will need to breakdown silos amongst its key players to build true R&D efficiencies and reduce development costs. At a firm level, pharmaceutical firms can help drive this change by forming multidisciplinary teams to help leverage

insights and capabilities across divisions and partner with innovative AI-driven biotech companies and innovators in the space.

Footnotes

1. Illumina. (2022). Genetic & rare disease: Empowering early discovery and intervention.
2. Cutler, D, M. (2020, January 14). Early returns from the era of precision medicine. Jama Network.
3. Morgan Stanley. (2022, September 9).Research: Why artificial intelligence could speed drug recovery.
4. The latest on drug failure and approval rates. Science. (n.d.). Retrieved December 5, 2022, from Pont, L. B., Fleming, B., Robke, L., Smietana, K., & Wurzer, S. (2022, May 31). Innovation sourcing in biopharma: Four practices to maximize success. McKinsey & Company.
5. Pont, L. B., Fleming, B., Robke, L., Smietana, K., & Wurzer, S. (2022, May 31). Innovation sourcing in biopharma: Four practices to maximize success. McKinsey & Company.

Glossary

Real World Evidence (RWE): clinical evidence about the usage and potential benefits or risks of an investigational therapy derived via real world data. Real world data in healthcare is data derived from clinical trial participants in real-world settings, including wearable sensors, electronic medical records, health insurance claims, and patient-reported data.