PUBLIC AND PRIVATE FUNDING OPPORTUNITIES TO ADVANCE A CIRCULAR U.S. BIOECONOMY AND MAINTAIN U.S. BIOTECHNOLOGY COMPETITIVENESS

Interim Report Informed by the Schmidt Futures Bioeconomy Task Force

December 1, 2021

About this Project

To seed the next wave of innovation in synthetic biology and the bioeconomy, Schmidt Futures launched the Task Force on Synthetic Biology and the Bioeconomy in October 2021 as part of a program to advance transformative bio-based and bio-enabled applications in areas such as clean energy, industry, agriculture, and health. Members of the Task Force are subject matter experts from academic disciplines, including physics, ethics, and synthetic biology; venture capitalists and industry leaders from both small and large companies; and leaders from biotechnology consortia.

Given the breadth of topics to address relating to the bioeconomy, this interim report is focused on identifying research needs for advancing biologically-based production and assessing infrastructure needs to support the U.S. bioeconomy. A follow up strategy document, planned for the spring 2022, will provide recommendations for additional topics, such as talent/workforce development, policy modernization, and catalytic actions to spur innovation. As Schmidt Futures contemplates its 2022 strategy document, input on this interim report and ideas for stakeholder convenings are welcomed. All input should be directed at the program co-leads listed below.

For this interim report, the Task Force members met regularly to debate a range of topics and developed two novel research products that informed the recommendations made. Information gathering for this report included interviews of more than 50 experts, literature reviews, and input from meetings and webinars. Schmidt Futures would like to broadly acknowledge and thank the many individuals that contributed to this effort, in addition to the Task Force members who dedicated their time to participate in this effort.

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With the exception of Schmidt Futures program co-leads, all members participated in their personal capacity. While the report generally reflects the observations, insights, and recommendations of the group, it should not be assumed that every member will have agreed with everything expressed herein.

Executive Summary

In the nearly 50 years since the first genetic engineering experiments, the United States has become the world's biotechnology powerhouse, with the resulting biology-based economy—the bioeconomy—generating nearly $960 billion in economic activity in 2016, about 5 percent of U.S. GDP,[1] with more than half of the total generated outside the biomedical sector, including the agricultural and industrial biotechnology sectors. Over the next two decades or less, a well-developed bioeconomy has the potential to transform manufacturing processes to use renewable biomass rather than petroleum to make the products of modern society, and in doing so, reduce the nation's dependence on fossil fuels, revitalize U.S. manufacturing and employment across the nation, create a more resilient supply chain, improve the nation's health, and contribute significantly to the goal of creating a net zero greenhouse gas economy. However, decentralized leadership, inadequate talent development, insufficient investment in both fundamental research and developing bioprocessing infrastructure, and international competition put the United States at risk of forfeiting that world-leading position and squandering the entrepreneurial drive and capital market interest that is trying to expand the bioeconomy. Without concrete action to address these concerns, the nation's economy, its national security, the health of its residents, and its opportunity to move to a net zero economy that creates good-paying jobs and keeps them in the country are in peril.

Schmidt Futures, a philanthropic initiative of Eric and Wendy Schmidt, convened a Task Force to chart a course for achieving the promise of platform technologies such as synthetic biology and artificial intelligence to contribute to what has recently been projected to become a future $4 trillion global bioeconomy. The Task Force deliberated the roadblocks and focused on identifying opportunities for translating basic science research into products for the general public by enabling large scale production of exciting bioeconomy products that are ready to move out of the lab, such as:

- a new generation of plastics that degrade to harmless chemicals in seawater and soil
- biologically produced, carbon-neutral cement
- alternative food protein sources that use less water and land and produce fewer greenhouse gas emissions
- climate change resilient plants, including salt- and drought-resistant crops
- textiles and dyes whose production slashes carbon dioxide emissions and reduces toxic waste
- soil microbes that reduce fertilizer use, improve the health of soils, and remove carbon dioxide from the atmosphere

This report from Schmidt Futures makes recommendations for public and private action that fall into two broad categories: foundational science and technology challenges and scale-up capacity bioproduction[2] infrastructure. These categories emerged as a consequence of the fact that most U.S. foundational life sciences research funded today is curiosity and discovery driven, not application driven, which results in these "non-academic" challenges that limit the ability to realize bioproduction goals going unexplored and underdeveloped in the United States. In addition, because other countries are investing in solving these challenges, U.S. companies are taking their technologies overseas for production and commercialization, a situation that if continued, promises to yield the same "innovate here, produce there" outcome that did so much damage to the U.S. manufacturing sector and the people it employed.

[1]Given that bioeconomy revenues have grown by more than 10 percent annually for decades, the 2021 estimate for the US bioeconomy could be close to $1.5 trillion

[2]Bioproduction refers to biologically based production, which is also called biomanufacturing.

Recommendations snapshot:

1. **The U. S. government should commit to remaining the global leader in biobased science and scale up manufacturing by establishing and funding a 5-year, $600 million[3] Bioproduction Science Initiative (BSI) that expands budgets and remits of relevant science agencies focused on advancing foundational science and technology development for current and future bioproduction, and is focused on addressing unmet research needs that hinder the translation of innovative technologies.**
   - The National Science Foundation (NSF) should serve as the lead agency for BSI and establish two regional innovation accelerators (RIAs) a year focused on bioproduction.
   - The RIAs should forge new partnerships with relevant federal science agencies to build on existing expertise, leverage earlier investments, and enable coordination for research acceleration.

2. **The U.S. government should invest $1.2 billion[4] in an extensive and flexible bioproduction infrastructure—one that can process multiple feedstocks using multiple organisms to produce multiple products at multiple scales—over two years to expand domestic bioproduction capacity in an equitable and strategic manner. Additional funding for maintaining and sustaining these investments will be needed over time.**
   - The Department of Commerce should undertake a comprehensive assessment of existing facilities and functionality, building from the work of this Task Force, to identify and realize opportunities for appropriate and equitable placement of future facilities.
   - A network of 10-15 new and refurbished bioproduction facilities, provided with incentives for early-stage technology development, will accelerate the transition from laboratory technologies to commercial deployment.
   - Additionally, the Department of Commerce should explore other financial incentives, such as those embodied in the CHIPS Act, to provide capital for small and large companies to meet their infrastructure needs.

3. **To remain globally competitive, the U. S. government should establish and sustain creative public-private partnerships with the goal of reducing the time it takes to successfully scale new products from several years to months.**
   - The Department of Commerce should incentivize partnerships between companies with deep artificial intelligence expertise and those with biomanufacturing facilities to provide services, facilities, and expertise for innovators.

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[3]Compared to the U.S. bioeconomy, which accounts for 5.1 percent of U.S. GDP, the semiconductor industry accounts for 1.2 percent of U. S. GDP, and the CHIPS Act proposed a $30M annual R&D investment in semiconductor research and development for the next 5 years. A commensurate investment for bioproduction would amount to $120M annually for R&D investment over 5 years.

[4]Estimates for new bioproduction facilities with existing technologies range from $100,000-$200 million and implementing new flexible, modular next-generation facilities will likely fall on the higher end. This Task Force considers $1.2B as an estimate to enable the expansion of the bioproduction infrastructure called for in this report that covers pilot, intermediate, and large-scale needs.

Public and Private Funding Opportunities to Advance a Circular U.S. Bioeconomy and Maintain U.S. Biotechnology Competitiveness

Interim Report Informed by the Schmidt Futures Bioeconomy Task Force

In the nearly 50 years since Herbert Boyer and Stanley Cohen conducted the first genetic engineering experiments, the United States has become the world's biotechnology powerhouse, with the resulting biology-based economy—the bioeconomy—generating nearly $960 billion in economic activity in 2016, alone, about 5 percent of U.S. GDP,[5] and fostering the growth of private industry and vibrant startup ecosystem. However, decentralized leadership, inadequate talent development, insufficient investment in both fundamental research and developing bioprocessing infrastructure, and international competition put the United States at risk of forfeiting that world-leading position. Without action to address these concerns, the nation's economy, its national security, its residents' health, and its opportunity to move to a net zero carbon economy that creates good-paying jobs and keeps them in the country are in peril.

> ***Net zero*** *refers to the balance between the amount of greenhouse gas the nation produces and the amount it removes from the atmosphere through innovation. We reach net zero when the amount we add is no more than the amount taken away.*

The United States has the science and engineering knowledge base, commercial and venture capital interest, plentiful renewable raw materials, an energized workforce and innovative that wants to address the perils of climate change, a small and growing segment of consumers demanding and willing to pay a premium for products that are less harmful to the environment, and other resources to jump start a concerted national effort to grow the bioeconomy far beyond its size today. Indeed, our game-changing expertise at manipulating and harnessing the building blocks of life can drive the global transition of using renewable biomass resources to replace the role of petroleum products and other non-renewable materials in driving economic activity. Should the nation capitalize on this opportunity and its many strengths, particularly its global leadership in genetic engineering, molecular biology, and biotechnology, as well as its strong position in artificial intelligence, the result will:

- enable the nation to reach its goal of establishing a net zero greenhouse gas emissions economy by 2050,
- lead to a healthier and more sustainable nation and planet,
- address food and water security,
- reduce the nation's dependence on foreign resources, reduce its balance of trade deficit, and strengthen and add resilience to the nation's supply chains,
- revitalize urban and rural economies and create economic opportunities for marginalized communities,
- capture the lion's share of what is projected to be a $4 trillion global industry[6] that will affect almost all human endeavors and wellbeing, and
- enable the U.S. bioeconomy to lead history's fourth industrial revolution, one as pivotal as the invention of the steam engine, the age of science and mass production, and the rise of digital technology.

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[5]Given that bioeconomy revenues have grown by more than 10 percent annually for decades, the 2021 estimate for the US bioeconomy could be close to $1.5 trillion

[6]https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives

Making this transition from a petroleum economy to a bioeconomy is not a pipedream, nor is there an intractable tradeoff between reducing ecological impact and growing economic opportunity. Rather, it is the well-considered conclusion of a broad swatch of the scientific community and entrepreneurs that the bioeconomy offers an important option to address climate change while also strengthening and growing the U.S. economy. Indeed, the U.S. government has invested over $5 billion over the past 15 years in research support for the bioeconomy, and the U.S. Department of Energy (DOE) projects that the United States could sustainably produce more than 1.3 billion tons of renewable biomass a year—without affecting food, animal feed, and export demands—while transitioning to low-carbon input agriculture and forestry that nurtures soil health. With a concerted and coordinated effort involving the federal government, academia, and the private sector, the transition to a bioeconomy has the potential to:[7]

- create 1.1 million high-paying and intellectually satisfying jobs,
- keep $260 billion dollars a year of economic activity from going overseas,
- contribute to the prosperity of rural, urban, and underserved and marginalized communities across the nation by using locally produced biomass for regional bioproduction,
- replace the transportation fuels that long-haul air travel and shipping might require even after electrification of the nation's transportation sector,
- produce chemicals and bioproducts from renewable biomass rather than from traditional chemical manufacturing, and produce entirely new materials that only nature can make economically,
- create a dependable, economic, and resilient domestic supply chain for producing and distributing all biobased products,
- develop large-scale, low-energy use DNA-based data storage to better capture the tremendous growth in data generated by human activity,
- raise the nutritional value of food and improve soil health, while reducing agriculture's greenhouse gas footprint, nitrogen runoff, and pesticide use,
- use marsh lands and forests more efficiently to improve their carbon- and water-holding capacity,
- create salt-tolerant, drought-tolerant, and disease-resistant crops to increase the resilience of agriculture, and
- reduce annual U.S. carbon dioxide emissions by 450 million tons, nearly 10 percent of the nation's emissions, or more, while also creating the possibility of developing biological processes that remove carbon dioxide from the atmosphere.

In addition, given the creativity of researchers in the public and private sectors, a biology-based economy, relying on the ability of nature to perform chemistry that humans have yet to master at scale, is likely to produce entirely new materials and production processes, just as the petrochemical-based economy has done. In fact, synthetic organic chemistry performed by humans may be reaching the limits of the possible and that nature is capable of extending the range of available chemicals and materials. Examples of bioeconomy products, available today, that are less damaging to the environment and less wasteful of precious resources include:[8]

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[7]An extensive list of bioeconomy products that are on the market, under development, or early-stage concepts is available at https://www.futurebioengineeredproducts.org/refs/market-status/

[8]For an extensive listing of companies with products either on the market or in development as of 2018, see http://go.bio.org/rs/490-EHZ-999/images/BIO_Chemical_Companies_Report_2018_FINAL.pdf

- plant-based meat substitutes with a much smaller environmental footprint,
- textiles, dyes, carpeting, and furniture whose production slashes carbon dioxide emissions and energy use,
- synthetic leather made by fungus,
- soil microbes that reduce fertilizer use, improve the health of soils, and remove carbon dioxide from the atmosphere,
- cosmetics and personal care items made from sustainable bioproduced chemicals with smaller greenhouse gas footprints and that do not rely on sourcing from animals,
- a new generation of plastics that degrade to harmless chemicals in seawater and soil,
- enzymes that improve efficiency and reduce energy use in traditional industries such as pulp and paper bleaching, textile processing, and food processing,
- biologically produced cement,
- sustainable fish feed made from methane,
- biodegradable and compostable plastic containers whose production is associated with a 200 percent reduction in greenhouse gases,
- high-performance biodegradable lubricants and greases,
- polyurethane foam from algae oils left over from omega-3 fatty acid production, and
- tailored enzymes that enable washing clothes in cold water.

At the same time, making this transition is not easy or inexpensive. This interim report, based on input from a Task Force[9] comprising experts covering a broad range of interests and expertise, provides a roadmap the nation can follow that will enable the United States to maintain its dominant global position in harnessing the modern molecular biology revolution and establish an equitable, vibrant and sustainable, circular bioeconomy that will provide economic, social, environmental, human health, and national security benefits for decades to come. Schmidt Futures will release a more comprehensive plan to power the growth of the U.S. bioeconomy in March 2022. This interim report focuses on steps to address foundational scientific and technological research needs and establish robust national capabilities for end-to-end bioproduction.

Before getting to the heart of our argument and the steps the nation needs to take, it is useful to define the terms bioeconomy, circular bioeconomy, and bioproduction. For the purposes of this report, we are using the definition of the bioeconomy developed by the National Academy of Sciences, Engineering, and Medicine in its 2020 report, Safeguarding the Bioeconomy:

> *"The U.S. bioeconomy is economic activity that is driven by research and innovation in the life sciences and biotechnology, and that is enabled by technological advances in engineering and in computing and information sciences."*

This report borrows from a number of sources for our definition of a circular bioeconomy:

> *A circular bioeconomy is one that forgoes the traditional linear economic model of "take-make-consume-throw away" for one that uses the power of biotechnology, design for bioproduction, and advanced analytics and information technology to create processes that result in a sustainable and regenerative economic cycle in which waste products serve as inputs to create highly valued products and materials, that are used as*

[9] https://schmidtfutures.com/task-force-on-synthetic-biology-and-the-bioeconomy/

long as possible, and reused without drawing down limited resources or generating wastes that are disposed into the atmosphere, landfills, or rivers, lakes, and oceans.

Finally, while some reports use the term biomanufacturing, this report uses the term bioproduction to be more forward-looking and inclusive of the variety of industrial and agricultural processes that commercial entities will use to make their products:

Bioproduction is the use of biological systems, including plants, microbial consortia, individual living cells, and or parts of living cells (known as cell-free systems), to produce commercially important products from biomass feedstocks and carbon dioxide in a broad range of economic sectors including health, nutrition, agriculture, industrial applications.

Note that this report does not focus directly on addressing the needs of the biopharmaceutical and biomedical sectors of the bioeconomy, though investments in foundational research for bioproduction outlined later could also benefit the biopharmaceutical and biomedical sector, just as biomedical research produced the very genetic tools and discoveries that are enabling the rest of the bioeconomy. Those areas are well-funded by both government and the private sector and have a significant installed infrastructure that differs from non-biomedical applications given manufacturing practices and regulatory specifications, among other things. In fact, leadership in the bioeconomy is in some ways a byproduct of sustained investment in biomedical sciences, suggesting that broader investment in non-medical bioproduction could drive even faster growth of the bioeconomy.

Moving Beyond Biofuels and Renewable Energy

Most media coverage of the nation's efforts to reduce greenhouse gas emissions and get to a net zero economy centers on renewable energy solutions such as electrification of the transportation industry. Certainly, renewable energy complemented by improving energy efficiency must play a significant role in moving to net zero, but the fact is, displacing fossil fuels with renewable energy can only address 55 percent of the nation's carbon emissions. Addressing the other 45 percent of the nation's carbon emissions requires changing the way we manufacture consumer and industrial products and the way we grow our food, and this provides an opportunity for the bioeconomy to contribute in significant ways.

A critical piece for addressing that opportunity is to enable of biobased chemicals to serve as the constituents of an estimated 96 percent of U.S.-manufactured products. In fact, that transition is already starting to happen, and some biobased chemicals already outcompete petrochemicals in several categories, generating at least $125 billion annually and accounting today for somewhere between 17 and 25 percent of U.S. fine chemical revenues. U.S. Department of Agriculture's (USDA) BioPreferred program has identified about 20,000 biobased products in commercial production.

One advantage bioproduction of chemicals has is the cost of building a bioproduction facility, which in many respects with current technologies is similar to a brewery. For example, bioproduction facilities with current technologies cost from $100,000 to $200 million, depending on its size, complexity, and ability to handle multiple production processes. The relatively low cost of a bioproduction facility means that the return on capital should be quite attractive to the capital markets. Experts consulted for this report expect operating expenses for a bioproduction facility to be relatively low as well.

In addition, because of the varied nature of biomass and its localized production, the most functional and economical way to build a biomass-to-chemicals industry is to co-locate biomass processing facilities close to their feedstock. For example, a bioprocessing facility could be located adjacent to a municipal waste treatment facility to turn that waste into chemicals, or as one U.S. company is doing, locating a bioproduction facility adjacent to a Chinese steel mill and uses its industrial emissions as a feedstock for bioproduction.[10] Co-locating bioprocessing facilities and their biomass feedstocks would create economic growth distributed across the nation and address the policy goal of revitalizing the economies of rural communities, as well as those that now—or once did—rely on fossil fuel production and those struggling because traditional manufacturing jobs disappeared. Adapting to the different nature of regionally produced biomass will require basic research on process control, and getting biomass to regional processing centers will require innovation in logistics.

Why Now?

Aside from the critical role that a circular bioeconomy must play in achieving the goal of reaching net zero by 2050, there is another compelling argument for a national investment in developing a circular bioeconomy: international competition and the risk of losing an opportunity to revitalize U.S. manufacturing. For the past several decades, the United States has been following an "innovate here, produce there" model, rather than the "innovate here, produce here" model that capitalized on the nation's comparative advantage over other nations in innovation to become a manufacturing powerhouse and the world's wealthiest economy. The "innovate here, produce there" model cost the nation the opportunity to fully capitalize on the electronics revolution and the explosive growth in photovoltaic deployment, two sectors that U.S. innovation made possible but have largely benefited manufacturers in China, Japan, and Korea, at least in part because of lower costs of labor that are not expected to be as an big issue with bioproduction. The result has been a loss of manufacturing capacity, jobs, and economic benefits, as well as the supply chain snafus that developed in 2020, caused inflation to spike in 2021, and costs U.S. businesses hundreds of millions of dollars.

Today, the United States is in danger of having the same thing happen with bioproduction. Because of underinvestment in process development research, process engineering, bioproduction infrastructure, and workforce development, a number of U.S. innovators in the bioproduction space are having to rely on testbed and bioproduction facilities in Mexico and Europe, turn to talent located in Europe to develop bioproduction processes at scale, and export their intellectual property in order to manufacture their products, just as their predecessors in the electronics and photovoltaic sectors did. Moreover, the existing bioeconomy that has developed in the U.S. Midwest around corn processing could be in peril if the demand for fuel ethanol and high fructose corn syrup were to decrease. Therefore, using the existing biomass resources to produce innovative products with sustainable markets could help ensure continued growth of the Midwest segment of the bioeconomy.

In addition, international competitors have clearly and explicitly described their intent to dominate the global stage in the 21st century using biotechnology, and are investing to implement associated long-term strategic goals. India and China, in particular, have clearly stated their intention to become a dominant global power via domestic development and mastery of biotechnology. To avoid falling behind and losing America's current advantage in biotechnology and molecular biology, the United States must begin to plan and execute on the same multi-decadal timescales as our competitors.

[10]Matsakas, M., Gao, Q., Jansson, S., Rova, U., and Christakopoulos, P. 2017. Green conversion of municipal solid wastes into fuels and chemicals, *Electronic Journal of Biotechnology* 26:69-83. https://doi.org/10.1016/j.ejbt.2017.01.004.

At the same time, dozens of recent reports, hearings, and developing legislation suggest the time is right to capitalize on the current momentum in support of revitalizing technology-based manufacturing in the United States. According to a recent Congressional Research Report focused specifically on the U.S. bioeconomy, Congress over the past few years has introduced several pieces of legislation directly related to the bioeconomy, including the Bioeconomy Research and Development Act of 2020, which was reintroduced in 2021; the Engineering Biology Research and Development Act of 2019; and the Securing American Leadership in Science and Technology Act of 2020, which was also reintroduced in 2021. The Senate has also passed the United States Innovation and Competition Act of 2021, which included the Bioeconomy Research and Development Act of 2021. These legislative efforts, if signed into law, would provide an excellent foundation for supporting the continued growth of the bioeconomy. Bioeconomy research would also fit under the provisions of the recently signed Infrastructure Investment and Jobs Act, otherwise known as the bipartisan infrastructure deal, as well as the recently announced, U.S.-led Net Zero World Initiative and the 2018 National Strategic Plan for Advanced Manufacturing.

Together, pending legislation represents a good starting point for supporting the nation's bioeconomy, but capitalizing on the full potential that the bioeconomy represents requires the U.S. government to make a more substantial commitment. Our subsequent report will consider recommendations for specific policy actions the federal government should take to further activate the U.S. bioeconomy—perhaps legislation analogous to the Creating Helpful Incentives to Produce Semiconductors for America (CHIPS) for America Act and the Facilitating American-Built Semiconductors (FABS) Act.

What's the Hold Up?

While the benefits of building a bioeconomy for the 21st century and beyond are both obvious and undeniable, the United States has a great deal of work ahead to address scientific, technological, infrastructure, and commercialization hurdles to turn potential into reality. Some of this work to address the scientific and technological hurdles is ongoing in academic and private sector laboratories, and to fully realize its potential requires the type of foundational research, development, and infrastructure support at which the federal government excels. For example, the U.S. government has a history of funding industrial revolutions by enabling the connection of digital design and simulation with manufacturing. The most notable examples are CAD/CAM for mechanical engineering and airplane manufacturing and the layout and simulation tools for designing semiconductor chips.

The molecular biology revolution, for that matter, owes its existence to federal funding of biomedical research, and federally funded research has already led to great progress in synthetic biology—the direct engineering of microbes and plants. However, there is a need, for example, to better generate, organize, catalog, and share all the data on the genes, proteins, and biosynthetic pathways that microbes and plants use. Doing so will enable bioengineers to use a wide array of digital design and production technologies for biotechnology that are the logical equivalent of those used by the industries that produced iPhones, Teslas, and 787s. Such capabilities would enable bioproduction facilities to accommodate the variable response of living systems that make them more difficult to scale than mass-producing cars or mobile phones. There is little doubt, too, that federal research support in this area will create additional platform technologies that lead to serendipitous advances, just as it did for DNA sequencing, DNA synthesis, and genome editing.

Infrastructure hurdles may be the bigger barrier to commercializing research advances. One significant barrier is the limited U.S. capacity of testbed and intermediate-scale facilities that innovators require to demonstrate they can scale-up their laboratory successes and produce enough bioproduct needed for the necessary testing and validation steps. Another barrier in this realm is the situation where innovators seeking to manufacture their biobased products at scale must deal with a patchwork of bespoke facilities and processes that were most likely not built with their products in mind. Investment in a network of new testbed facilities, as well as establishing data and technology transfer standards akin to application programming interfaces used in the software industry would allow direction application of data from the laboratory to high-performance bioproduction, would help new products reach markets faster. So, too, would developing biotechnology operating systems that can drive experiments, optimize production processes, facilitate technology transfer implementation, and serve to integrate basic product development with systems that manage customer-facing production and compliance. Given the variability of biomass composition biomanufacturers need standardization of tasks ranging from data gathering and annotation to root cause analysis, which together facilitate the use of modern process development and management tools in the same way that the chemical industry deals with much smaller variability in its raw materials.

Beyond that, there are the one-time costs involved in transitioning from a petroleum-based throw-away economy to a circular bioeconomy, costs estimated to total around $145 billion over the next 30 years[11]—or a little over 25 percent of the new federal spending included in the bipartisan infrastructure bill—but these are limited in duration and repaid multiple times over once the transition is complete. As the old saying goes, if we stopped doing things the old, unsustainable way—in this case, turning sequestered carbon in the form of oil, natural gas, and coal, into carbon dioxide and other products that cause environmental damage and endanger life on Earth—we could more than afford to do things a better way.

Another constraint on developing bioproduction capabilities here is that there is a severe shortage of bioprocess engineering talent in the United States, one that raises the need for education in bioprocess engineering at all levels, from community college to graduate school. While our subsequent report will dive more fully into workforce needs, suffice it to say that other countries are actively addressing this issue. The European Union, for example, has high quality chemical engineering and process development research and training programs, and U.S. companies are increasingly forced to rely on foreign-trained talent. It is common today to hear companies say they have to rely on Dutch process engineers, for example, when trying to hire for their facilities.

Finally, there are regulatory and policy considerations that the nation needs to modernize to support the bioeconomy. Our subsequent report will discuss ways to address those, and will also define a set of bioeconomy-related grand challenges and actions that would benefit a range of communities and set forth a plan to implement them.

What Do We Need to Do to Enable a U.S. Circular Bioeconomy?

The research, development, and infrastructure opportunities that this report highlights and makes recommendations for public and private action fall into two broad categories: foundational science and technology challenges and end-to-end bioproduction capacity (see Figure 1). Addressing the major scientific and technological challenges to creating a circular bioeconomy and moving toward a net zero would enable the country to unlock the wealth of knowledge, entrepreneurial drive, and venture capital resources that few if any other nations possess together. Increasing end-to-end bioproduction capacity

[11] Williams, J. H., Jones, R., Haley, B., Kwok, G., Hargreaves, J., Farbes, J., et al. (2021). Carbon-neutral pathways for the United States. *AGU Advances*, 2, e2020AV000284. https://doi.org/10.1029/2020AV000284

would enable the nation to return to the innovate here, produce here model that would grow the U.S. bioeconomy and create millions of high-paying bioproduction jobs.

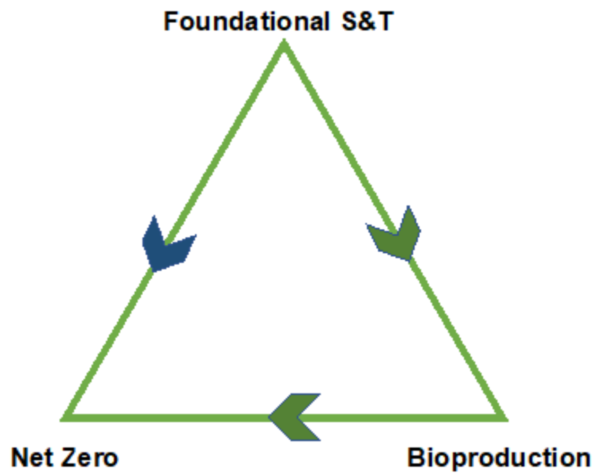

FIGURE 1 Relationship between developing foundational science & technology capabilities, developing bioproduction capacity, and net zero goals. The green arrows designate a pathway to net zero that relies on bioproduction and reflects the subject matter of this report. The blue arrow represents other paths to net zero that do not depend on bioproduction.
Credit: This figure was created with the assistance of Sifang Chen, Ph.D., a postdoctoral fellow with the Engineering Biology Research Consortium

U.S. government funding in these areas would be directed to address challenges and eliminate barriers that would unleash the power and capabilities of the private sector to create markets and drive economic prosperity, and also address the national imperative to move to a sustainable net zero carbon economy that benefits all Americans. In addition, federal investments in foundational science and technology have a long history of leading to unanticipated future applications, including the research that led to the molecular biology revolution that serves as the bedrock of the bioeconomy.

At the same time, there is a key role for industry to play in these efforts, particularly in terms of sharing knowledge and expertise through research partnerships with government and academia. For example, fostering partnerships between large technology companies with expertise in artificial intelligence and bioproduction companies, with knowledge of scale-up challenges and the ability to generate copious data on their processes, could dramatically reduce the time that it takes to reach commercial production capacity. In fact, much of the startup and investment activity in the bioeconomy has focused on the confluence of automation, software, and biology.

Certainly, other organizations have developed roadmaps that are broadly supportive of funding foundational science and technology research that would aid in developing a vibrant, bioeconomy. In particular, the Engineering Biology Research Consortium has produced several roadmaps targeted at specific areas of basic research relevant to the bioeconomy, including its most recent on engineering biology and materials science.[12] What makes this effort different is its specific focus on research and development activities needed to expand end-to-end bioproduction capacity on the scale needed to evolve the U.S. bioeconomy toward a circular bioeconomy and to accelerate the transition to a net zero economy.

[12]The Engineering Biology Research Consortium's roadmaps are available at https://roadmap.ebrc.org/

FOUNDATIONAL SCIENCE AND TECHNOLOGY CHALLENGES

Achieving the biggest return on the nation's investments, both past and future, requires the U.S. government to accelerate research in foundational bioengineering and bioproduction. Up to this point, federal research support has enabled researchers to develop an ever-growing set of tools, such as CRISPR, to manipulate DNA at will and use those tools to develop plants, microorganisms, and cell-free systems capable of producing a wide range of commercially valuable chemicals and materials. Now, to advance the nation's bioproduction capabilities, research and development efforts need to focus on creating rational design for bioproduction processes that would involve the following:

- modeling, designing, and testing metabolic pathways to make molecules and products that do not exist in nature,
- developing the rules, data analysis tools, computer modeling capabilities, and data-driven approaches to model building, that would enable biotechnologists to rapidly identify and produce the exact genetic modifications in the most suitable organism or cell-free system required to create those pathways and generate the desired biochemical product,
- conducting data-driven discovery using emerging machine learning and artificial intelligence approaches now being employed by chemical engineers, materials scientists, and some early adopters in industrial biotechnology,
- accurately projecting laboratory-scale results to industrial-scale processes, and
- doing all of this in a matter of days and weeks instead of months and years.

Concurrent with that effort should be research aimed at extending existing DNA production methodology to enable manufacturing entire genes or even whole genomes with high fidelity. This effort would include developing genetic tools for precisely editing plant and microbial genomes at multiple sites simultaneously to improve existing metabolic pathways and create new ones as part of rational design. Given the importance of biomass to the future bioeconomy, there needs to be a greater research emphasis on plant genomics and higher throughput genomic manipulations of plant genomes, such as the successful National Science Foundation (NSF)-funded effort to assemble, annotate, and compare 26 diverse maize genomes, in order to increase the productivity of food and feed crops and to develop varieties that be grown on marginal lands. Another research goal should be to identify organisms, and even collections of organisms that work together, that could serve as new "chassis" for bioproduction, expanding the breadth of products that can be manufactured routinely.

Creating the biobased systems capable of producing valuable chemicals and materials is only a start. What must happen next is for process and chemical engineers to develop the systems and capabilities needed to produce biobased products on a commercial scale. An analogy would be turning a home-based, one-carboy beer fermenter into a full-fledged brewery capable of producing enough beer to stock every liquor store, bar, and restaurant. While there are a number of companies already skilled at doing this for existing products, the vibrant domestic start up ecosystem is struggling to develop and access these capabilities for a number of reasons, which are detailed below in the section on increasing end-to-end bioproduction capacity.

Scaling biobased production from the benchtop to commercial scale is not straightforward at present owing to a number of factors, including the inherent variability that comes from working with a living organism, and research is needed to develop methods of dealing with the variability and increasing the efficiency of what can be extracted from biological feedstocks. In addition, the government can create a market for the individual carbon fractions that bioproduction would generate, from one carbon to six carbon, as well as lignin for aromatics, to create a carbon building-block pipeline for the bioeconomy as these fractions can plug into existing value chains and infrastructure (Figure 2). Research into the tolerance for impurities and blends of biomass will also enable this transition.[13]

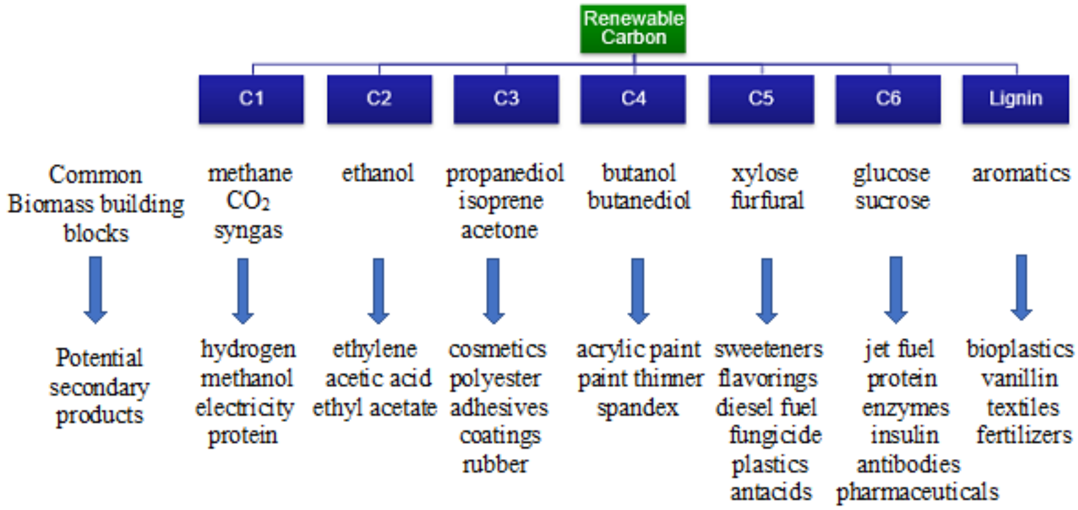

FIGURE 2 A hypothetical biomass-utilizing, carbon building-block pipeline would produce carbon feedstocks for production of the wide range of consumer and industrial products.
Credit: Luis Cascão-Pereira

This is one place where modeling and simulation capabilities need to play a larger role than is possible today. To support the development of those capabilities, funding is needed to establish an easily accessible national computational and database infrastructure that would better support the design-build-test-learn process common in engineering for biology by enabling better simulation. This infrastructure would provide process engineers with the ability to perform scale-up experiments and refine operating conditions before moving a laboratory-based process to pilot plant scale and then on to commercial production scale. Currently, scale-up is an expensive and time-consuming process that would benefit from a concerted research effort focused specifically on optimizing and standardizing bioproduction scale-up processes.

An area that has not gotten much attention, but definitely needs it to enable a future circular bioeconomy, centers on how to process the varied feedstocks that will be available to biotechnologists, including forest-based biomass of many types, grasses and crops, agriculture and aquaculture byproducts, food production byproducts and waste, municipal waste, waste water, and carbon dioxide produced by other processes, among others depending on where a bioproduction facility would be located and even what season it is when production occurs.

Biomass feedstock variability can make any attempts at pre-determining optimal process conditions futile. Bioproduction facilities can learn from the petroleum industry, which uses advanced computer modeling to tune process conditions and fully convert each batch of crude into a pre-established suite of chemicals. By applying the same type of analytic tools and modeling capabilities, bioproduction facilities will be able to adapt their processes to accommodate the variability in biomass feedstocks that result from seasonal and geographic variation.

Once the nation has enabled feedstock flexibility or further developed the capabilities to use diverse sources of renewable biomass to power the bioeconomy, there may be an opportunity to use one of society's most vexing waste problems, plastics. Researchers are working on ideas for how to

[13]Narani, A., Coffman, P., Gardner, J., Li, C., Ray, A. E., Hartley, D. S., Stettler, A., Konda, N. V. S. N. M., Simmons, B., Pray, T. R., and Tanjore, D. Predictive modeling to de-risk biobased manufacturing by adapting to variability in lignocellulosic biomass supply. Bioresource Technology. 2017 Nov;243:676-685. doi:10.1016/j.biortech.2017.06.156.

deconstruct existing plastics into smaller molecules that could then serve as feedstocks for biological processes. One advantage of this approach is that there is an already existing collection and sorting system for plastics. However, the processes needed to break down plastics into usable feedstocks are a relatively new and developing technology, and research is needed on how to best use that feedstock in combination with biomass feedstocks. That being said, major polymer producers around the globe are investing in chemical recycling infrastructure and anticipating some of these processes coming to fruition in the next 15 years. It behooves the United States to make larger strategic investments now to capitalize on this alternative feedstock.

The nation's extensive expertise in biotechnology and artificial intelligence puts the United States in an ideal position to address the research needs listed above with appropriate government support. However, our analysis of federal spending to support the research needed to develop a vibrant U.S. circular bioeconomy reveals that such spending has been flat for years (Figure 3).[14] That situation must change, and change now, if the nation is truly serious about rebuilding its manufacturing capabilities, creating millions of good-paying jobs spread equitably across the nation, and reaching the goal of building a net zero economy. The magnitude of the funding needed to accomplish that goal is likely to be a fraction of the cost of the recently passed bipartisan infrastructure deal, and the return on that investment will more than justify it.

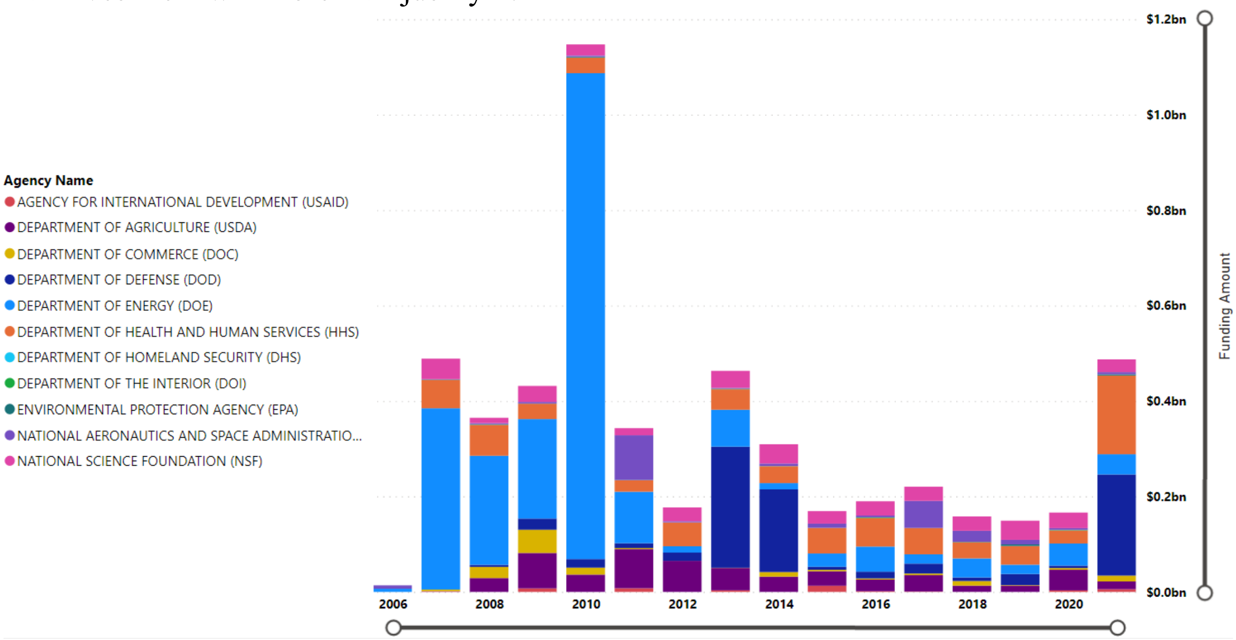

FIGURE 3 Federal research funding for bioeconomy-related areas by federal agency (2006-2021).
Method: The above visualization was created using USASpending.gov, the official open data source on federal spending. The award type selected was grants that exclude services such as consulting, military contracts, and IT infrastructure modernization. Research was done using the terms "biomass, biotechnology (biotech), biofuels, feedstock, bioeconomy, bionutrients, bioprocessing, biomanufacturing, synthetic biology, cell-free synthesis, cellular agriculture, downstream processing, scale-up manufacturing, biological technologies, and solid-state fermentation." The Awarding Agencies selected were the Department of Agriculture (USDA), Department of Commerce (DOC), Department of the Interior (DOI), Department of Defense (DOD), Department of Energy (DOE), National Aeronautics and Space Administration (NASA), Department of Health and Human Services (HHS), Agency for International Aid (USAID), Department of Homeland Security (DHS), Environmental Protection Agency (EPA), National Science Foundation (NSF), Department of Veterans Affairs (VA), and the Smithsonian Institute.
Credit: Kathryn Hamilton and John Haley, Aurora North America

[14]It's worth noting that investments by HHS (likely related to COVID-19) and DOD (for BioMADE) account for a significant increase for 2021.

END-TO-END BIOPRODUCTION CAPACITY

While the scientific, engineering, and technology communities are ready to tackle the foundational science and technology challenges discussed above over the next five years with appropriate support, establishing a nationwide, end-to-end bioproduction capacity to move from the desktop to commercial production requires a larger-scale effort—and commitment on the part of the U.S. government—that will play out over the next 3 to 15 years. This effort will require advances in several areas, including research and development, infrastructure development, science and regulatory policy, and strategies to develop alternative feedstocks. One area that has received some attention concerns the risks that future biotechnology products might pose. The National Academies of Sciences, Engineering, and Medicine has examined this subject in detail and concluded that there are no new or unique risk endpoints associated with current or future products of the bioeconomy that the scientific community and regulators have not had to address already, but that the complexity, scope, scale, and tempo of bioeconomy products that are likely to come before regulators may stress regulatory agencies in terms of capacity and expertise.[15]

Development, Testbeds, and Deployment

In biotechnology, product and process are highly integrated. Process innovation at universities in Europe is much more advanced, while it is largely non-existent in the United States, where manufacturing is considered an industry of the past that is not exciting for students or faculty. Indeed, it is difficult to hire true process engineering talent in the United States, and though biological engineers coming out of university are ready to work in microbiology or synthetic biology, they are not properly trained to scale technology or work on process design.

To incentivize industry and academia to pursue innovation that offers 10-fold improvements in bioproduction technology—the scale needed to achieve a commercially viable alternative to a petroleum-based economy—funding should be directed to addressing grand challenges in bioproduction, with relevant metrics of success, that the nation's research community could address within a 5-year timeframe, much as the semiconductor and nanotechnology industries addressed their grand challenges with federally funded initiatives. Often, bioproduction needs improvements beyond using fermentation, a place where chemical engineers could play a vital role by applying the skills they developed for chemical production to a new industry with tremendous growth prospects and societal benefits.

Aside from dedicating funds to addressing grand challenges in bioprocessing and bioproduction, another step would be to follow the model used by the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs to create the nanolithography industry. Increasing SBIR/STTR funds dedicated to bioprocessing and bioproduction improvement by 10-fold would spur innovation, as would developing mechanisms to ease the transition out of the SBIR/STTR funding model and changing the statutory requirements regarding commercialization assistance that may hinder small business commercialization prospects and business development in the long run.[16]

Also needed in this realm is support for what are known as testbed facilities or sandboxes: scale-up facilities with expertise available with which to contract to help rapidly transfer scale-up knowledge to innovators. The Bioindustrial Manufacturing and Design Ecosystem, or BioMADE, is one example.

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[15]National Academies of Sciences, Engineering, and Medicine 2017. *Preparing for Future Products of Biotechnology*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24605

[16]National Academies of Sciences, Engineering, and Medicine. 2020. *Review of the SBIR and STTR Programs at the Department of Energy*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25674

This institute, with a focus on catalyzing and reducing the risk of investments in relevant infrastructure, is supported by a seven-year award that includes at least $87.5 million in federal funds from the Department of Defense (DoD) and more than $180 million in cost sharing from non-federal sources. This and similar facilities would serve the bioproduction industry in the same way that ARPANET paved the way for the internet to develop. Other examples include the National Cancer Institute's Nanotechnology Characterization Laboratory, which provides analytical expertise needed to commercialize nanotechnology-based products but that are too expensive for small companies to afford and require hard-to-find expertise, and the National Renewable Energy Laboratory's National Wind Technology Center, which provides field validation sites and composites manufacturing pilot facilities that have played a critical enabling role in the advancement of wind energy technology that has benefited the entire industry. A network of such industry-enabling facilities will offer the ability to evaluate multiple bioengineering technologies with a fail-fast approach.

Infrastructure Development

An important sticking point today in translating laboratory research to commercial production is the paucity of testbed facilities where innovators develop their scale-up procedures and innovative manufacturing technologies in partnership with experts in process and chemical engineering that will enable them to bring their products to market faster and at reduced costs. The National Institute of Standards and Technology (NIST) established the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) as a public-private partnership in 2016 to address just that challenge for the biopharmaceutical industry. Investing in the fundamental science of bioprocessing in the precompetitive space, as NIIMBL is doing for biopharmaceutical production, will benefit the entire industry, both in terms of the knowledge gained and by providing innovators with the opportunity to demonstrate that their processes are reproducible at an intermediate scale before the capital markets will step in to fund building a commercial-scale facility. The federal government can play a catalytic role here by establishing a network of regional testbed facilities—facilities that can process multiple feedstocks using multiple organisms to produce multiple products at multiple scales—enabling innovators to work out their scale-up processes and generate the performance data that would lay the groundwork for moving to commercial production. Doing so would reduce the risk that currently keeps the capital markets on the sidelines.

While there are domestic contract bioproduction facilities, many of them serve the biopharmaceutical industry and thus operate under GMP standards. Because of the fees these for-profit contract facilities charge, bioeconomy startups have difficulty competing with biopharmaceutical companies when trying to develop products that have a lower price per pound than a biomedical product or even a cosmetic ingredient. The federal government has made a significant down payment toward addressing some of the needed bioproduction capacity limitations. BioMADE is the newest example of a public-private partnership testbed bioproduction facility that, once built, will be dedicated to address some of the needs of the bioeconomy. Another such facility, the Advanced Biofuels and Bioproducts Process Development Unit (ABPDU) was funded in 2009 as part of the American Recovery and Reinvestment Act as an infrastructure investment. This DOE facility, located at Lawrence Berkeley National Laboratory, is so in demand today that it is turning away potential customers. Despite these initial federal bioproduction investments, many companies are now forced to go to contract manufacturers in Belgium, Canada, China, Germany, India, Mexico, the Netherlands, Slovakia, Slovenia, and elsewhere to access needed infrastructure that is not available domestically. In addition, there is no comprehensive, publicly available resource that documents the location and functionality of existing domestic bioproduction facilities, as exists in Europe.[17] As a consequence, this Task Force has produced an initial compilation of existing bioproduction facilities and infrastructure that might serve as the basis of a future public database demonstrating the location and whether the asset is publicly or privately affiliated (Figure 4).

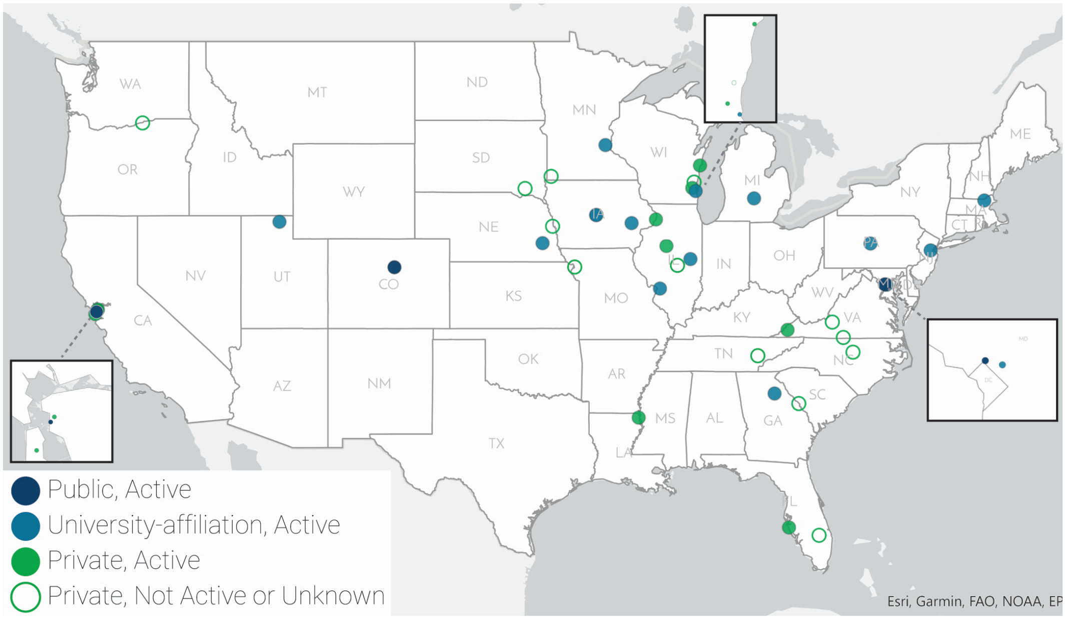

FIGURE 4 Public and Private Affiliated Bioproduction Facilities. The green, teal, and navy-blue colors respectively represent biomanufacturing plants that are privately owned, university-affiliated, or public assets. The filled and empty circles respectively represent if the plant operations are active or not/unknown.
Credit: This figure was created with the assistance of Albert Hinman, Ph.D., a postdoctoral fellow with the Engineering Biology Research Consortium

Regarding international competitiveness, if U.S. leadership is the goal, it is imperative for the United States to act now to establish more of these facilities given that other nations have already taken this step. The United Kingdom, for example, has established the National Biologics Manufacturing Centre, Centre for Process Innovation, and Industrial Biotechnology Innovation Centre to aid its nascent bioproduction industry. In the solar energy field, the failure of the federal government to help fledgling companies get past the intermediate stage of development played a significant role in China's rise as the world's predominant supplier of photovoltaic cells. If the United States does not act now and over the next five years to invest in bioproduction infrastructure strategically and aggressively, the same could happen to the U.S. bioeconomy.

Beyond funding the testbed facilities, the federal government could expand bioproduction capacity by incentivizing the use of existing scale-up infrastructure housed within established companies. The U.S. government could also implement tax breaks, subsidies, loan guarantee programs and other financial incentives for further investment in bioprocessing infrastructure and for retrofitting existing facilities, including existing idled cellulosic ethanol and pharmaceutical facilities, as well as other corn-to-ethanol facilities pivoting to additional bioproduction opportunities.

In addition, the U.S. government could support a nascent bioproduction hardware industry, perhaps by creating plug-and-play centers that provide a continuous stream of bioproduction partners.

[17] https://biopilots4u.eu/

Such centers could also have a research focus of working toward designing modular production systems that would enable companies to expand production relatively easily as demand for their produces increases. Currently, many startup companies in the bioeconomy are having to design and build their own hardware, such as novel bioreactors, to improve process yields because venture capital shies away from funding standalone equipment manufacturing firms.

RECOMMENDATIONS

The discussion above describes the key assets the United States possesses and the critical areas of research, development, and infrastructure needs that the nation must develop further to fully capitalize on those assets. As alluded to earlier in the report, there are regulatory and policy considerations that are essential elements of a holistic strategy for support the US bioeconomy. This Task Force will inform a holistic strategy in March 2022, but here we focus on the specific actions needed to move laboratory successes into testbeds and eventually into commercial production scales to advance the current U. S. bioeconomy and to build the necessary foundation for a future circular U.S. bioeconomy that moves toward net zero greenhouse gas emissions. We identified the following three needs: 1) establish a strategic bioproduction research initiative to catalyze private and public sector innovations needed to overcome existing barriers to translation; 2) establish and sustain creative public-private partnerships to unlock the decades of tacit knowledge and data within industry to accelerate technology translation; 3) create and sustain a network of next-generation bioproduction testbeds through infrastructure investments to stem the trend of off-shore technology loss.

Recommendations:

1. **The U. S. government should commit to remaining the global leader in biobased science and scale up manufacturing by establishing and funding a 5-year, $600 million[18] Bioproduction Science Initiative (BSI) that expands budgets and remits of relevant science agencies focused on advancing foundational science and technology development for current and future bioproduction, and is focused on addressing unmet research needs that hinder the translation of innovative technologies.**

   Broadly speaking, innovation in bioproduction capability can be achieved by improving predictability of living systems at scale and enabling modularity in bioproduction. Federal science agencies have made initial efforts toward these priorities, but bolder and larger efforts are needed to catalyze necessary innovation. The BSI should enable research focused on the priorities articulated in detail in this report and summarized at a high-level here:

   - Creating software-enabled metabolic pathway design programs grounded in rules, data, and simulation capabilities for generating novel molecules and products.
   - Expanding genetic and characterization tools for microbes, plants, and animal cells with proven or high potential for bioproduction, including those for reading, multiplexed editing, and writing whole genomes.
   - Developing microfluidic and digital tools to enable a predictive understanding of potential successes of transitions from laboratory-scale to industrial-scale processes through simulations, testing, data collection, and iteration.

[18]Compared to the U.S. bioeconomy, which accounts for 5.1 percent of U.S. GDP, the semiconductor industry accounts for 1.2 percent of U. S. GDP, and the CHIPS Act proposed a $30M annual R&D investment in semiconductor research and development for the next 5 years. A commensurate investment for bioproduction would amount to $120M annually for R&D investment over 5 years.

- Enabling circularity through development of next-generation bioproduction capabilities, including modular production hardware, novel software control systems, upstream flexibility in processing local, and expanded feedstocks repertoires, as well as innovating downstream processing and formulation activities for future biological inputs.

The National Science Foundation (NSF) should serve as the lead agency for BSI and establish two regional innovation accelerators (RIAs) a year focused on bioproduction. NSF supports fundamental research and education in all non-medical fields of science and engineering, and its stated mission is "to promote the progress of science, to advance the national health, prosperity, and welfare, and to secure the national defense." Given this program's inclusive remit, NSF is the ideal home for this multi-disciplinary bioproduction science initiative. Through the RIAs and complementary traditionally funded research, NSF can implement the research priorities described above, expand existing relevant commitments, forge new innovative industry partnerships, and advance their preliminary explorations of circular bioeconomy research.

The RIAs should forge new partnerships with relevant federal science agencies to build on existing expertise, leverage earlier investments, and enable coordination for research acceleration.
The FY2022 NSF Budget Request to Congress [19] describes the RIAs to be a vehicle for partnerships (industry, academies, state and local governments), but partnership between federal agencies is not included in that description. Enabling partnerships between agencies with existing expertise could further accelerate the bioeconomy and serve to begin breaking down the silos across application areas. For example, the RIAs could work with Department of Energy (DOE) programs such as the ABPDU, the Agile BioFoundry, and the Feedstock-Conversion Interface Consortium, as well as USDA's Feedstock Flexibility program to advance foundational research expanding the array of future bioeconomy feedstock options.

2. **The U.S. government should invest $1.2 billion[20] in an extensive and flexible bioproduction infrastructure—one that can process multiple feedstocks using multiple organisms to produce multiple products at multiple scale—over two years to expand domestic bioproduction capacity in an equitable and strategic manner. Additional funding for maintaining and sustaining these investments will be needed over time.**

   To maximize the potential of the U. S. bioeconomy and regain competitiveness, additional pilot- and intermediate-scale facilities with inherent flexibility and modularity are needed and must be prioritized.

   The Department of Commerce should undertake a comprehensive assessment of existing facilities and functionality, building from the work of this Task Force, to identify and realize opportunities for appropriate and equitable placement of future facilities. Considerations for implementing this expansion include access to feedstock, a trained workforce (or where a potential workforce could be developed with training/re-skilling programs),

[19]https://www.nsf.gov/about/budget/fy2022/pdf/52_fr2022.pdf
[20]Estimates for new bioproduction facilities with existing technologies range from $100,000-$200 million and implementing new flexible, modular next-generation facilities will likely fall on the higher end. This Task Force considers $1.2B as an estimate to enable the expansion of the bioproduction infrastructure called for in this report that covers pilot, intermediate, and large-scale needs.

academic and industrial partners to operate these facilities, and considerations for where this new industrial activity could most benefit communities.

A network of 10-15 new and refurbished bioproduction facilities, provided with incentives for early-stage technology development, will accelerate the transition from laboratory technologies to commercial deployment.

Previous federal bioproduction infrastructure investments such as the DOE's ABPDU, established with the American Recovery and Reinvestment Act, NIST's NIIMBL, DOD's Advanced Regenerative Manufacturing Institute, have proven valuable in generating important returns on federal investment since they were brought online, and the new DoD BioMADE facility is expected to deliver significant returns as well. However, these assets are insufficient to meet the growing demand by U.S. innovators who are increasingly forced to develop their technologies in foreign countries.

Additionally, Commerce should explore other financial incentives, such as those embodied in the CHIPS Act, to provide capital for small and large companies to meet their infrastructure needs.

Such incentives could be in the form of tax incentives and loan guarantees to enable companies to fund their own new facilities and/or acquire and refurbish existing infrastructure as their technology reaches maturation. This approach has the potential to revitalize communities whose existing bio- or chemical refineries have gone unused.

3. **To remain globally competitive, the U. S. government should establish and sustain creative public-private partnerships with the goal of reducing the time it takes to successfully scale new products from several years to months.**

Given the lack of relevant academic research programs, most U.S. expertise in bioproduction exists in companies and in the few publicly-funded facilities currently in operation. Therefore, action is needed to unlock the decades of valuable tacit knowledge and data within industry to accelerate technology translation and unleash a wave of innovation.

The Department of Commerce should incentivize partnerships between companies with deep artificial intelligence expertise and those with biomanufacturing facilities to provide services, facilities, and expertise for innovators.

Beneficial new public private partnerships could help address scale-up barriers that innovators face, such as lack of access to bioproduction facilities, inexperience to transition technology across scales, and transfer know-how and tacit knowledge. Participation in these partnerships could be contingent upon dedicating a percentage of bioproduction hours to serve the larger bioeconomy community and enable its products to be economically competitive from the outset or by providing training opportunities/internships for the future bioeconomy workforce.

Concluding remarks

A convergence in platform technologies such as artificial intelligence and synthetic biology has the potential to accelerate biotechnology solutions in a wide range of economic sectors and advance the United States toward a resilient, sustainable net zero economy. As a result of the U. S. government's incredible foundational investments that led to the creation of biotechnology, the nation is in an ideal position to capitalize on that investment by building an economy rooted in biotechnology. Indeed, as the world embraces a circular bioeconomy, the United States should leverage its unmatched biotechnology expertise to capture a leadership position in a global circular bioeconomy grounded in biotechnology, which most countries are failing to do. To do that, however, the U.S. government needs to make additional investments to facilitate the transition from laboratory scale to commercial scale.

As this report spells out, the U.S. bioeconomy is poised to deliver significantly substantial economic and public benefit, but U. S. government investments in bioeconomy-related research have remained stagnant for the last several years despite the rapid rise of new enabling capabilities such as artificial intelligence and genome editing tools that could greatly accelerate achievement of a possible $4 trillion future global bioeconomy. However, a strategic new investment on the order of $2 billion for bioproduction research and development and infrastructure support is required to realize this potential over the next 5 years.

The lack of domestic bioproduction facilities and a public database such as the European Pilots4U hinders U.S. industry access to assets that can help mature its technologies. In fact, several U.S. companies with novel technologies have moved their efforts overseas because of the lack of domestic capacity, thus allowing other countries to capture technology rights that would otherwise stay in the United States. It is imperative that the United States address this capacity gap now, and the recommendations above provide a roadmap for doing that just that. In addition, the opportunity exists for creating a novel "business-to-business" information technology infrastructure that the proposed bioproduction scaling facilities could implement, enabling innovators to design their innovative technologies with compatibility for scaling in mind.

In summary, biotechnology, through innovation in bioproduction capabilities, should be another tool in the toolbox for a net zero future by providing better bioproduction processes, innovative technologies that are cleaner and safer for workers and their communities, and applications for fighting and adapting to climate change. This is the time for the United States to make the needed investments and seize the once in a lifetime opportunity to create a future circular bioeconomy based on this "next big thing."