AllianceBernstein®

The Synthetic Biology Revolution

Investing in the Science of Sustainability

The revolutionary technology of synthetic biology is poised to make a profound impact on the way a vast array of products are manufactured, from lab-grown meat to cosmetics to biodegradable packaging. Yet investors are still paying relatively little attention to the huge business potential. In this paper, we explain the science and show how its growing impact on more industries will create exciting opportunities for equity investors.

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If the technology for making diabetes medicine hadn't changed since the 1930s, today we'd need an area larger than the surface of the earth for raising pigs, harvesting insulin from their pancreases to help hundreds of millions of diabetics around the world.

That isn't necessary because of a breakthrough in the 1970s: the invention of synthetic biology. Scientists at start-up Genentech found that inserting the human insulin gene into a yeast cell encouraged the production of that critical protein for treating diabetes. This pioneering application of synthetic biology spawned the biotechnology industry, which now harnesses the power of DNA to produce a growing number of life-changing medicines.

Today, we're just scratching the surface of this revolutionary technology. What started in the healthcare industry is expanding into many sectors. Over time, synthetic biology is likely to make a profound impact on our world by changing the way a vast array of products are manufactured, from lab-grown meat to cosmetics to biodegradable packaging. McKinsey estimated in a May 2020 report that as much as 60% of the global economy's physical inputs could be made using synthetic biology, resulting in direct economic benefits of at least $1.7 trillion between 2030 and 2040 (*Display 1, left, next page*).

How does synthetic biology work and why does it matter for equity investors? In this paper, we'll lay out the basics of the science. We'll show how exponential cost curves and a convergence of powerful technologies are accelerating progress in synthetic biology and rapidly expanding into new applications. In our view, the growing impact on industries will create many attractive investment opportunities, while the global push for sustainability will add catalysts for adoption. Like the internet revolution, companies that enable or effectively harness synthetic biology will thrive, challenging existing profit pools for incumbents. Simply put: investors can't ignore the broad, disruptive potential of synthetic biology.

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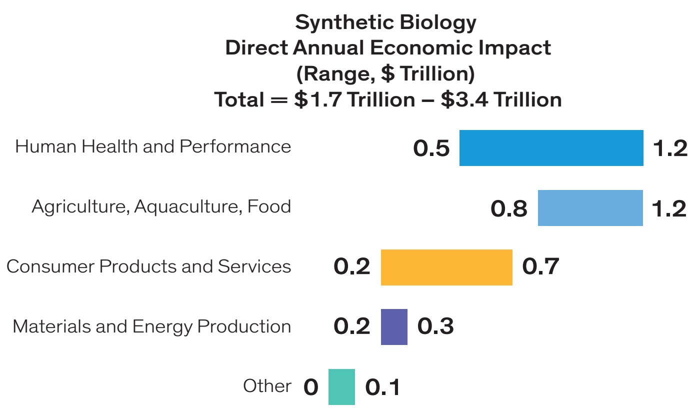
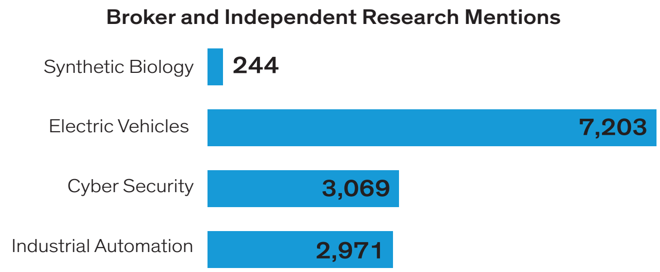
DISPLAY 1: SYNTHETIC BIOLOGY: SCANT RESEARCH COVERAGE DESPITE HUGE POTENTIAL





Past performance and current analysis do not guarantee future results.

***** These impact estimates are not comprehensive; they include only potential direct impact of the visible pipeline of applications identified and assessed. Estimates do not represent GDP or market size (revenue), but direct economic impact—broader knock-on economic effects are not included. Estimates are relative to the 2020 economy; they do not include changes in variables such as demographics and inflation. Numbers may not sum to total due to rounding.

† Broker and independent research mentions refers to the number of times the themes have been referenced in broker or independent research over the past two years.

Left chart as of May 13, 2020. Right chart as of October 15, 2021 | **Source**: AlphaSense, McKinsey Global Institute and AllianceBernstein (AB)

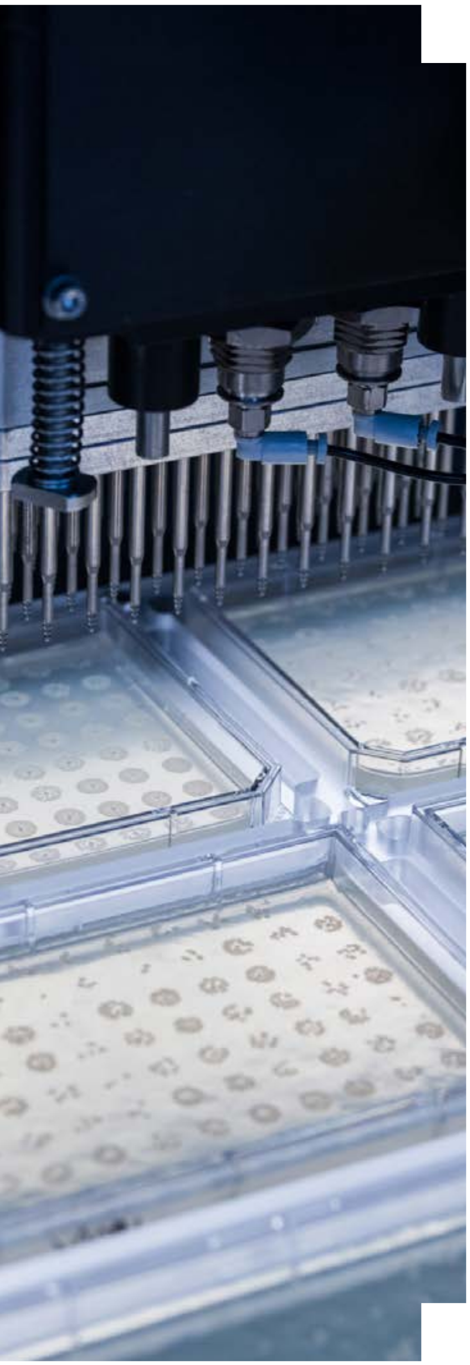
Our research suggests that synthetic biology is still receiving relatively little attention from investment analysts despite its huge potential (*Display 1, right, above*). Many investment firms will struggle to access that potential, because asset managers' typically siloed sector research isn't well-suited for the cross-sector changes synthetic biology will unleash. Portfolio managers will need to collaborate across industries while applying fundamental research to new products, companies and markets to capture this transformative investment opportunity.

The last major advancement in material science occurred at the turn of the 20th century with the invention of plastics as a byproduct of oil.

That's about to change. From using CO_2 in the air as a production input to creating completely biodegradable products, synthetic biology will transform the environmental footprint of our daily lives, fueled by the drive for sustainability. While the technology has risks, we believe that it will open a world of new ideas that equity investors can't even imagine today.

Over a decade ago, we began researching the potential for plummeting DNA sequencing costs to revolutionize the healthcare industry. That research spawned powerful investment ideas, and DNA is taking a great leap into many more industries; we believe this genomics revolution is just getting started.

The Science: Harnessing the Cell as a Factory



A colony picker, used to identify new bacterial strains that can create new products

Photo courtesy of Ginkgo Bioworks

Biology—what happens inside living organisms—starts with a genome, a long strand of DNA made up of base pairs of nucleotide "letters" A, T, C and G. Think of them as a four-letter alphabet spelling out instructions for your body's cells, or as similar to the 0 and 1 binary computer code. DNA is the programming language of life.

DNA is organized into genes, which contain a specific pattern of the nucleotide letters A, T, C and G. The gene for hair color, for instance, will inhabit a specific stretch of your genome with a particular DNA pattern. Differences in the base pairs within our genomes make us different, in everything from appearances to health outcomes.

When these biological instructions are needed, DNA is transcribed into RNA in a cell. RNA is similar to DNA, like a mirror image or biological photocopy of the specific stretch of genome. This piece of RNA is then translated into a specific pattern of amino acids, which are the building blocks of proteins. It's the fundamental process in biology: DNA is transcribed into RNA, which is translated into proteins.

Proteins perform many functions in your body. Your hair gene contains base pairs of DNA that will be transcribed into RNA and translated into a protein—in this case, pigments that determine hair color. Proteins can also function as antibodies, the part of your immune system that recognizes viruses like the coronavirus that causes COVID-19.

This basic biological process also occurs in non-human cells, including plants, animals and less complex living organisms like bacteria. Yeast cells, for instance, contain DNA that encodes for a protein (an enzyme) that breaks down sugar and turns it into alcohol—a key part of the brewing process. Genentech inserted the human gene for insulin into the yeast cell DNA. When fed and kept in a comfortable environment, those yeast cells went through the same DNA-to-RNA-to-protein process. The final result was insulin fit for treating diabetics. This is one example of how synthetic biology works, and how biotech drugs are "brewed."

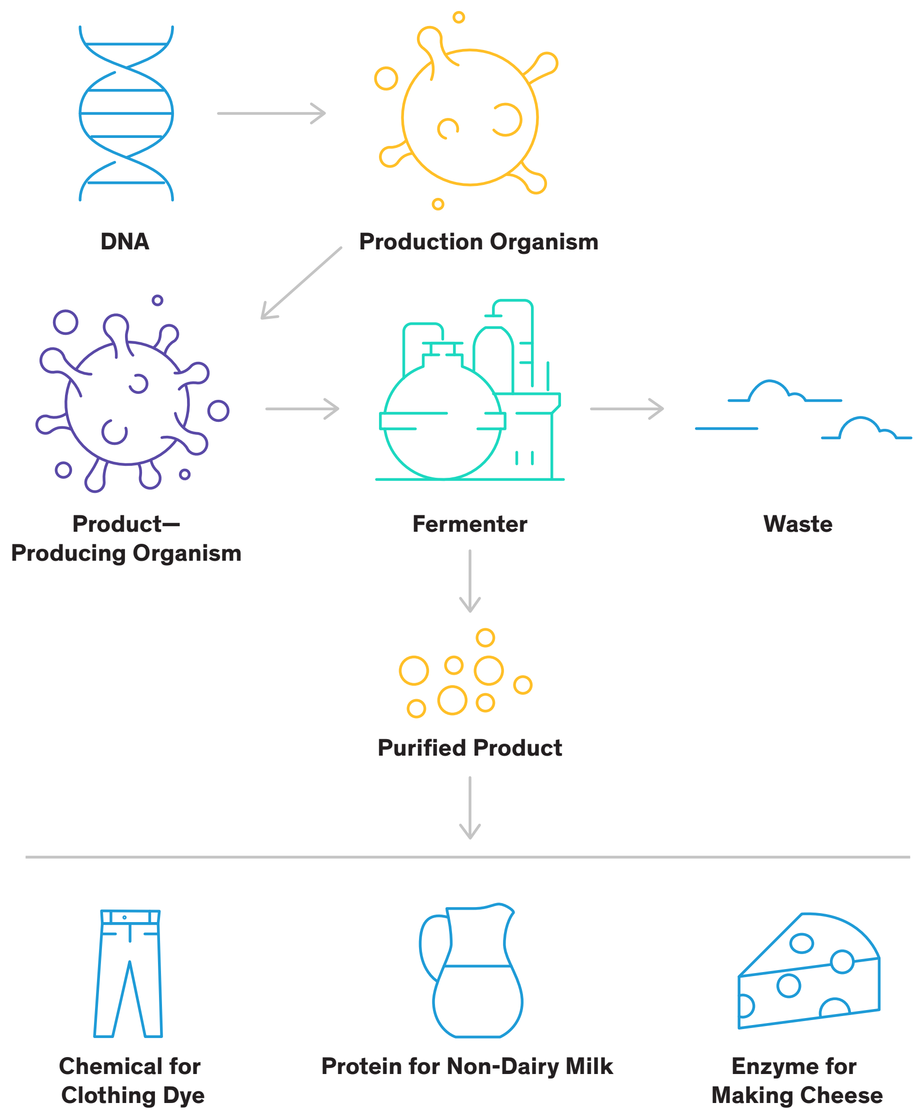
In recent decades, synthetic biology research has built on Genentech's invention, developing new products beyond human-protein medicine. Non-human genes can be added to cells, such as yeast cells, which can then produce useful materials. The relevant gene from a clam or mussel can be expressed in a bacteria cell to produce an adhesive, for example. And entirely new genomes can be built to produce new proteins like enzymes—catalysts in changing one molecule into another.

The enzyme that yeast produces, alcohol dehydrogenase I, converts glucose to alcohol. New enzyme proteins designed from scratch can convert one molecule into another. Pharmaceutical researchers created an enzyme that breaks down the Artemisia annua plant to yield anti-malarial compound artemisinin. This approach lowered production costs, enabling drugmakers to expand access to the critical life-saving medicine around the world. Multiple enzymes can even be linked in a chain of production. Picture a tire manufacturing line. One enzyme converts rubber into a circle, another cuts the tire treads. These enzymatic processes link to create an end product.

Synthetic biology products are physically produced in a brewery-like environment. In a typical process, the production organism cells (yeast, for instance) are grown and fed, and the downstream output (purified protein, for example) is harvested (*Display 2*).

One example of synthetic biology applied outside the biotechnology industry is squalene, a natural moisturizer found in many cosmetics. Your body's skin cells produce squalene, but production slows down as you age. Historically, this cosmetic ingredient was obtained from shark livers, leading to the slaughter of millions of deep-sea sharks annually to satisfy demand. That is, until California-based Amyris discovered a way to produce squalene using synthetic biology, which became commercially available in 2011. The company genetically engineered a yeast cell that could ingest sugar cane and produce squalene more cheaply and sustainably than shark harvesting.

DISPLAY 2: HOW DOES SYNTHETIC BIOLOGY WORK?



Source: AOCS, Good Food Institute and AB

Technology Convergence: Unleashing the Power of Gene Sequencing

Exponentially developing and converging technologies are turbocharging the pace of discovery and new product development in synthetic biology. Thematic investors are often attracted to trends like these because people tend to underestimate the longer-term result of exponential growth, which challenges familiar linear thought processes.

Think about computing. Decades ago, the power of today's computers was unfathomable. But decades of Moore's Law at work, with chips' processing power doubling every two years, opened vast markets for computing at ever-lower prices and entirely new applications. Early predictions about the ultimate sales volumes of computers or cell phones have proved laughably low. New applications have created enormous new markets and shareholder returns for businesses like Google, Amazon and Facebook.

Liquid handling robots used to automate high-throughput screening of biological samples
Photo courtesy of Ginkgo Bioworks

Over the past two decades, the price of reading DNA, referred to as DNA sequencing, has declined faster than Moore's Law would imply (*Display 3*). The price of reading a human genome has declined by a factor of roughly one million—from hundreds of millions of dollars in the early 2000s to hundreds of dollars today. This progress has greatly accelerated discoveries linking DNA to protein and function, unearthing new ways to deploy synthetic biology.

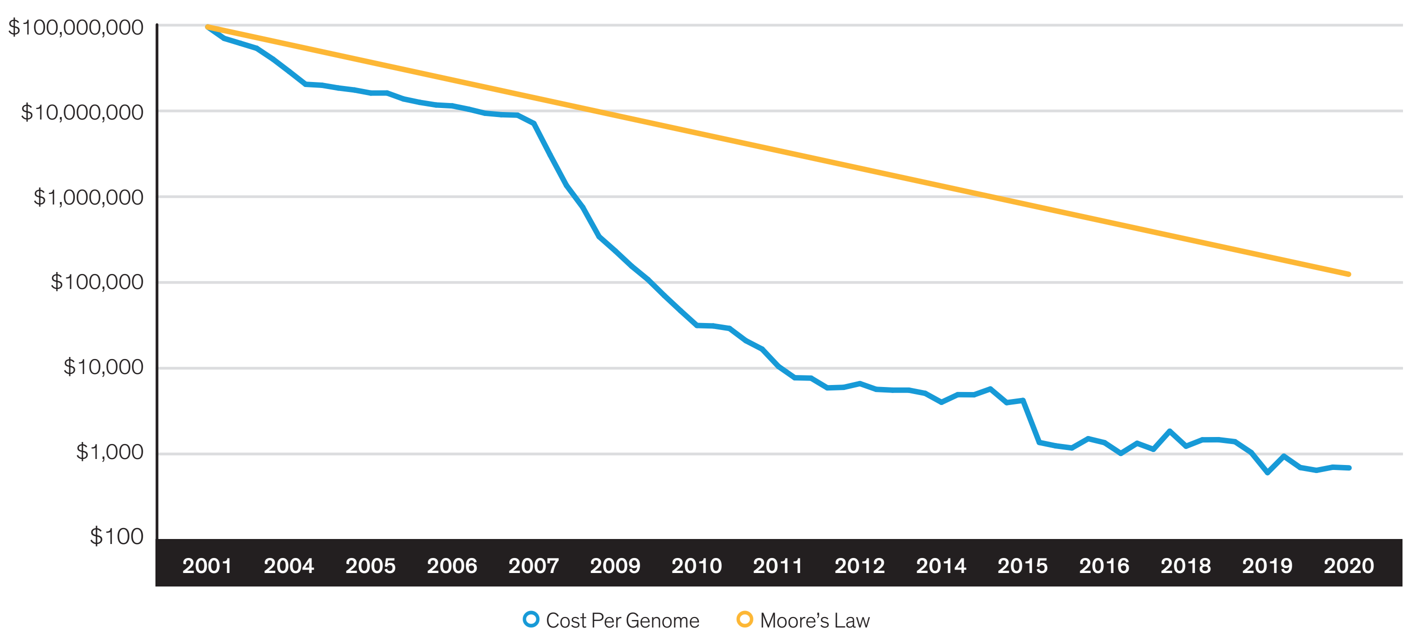
One result of ever-cheaper DNA sequencing is a fast-growing trove of genomic data, and the ability to process that data has improved. The human genome contains roughly 3 billion base pairs. In 2012, researchers at the University of Leicester printed out a single human genome on paper: it filled 130 books that would take an estimated 95 years to read. Today, analyzing genomic information is much less daunting because of advances in big data such as cheap processing power and data-science tools like artificial intelligence and machine learning. Armed with these superpowers, scientists can recognize patterns, linking DNA changes to bodily functions and health outcomes.

In addition to DNA sequencing and computing costs, the price of creating new DNA from scratch, called DNA synthesis, is also rapidly declining. When Genentech inserted the insulin gene into a yeast cell, it needed the human gene and DNA. Researchers can now order cheap stretches of DNA online, uploading the string of A, T, C and G that they want. This advance enables entirely new experiments: What if a slightly different version of the insulin gene were inserted into the yeast cell? What other genes and proteins can a yeast cell produce?

If DNA is the programming code for life, reading DNA is akin to passively consuming information on your computer. DNA synthesis, in contrast, is using your keyboard to create something new. Until recently, DNA synthesis was prohibitively expensive. Imagine how different our lives with computers would be if pressing a single key on your keyboard cost $5. Then imagine how empowering it would be if that price fell to 5 cents—and ultimately to a negligible cost. That's an illustration of the power of cheap, easy DNA synthesis.

DISPLAY 3: GENE SEQUENCING COSTS HAVE DECLINED FASTER THAN MOORE'S LAW

DNA Sequencing Costs



Past performance and current analysis do not guarantee future results.

Moore's Law states that the number of transistors on a microchip doubles about every two years.

As of August 31, 2020 | **Source**: National Human Genome Research Institute

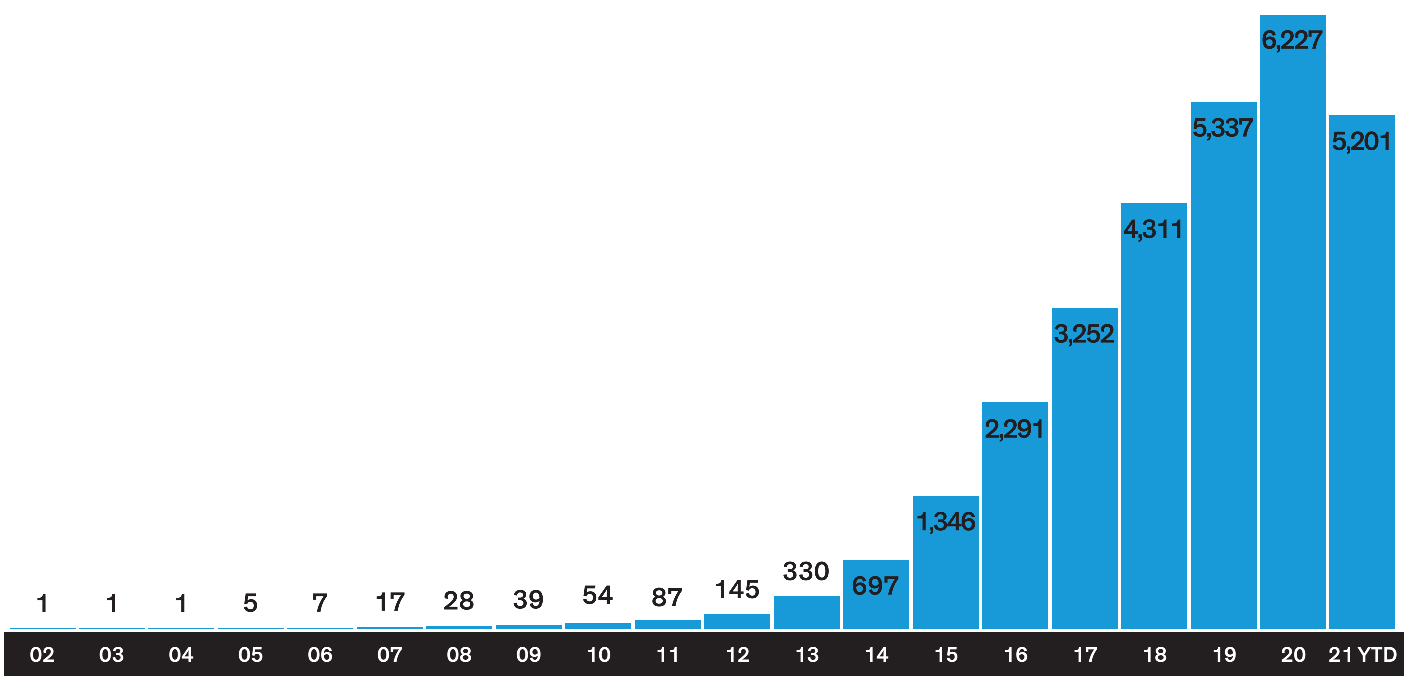
Genomics and synthetic biology, in addition to enjoying exponential cost curves, is benefiting from the recent discovery of a tool for cheaply and accurately altering an existing genome. Called gene editing, it's like the copy/paste function in Microsoft Word. And it's so easy to use that anyone can order a gene-editing kit online and experiment in their own home. Researchers can now take that 130-book genetic tome and make precise changes to it, inserting new DNA they've created and watching what happens.

In genomics, one of the most challenging questions is how to link millions of genetic differences to their actual meaning in terms of body function. Until recently, researchers were "stuck" using existing genomes, hoping to learn from the small number that featured rare mutations. They would experiment with single cells such as a bacteria, bombarding the genome with radiation to induce random changes. Compared with current capabilities, this process is like watching monkeys type randomly on keyboards until a coherent piece of writing emerges.

Now, with gene editing, scientists can make a targeted change in a genome and then observe. Research into gene editing technology is becoming pervasive—mentioned in more than 6,200 scientific publications in 2020, compared with less than 100 a decade ago (*Display 4*). It has transformed the field from observing differences to engineering alterations, turbocharging our ability to understand DNA and manipulate physical matter. Researchers aren't limited by nature's genomes or proteins anymore. The potential combinations of amino acids that can form proteins vastly exceeds the number of atoms in the universe. Cheap DNA sequencing and synthesis, data analytics, and gene editing have unleashed a modern-day gold rush to discover the next blockbuster synthetic biology product.

DISPLAY 4: GENE EDITING TECHNOLOGY RESEARCH IS MUSHROOMING

CRISPR* Research Publications Per Year



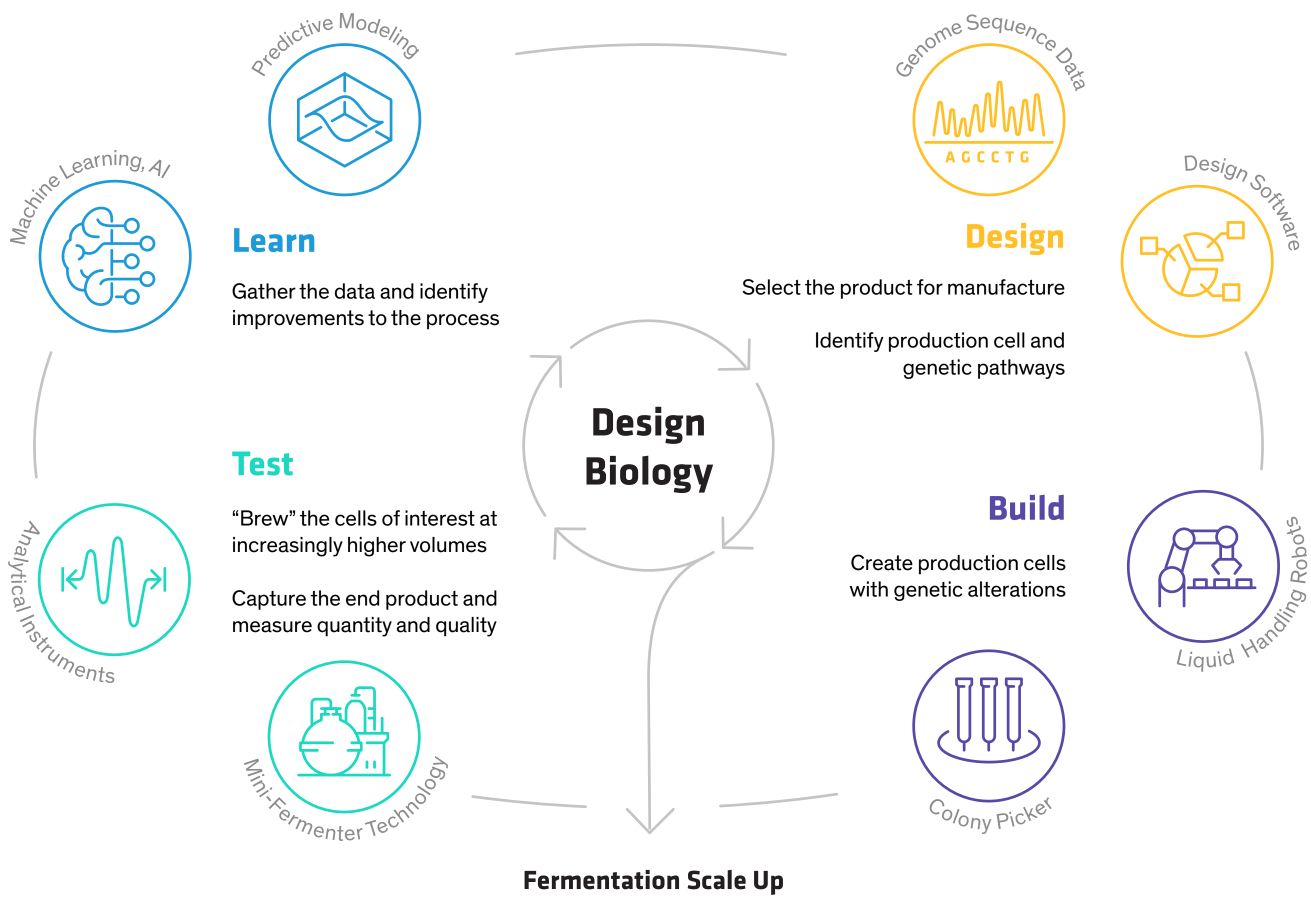
Past performance and current analysis do not guarantee future results.

*****CRISPR is a gene-editing technology.

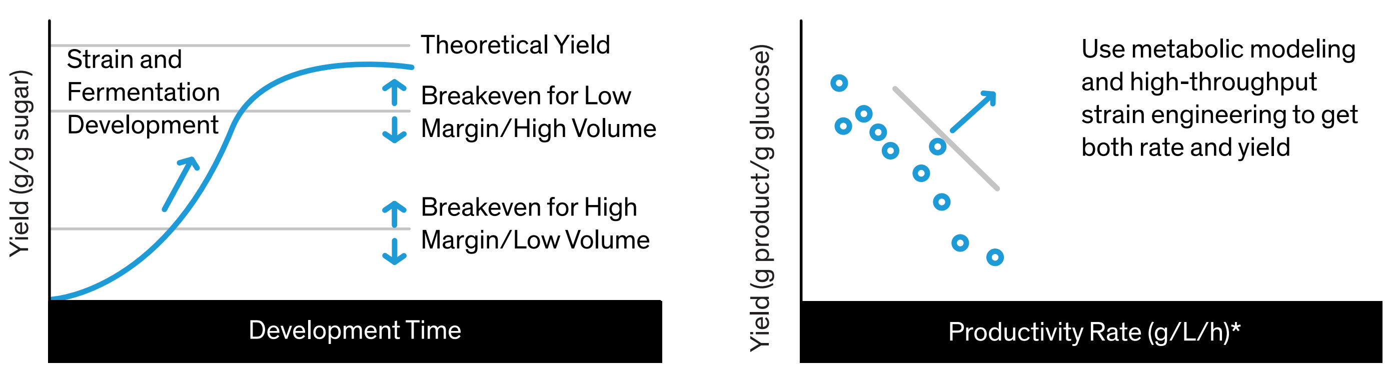
As of September 24, 2021 | **Source**: National LIbrary of Medicine: National Center for Biotechnology Information

DISPLAY 5: TECHNOLOGICAL ADVANCES AMPLIFY THE POWER OF ENGINEERING PROCESSES

Design-Build-Test-Learn Synthetic Biology Engineering Process



High-Volume Glucose Products: Production and Yield Benefits of Synthetic Biology



* Grams per liter per hour.

Source: Archer Daniels Midland and AB

Converging technologies (DNA sequencing, DNA synthesis, gene editing and artificial intelligence) that are additive lead to results that are larger than the sum of their parts (*Display 5, upper graphic, previous page*). Without the power of big data, interpreting DNA data would be nearly impossible. Without gene editing and synthesis technologies, scientists would be limited in how far they could explore new genetic possibilities. We can see the benefits by looking at an individual project for designing a cell that can take a specific feedstock—in this case, sugar—and transform it more efficiently into an end product (*Display 5, lower graphic, previous page*). This illustration from multinational food processor Archer Daniels Midland, shows how the converging drivers of synthetic biology are making the technology more competitive with traditional manufacturing methods.

There are examples from other industries—Uber, for instance. The firm sits at the convergence of ubiquitous smart phone adoption and cheap GPS technology—its "magic" is tracking the cab you hailed on your phone while you wait. Netflix is another great example. Started as a mail-order service for DVDs, the company really took off when ubiquitous broadband adoption offered fast enough internet to stream videos right to your TV, with sophisticated software that suggests personalized content. Likewise, the convergence of technologies in synthetic biology will surely create some of tomorrow's big new companies.

What does all this mean for investors?

Cost declines and discoveries in synthetic biology will shrink profits for disrupted incumbents, while creating opportunities for new leaders. Projections for the promise of synthetic biology can't be based on today's cost and technological capabilities when both are progressing rapidly. This includes the pace at which synthetic biology penetrates products and industries outside healthcare. Based on our scouring of broker research and company news articles, synthetic biology is not a hot topic—so investors are likely underestimating its impact.

Like many transformative technologies, synthetic biology is a "trend break"—a shift in profit pools among companies. Because this disruption will undermine incumbents, investors should beware of focusing on large benchmark firms that reached their size and stature on the back of yesterday's innovations and technologies. However, this process will likely take place over many years, so its impact won't be captured in detailed one-to-two-year forward broker forecasts. This is precisely the bias and variant perspective thematic investors seek to exploit.

From Personalized Medicine to Personalized Everything

As mentioned earlier, the biotech industry was an early adopter of synthetic biology. The impact of that technology on medicine provides perspective on the potential disruption as it spreads to other sectors.

Synthetic biology has completely transformed the nature of industrial scale in the medical industry, including drug discovery. Historically, drugmakers would screen as many compounds as possible against a targeted disease to generate "hits" that might indicate effectiveness. Pharma companies would scour the globe for natural compounds such as flowers from Madagascar, tree bark from North America and snake venom from Africa. The more compounds screened, the higher chance of success. This approach was successful for many years—until synthetic biology flipped it on its head.

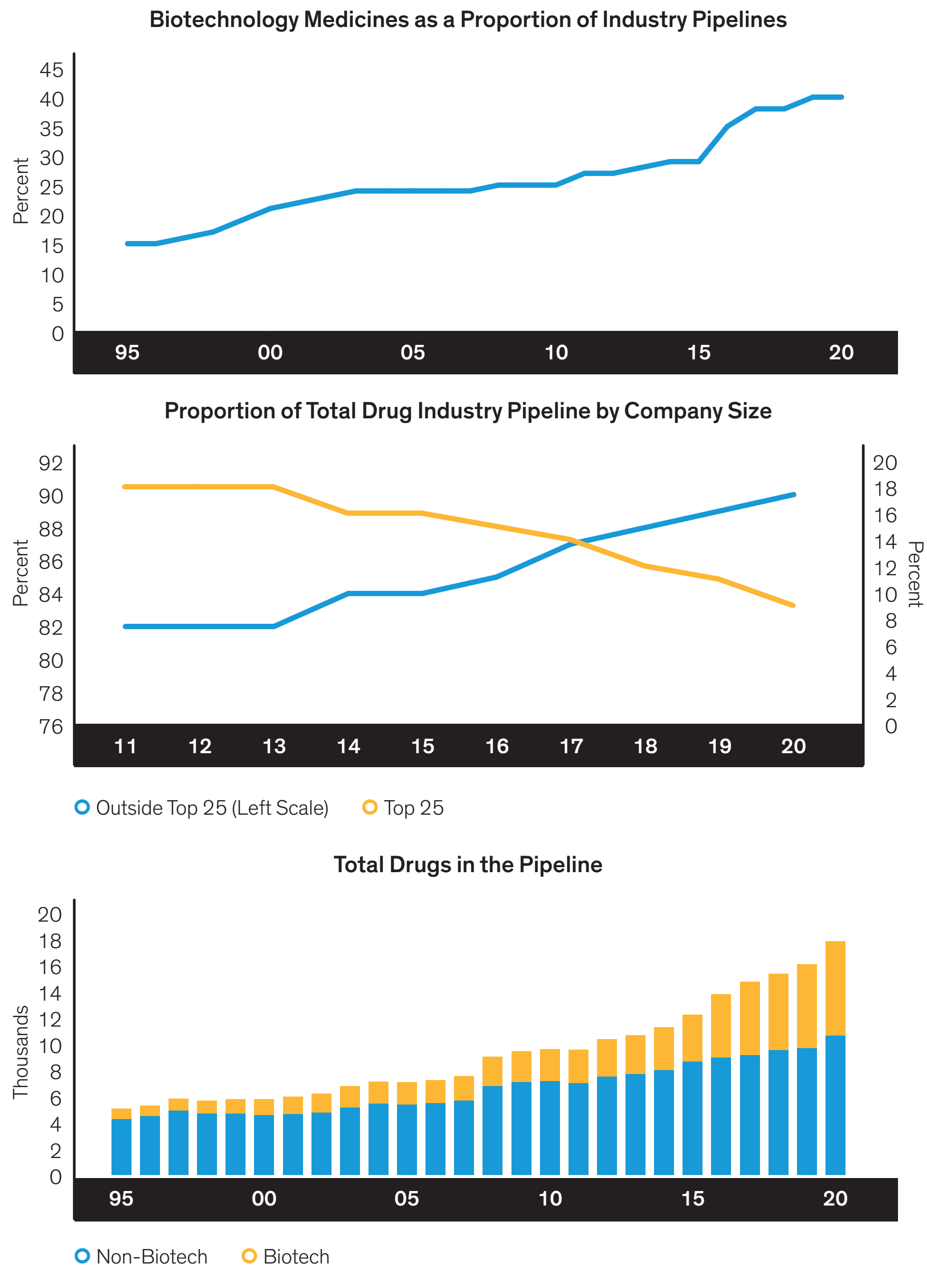
These days, researchers can tailor proteins to the targeted disease, bolstering drug efficacy and speeding discovery. We all witnessed Moderna's lightning creation of a prototype mRNA-based COVID-19 vaccine, just days after the genome sequencing of the novel coronavirus in 2020. What's more, under the old pharmaceutical model, the scale required for screening and marketing a mildly more effective product made searching for targets against rare diseases uneconomical. Today's new biotech tools have changed the calculus, enabling companies to profitably design treatments for rare diseases that affect a smaller number of patients.

Photo courtesy of Ginkgo Bioworks

The industry is also moving slowly toward designing completely personalized medicines for individual patients.

This will transform how medicines are sold. Fewer armies of pharma sales reps will buy pizza for doctors' offices and hand out branded pens to generate prescriptions for thousands or millions of patients. Instead, drugs will increasingly target specific patients, with genetic tests guiding doctors to the most effective therapies. New biotech medicines had no presence in the drug industry's pipeline when they emerged in the 1970s; today, they account for more than 40% of that pipeline (*Display 6*). In this flourishing ecosystem, smaller biotech companies are eagerly adopting new genomic technologies. Smaller pharmaceutical developers today account for roughly 90% of the drugs in research pipelines. Large pharma incumbents are feeling the pressure of this thematic disruption dynamic.

DISPLAY 6: BIOTECH IS REDEFINING THE MARKET FOR MEDICINE



Past performance and current analysis do not guarantee future results.

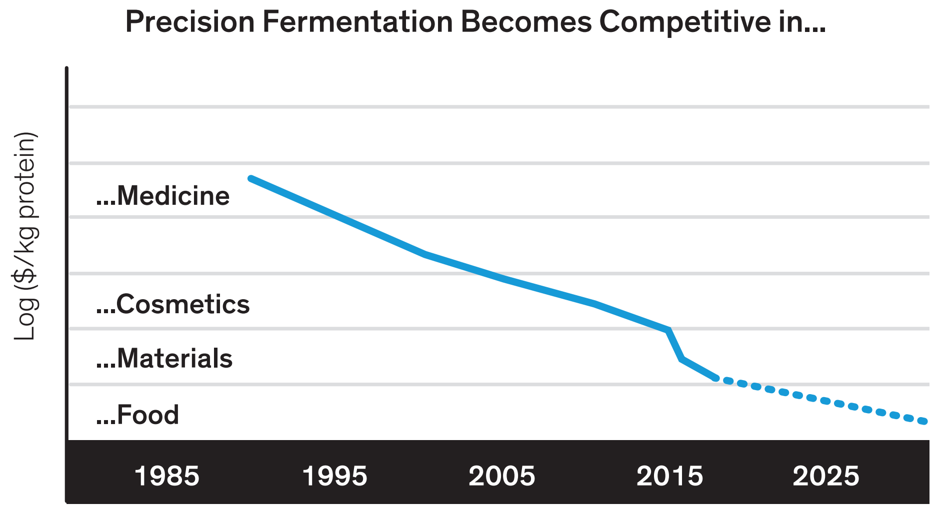
As of February 28, 2021 | **Source**: Pharmaprojects®—Informa, 2021

Dress designed by Stella McCartney using Microsilk™, replicating the silk fibers produced by spiders

Photo courtesy of Bolt Threads

On a per-kilogram basis, biotechnology drugs are among the most expensive products in the world. However, as the cost of synthetic biology (also known as "precision fermentation") keeps falling, more and more products and industries will face disruption (*Display 7*).

DISPLAY 7: SYNTHETIC BIOLOGY IS DISRUPTING MORE INDUSTRIES AS COSTS FALL



Past performance and current analysis do not guarantee future results.

As of September 2019 | **Source**: RethinkX

Fermenter used in a biotech laboratory
Getty Images

Moving Beyond Biotech

What will be the impact of synthetic biology outside of biotech?

Synthetic biology is spreading rapidly from the biotech industry to higher-value niche materials and ingredients. Examples include additives, scents, flavorings and texturants in packaged food or personal care products. In a classic pattern of disruptive technologies, synthetic biology has gained a toehold in niche products, enabling it to fly under the radar and be ignored by industry incumbents thriving on larger markets.

Historically, the notion of scale in the materials industries was represented by manufacturing capacity. Companies with the largest factories could apply their fixed costs over a larger production volume, providing greater economies of scale and pricing leverage versus competitors. Synthetic biology also inverts that notion of scale, riding the rapidly declining costs of DNA sequencing and computing. Powered by the efficiency of synthetic biology, the technology can reach price parity with traditional manufacturing methods at ever-lower production quantities.

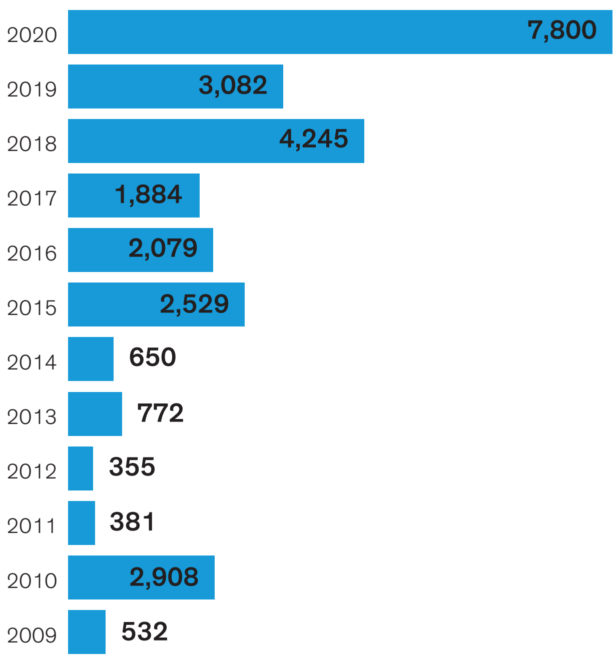
That parity is already arriving in a growing number of materials markets. Eventually, as the technology enables manufacturers to produce smaller volumes at the same price, innovation is likely to explode. In the past, scale was key—the volume of the same product was the primary metric. Tomorrow, smaller production batches will facilitate the development of materials for smaller volumes of applications. Just as new medicines target specific genomes, food ingredients might be developed for hyper-specific markets and applications, making products both more effective and more appealing for consumers who increasingly value personalization and variety.

Pharmaceutical and biotech companies typically invest a high proportion of sales into research and development (R&D). This spending has ramped up as companies race to keep up with accelerating industry innovation, and as declining barriers bring new entrants, helped by cheaper and easier synthetic biology technology. Likewise, companies in a wider array of industries may need to invest more into R&D as the focus moves toward products fit for purpose rather than a focus on manufacturing scale for larger-volume goods.

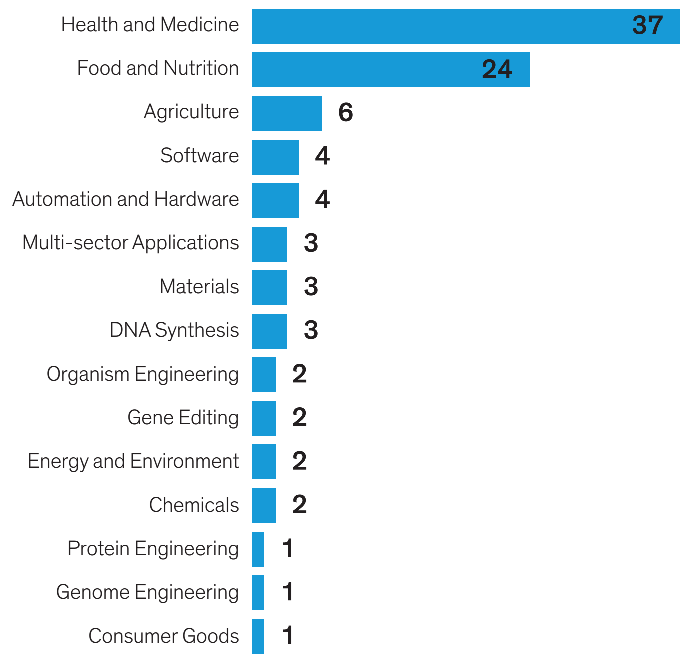
Greater adoption of synthetic biology may prompt realignment in supply chains, with materials companies moving further upstream to secure access to "feedstock" such as sugarcane, used to feed production cells during the manufacturing process. Conversely, other companies may move downstream, closer to the end product, through more innovation. Smaller and more efficient volumes could support manufacturing localization and improve the economics of materials production. In particular, this could help mitigate volatile "boom/bust" profit cycles caused partly by high fixed costs and large increases in capacity that may not be in sync with the pace of demand growth.

DISPLAY 8: INVESTMENT IN SYNTHETIC BIOLOGY HAS JUMPED

Synthetic Biology Funding (USD millions)



Deal Count by Industry (1H: 2021)



Past performance and current analysis do not guarantee future results.

Financing sources included are private, public and non-dilutive grant financing.

Left chart as of December 31, 2020. Right chart as of June 30, 2021 | **Source**: SynBioBeta

Funding for synthetic biology rose sharply in 2020, reflecting enthusiasm for new applications of the technology, including those in sectors outside healthcare (*Display 8*). As synthetic biology spreads to other industries and costs continue to decline, companies that enable this research and production—"pick-and-shovel" makers—will benefit, in our view. The power of genomics will be leveraged to help discover new products, as well as to improve the production cells' manufacturing efficiency.

We believe this "gold rush" will drive higher demand for DNA sequencing instruments and consumables.

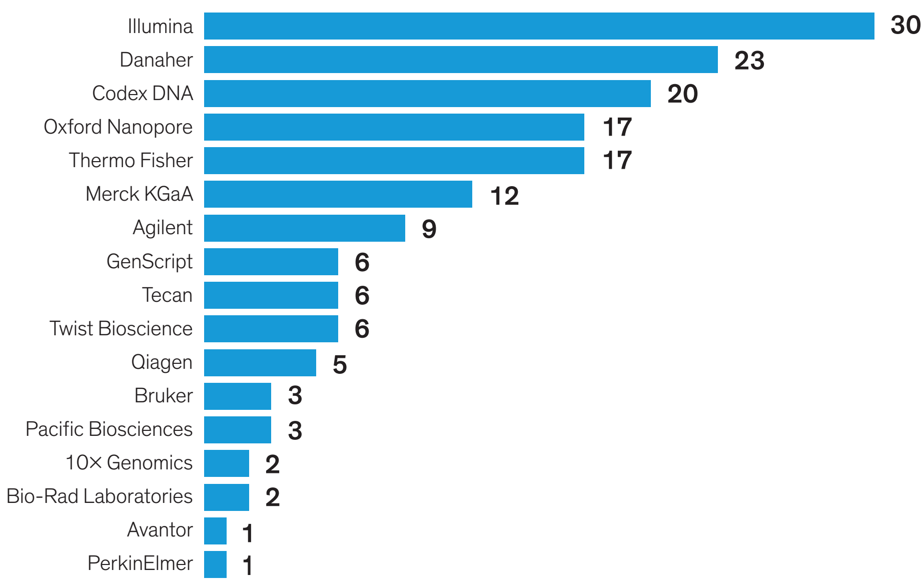
But researchers can't just throw a sample into the current generation of DNA sequencing instruments and get an answer. Many front-end steps are necessary to extract DNA and prepare it for sequencing.

The output of experiments must also be analyzed: What was the protein or molecule end product? And is it suitable for the application we had in mind? Other analytical technologies like chromatography and mass spectrometry will play a role. Moving samples around a lab between different testing modalities is becoming more efficient and accurate thanks to liquid handling automation equipment—essentially, robots for synthetic biology labs.

Partnering with AB's data science group, we built a proprietary tool that combs through synthetic biology research papers, identifying the specific products cited in research papers (*See "Big Data Provides Early Insight for New Applications" on page 15*). Mapping those products to vendors, we're identifying the most relevant publicly traded companies, using fundamental research to pinpoint attractive investment candidates (*Display 9*).

DISPLAY 9: PUBLIC COMPANIES ARE FEATURED IN SYNTHETIC BIOLOGY STUDIES

Number of Citations in Synthetic Biology Research Papers



Past performance and current analysis do not guarantee future results.

Based on a tool developed by AB's data science team, which scrapes the methods section of synthetic biology papers on bioRxiv and maps those vendors to public companies.

As of September 27, 2021 | **Source**: bioRxiv and AB

Popularity of SynBio Products by Frequency of Mentions

Big Data Provides Early Insight for New Applications

When researching a nascent technology like synthetic biology, investors must detect scientific developments with disruptive potential to get ahead of the market. But connecting the dots between academic research, nascent companies and promising products is no easy task.

Big data and artificial intelligence can help. Our data science team created tools to develop insight by scraping about 1,200 synthetic biology research papers published globally since 2014 and filed on bioRxiv, a public repository of scientific studies. Since the database contains peer-reviewed published papers and working papers, it includes ideas at the vanguard of the field—in some cases, years before industrial applications are developed.

After downloading the full text of each paper, natural language processing (NLP) was used to identify brands and products that are becoming more popular, targeting a group of 17 companies and their subsidiaries. To maximize detection accuracy, the system was designed to correct for spelling errors and variations in how academics refer to brands or companies. Products were targeted across the synthetic biology ecosystem, including assembly, gene sequencing tools and PCR, used to make copies of genes for research.

Findings are displayed in a dashboard that helps portfolio managers and analysts see which companies are playing a growing role in synthetic biology and monitor the evolving real-time popularity of companies, products and terms *(Display, above)*. With these advanced data tools, analysts can catch new developments early while tracking long-term trends. We believe these tools are essential for equity investors to uncover the strategic potential impact of synthetic biology across sectors and industries. Hard data gleaned from AI can complement a fundamental analyst's hypothesis and bolster conviction in an investment case.

From Burgers to Skis: More Products Embrace Synthetic Biology

Synthetic biology isn't science fiction. You may have consumed a product that contains an ingredient or material made using synthetic biology without even knowing. Companies are increasingly adopting synthetic biology not only to improve the quality and performance of their products, but to also make them more environmentally friendly. Here are some examples.

Burgers: Can a vegan burger feel like the real thing? The Impossible Burger uses heme, a protein normally found in blood, to create a pink color when cooked and a "meaty" flavor. To produce heme, the company inserts the gene from a soy plant into a yeast cell for fermentation.

Watch Straps: Using DNA from spiders, Omega produces an extraordinarily resilient watch strap. Its synthetic biology process produces spider silk and turns it into a fiber called Biosteel that's strong enough to catch a jumbo jet. It's also completely biodegradable.

Pet Food: Dogs might not be natural vegetarians. But Wild Earth has created a pet food based on a fungus-based protein that's healthier and more environmentally friendly than a meat meal. The company claims 92% of 3,000 customers surveyed say their dogs like the taste too.

Cement: The cement industry generates 8% of global carbon emissions. To replace cement, Biomason uses bacteria that mimics the growth of corals in nature. Its synthetic cement is three times stronger than real cement and generates much less pollution in manufacturing.

Skis: By fermenting algae, WNDR Alpine skis produces new types of oils to make and laminate high-performance skis. The process sidesteps the use of petroleum in manufacturing while providing the company with vertical integration and greater control over its supply chain.

Shifting Profit Pools Will Create Winners and Losers Among Adopters

Synthetic biology is a fundamentally new way of making things. Like any new transformative technology, there will be early and late adopters—and the performance divergence between the two will present opportunities for investors to achieve differentiated returns.

Consider how the internet changed the way companies sell products. Initially, start-ups won market share, aided by flexible business models that typically didn't rely on a fixed infrastructure of stores. Incumbent companies, meanwhile, are often locked into existing business models and supply chains. Eventually, later adopters caught on and invested more in internet-based selling. A similar trend unfolded much earlier with electricity, which took decades to achieve full adoption in factories despite providing enormous productivity gains. Switching costs can impede established businesses and delay adoption.

Where is synthetic biology today on that trajectory? Start-ups are harnessing synthetic biology to challenge industry incumbents across a growing array of end markets. New materials companies are developing synthetic biology-based products like nylon, vitamin E and vanilla flavoring. Cell-based meat companies are aiming to displace traditional meat products (*See "From Burgers to Skis: More Products Embrace Synthetic Biology," left*).

The timing and magnitude of industry disruption will depend on many factors, including the price elasticity of inputs, product development cycles and regulation, and consumer tastes. For investors, this means that a company-by-company bottom-up research process within sectors is needed to identify opportunities; simply investing in affected sectors or industries won't do. Think about how opportunities in the technology industry evolved over time—from semiconductor to personal computer manufacturers, then e-commerce followed by social media and gaming companies.

Synthetic biology's adoption probably won't happen in a straight line. But we expect it to be embraced in bursts as price points and technology developments open more applications and industry incumbents step up investment. In the automotive industry, falling battery prices, Tesla's success and environmental concerns have arguably prompted traditional carmakers to suddenly ditch small pilot projects and dive headfirst into electric vehicles. In synthetic biology, similar dynamics could shake up consumer product markets. As this theme develops in the coming years, we believe that active investing is crucial to harness the most promising opportunities at specific points in the synthetic biology ecosystem (*See "Investing Questions for the Synthetic Biology Revolution" on page 17*).

Investing Questions for the Synthetic Biology Revolution

Investing in early-stage technologies always presents unique challenges along with exceptional opportunities. Here are some questions that we think investors should ask to evaluate the potential of companies to benefit from synthetic biology.

Are products economically viable?

Synthetic biology attracted attention and funding in the early 2000s when companies tried to develop new biofuels. Despite the huge market potential, early synthetic biology–based products couldn't compete on cost with cheap and abundant natural fossil fuels. Some of those companies still exist and have become more selective with the materials, ingredients and enzymes in development. While synthetic biology costs are rapidly declining, production costs must be competitive with traditional industrial processes for a product to succeed.

Will consumers accept synthetic biology products?

Even products that make economic sense will face penetration hurdles. Verify whether companies and consumers will embrace products created from entirely new materials using synthetic biology.

Can companies overcome switching costs and supply-chain rigidity?

Some companies may struggle to adopt new synthetic biology manufacturing processes. It took decades for companies to fully integrate electricity in manufacturing due to the upfront costs and lower efficiency initially. Overcoming these challenges will help determine the pace of sales growth.

How will manufacturing be scaled up?

Scaling up manufacturing capacity of new synthetic biology products is a big challenge. Technical specifications of processes and access to production-scale capacity is an important consideration and often a large expense.

Will early adopters stay committed?

Investors should verify whether synthetic biology efforts extend beyond "proof of concept" or "pilot projects" as an indication of a company's commitment to the technology. Building internal expertise—R&D, corporate venture capital investments or synthetic biology partnerships—may signal a company's true early interest. Watch for red flags such as an incumbent company that shows no interest in synthetic biology when peers are racing ahead.

Is the price right?

As with any investment, valuation is crucial. Investors shouldn't just buy companies with the most exposure to synthetic biology or those getting media attention. Often, the best opportunities can be found in companies that are indirect beneficiaries of the theme, with attractive growth potential at a more reasonable price.

Photo courtesy of Genomatica

Manufacturing Is a Key Bottleneck

It's not all doom and gloom for larger materials incumbents.

A sustainable leather-like material called Mylo™, engineered from mycelium, a fungus that grows naturally

Photo courtesy of Bolt Threads

Discovering a new protein enzyme or a way to coax yeast cells into producing a useful product is one thing; increasing production quantities to commercial scale is a big challenge. Anyone who's tried to brew beer or bake bread at home knows that yeast cells must be fed and kept comfortable to be productive. New potential products from yeast fermentation must be weighed against the amount of material needed to feed yeast cells (at-home bakers keep a lot of flour in their pantry), and against the additional downstream waste brewing will create that must be filtered down to obtain the final product.

These and other factors are important to evaluate production costs versus legacy manufacturing methods. In some instances, existing manufacturing processes have been optimized over decades (or thousands of years in the case of agriculture/naturally grown products). Companies that have historically developed and produced biologic products like microbes and enzymes have valuable experience and data around optimizing genomic engineering to ensure economic production at commercial scale. They also possess manufacturing bases and capital to expand. The cost of setting up new synthetic biology manufacturing capacity today can generally cost $50 million to $100 million depending on the production volume—a tall order for smaller start-ups. For niche firms focused on a small number of products, it might take years to fill such a plant, if ever. And since manufacturing capacity across the industry is so tight, it can be difficult to secure outsourced manufacturing capacity at attractive prices.

We believe that select materials companies with experience in biologic products can leverage their proficiency and synthetic biology to expand into new markets, creating attractive investment candidates. For instance, novel enzymes are finding their way into a wider array of end products, like household cleaners. Manmade engineered microbes could open vast new agriculture markets. What's more, the expansion of manufacturing capacity presents a compelling need for private capital that's aligned with the estimated $90 trillion of investment required for the world to achieve the UN Sustainable Development Goals (SDGs), creating future opportunities (*See "The Sustainability Catalyst" on page 19*).

The Sustainability Catalyst

The UN SDGs are a good roadmap for thematic investors focused on sustainability.

Synthetic biology applications offer innovative products and solutions that address many of the 17 SDGs and 169 detailed sub-targets.

Efforts to create meat and dairy alternatives can help feed the growing global population, ensure sustainable food production systems and resilient agriculture, and eradicate extreme poverty, as defined in sub-targets of SDGs 1 and 2. Synthetic cement addresses SDGs 9 and 11, aimed at upgrading infrastructure around the world with a focus on cleaner and environmentally sound technologies and industrial processes. Innovative biodegradable packaging products help reduce waste generation, a key target of SDG 12.

Identifying synthetic biology companies, research and products that are aligned with the SDGs is a good investing strategy, in our view. In particular, we believe that investors should hunt for opportunities within the SDGs that are most likely to require substantial private sector innovation and market access.

A comprehensive, sustainable approach also requires a thorough review of environmental, social and governance (ESG) issues. For example, synthetic biology companies must take precautions to ensure that genetic tools aren't used for nefarious purposes and to prevent new products from being released unsafely into natural environments. Food ingredients and products must be proved safe for human consumption. Production life cycles should be scrutinized for undesirable side effects such as the burden feedstock sources might place on local resources and water supplies. Companies will also be pressed to retain and attract top talent in high-tech fields such as genomics and AI—an important human capital issue for investors to keep in mind.

By drawing clear connections from the SDGs to synthetic biology companies while engaging with management on material ESG issues, we believe that active investors can identify pioneers that offer truly sustainable solutions to some of the world's most pressing problems.

Sustainability Is Fueling Growth

Along with falling prices and performance improvements, sustainability is another catalyst for adopting synthetic biology. Products made with this technology can be much more sustainable than those made using traditional energy-intensive chemical synthesis and traditional agriculture. McKinsey estimates that by 2040 to 2050, direct applications of synthetic biology could reduce annual average man-made greenhouse gas emissions by 7% to 9% from 2018 emissions levels.

For example, Perfect Day, a food technology company based in Berkeley, California, estimates that its “process for producing animal-free milk protein reduces greenhouse gas emissions by up to 97% compared to conventional dairy processes for whey.”

In addition to a lower-production carbon footprint, synthetic biology products can also be designed to be more biodegradable. Paradise Packaging, based in northern California, is using synthetic biology to produce a sturdy wood-like material for product packaging that completely biodegrades in 30–45 days.

UK-based Colorifix uses the DNA that encodes for color pigments in living organisms to produce dyes for clothing and other products. The company says its process uses at least 68% less water than conventional dyeing practices, and up to 90% less than synthetic fiber processes.

Companies across sectors and geographies are under intensifying pressure from consumers and investors to reduce their environmental footprints. Many firms aim to reduce greenhouse gas emissions in accordance with the Paris Agreement. Synthetic biology can help. Athletic apparel manufacturer Lululemon, based in Vancouver, Canada, announced plans in August 2021 to replace oil-based nylon in its garments with a material made using synthetic biology, helping the company achieve longer-term environmental sustainability targets. Nike made a similar announcement in 2021: a partnership with a company that discovered a way to make a plastic replacement material by pulling greenhouse gasses out of the air—a negative carbon footprint. In addition to the tech tailwind and consumers’ greater awareness of and commitment to sustainability, investors and companies will help advance the adoption of synthetic biology.

Cross-Sector Disruption Poses Investing Challenge

Because disruption isn’t confined to a single industry, some investors could face challenges in tapping the opportunities; others may thrive.

For decades, synthetic biology has predominantly been used by biotech companies, and investment analysis typically occurs in industry silos—healthcare analysts look at medical companies and technologies, consumer analysts focus on consumer companies, and so on. In the case of synthetic biology, investors in biotech and life science tools are familiar with the technology and principles, but not with the end markets, such as ingredients, food and materials. Meanwhile, materials and consumer analysts are unfamiliar with the technology and tools of synthetic biology.

This is a less holistic approach to investing in synthetic biology—cross-sector collaboration isn’t always the norm for investment firms.

Shares of one synthetic biology company, Zymergen, declined by roughly 75% on August 4, 2021 after the company disclosed that its lead product was seeing less customer uptake than expected. During a call hosted by Zymergen with the investment community, one industry analyst commented that he and his peers were being asked to evaluate electronics, consumer products and agriculture. Because this was “beyond their scope,” healthcare analysts were forced to rely on company information. Fundamental investors need to form an independent view that doesn’t simply depend upon company projections. In our view, this depends on ongoing collaboration and cross-sector analyst participation. Meetings with players throughout the synthetic biology ecosystem include analysts covering industrial, material, consumer, technology and life science sectors, providing a broader, differentiated perspective.

Evaluating the Risks: Consumer Acceptance and Regulation

The development of synthetic biology will face risks. Two key issues that will affect its trajectory are consumer acceptance and regulation.

Some consumers may be repulsed by products, particularly food, that are "grown in a lab" (though they might also be horrified to see the inner workings of an industrial-scale slaughterhouse). So the incursion of synthetic biology into products we use and consume on a daily basis will likely be gradual. Consider the concept of driverless cars. Many of us would be hanging onto our seatbelts with white knuckles in a completely driverless car at 65 miles per hour today, but driverless features will be rolled out gradually. We've already seen cruise control, lane assist, even self-parking features—one day, years from now, we'll realize we're not actually driving.

Similarly, many people don't stop to think about how their diabetes drug is made today, but they also don't wonder how the vanilla in their ice cream was manufactured. Synthetic biology's adoption will be gradual and will keep improving as the technology advances. Consider the video game industry. In the 1980s and 90s, video games were a niche entertainment with clunky graphics and kludgy gameplay. But the games kept improving, riding the Moore's Law computing wave, driving higher adoption. Today, video games are dominant in visual entertainment, with development of virtual reality "metaverses" under way.

Now, consider the market for artificial meat—a potentially large addressable market for synthetic biology. Many of today's meat lovers will say that the taste and texture profile of plant-based burgers and sausages is inferior to animal protein products. But labs around the world full of PhDs and the most advanced scientific tools are working on creating better plant-based and lab-grown protein products. It seems inevitable, in our view, that synthetic products will keep advancing until a person can eat a perfectly marbled cut of beef that rivals or surpasses what's naturally obtainable from a cow.

Despite the lesser quality of today's plant-based meat offerings, consumers have adopted them rapidly since their launch over the past several years. In addition to seeking the health and environmental benefits, consumers—particularly younger ones—increasingly want variety and are willing to try new things. This trend is notable in developing economies like China's, where consumption habits are less hardened. Leading consumer packaged goods (CPG) companies recognized this trend long ago and are already starting to adopt synthetic biology materials and ingredients. As experts in advertising and marketing, and in creating consumer awareness and adoption, we see the CPG industry's adoption as a positive driver for synthetic biology.

Regulation will also play a big part in determining the success of synthetic biology products. The biomaterials industry learned a powerful lesson from society's pushback against genetically modified organisms (GMOs) since the first products were introduced years ago. This has prompted more active engagement between the industry and policymakers.

New genetic technologies have arguably advanced faster than regulation. For instance, you don't need to insert foreign DNA into a cell (the definition of a GMO) when you can use a tool like CRISPR-Cas9 to perform a "copy and paste" on a cell's DNA. And in a typical synthetic biology process, the organism whose genetics have been altered—such as a yeast cell—is discarded as waste and isn't part of the final product. Governments across the world have agreed on some of the world's major challenges as laid out in the UN SDGs. Synthetic biology can play a prominent role in sustainable development efforts.

Instead of seeking stricter regulation on new technologies that promote company and high-tech job formation, governments are increasingly competing against each other to provide a supportive environment for innovators. Examples include municipalities developing forward-thinking protocols for drone flights, driverless cars and cryptocurrencies. In 2018, Sonny Perdue, then US Secretary of Agriculture, summed up this dynamic: "We don't want this new technology to feel like they've got to go offshore or outside the United States to get a fair regulatory protocol." Singapore and Qatar are actively promoting cell-cultured meat technology in the interest of food security.

While the path of regulation is uncertain and difficult to predict, we're optimistic and believe that investors can gain exposure to the synthetic biology theme without incurring unnecessarily high levels of public policy risk.

Prepare to Invest in the "Century of Biology"

Synthetic biology is just now taking its first steps beyond the biotechnology industry. Although current efforts are largely focused on replacing existing materials and ingredients, the limit of potential applications is nearly unfathomable.

Just a few decades ago, many drugs were simple pills or injected concentrates of small, less complex chemicals. Fast forward to today: new cancer treatments involve removing a patient's immune cells, editing the genomes to target specific molecules on the surface of cancer cells (based on the genetic mutations specific to that individual), and injecting the cells back into the patient. Millions of people globally have received an mRNA-based vaccine for COVID-19. That vaccine is essentially a virus that changes the genome of certain cells in your body, programming them to produce an antigen, a molecule that prompts an immune response that trains your body to recognize and neutralize coronavirus in the future.

Treatments like these would have been unthinkable years ago. What might come next?

Imagine programming a tree cell to grow into the shape of a house, or planting trees whose leaves contain phosphorescent cells that light up at night to replace streetlights. Or using the packaging from everyday products you consume to fertilize your lawn. Farmers may one day tend fields with custom-built microbes that obviate the need for aggressive use of fertilizers and pesticides. Future applications of synthetic biology could unearth entirely new form factors and products beyond our imagination today. As new products are developed and commercialized, we believe synthetic biology will create attractive investment opportunities and financial returns while contributing to positive social and environmental outcomes.

We predicted a decade ago that DNA sequencing would have a dramatic impact on the healthcare industry. It has. This disruption is poised to spread to many different markets and industries, creating significant new opportunities as well as challenges for certain companies. We believe that investors need to leverage deep research and active, cross-sector thematic investing in order to continue profiting from the "century of biology."

A handbag made from Mylo™, the fungus-based material that looks and feels like leather

Photo courtesy of Bolt Threads

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