NATIONAL ACADEMIES Sciences Engineering Medicine

Successes and Challenges in Biomanufacturing – A Workshop

Meeting Book and Resources

October 24-25, 2022

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NOTE: All information included in this document is publicly available. Agency and office descriptions are taken directly from USG websites.

NATIONAL ACADEMIES Sciences Engineering Medicine

BOARD ON LIFE SCIENCES

Successes and Challenges in Biomanufacturing – A Workshop

National Academies of Science, Engineering, and Medicine

AGENDA AT A GLANCE

Purpose The goals of the workshop are to:

- Present a diverse array of case-studies that highlight specific successes, failures, and challenges of researching, developing, and bringing products to market in all different sectors of the biomanufacturing industry. Case-studies should touch on both technical and policy challenges encountered during the process.
- Discuss technical challenges in biomanufacturing and identify which bottlenecks are ubiquitous across different sectors, and which are sector-specific.
- Discuss methods and opportunities to overcome these challenges and engage experts in other areas of manufacturing, as well as international partners, for possible solutions in order to overcome these challenges.
- Discuss approaches that other countries are taking related to R&D, technology transfer, and policy, and dissect what opportunities the U.S. might have in adopting some of these practices or policies.
- Understand the role that biomanufacturing can play in achieving a sustainable future through a circular bioeconomy, and thinking through the steps that are needed to reach this goal.
- Discuss issues related to scaling-up of productions from small research testing to full-scale production
- Discuss current gaps in the biomanufacturing workforce and what is needed to train a new generation that can contribute to a future of sustainability.
- Look at the current landscape of regulation and standards in biomanufacturing and understand what issues exist and how those might be addressed.
- Understand what could be changed related to enhancing the understanding of biomanufacturing to the outside world.

8:45AM–5:30PM ET

October 24, 2022:

8:45-9:00AM	Opening Remarks from Workshop Planning Group
9:00-9:15AM	Opening Remarks from Schmidt Futures
9:15-10:15AM	Keynote
10:30-11:30AM	Breakout Session: Identifying Key Challenges in Different Biomanufacturing Sectors
11:30-12:30PM	Panel: Challenges in Biomanufacturing Contributing to a Circular Bioeconomy
1:30-2:30PM	Panel: Regulation and Standards of Biotechnologies in the U.S. and Abroad
2:30-3:30PM	Panel: Needs for the Future Biomanufacturing Workforce
3:45-4:45PM	Panel: Key Considerations that Prevent the Advancement of Biomanufacturing
4:45-5:30PM	Breakout: Digest Key Takeaways from the Day
6:30PM	Evening Reception (In-person only)

Successes and Challenges in Biomanufacturing – A Workshop

National Academies of Science, Engineering, and Medicine

Slido Link

https://app.sli.do/event/ggniY4gy8fM6ZV1FrVWjCB

Slido QR Code

CLICK HERE TO WATCH THE MEETING

MONDAY, OCTOBER 24, 2022

8:45am–9:00am ET

Opening Remarks from Workshop Planning Group (in-person and virtual)
Steven Moss, National Academies – Board on Life Sciences
Kristala L. J. Prather, MIT (Workshop Planning Committee Chair)

9:00am–9:15am

Opening Remarks from Schmidt Futures (in-person and virtual)
Elizabeth Young McNally, Schmidt Futures
Mary Maxon, Schmidt Futures
Andrea Hodgson, Schmidt Futures

9:15am–10:15am

Keynote (in-person and virtual)

Moderator
Kristala L. J. Prather, MIT

Speakers
Paula Hammond, MIT and President's Council of Advisors on Science and Technology (Virtual)
Susan S. Margulies, National Science Foundation – Directorate for Engineering

***Goals of the session*:**

- Understand the biomanufacturing focus and interests of the federal government and identify the knowledge, technical, and policy gaps that they are most interested in solving
- Discuss opportunities for experts from industry and academia to help advise a path forward and begin to think through the existing challenges.

10:15am–10:30am

Break

10:30-11:30

Breakout Session: Identifying Key Challenges in Different Biomanufacturing Sectors (in-person and virtual)

During this time, in-person participants will have the opportunity to discuss the prompts in small groups. For all virtual participants, please use the links below to provide input to the workshop

In-person participants, please refer to handout showing the break-out groups
Virtual participants, please participate in identifying key questions and challenges to be addressed by the workshop using these links:

- Key Questions to be Addressed over the Workshop
- Challenges Facing Biomanufacturing

Questions for all participants

- What is one question you hope will be addressed over the course of the workshop?
- What do you feel are the one or two biggest challenges facing biomanufacturing from your own experience and expertise?

Goals of the Session

Make introductions amongst the in-person group, and start to brainstorm questions and ideas that we hope to see discussed over the course of the workshop.

11:30am-12:30pm **Panel: Challenges in Biomanufacturing Contributing to a Circular Bioeconomy (in-person and virtual)**

Moderator

Jim Philp, Orgainsation for Economic Co-operation and Development (OECD) (Virtual)

Panelists

Corinne Scown, Lawrence Berkeley National Laboratory (Virtual)
Brian Fahie, Biogen
Dina Petranovic Nielsen, Novo Nordisk Foundation
Guillaume Lamy, ARD (Virtual)
Jukka Kantola, World Bioeconomy Forum

Goals of the Session

- Begin to understand where biomanufacturing might have the most substantial impact related to environmental sustainability.
- Identify key challenges that need to be addressed before biomanufacturing can be impactful to global environmental sustainability goals.
- Understand what different biomanufacturing sectors are doing to improve environmental sustainability and contribute to a circular bioeconomy, and see if there are lessons to be learned across sectors.
- Explore the international focus on biomanufacturing for sustainability, and understand what key domestic challenges might be overcome by adopting international practices and/or forming international collaborations.
- Explore tools that are available to help assess environmental sustainability and understand how they can be applied to different sectors of biomanufacturing.

12:30pm-1:30pm **Lunch**

1:30pm–2:30pm **Panel: Regulation and Standards of Biotechnologies in the U.S. and Abroad (in-person and virtual)**

Moderator

Emily Grayek, Carnegie Mellon University

Panelists

Jeffrey Baker, National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)
Sheng Lin-Gibson, National Institute of Standards and Technology
Anastasia Bodnar, United States Department of Agriculture
Manuel Porcar Miralles, University of Valencia

Goals of the Session

- Learn about the current landscape of standards and regulation related to biomanufacturing in different sectors, and understand the key similarities and differences.

- Understand the push and pull between biotechnology regulation serving as a mechanism for protection versus regulation acting as a bottleneck for getting products to market.
- Identify current challenges in establishing standards for emerging biotechnologies, such as the use of genetically engineered microbes and cell and gene therapy technologies.

2:30pm-3:30pm **Panel: Needs for the Future Biomanufacturing Workforce (in-person and virtual)**

Moderator
Emily Aurand, Engineering Biology Research Consortium

Panelists
Tom Tubon, BioMADE
Natalie Kuldell, BioBuilder
Erica Monique Vilsaint, North Carolina Community College System & BioNetwork (Virtual)
Jason Ryder, University of California, Berkeley and Joywell Foods

Goals of the Session
- Understand the landscape of workforce development and educational opportunities for biomanufacturing at all degree levels.
- Identify the current challenges in developing a biomanufacturing workforce and discuss how different sectors such as academia, industry, and government can begin to address these challenges.
- Explore opportunities for fostering diversity and equity in the biomanufacturing workforce
- Understand the needs of different sectors in developing a biomanufacturing workforce

3:30pm-3:45pm **Break**

3:45pm-4:45pm **Panel: Key Considerations that Prevent the Advancement of Biomanufacturing (in-person and virtual)**

Moderator
Sarah Richardson, MicroByre

Panelists
Stephen Sofen, Abata Therapeutics
Pulakesh Mukherjee, Imperative Ventures
Jenny Rooke, Genoa Ventures (Virtual)

Goals of the Session
- Understand the reasons that funders and developers might be disinterested in biomanufacturing, and what considerations lead to these decisions.
- Exploring patterns of mistakes that are made over and over again in the advancement of biotechnology.
- Understand the key areas that panelists feel will never benefit from biomanufacturing, and understand the reasons why.
- Explore the reasons or calculations that led the panelists to these decisions.

4:45pm-5:30pm **Breakout: Digest Key Takeaways from the Day (in-person and virtual)**
-**In-person participants** should go back to their break-out group from the beginning of the day
-**Virtual participants** can contribute using this link: Key Takeaways from Day 1

Goal of the session
- Come up with 3 key takeaways or universal challenges that were identified during the first day of the workshop

5:30pm **Adjourn Day 1**

Slido Link **Slido QR Code**

https://app.sli.do/event/ggniY4gy8fM6ZV1FrVWjCB

CLICK HERE TO WATCH THE MEETING

TUESDAY, OCTOBER 25, 2022

8:45am-9:00am ET

Opening Remarks and Digestion of Day 1 (in-person and virtual)

Deepti Tanjore, Advanced Biofuels and Bioproducts Process Development Unit (ABPDU)

9:00am-10:00am

Panel: Key Challenges Identified from Different Innovation Ecosystems (in-person and virtual)

Moderator
Krishnendu Roy, Georgia Institute of Technology and the NSF Engineering Research Center for Cell Manufacturing Technologies (CMAT)

Panelists
Maureen Toohey, BioFabUSA
Kelvin Lee, NIIMBL
Douglas Friedman, BioMADE

Goals of the Session

- Understand the landscape, reach, and goals of innovation ecosystems, especially the manufacturing USA groups that are present.
- Understand how to balance the goals of the different translational ecosystems in order to universally advance biomanufacturing
- Explore the challenges that are present when dealing with the interface of different sectors such as academia and industry, and ask how the innovation ecosystems are working to overcome those challenges.
- Explore what biomanufacturing challenges have been identified as universal bottlenecks to advancement across all three sectors represented by the manufacturing USA institutes.

10:00am-11:00am

Theme 2: Successes and Lessons Learned

Keynote: Translating Lessons from Different Sectors of Biomanufacturing (in-person and virtual)

Moderator
Kristala L.J. Prather, MIT

Panelists
Don Parsons, Moderna Therapeutics
Jennifer Holmgren, LanzaTech (Virtual)

Goals of the Session

- Explore biomanufacturing case-studies from different sectors of industry
- Understand how lessons learned from these case-studies can be used to address challenges and bottlenecks in other sectors despite the different political and economic landscape that is present.

11:00am-11:15am **Break**

11:15am-12:30pm **Panel: Sensors, Data, Analysis, and Process Control for Biomanufacturing (in-person and virtual)**

Moderator
Deepti Tanjore, *ABPDU*

Panelists
Richard Braatz, MIT
Stephen Balakirsky, Georgia Institute of Technology
Theresa Kotanchek, Evolved Analytics
Chong Yung, Agilent

Goals of the Session

- Explore specific case-studies from different sectors related to process control and data analytics to enhance biomanufacturing processes
- Understand how these technical successes might be applied to other areas of biomanufacturing and be used to overcome some of the key challenges identified over the course of the workshop.
- Understand what advances are most needed for biomanufacturing process analytics
- Explore what technologies and methodologies can be adopted from other fields of science, engineering, and manufacturing to enhance biomanufacturing

12:30pm-1:30pm **Lunch**

1:30pm-2:45pm **Panel: Infrastructure and Tools for Scaling-up for Biomanufacturing (in-person and virtual)**

Moderator
Emily Greenhagen, Ginkgo Bioworks

Panelists
Greg Russotti, Century Therapeutics
Brett Schreyer, SciFi Foods
Kris Tyner, Culture Biosciences (Virtual)
Charles Isaac, Fermic (Virtual)

Goals of the Session

- Explore specific case-studies related to infrastructure and tools for scale-up capabilities in biomanufacturing.
- Understand what infrastructure and capabilities are still needed domestically for all different sectors of biomanufacturing.
- Understand how different sectors work to accomplish scale-up, and if there are lessons to be learned in increasing production testing.

2:45pm-3:45pm **Research and Development Successes and Needs for Platforms and Organisms (in-person and virtual)**

Moderator

Sarah Richardson, MicroByre

Panelists
Nili Ostrov, Cultivarium (Virtual)
Rahul Singhvi, National Resilience (Virtual)

Goals of the Session

- Explore specific case-studies related to technological advances in platforms and organism use related to different sectors of biomanufacturing.
- Understand how lessons-learned from advances in platforms and organism use in specific sectors of biomanufacturing might be applied to other areas.
- Discuss limitations and needs that should be addressed by future research into platforms and organisms, in order for biomanufacturing to continue to advance.

3:45pm-4:00pm **Break**

4:00pm-4:45pm **Final Breakout to Discuss Communication of Biomanufacturing and Synthesize Key Takeaways from Day 2 (in-person and virtual)**

In-person participants please break-out into groups for discussion
Virtual participants please contribute to the conversation using this link: Communication of Biomanufacturing

All participants will be working toward answering the following questions

- Who are the key biomanufacturing stakeholders?
- What are the gaps in communication around biomanufacturing that currently exist?
- What communications tools can we use to address those gaps in knowledge? What key messages should the biomanufacturing community be trying to get out to a broader audience?

Goals for the Session

- Explore opportunities for effective communication of biomanufacturing to the greater public.
- Discuss final takeaways from the workshop and come up with key messages for industry, academia, and government.
- Figure out what are the next steps after the workshop is complete.

4:45pm-5:30pm **Report Out and Final Comments**

5:30pm **Adjourn Workshop**

PLANNING COMMITTEE BIOGRAPHIES

DR. KRISTALA L. J. PRATHER, (Chair) is the Arthur D. Little Professor in and Executive Officer of the Department of Chemical Engineering at MIT. She received an S.B. degree from MIT in 1994 and Ph.D. from the University of California, Berkeley (1999), and worked 4 years in BioProcess Research and Development at the Merck Research Labs prior to joining MIT. Her research interests are centered on the design and assembly of recombinant microorganisms for the production of small molecules, with additional efforts in novel bioprocess design approaches. Prather is the recipient of an Office of Naval Research Young Investigator Award (2005), a Technology Review "TR35" Young Innovator Award (2007), a National Science Foundation CAREER Award (2010), the Biochemical Engineering Journal Young Investigator Award (2011), the Charles Thom Award of the Society for Industrial Microbiology and Biotechnology (2017), and the Andreas Acrivos Award for Professional Progress in Chemical Engineering of the American Institute of Chemical Engineers (AIChE, 2021). Additional honors include selection as a Fellow of the Radcliffe Institute for Advanced Study (2014-2015), the American Association for the Advancement of Science (AAAS; 2018), the American Institute for Medical and Biological Engineering (AIMBE; 2020), and AIChE (2020).

MS. EMILY GREENHAGEN, has 17 years of experience serving the bioeconomy, leading development and successful commercialization across a range of organisms and applications. She is currently serving as Transformation Lead for an internal company-wide initiative focused on scaling Ginkgo's operations, and immediately prior served as Ginkgo's Head of Deployment for five years, during which Ginkgo progressed eight products to commercial manufacturing. Prior to her work at Ginkgo, Emily contributed to strain engineering and fermentation process development across a range of products and organisms at Microbia (now DSM), and biofuels companies Qteros and Novogy. Emily holds a bachelor's degree in biology from MIT, and helps to inform how we can best train the bioeconomy workforce of the future by serving on the external advisory board for Penn State's Center of Excellence in Industrial Biotechnology, and engaging in initiatives such as the World Economic Forum's Accelerating the Biomanufacturing Revolution.

DR. BRIAN D. KELLEY, Brian Kelley is the Senior Vice President of Process Development at VIR Biotechnology. VIR is addressing some of the world's most challenging infectious diseases using a broad portfolio of biologic modalities, in both the developed and developing worlds. Formerly, Brian was Vice President of Bioprocess Development at Genentech, covering bioprocess development, validation, and technology transfer. Prior to this, he worked 15 years at Genetics Institute/Wyeth in Andover, MA. He was an adjunct faculty member at Tufts University for 15 years where he taught graduate classes in biotechnology. He obtained his B.S. in Chemical Engineering from the University of Wisconsin-Madison, and his Ph.D. from MIT. Brian is a member of the National Academy of Engineering, has chaired the Recovery of Biological Products Board, and has been recognized by the American Chemical Society's Biotechnology division with the Michaels Award.

DR. JAMES PHILP, is currently a Policy Analyst at the OECD in Paris. His areas of interest are industrial biotechnology, synthetic biology and sustainability. He started his career in the microbiology of radioactive waste disposal and spent in total 8.5 years working for Saudi Aramco as an oilfield biotechnologist. He was an academic at Edinburgh Napier University for over 15 years, researching and teaching environmental biotechnologies such as bioremediation and bio-based production e.g. biosurfactants. He is a Fellow of the Royal Society of Chemistry (FRSC) and an Associate Fellow of the Institution of Chemical Engineers (AFIChemE). His first degree is in microbiology from the University of Edinburgh, with a Masters in Water Management from Edinburgh Napier University. For his PhD he studied microbial corrosion processes associated with the deep disposal of high level radioactive waste. He is the author of over 300 articles.

DR. SARAH RICHARDSON, Sarah is the CEO of MicroByre, a startup venture dedicated to domesticating novel bacteria for biomanufacturing. She founded MicroByre in 2017 with an award from the Department of Energy

through Cyclotron Road. Sarah's primary expertise is in industrial biotechnology, with specialties in microbiology and computer science. She is often asked to advise large scale collaborations at the intersection of computational science and biology: she worked on the NCI/DOE Collaborations Working Group for the Frederick National Laboratory Advisory Committee from 2018-2021 and is currently an advisor to the DOE Pacific Northwest National Laboratory's Predictive Phenomics Initiative Science Advisory Committee. She is also the Industry Assessment subcommittee chair for the BioMADE Education and Workforce Development Committee. In 2020 she received the Next Generation Award from the Association for Women in Science. She was named a 2015 SynBio LEAP fellow for vision and excellence in leadership and won the L'Oréal Postdoctoral Women in Science Fellowship that same year. Her Ph.D. at the Johns Hopkins School of Medicine was in Human Genetics & Molecular Biology; her thesis was on the design and construction of a synthetic yeast genome. She went on to be the Distinguished Postdoctoral Fellow in Genomics at the Lawrence Berkeley National Laboratory, first in the laboratory of Eddie Rubin at the Joint Genome Institute and then under Jay Keasling at the Joint Bioenergy Institute. Her work at LBNL centered on non-model microorganisms and cryptic CRISPR systems.

DR. KRISHNENDU ROY, is currently Regents' Professor and Robert A. Milton endowed Chair in Biomedical Engineering at Georgia Tech, where he also serves as the Director of the NSF Engineering Research Center (ERC) for Cell Manufacturing Technologies (CMaT) and The Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M) - as well as the Director of the Center for ImmunoEngineering. He has been the Technical Lead of the NIST/AMTech National Cell Manufacturing Consortium (NCMC), a national public-private partnership, focused on addressing the challenges and solutions for large scale manufacturing of therapeutic cells. Dr. Roy's research interests are in the areas of scalable cell manufacturing, Immuno-engineering, stem-cell engineering and controlled drug and vaccine delivery technologies, with particular focus in biomedical materials. In recognition of his seminal contributions to these fields, Dr. Roy has been elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE), the Biomedical Engineering Society (BMES), and the Controlled Release Society (CRS). He serves as a member of the Editorial Boards of the Journal of Controlled Release, the European Journal of Pharmaceutics and Biopharmaceutics, the Journal of Immunology and Regenerative Medicine, all from Elsevier, as well as the AIChE Journal of Advanced Biomanufacturing and Bioprocessing. He is a member of the Forum on Regenerative Medicine of the National Academies of Science, Engineering and Medicine (NASEM), and a Board Member of the Standards Coordinating Body (SCB) for Cell and Regenerative Therapies.

DR. DEEPTI TANJORE, is Director of the ABPDU and interfaces with several scientists from industry, academia, and start-ups that are each individually trying to resolve scale-up challenges for their synthetic biology–based technologies. Deepti's interests lie in articulating industry-wide issues and developing technologies that no single company is incentivized to pursue. Her research at ABPDU focuses on modeling the impact of bioprocess conditions on microbial heterogeneity and developing in-line analytical tools for real-time adaptation of process development in bioreactors. Deepti has a PhD in Biological Engineering from Pennsylvania State University and is currently enrolled for an MBA from University of California - Berkeley.

SPEAKER/ PANELIST BIOGRAPHIES

DR. PAULA T. HAMMOND is an Institute Professor at the Massachusetts Institute of Technology, and the Head of the Department of Chemical Engineering. She is a member of MIT's Koch Institute for Integrative Cancer Research, the MIT Energy Initiative, and a founding member of the MIT Institute for Soldier Nanotechnology. The core of her work is the use of electrostatics and other complementary interactions to generate functional materials with highly controlled architecture. Her research in nanomedicine encompasses the development of new biomaterials to enable drug delivery from surfaces with spatio-temporal control. She also investigates novel

responsive polymer architectures for targeted nanoparticle drug and gene delivery, and has developed self-assembled materials systems for electrochemical energy devices.

Professor Paula Hammond was elected into the National Academy of Engineering in 2017. She was elected into the National Academy of Medicine in 2016, and into the 2013 Class of the American Academy of Arts and Sciences. She won the ACS Award in Applied Polymer Science in 2018, and she is also the recipient of the 2013 AIChE Charles M. A. Stine Award, which is bestowed annually to a leading researcher in recognition of outstanding contributions to the field of materials science and engineering, and the 2014 AIChE Alpha Chi Sigma Award for Chemical Engineering Research. She was selected to receive the Department of Defense Ovarian Cancer Teal Innovator Award in 2013, which supports a single visionary individual from any field principally outside of ovarian cancer to focus his/her creativity, innovation, and leadership on ovarian cancer research. By developing degradable electrostatically assembled layer-by-layer (LbL) thin films that enable temporal and even sequential controlled release from surfaces, Paula Hammond pioneered a new and rapidly growing area of multicomponent surface delivery of therapeutics that impacts biomedical implants, tissue engineering and nanomedicine. A key contribution is her ability to introduce not only controlled release of sensitive biologics, but her recent advances in actually staging the release of these drugs to attain synergistically timed combination therapies. She has designed multilayered nanoparticles to deliver a synergistic combination of siRNA or inhibitors with chemotherapy drugs in a staged manner to tumors, leading to significant decreases in tumor growth and a great lowering of toxicity. The newest developments from her lab offer a promising approach to messenger RNA (mRNA) delivery, in which she creates pre-complexes of mRNA with its capping protein and synthesized optimized cationic polypeptides structures for the co-complexation and stabilization of the nucleic acid-protein system to gain up to 80-fold increases in mRNA translation efficiency, opening potential for vaccines and immunotherapies. Professor Hammond has published over 320 papers, and over 20 patent applications. She is the co-founder and member of the Scientific Advisory Board of LayerBio, Inc. and a member of the Scientific Advisory Board of Moderna Therapeutics.

DR. SUSAN S. MARGULIES leads the U.S. National Science Foundation's Directorate for Engineering in its mission to transform our world for a better tomorrow by driving discovery, inspiring innovation, enriching education, and accelerating access. The NSF's Engineering Directorate provides over 40 percent of federal funding for fundamental research in engineering at academic institutions, leading to innovative technologies and sustainable impacts in health, agriculture, clean energy and water, resilient infrastructure, advanced manufacturing and communication systems, and many other areas. NSF support also builds the Nation's workforce capacity in engineering and supports the diversity and inclusion of engineers at all career stages. Projects span frontier research to generate new knowledge, problem-driven research to identify new solutions to societal challenges, and application-driven research to translate discoveries to uses that enhance prosperity, equity and quality of life for all Americans.

Margulies joined the NSF as the assistant director for the Directorate for Engineering in August 2021 after leading the Wallace H. Coulter Department of Biomedical Engineering at the Georgia Institute of Technology and Emory University. While on detail at the NSF, she is a professor and Georgia Research Alliance Eminent Scholar at Georgia Tech and Emory. Margulies is internationally recognized for pioneering studies to identify mechanisms underlying brain injuries in children and adolescents and lung injuries associated with mechanical ventilation, leading to improved injury prevention, diagnosis and treatments.

Margulies' transdisciplinary scholarly impact has been recognized by her election as fellow of the American Society of Mechanical Engineers, the Biomedical Engineering Society, and the American Institute for Medical and Biological Engineering, and as a member of the National Academy of Engineering and the National Academy of Medicine.

DR. CORINNE SCOWN is the Vice President and founder of the Life-cycle, Economics, and Agronomy Division (LEAD) at the Joint BioEnergy Institute (JBEI), Deputy Director for Research of the Energy Analysis and Environmental Impacts (EAEI) Division at Lawrence Berkeley National Lab, Head of Sustainability at the Energy and Biosciences Institute (EBI), and Co-Founder of Cyklos Materials. Scown's expertise includes life-cycle assessment, techno-economic analysis, biofuels and bioproducts, and co-management of energy and water. She has led projects funded by the U.S. Department of Energy, California Energy Commission, California Air Resources Board, and Energy Biosciences Institute. She also frequently collaborates with companies ranging from small startups to large multinational corporations in the bioenergy and bioproducts domain. Scown earned a B.S. in civil engineering with a double-major in engineering and public policy at Carnegie Mellon University, and she received her Ph.D. and M.S. in civil and environmental engineering at UC Berkeley.

DR. BRIAN FAHIE is the Global Head of the Analytical Development team at Biogen supporting the entire product development portfolio (Proteins, Small Molecules, Antisense Oligonucleotides, Gene Therapy, and Devices) within Product Technical Development at Biogen. Brian is also responsible for leading the Product Technical Development team responsible for Sustainability initiatives across the entire development portfolio, including laboratory infrastructure, as part of Biogen's commitment to become fossil fuel independent by 2040, a part of Biogen's Healthy Climate Healthy Lives initiative.

MR. JUKKA KANTOLA has broad experience of the woody biomass related industries. He has held various executive positions in Europe and in Asia. Hence, he has a profound understanding of the challenges and opportunities of these economies. Jukka is well-known in the bioeconomy sector and is a passionate advocator of the circular bioeconomy. Through his companies he has advanced on the versatile valorisation of biomass for innovative applications. He has played an active role in advocating the bioeconomy in practice. In the past years he has been involved in facilitating new biorefinery ventures, a relatively new phenomenon in the forest industry. He also founded The World BioEconomy Forum in 2018, which has become one of the major platforms for the circular bioeconomy. Jukka holds a Master of Science degree from Aalto University, Finland. He also holds an eMBA from Rutgers University.

DR. DINA PETRANOVIC NIELSEN graduated in 1999 from University in Zagreb (Croatia) in Molecular Biology, and obtained her PhD in 2004 in Molecular Microbiology from University Paris XI (France). After that she did two postdocs in microbial genetics and yeast systems biology, at Technical University of Denmark, before starting her own research group at Chalmers University of Technology in Sweden, in 2008, focusing on using yeast as a model for study of protein misfolding and pathways of proteostasis, cell stress and aging in bioproduction or as a model for human misfolding diseases. In 2019 Dina joined the Novo Nordisk Foundation where she was appointed as Senior Scientific Manager for Biotechnology and after few years she took the position of the Chief Scientific Officer and Chief Partnership Officer at the Novo Nordisk Center for Biosustanability.

MR. GUILLAUME LAMY (Master's Degree in Biochemistry Engineering), has joined ARD as the Commercial Director in 2019, as well as the General Manager of its affiliate Wheatoleo. Prior to ARD and Wheatoleo, Guillaume spent more than 15 years in different Business Development & Marketing roles in Air Liquide, whether in Europe and Asia, including the Management of the Business & Marketing operations in the US for 6 years through Seppic affiliate in pharmaceutical, food and nutraceutical applications.

DR. EMILY GRAYEK is a postdoctoral researcher in Carnegie Mellon University's Department of Engineering and Public Policy. She researches the public perception of biotechnology as part of a national network working to improve the assessment of critical technologies. Her prior work has applied decision science methods to study a variety of topics including risk perception of breast cancer screening, the assessment of digital health app trials, and characterizing how critical care providers approach prognostication.

DR. JEFFREY C. BAKER holds a bachelor's degree in biochemistry and molecular biology from Northwestern University, doctorate in biochemistry from the University of North Texas, and pursued post-doctoral studies at the University of California, Berkeley. He joined Eli Lilly & Co in 1988 and led the development and manufacture of both first in class and legacy biologics. Dr. Baker received the Lilly President's Award twice, for development and launch of Humalog, the first insulin analog, and for development and launch of drotrecogen alfa, the first recombinant protein therapeutic manufactured from human cells. Dr. Baker left Lilly to be Sr. Director of Manufacturing Science and Technology at MedImmune, a subsidiary of AstraZeneca, and, in 2011 was appointed Deputy Director of the Office of Biotechnology Products in the Center for Drug Evaluation and Research (CDER) at FDA. Dr. Baker has received six CDER awards or citations for leadership and program development and in 2018 received an FDA Honors Award for contributions to "modernizing the U.S. regulatory system for biotechnology products through sustained creative leadership and collaboration." In 2019 Dr. Baker was detailed to the Advanced Manufacturing National Program Office at NIST where he worked with NIST and ManufacturingUSA programs on biopharmaceutical elements of the National Strategic Plan for Manufacturing in the United States and to speed the deployment of advanced technologies into biopharmaceutical manufacturing. He was recalled to FDA 2020 where he participated in CDER responses to the global pandemic and interagency advanced manufacturing programs through the Office of the Commissioner. He retired from the Agency in April of 2021. He remains active in the biotech community as a Senior Fellow in the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), participating in conferences, and working with several universities as a both a lecturer and advisor on program development.

DR. ANASTASIA BODNAR is an Agricultural Biotechnology Advisor and the Biotechnology Coordinator for the United States Department of Agriculture. Dr. Bodnar has served in multiple roles across USDA. She was a Regulatory Risk Assessor focusing on ecological risk assessments in the Office of Pest Management Policy and a Senior Science Advisor working on agricultural trade policy at the Foreign Agricultural Service. At the Animal and Plant Health Inspection Service, she worked on biotechnology regulatory policy and on risk analysis for invasive pest management. Dr. Bodnar began her career in the U.S. Army, focusing on public health, pest management, and environmental safety, and entered civilian service as a Presidential Management Fellow at the National Institutes of Health. Her Ph.D. in genetics, with a minor in sustainable agriculture, is from Iowa State University, and her B.S. in biology is from the University of Maryland, College Park. She also has a Certificate in Public Leadership from Brookings Executive Education.

DR. SHENG LIN-GIBSON is the Chief of the NIST Biosystems and Biomaterials Division. She oversees a multidisciplinary research portfolio that includes regenerative medicine and advanced therapies, precision medicine, synthetic and engineering biology, and complex microbial systems. She leads and coordinates the development of global standards for emerging biotechnology and biomanufacturing. She has coauthored over 80 peer-reviewed publications, serves on many Interagency Working Groups as well as numerous expert review panels and advisory boards. She has received two Department of Commerce Gold Medals.

DR. MANUEL PORCAR MIRALLES is an Applied Microbiologist and Synthetic Biologist. He has a degree in Biology (University of Valencia) and a PhD in Agronomic Engineering (UPNA, Pamplona, Spain). During four years, he worked as a postdoc at Institut Pasteur (Paris, France) working on both bacteriology (Bacillus thuringiensis) and virology (dengue virus receptor). He later worked at the Joint Genome Institute (DoE/University of Berkeley), on the characterization of extremophilic communities from Spain and California. He has published near 100 articles in peer-reviewed scientific journals, most of them of the Q1, including journals such as Nature Biotechnology, EMBO Reports, BioEssays or ACS Synthetic Biology. He has been PI in several research projects, coordinated several major EU projects on Synthetic Biology and biotechnology (BIOROBOOST and MICRO4BIOGAS); and led research contracts with private companies. He has five patents on applied microbiology and bioprocesses, and he periodically carries out a vast range of science popularization activities for journals, newspapers and radios. He has been an expert member of the Spanish Commission for Biosafety during four years, he is an expert evaluator of the European Commission and, beyond his work in microbiology and

molecular biology, he has developed Responsible Research and Innovation (RRI) approaches in the field of Synthetic Biology. He is co-founder and CEO of an award-winning spin-off of the University of Valencia, DARWIN BIOPROSPECTING EXCELLENCE, aiming at developing microbial solutions for the industry.

DR. EMILY AURAND is the Director of Roadmapping and Education at EBRC and serves as the executive editor of EBRC's technical research roadmaps and director of the EBRC Industry Internship Program. Prior to EBRC, Emily was an American Association for the Advancement of Science (AAAS) Science & Technology Policy Fellow at the National Science Foundation. At NSF her work in the Division of Chemical, Bioengineering, Environmental, and Transport Systems (CBET) included evaluation and assessment of the Synthetic Biology and Biomanufacturing portfolios, collaboration on the strategic reorganization of CBET programmatic concentrations, and development and implementation of novel funding initiatives, in addition to serving as a subject matter expert (a biologist amongst engineers). During her AAAS fellowship, Emily also served as a co-chair of the Fellows' Science Diplomacy Affinity Group, which explores how science and technology cooperation can be used as a tool for diplomacy. Emily received a B.S. in Biomedical Sciences from Colorado State University and a Ph.D. in Neuroscience from the University of Colorado. She continued her academic training in Trieste, Italy with a neuroengineering post-doctoral fellowship at the International School for Advanced Studies (SISSA). Her scientific research experience spans the fields of developmental neurobiology, biomaterial development, and neural tissue engineering and biocompatibility.

DR. JASON RYDER is a bioprocess engineer, entrepreneur, and educator with experience in process and product development, engineering design, scale up, and commercialization in the industrial biotech and food tech sectors. His professional work has ranged from small molecules to proteins with applications spanning sustainable chemicals, fuels, materials, and foods. Jason is also the Chief Technology Officer and Co-Founder of Joywell Foods, a food technology company building a new category of food and beverages based on naturally sweet proteins. Prior to Joywell, Jason spent time in senior technical leadership roles at Amyris, Bolt Threads, and Hampton Creek / Eat JUST. Jason earned a B.S. in Chemical Engineering from the University of Alabama and a Ph.D. in Chemical Engineering from the University of California at Berkeley. In 2018 he joined the UC Berkeley faculty in the Department of Chemical and Biomolecular Engineering, where he currently serves as Adjunct Professor and Executive Director of the Master of Bioprocess Engineering (MBPE) program.

DR. NATALIE KULDELL leads BioBuilder, a nonprofit organization that inspires the next generation of innovators with authentic science and engineering. BioBuilder's synthetic biology curriculum breeds excitement by helping students and teachers design and then build biotechnologies that solve real problems throughout the US and around the world. A BioBuilder textbook was published by O'Reilly Media. BioBuilder opened a community lab in Kendall Square's LabCentral in 2017, and a second in 2021 inside Ginkgo Bioworks. Dr. Kuldell studied Chemistry as an undergraduate at Cornell, completed her doctoral and post-doctoral work at Harvard Medical School, and taught at Wellesley College before joining the Department of Biological Engineering faculty at MIT in 2003. She is the 2020 recipient of the Margret and H.A. Rey Curiosity Award and the Million Women Mentors STEM Trailblazer Award.

MS. ERICA MONIQUE VILSAINT, BS, MAS, ELPHD-AWCPE Ph.D student: Executive Director of BioNetwork and Life Sciences, North Carolina Community College System (NCCCS). Erica has a bachelor's in Biological Sciences and a master's in Animal Science from North Carolina State University (NCSU). She remains academically engaged through MBA coursework with NC State's Poole College of Management business program and admission to NC State's College of Education's Educational Leadership, Policy, and Human Development doctoral program, where her program area of study is Adult, Workforce, and Continuing Professional Education. Erica has held biopharmaceutical and bioanalytical industry-based positions in quality assurance and control and process improvement. Her roles in professional development and marketing at the Biomanufacturing Training and Education Center (BTEC) of NCSU's College of Engineering focused on workforce development in biopharma and lifelong learning through training and education. Erica's newest appointment is as

the Executive Director of BioNetwork and Life Sciences, which allows her to continue life science contributions as the primary contact for biotechnology-related business and industry, and collaborate with other members of the NC Community College System to achieve specific education and training objectives relative to NC Community College's guiding goals of student success, student access, and program quality. She is committed to diversity, equity, inclusion, and accessibility (DEIA), serving as BioMADE's Education and Workforce Development DEIA subcommittee co-chair.

DR. THOMAS TUBON is currently appointed as the Chief Workforce Development Officer for the BioIndustrial Manufacturing and Design Ecosystem (BioMADE) Manufacturing Innovation Institute. BioMADE joins eight DoD-sponsored institutes as part of the Manufacturing USA network and is the16th institute that was created to develop an end-to-end ecosystems for domestic manufacturing to secure America's future through manufacturing innovation, education, and collaboration. Dr. Tubon leads the Education and Workforce Development initiatives for BioMADE, with a specific focus on bioindustrial manufacturing and engineering biology. Prior to his appointment with BioMADE, Dr. Tubon served as a Professor in the Biotechnology Program at Madison Area Technical College for 13 years. During this time, he led several National Science Foundation Advanced Technological Education grant projects to establish and scale an emerging technology program in Stem Cells and Cell Manufacturing and oversee a Coordination Network project for Advanced Manufacturing of Cell and Tissue Products. While at Madison College, Dr. Tubon was responsible for the development of bioscience workforce and strategic implementation of programs for local, regional, and national-level adoption and scale-up. In this role, he has facilitated the creation of a broad network of industry, community, and academic stakeholders, that promote career pathways in Science, Technology, Engineering, and Mathematics (STEM). Dr. Tubon has served as a CoPI on the NSF ATE InnovATEBIO Center for Biotechnology Education, and the NSF Advancing Research Impact in Society (ARIS) Center leadership team for workforce development and strategic partnerships. Dr. Tubon holds a Ph.D. in Molecular Genetics from Stony Brook University and Cold Spring Harbor Laboratory and a BS in Molecular Biology from San Diego State University.

DR. STEPHEN SOFEN, CTO, Abata Therapeutics. Dr. Sofen is an accomplished CMC leader with over 20 years of biotech and pharma experience. He previously worked on development and manufacturing commercialization projects including global CMC regulatory filings at established biotech companies Genzyme and Biogen, as well as start-ups CRISPR Therapeutics, Kaleido Biosciences and now Abata. The projects span numerous platform technologies including small molecules, mono- and polyclonal antibodies, recombinant proteins, autologous and allogeneic gene edited cell therapies, viral vectors, and polymeric drugs delivered by parenteral and oral administration. Licensed products include Clolar, Fludara, Hectorol, Kynamro, Campath, Thymoglobulin, Leukine, and Renvela.

DR. PULAKESH MUKHERJEE is a partner at Imperative Ventures. Before co-founding Imperative, Pulakesh spent ten years at BASF Venture Capital sourcing and executing investments in the energy, agriculture, chemical, and industrial sectors. During that time he served as a director or observer on the boards of early-stage technology companies. Prior to his role in venture capital, Pulakesh gained over ten years of experience in international business development, sales, marketing, and chemical process scale-up while working at BASF. He serves on numerous industry advisory boards, including the NREL Investor Advisory Board, Activate, and Rocky Mountain Institute. Pulakesh has a PhD from Stanford University and a M.Sc. from IIT Kanpur, India. He has published in peer-reviewed journals and has co-authored more than 15 patents.

DR. JENNY ROOKE is the Founder and Managing Director of Genoa Ventures, where she leverages her unique toolkit of genetics domain expertise, strategic business acumen, and venture investing to launch and empower the next generation of category-defying companies at the convergence of biology and technology. She has over fifteen years of investing experience, beginning at Fidelity Biosciences in 2006 as a Kauffman Fellow. After Fidelity, Jenny helped establish the investing function at the Gates Foundation, funding companies in genetic engineering, diagnostics, and synthetic biology. Jenny began her own investing practice in 2014, building the

largest life sciences syndicate on AngelList, and achieving one of the highest-performing AngelList syndicates of any sector. Her prior investments include Zymergen (NASDAQ:ZY), Caribou (NASDAQ:CRBU), Intabio (acquired by Danaher Sciex), Accuri (acquired by Becton Dickinson), and Topaz (acquired by Sanofi). Prior to her investing career, Jenny was a management consultant with McKinsey for the pharma and biotech sector. She also served in executive management roles at U.S. Genomics, leading Corporate Development and Research & Development. Jenny studied physics and software engineering at Georgia Tech and has a PhD in genetics from Yale University, where she was a National Science Foundation Fellow.

DR. DOUGLAS FRIEDMAN is CEO of BioMADE, the Bioindustrial Manufacturing Innovation Institute. In founding BioMADE, Doug seeks to secure the growth of the U.S. industrial biomanufacturing ecosystem and advance the bioeconomy. He is also President of the Engineering Biology Research Consortium (EBRC), a nonprofit membership organization focused on advancing precompetitive technologies in a safe, secure, sustainable, and ethical manner. At EBRC, Doug focuses on strategic initiatives, serves on the board and key leadership groups, and mentors science policy postdoctoral fellows. He was the inaugural Executive Director of EBRC from 2016 to 2021. His primary scientific and technical interests lie in the fields of synthetic biology, biomanufacturing, and modern biotechnology. Doug's policy interests include development of sustainable biotechnology, safeguarding the bioeconomy, and accelerating technical advancement by building diverse, robust community partnerships. He regularly serves as a subject matter expert on emerging biotechnologies, biotechnology policy, and national security topics at the interface of the biological and chemical sciences. Doug participates in more than a dozen external scientific and policy committees and boards. Prior to his role at EBRC, Doug was a study director and senior program officer with the Board on Chemical Sciences and Technology at the National Academies of Sciences, Engineering, and Medicine. His primary portfolio focused on the advancement of science and engineering at the interface of chemistry and biology, often as they related to national security. Earlier in his career, Doug performed research in physical organic chemistry and chemical biology in academia and industry. He earned a Ph.D. in Chemistry from Northwestern University and a B.S. in Chemical Biology from the University of California, Berkeley.

DR. KELVIN H. LEE is Gore Professor of Chemical and Biomolecular Engineering at the University of Delaware and is Director of NIIMBL: the National Institute for Innovation in Manufacturing Biopharmaceuticals, one of 16 Manufacturing USA Institutes. He previously served as Director of the Delaware Biotechnology Institute. He received a BSE in Chemical Engineering from Princeton and PhD in Chemical Engineering from Caltech. He spent several years in the Biotechnology Institute at the ETH in Zurich, Switzerland and also completed a postdoc in Caltech's Biology Division. Prior to his current appointment, he was on the faculty at Cornell University where he held the titles of: Samuel C. and Nancy M. Fleming Chair Professor, Professor in the School of Chemical and Biomolecular Engineering, Director of the Cornell Institute for Biotechnology, and Director of the New York State Center for Life Science Enterprise. He has been recognized with a number of awards including: AIMBE Fellow, AAAS Fellow, Fellow of the National Academy of Inventors, Inaugural Winner of the American Electrophoresis Society Lifetime Achievement Award, AIChE Professional Progress Award, Biotechnology and Bioengineering Elmer Gaden Award, and the ACS BIOT Marvin Johnson Award. He is currently also serving as interim Vice President for Research, Scholarship, and Innovation at the University of Delaware.

MS. MAUREEN K. TOOHEY is the Deputy Executive Director for ARMI and serves as Secretary of the Board where she manages all facets of building an entirely new sector through an industry, government and academic collaboration accelerating the deployment of emerging large-scale manufacturing of engineered tissues and tissue-related technologies. Drawing from her past experiences as an entrepreneur, intellectual property expert, and new business development professional, Maureen brings a unique perspective to ARMI’s efforts to foster innovation, encourage collaboration, and drive economic growth. Toohey is the founding member of the Toohey Law Group LLC where she counsels clients regarding the strategic protection and transfer of intellectual property rights, supervises the prosecution of intellectual property portfolios, and litigates intellectual property disputes. Prior to founding the Toohey Law Group in 2007, Maureen served as General Counsel for DEKA Research &

Development Corporation. Maureen also practiced in the Silicon Valley Office of Weil, Gotshal & Manges LLP. Toohey received a B.S. in Chemistry from the United States Naval Academy at Annapolis, MD. After serving on active duty in the United States Navy, she attended law school at the University of Virginia School of Law and received her J.D. in 1996. Additionally, Maureen is active in the Federal Circuit Bar Association, AIPLA, and IP Law Section of the ABA, and serves as an advisor to FIRST (For Inspiration and Recognition of Science and Technology), a non-profit organization dedicated to inspiring young people to pursue a career in science and engineering.

DR. DONALD PARSONS is Vice President, Early Technical Development and Lipid Nanoparticle Process Development at Moderna Therapeutics in Norwood, Massachusetts, USA. The research of his team focuses on the fundamental process science behind the manufacture of lipid nanoparticles for mRNA delivery; and the development and scaleup of these processes. Additionally, he plays a matrix leadership role coordinating CMC activities for Moderna's early-phase clinical pipeline; as well as leading Moderna's small molecule process chemistry efforts. Prior to his tenure at Moderna, Don spent six years with BIND Therapeutics in Cambridge, Massachusetts, where he led analytical development and process chemistry functions supporting the development and clinical translation of small molecule-loaded polymeric nanoparticles as Vice President, Pharmaceutical Development. Don has extensive experience in the clinical translation of complex drug delivery systems, including process development, analytical characterization, and application of Quality by Design principles to these systems.

Dr. Parsons is Vice President, Early Technical Development and Lipid Nanoparticle Process Development at Moderna. He has over 25 years of experience in the pharmaceutical industry leading nanoparticle and small molecule process and analytical development. In his role at Moderna he leads the development of manufacturing processes for lipid nanoparticle products as well as small molecule process chemistry; he also plays a matrix leadership role coordinating CMC activities for Moderna's early-phase clinical pipeline. Prior to his tenure at Moderna, Don spent six years with BIND Therapeutics in Cambridge, Massachusetts, where he led analytical development and process chemistry functions as Vice President, Pharmaceutical Development. Dr. Parsons has extensive experience in the clinical translation of complex drug delivery systems, including process development, analytical characterization, and application of Quality by Design principles to these systems. He has a B.A. in Chemistry from Dartmouth College (1987) and a Ph.D. in Physical Chemistry from University of Wisconsin-Madison (1994).

DR. JENNIFER HOLMGREN is CEO of LanzaTech. Under Jennifer's guidance, LanzaTech is developing a variety of platform chemicals and fuels, including the world's first alternative jet fuel derived from industrial waste gases. She is also the Director and Chair of the LanzaJet Board of Directors. Prior to LanzaTech,

Jennifer was VP and General Manager of the Renewable Energy and Chemicals business unit at UOP LLC, a Honeywell Company. While there, she was a key driver of their leadership in low carbon aviation biofuels. Jennifer has authored or co-authored 50 U.S. patents and more than 30 scientific publications and is a member of the National Academy of Engineering. She is on the Governing Council for the Bio Energy Research Institute in India. The institute has been set up by the DBT (Department of Biotechnology, Indian Government) and IOC (Indian Oil Corporation). She also sits on the Advisory Council for the Andlinger Center for Energy and the Environment at Princeton University, the National Academies' Board on Energy and Environmental Systems (BEES), the Halliburton Labs Advisory Board, the Universiti Teknologi PETRONAS International Advisory Council, and the Founder Advisory for The Engine, a venture capital fund built by MIT that invests in early-stage science and engineering companies.

Jennifer holds a B.Sc. degree from Harvey Mudd College, a Ph.D. from the University of Illinois at Urbana-Champaign and an MBA from the University of Chicago.

DR. RICHARD BRAATZ is the Edwin R. Gilliland Professor of Chemical Engineering and Associate Faculty Director of the Center for Biomedical Innovation at the Massachusetts Institute of Technology (MIT), where he conducts research into advanced biopharmaceutical manufacturing systems. In this role, he leads process data analytics, mechanistic modeling, and control systems for several projects on campus, including those focused on monoclonal antibody, viral vaccine, and gene therapy manufacturing. Dr. Braatz received an M.S. and Ph.D. from the California Institute of Technology and was the Millennium Chair and Professor at the University of Illinois at Urbana-Champaign and a Visiting Scholar at Harvard University before moving to MIT. Dr. Braatz has collaborated with more than 20 companies including Novartis, Pfizer, Merck, Bristol-Myers Squibb, Biogen, Amgen, and Takeda. Honors include the AIChE Computing in Chemical Engineering Award, the AIChE Excellence in Process Development Research Award, and the IEEE Control Systems Society Transition to Practice Award. He has published over 300 journal papers and three books. Dr. Braatz is a Fellow of IEEE, IFAC, AIChE, and AAAS and a member of the U.S. National Academy of Engineering.

DR. CHONG WING YUNG is currently the Associate Director of University Relations & External Research and a Master Scientist at Agilent Technologies. Chong joined Agilent in 2011 as a Staff Scientist in Agilent Labs and has made key contributions to the invention and development of commercial cell analysis and genome engineering technologies. In 2018, he joined University Relations and leveraged his technical expertise and distinctive creativity to lead the global flagship research programs – Application and Core Technology University Research (ACTUR), Agilent Early Career Professor Award (AECPA), Thought Leader Award (TL) – and drive broad technological impact and business value at Agilent. He also leads institute-specific partnerships like the Agilent Biodesign Program at Berkeley and Agilent Fellowship programs at Stanford and USC to advance innovations in science and technology, as well as education. In his early career, Chong was a bioprocess specialist at Genentech's research bioprocess development and biomanufacturing facilities. Chong was a CIMIT Postdoctoral Fellow at Harvard University and completed his Ph.D. in Chemical Engineering at the University of Maryland, College Park, and B.S. in Chemical Engineering at UCI. He has been a member of the US Frontiers of Engineering - National Academy of Engineering since 2013. In his free time, he enjoys volunteering with Science is Elementary to do STEM educational outreach for underprivileged children at local Title 1 schools and spending quality time outdoors with his wife and two young children.

DR. STEPHEN BALAKIRSKY is a Regents' Researcher with the University System of Georgia, the Chief Scientist for the Aerospace, Transportation & Advanced Systems Laboratory at the Georgia Tech Research Institute (GTRI), and the Director of Technical Initiatives at the Petit Institute for Bioengineering and Bioscience at the Georgia Institute of Technology (GaTech). Dr. Balakirsky's research interests include bio-automation, robotic architectures, planning, robotic standards, and autonomous systems testing. His work in knowledge driven robotics couples real-time sensors and knowledge repositories to allow for flexibility and agility in robotic systems ranging from assembly and manufacturing systems to surveillance and logistics systems. The framework promotes software reuse and the ability to detect and correct for execution errors. Previously, Dr. Balakirsky worked as a project manager at the National Institute of Standards and Technology (NIST) and was a senior research engineer at the Army Research Laboratory (ARL). At ARL, Dr. Balakirsky performed mobile robotics research in several areas, including command and control, mapping, human-computer interfaces, target tracking, vision processing and tele-operated control. Dr. Balakirsky obtained his doctorate in engineering from the University of Bremen in Bremen, Germany and his master's and bachelor's degrees in electrical engineering from the University of Maryland in College Park, MD.

DR. THERESA KOTANCHEK is the CEO of Evolved Analytics LLC, a data science, predictive analytics and augmented intelligence software and solutions provider. Her technical interest is in the creation and application of systems to accelerate the design, development, manufacture, and commercialization of sustainable chemical, material, and biological products and processes. Prior to assuming her current role, Dr. Kotanchek spent 23 years in executive and leadership positions at The Dow Chemical Company. There her responsibilities included Vice President for Sustainable Technologies, Innovation Sourcing, and Information Research; Chief Technology Officer

of Asia Pacific; Global Director of Dow Ventures; Global R&D Director of Dow Plastics, and Corporate Director of Materials Science and Engineering. Theresa holds a PhD in Materials Science, a MS in Ceramic Science, and a BS in Ceramic Science & Engineering from The Pennsylvania State University. She is member of the National Academy of Engineering and currently chairs NASEM's National Materials and Manufacturing Board.

DR. KRISTINA TYNER is the Senior Director of Bioprocessing and microbial fermentation subject matter expert at Culture Biosciences. In addition to creating technical content resources for customers, she works onboarding new customers and assists with technical transfer and successful scale-down into Culture's reactors. Prior to joining Culture, Kris worked at Zymergen overseeing tech transfer and scale-down of fermentation processes, including scale-down into 96-well plates for high-throughput screening and providing technical guidance across fermentation projects. Kris also worked at OPX biotechnologies as a senior scientist in Physiology and Bioprocess Research. Throughout her career, Kris has worked with a wide variety of organisms including bacteria, yeast, and filamentous fungi. Kris received her degree in Genetics and Microbiology from Monash University in Melbourne, Australia. She then completed graduate studies in molecular, developmental and cellular biology studying signaling in muscle stem cells at the University of Colorado Boulder and a postdoctoral fellowship at National Jewish Health working on cell signaling in macrophages.

MR. CHARLES ISAAC Charles Isaac us the Manufacturing Technology Transfer Director at Fermic, a Mexico City based biomanufacturing contract manufacturing organisation. His career has been focused on the scale up and commercialisation of bioproduct. Charles professional career began after receiving Masters degrees in Microbiology and Business Administration. His experience in large scale production of bio-products started at Karl Strauss Breweries in San Diego. Charles worked for several start-ups biotechs in San Diego with the highlight being roles at Diversa/Verenium Corp where dozens of bioproducts were developed and scaled up to commercial production. bp's acquisition of Verenium's biofuels business led Charles a Technology Manager role in the bp Office of the Chief Scientist where he served for 7 years leading technology development projects and as Secretary of the bp Science Council. Charles led the buildout and development of a high throughout medium scale strain selection lab at Zymergen before taking his role a Fermic. At Fermic Charles works with new and existing clients to transfer their processes, fermentation and DSP, to the Fermic site and oversees the on-going commercial operations at the 2.3 million litre capacity facility.

DR. GREG RUSSOTTI is the Chief Technology Officer at Century Therapeutics, a company developing iPSC-derived, allogeneic immune cell therapy products for hematology/oncology indications. Before joining Century in January 2020, Greg was Vice President of Cell Therapy Development and Operations at Celgene. During his 13 year tenure at Celgene, he guided CMC efforts for five different cell therapy products to IND and clinical stage development. Greg was also a leader in establishing in-house clinical manufacturing at Celgene and in building Celgene's first commercial CAR T manufacturing facility. Prior to Celgene, Greg held various leadership roles at Merck Research Laboratories, developing vaccines and monoclonal antibodies for clinical and commercial manufacturing. Greg received his B.S. and M.S. degrees in Chemical Engineering from Rensselaer Polytechnic Institute and his Ph.D. in Chemical and Biochemical Engineering from Rutgers University.

DR. H. BRETT SCHREYER has a BS and PhD in chemical engineering and for over 20 years has focused his energy on harnessing microorganisms and mammalian cells to produce products that are either challenging to manufacture by pure chemical means or the process is not environmentally sound. His passion is to convert ideas that have been realized in the lab and make them a reality, to bridge the gap from 'proof-of-concept' to large scale production. Brett has years of experience in scaling up bioprocesses for the production of renewable and bio-based chemicals. He takes processes established in bench-scale fermenters and optimizes them for large scale production, confirms process performance at pilot scale, and designs processes and equipment for large-scale equipment. The many scale-up projects Brett has worked on includes managing for Genomatica the piloting of a fermentation process that led to a successful production campaign of over 2.2 million kg of a renewable chemical in 500m3 fermenters and a piloting and demonstration campaign that culminated in designing 400m3

aerobic fermenters while he was at Verdezyne. As Director of Process Engineering at SCiFi Foods, he is currently applying his expertise in industrial biotech to cultivated meat by navigating the path towards large scale cultivated beef production to produce sustainable food at cost competitive prices.

DR. NILI OSTROV is the Chief Scientific Officer at Cultivarium, a non-profit startup developing open source tools to accelerate research and development of non-model microorganisms for biotechnology. Previously, she was the Director of Molecular Diagnostics at Pandemic Response Lab, a high-throughput diagnostic and genome biosurveillance COVID-19 facility established for New York City. Trained in Microbiology, Chemistry and Genetics, Nili has led several technology development projects in the field of synthetic biology. She received her PhD from Columbia University where she used baker's yeast as an environmental sensor. As a fellow at Harvard, she spearheaded construction of synthetic chromosomes, and established genome-scale engineering methods for non-model microbes. At Cultivarium, Nili is interested in bridging the gap between academic and industrial biotechnology.

DR. RAHUL SINGHVI Rahul Singhvi is a global leader in the Life Sciences industry and serves as the Chief Executive Officer of Resilience. Most recently, Rahul was an Operating Partner at Flagship Pioneering, a Boston-based life sciences innovation firm where he was responsible for founding and operating companies launched from Flagship's innovation foundry, Flagship labs. Before joining Flagship, Rahul was the Chief Operating Officer of Takeda's Vaccine Business Unit where he was responsible for worldwide vaccine CMC and manufacturing operations. During his six-year tenure at Takeda, the vaccine business grew to over 500 employees and created an industry leading late-stage pipeline of vaccine candidates against dengue, norovirus, and zika. Before Takeda, Rahul was President and CEO of Novavax, Inc. (Nasdaq: NVAX) where he transformed the company from a specialty pharmaceutical business to a vaccine development company with vaccine candidates against influenza (funded by BARDA) and respiratory syncytial virus (RSV). Rahul's professional career began at Merck & Co in 1994, where he held several positions in R&D and manufacturing. Rahul serves on the Executive Advisory Board of the Leonard Davis Institute (LDI) of Health Economics at the University of Pennsylvania and on the Scientific Advisory Board of the anti-microbial resistance research group at the Singapore MIT Advance Research and Technology program. He is a mentor instructor in the Undergraduate Projects Opportunity Program (UPOP) at MIT and is a visiting lecturer at the University College London (UCL). Dr. Singhvi graduated as the top ranked chemical engineer from the Indian Institute of Technology, Kanpur, India and obtained both his M.S. and Sc.D. chemical engineering degrees from MIT. He received an MBA from the Wharton School of the University of Pennsylvania, where he graduated as a Palmer Scholar.

STATEMENT OF TASK

The National Academies of Sciences, Engineering, and Medicine (The National Academies) will appoint a committee of experts to organize and convene a workshop to explore domestic and international advancements in biomanufacturing. The workshop will highlight examples of recent achievements in biomanufacturing and explore outstanding needs across science and policy to further enhance the circular bioeconomy. The activity will be an opportunity to bring together experts across diverse and relevant fields, such as the life sciences, biotechnology, engineering, and computer and information sciences, and policy to foster collaborative discussion and engagement in considering areas of mutual interest and greatest near-term impact in achieving and leveraging biomanufacturing.

Workshop presentations and discussions will include:

- Exploration of case studies from recent successes in the U.S. and internationally on the successful development of biomanufactured products and their application. Case studies will explore lessons learned with an emphasis on practices that could be applied in different contexts.
- Understanding challenges and bottlenecks that are related to specific types of biomanufacturing, and identifying those challenges that are universal across different biomanufacturing platforms. This could include challenges related to the science and engineering of biomanufacturing, scale-up, federal regulation, workforce gaps, and other factors that impact the transition to more sustainable biomanufacturing practices.
- Opportunities to learn from international practices in biomanufacturing, and to foster domestic and international collaboration. This includes leveraging collaborative platforms to expand biomanufacturing development and application.
- Exploration of international strategic plans that include the application and development of a circular bioeconomy to achieve net zero goals.
- Exploration of gaps in domestic infrastructure and coordination, and identification of successful international practices that could be deployed

The presentations and discussions at the workshop will be documented in a workshop proceedings-in-brief, written by a designated rapporteur in accordance with institutional guidelines.

READ-AHEAD MATERIALS (START ON NEXT PAGE)

Read Ahead 1: Executive Order on Advancing Biotechnology and Biomanufacturing

Read Ahead 2: Case Studies – Therapies of the State

Read Ahead 3: Case Studies – Schmidt Bioeconomy Task Force Strategy

SEPTEMBER 12, 2022

Executive Order on Advancing Biotechnology and Biomanufacturing Innovation for a Sustainable, Safe, and Secure American Bioeconomy

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. Policy. It is the policy of my Administration to coordinate a whole-of-government approach to advance biotechnology and biomanufacturing towards innovative solutions in health, climate change, energy, food security, agriculture, supply chain resilience, and national and economic security. Central to this policy and its outcomes are principles of equity, ethics, safety, and security that enable access to technologies, processes, and products in a manner that benefits all Americans and the global community and that maintains United States technological leadership and economic competitiveness.

Biotechnology harnesses the power of biology to create new services and products, which provide opportunities to grow the United States economy and workforce and improve the quality of our lives and the environment. The economic activity derived from biotechnology and biomanufacturing is referred to as "the bioeconomy." The COVID-19 pandemic has demonstrated the vital role of biotechnology and biomanufacturing in developing and producing life-saving diagnostics, therapeutics, and vaccines that protect Americans and the world. Although the power of these technologies is most vivid at the moment in the context of human health, biotechnology and biomanufacturing can also be used to achieve our climate and energy goals, improve food security and sustainability, secure our supply chains, and grow the economy across all of America.

For biotechnology and biomanufacturing to help us achieve our societal goals, the United States needs to invest in foundational scientific capabilities. We need to develop genetic engineering technologies and techniques to be able to write circuitry for cells and predictably program biology in the same way in which we write software and program computers; unlock the power of biological data, including through computing tools and artificial intelligence; and advance the science of scale-up production while reducing the obstacles for commercialization so that innovative technologies and products can reach markets faster.

Simultaneously, we must take concrete steps to reduce biological risks associated with advances in biotechnology. We need to invest in and promote biosafety and biosecurity to ensure that biotechnology is developed and deployed in ways that align with United States principles and values and international best practices, and not in ways that lead to accidental or deliberate harm to people, animals, or the environment. In addition, we must safeguard the United States bioeconomy, as foreign adversaries and strategic competitors alike use legal and illegal means to acquire United States technologies and data, including biological data, and proprietary or precompetitive information, which threatens United States economic competitiveness and national security.

We also must ensure that uses of biotechnology and biomanufacturing are ethical and responsible; are centered on a foundation of equity and public good, consistent with Executive Order 13985 of January 20, 2021 (Advancing Racial Equity and Support for Underserved Communities Through the Federal Government); and are consistent with respect for human rights. Resources should be invested justly and equitably so that biotechnology and biomanufacturing technologies benefit all Americans, especially those in underserved communities, as well as the broader global community.

To achieve these objectives, it is the policy of my Administration to:

(a) bolster and coordinate Federal investment in key research and development (R&D) areas of biotechnology and biomanufacturing in order to further societal goals;

(b) foster a biological data ecosystem that advances biotechnology and biomanufacturing innovation, while adhering to principles of security, privacy, and responsible conduct of research;

(c) improve and expand domestic biomanufacturing production capacity and processes, while also increasing piloting and prototyping efforts in biotechnology and biomanufacturing to accelerate the translation of basic research results into practice;

(d) boost sustainable biomass production and create climate-smart incentives for American agricultural producers and forest landowners;

(e) expand market opportunities for bioenergy and biobased products and services;

(f) train and support a diverse, skilled workforce and a next generation of leaders from diverse groups to advance biotechnology and biomanufacturing;

(g) clarify and streamline regulations in service of a science- and risk-based, predictable, efficient, and transparent system to support the safe use of products of biotechnology;

(h) elevate biological risk management as a cornerstone of the life cycle of biotechnology and biomanufacturing R&D, including by providing for research and investment in applied biosafety and biosecurity innovation;

(i) promote standards, establish metrics, and develop systems to grow and assess the state of the bioeconomy; to better inform policy, decision-making, and investments in the bioeconomy; and to ensure equitable and ethical development of the bioeconomy;

(j) secure and protect the United States bioeconomy by adopting a forward-looking, proactive approach to assessing and anticipating threats, risks, and potential vulnerabilities (including digital intrusion, manipulation, and exfiltration efforts by foreign adversaries), and by partnering with the private sector and other relevant stakeholders to jointly mitigate risks to protect technology leadership and economic competitiveness; and

(k) engage the international community to enhance biotechnology R&D cooperation in a way that is consistent with United States principles and values and that promotes best practices for safe and secure biotechnology and biomanufacturing research, innovation, and product development and use.

The efforts undertaken pursuant to this order to further these policies shall be referred to collectively as the National Biotechnology and Biomanufacturing Initiative.

Sec. 2. Coordination. The Assistant to the President for National Security Affairs (APNSA), in consultation with the Assistant to the President for Economic Policy (APEP) and the Director of the Office of Science and Technology Policy (OSTP), shall coordinate the executive branch actions necessary to implement this order through the interagency process described in National Security Memorandum 2 of February 4, 2021 (Renewing the National Security Council System) (NSM-2 process). In implementing this order, heads of agencies (as defined in section 13 of this order) shall, as appropriate and consistent with applicable law, consult outside stakeholders, such as those in industry; academia; nongovernmental organizations; communities; labor unions; and State, local, Tribal, and territorial governments to advance the policies described in section 1 of this order.

Sec. 3. Harnessing Biotechnology and Biomanufacturing R&D to Further Societal Goals. (a) Within 180 days of the date of this order, the heads of agencies specified in subsections (a)(i)-(v) of this section shall submit the following reports on biotechnology and biomanufacturing to

further societal goals related to health, climate change and energy, food and agricultural innovation, resilient supply chains, and cross-cutting scientific advances. The reports shall be submitted to the President through the APNSA, in coordination with the Director of the Office of Management and Budget (OMB), the APEP, the Assistant to the President for Domestic Policy (APDP), and the Director of OSTP.

(i) The Secretary of Health and Human Services (HHS), in consultation with the heads of appropriate agencies as determined by the Secretary, shall submit a report assessing how to use biotechnology and biomanufacturing to achieve medical breakthroughs, reduce the overall burden of disease, and improve health outcomes.

(ii) The Secretary of Energy, in consultation with the heads of appropriate agencies as determined by the Secretary, shall submit a report assessing how to use biotechnology, biomanufacturing, bioenergy, and biobased products to address the causes and adapt to and mitigate the impacts of climate change, including by sequestering carbon and reducing greenhouse gas emissions.

(iii) The Secretary of Agriculture, in consultation with the heads of appropriate agencies as determined by the Secretary, shall submit a report assessing how to use biotechnology and biomanufacturing for food and agriculture innovation, including by improving sustainability and land conservation; increasing food quality and nutrition; increasing and protecting agricultural yields; protecting against plant and animal pests and diseases; and cultivating alternative food sources.

(iv) The Secretary of Commerce, in consultation with the Secretary of Defense, the Secretary of HHS, and the heads of other appropriate agencies as determined by the Secretary of Commerce, shall submit a report assessing how to use biotechnology and biomanufacturing to strengthen the resilience of United States supply chains.

(v) The Director of the National Science Foundation (NSF), in consultation with the heads of appropriate agencies as determined by the Director, shall submit a report identifying high-priority fundamental and use-inspired basic research goals to advance biotechnology and biomanufacturing and to address the societal goals identified in this section.

(b) Each report specified in subsection (a) of this section shall identify high-priority basic research and technology development needs to achieve the overall objectives described in subsection (a) of this section, as well as opportunities for public-private collaboration. Each of these reports shall also include recommendations for actions to enhance biosafety and biosecurity to reduce risk throughout the biotechnology R&D and biomanufacturing lifecycles.

(c) Within 100 days of receiving the reports required under subsection (a) of this section, the Director of OSTP, in coordination with the Director of OMB, the APNSA, the APEP, the APDP, and the heads of appropriate agencies as determined through the NSM-2 process, shall develop a plan (implementation plan) to implement the recommendations in the reports. The development of this implementation plan shall also include the solicitation of input from external experts regarding potential ethical implications or other societal impacts, including environmental sustainability and environmental justice, of the recommendations contained in the reports required under subsection (a) of this section. The implementation plan shall include assessments and make recommendations regarding any such implications or impacts.

(d) Within 90 days of the date of this order, the Director of OMB, in consultation with the heads of appropriate agencies as determined through the NSM-2 process, shall perform a budget crosscut to identify existing levels of agency spending on biotechnology- and biomanufacturing-related activities to inform the development of the implementation plan described in subsection (c) of this section.

(e) The APNSA, in coordination with the Director of OMB, the APEP, the APDP, and the Director of OSTP, shall review the reports required under subsection (a) of this section and shall submit the reports to the President in an unclassified form, but may include a classified annex.

(f) The APNSA, in coordination with the Director of OMB, the APEP, the APDP, and the Director of OSTP, shall include a cover memorandum for the reports submitted pursuant to subsection (a) of this section, along with the implementation plan required under subsection (c) of this section, in which they make any additional overall recommendations for advancing biotechnology and biomanufacturing.

(g) Within 2 years of the date of this order, agencies at which recommendations are directed in the implementation plan required under subsection (c) of this section shall report to the Director of OMB, the APNSA, the APEP, the APDP, and the Director of OSTP on measures taken and resources allocated to enhance biotechnology and biomanufacturing, consistent with the implementation plan described in subsection (c) of this section.

(h) Within 180 days of the date of this order, the President's Council of Advisors on Science and Technology shall submit to the President and make publicly available a report on the bioeconomy that provides recommendations on how to maintain United States competitiveness in the global bioeconomy.

Sec. 4. Data for the Bioeconomy. (a) In order to facilitate development of the United States bioeconomy, my Administration shall establish a Data for the Bioeconomy Initiative (Data Initiative) that will ensure that high-quality, wide-ranging, easily accessible, and secure biological data sets can drive breakthroughs for the United States bioeconomy. To assist in the development of the Data Initiative, the Director of OSTP, in coordination with the Director of OMB and the heads of appropriate agencies as determined by the Director of OSTP, and in consultation with external stakeholders, shall issue a report within 240 days of the date of this order that:

(i) identifies the data types and sources, to include genomic and multiomic information, that are most critical to drive advances in health, climate, energy, food, agriculture, and biomanufacturing, as well as other bioeconomy-related R&D, along with any data gaps;

(ii) sets forth a plan to fill any data gaps and make new and existing public data findable, accessible, interoperable, and reusable in ways that are equitable, standardized, secure, and transparent, and that are integrated with platforms that enable the use of advanced computing tools;

(iii) identifies — based on the data types and sources described in subsection (a)(i) of this section — security, privacy, and other risks (such as malicious misuses, manipulation, exfiltration, and deletion), and provides a data-protection plan to mitigate these risks; and

(iv) outlines the Federal resources, legal authorities, and actions needed to support the Data Initiative and achieve the goals outlined in this subsection, with a timeline for action.

(b) The Secretary of Homeland Security, in coordination with the Secretary of Defense, the Secretary of Agriculture, the Secretary of Commerce (acting through the Director of the National Institute of Standards and Technology (NIST)), the Secretary of HHS, the Secretary of Energy, and the Director of OMB, shall identify and recommend relevant cybersecurity best practices for biological data stored on Federal Government information systems, consistent with applicable law and Executive Order 14028 of May 12, 2021 (Improving the Nation's Cybersecurity).

(c) The Secretary of Commerce, acting through the Director of NIST and in coordination with the Secretary of HHS, shall consider bio-related software, including software for laboratory equipment, instrumentation, and data management, in establishing baseline security standards for the development of software sold to the United States Government, consistent with section 4 of Executive Order 14028.

Sec. 5. Building a Vibrant Domestic Biomanufacturing Ecosystem. (a) Within 180 days of the date of this order, the APNSA and the APEP, in coordination with the Secretary of Defense, the Secretary of Agriculture, the Secretary of Commerce, the Secretary of HHS, the Secretary of Energy, the Director of NSF, and the Administrator of the National Aeronautics and Space Administration (NASA), shall develop a strategy that identifies policy recommendations to expand domestic biomanufacturing capacity for products spanning the health, energy, agriculture, and industrial sectors, with a focus on advancing equity, improving biomanufacturing processes, and connecting relevant infrastructure. Additionally, this strategy shall identify actions to mitigate risks posed by foreign adversary involvement in the biomanufacturing supply chain and to enhance biosafety, biosecurity, and cybersecurity in new and existing infrastructure.

(b) Agencies identified in subsections (b)(i)-(iv) of this section shall direct resources, as appropriate and consistent with applicable law, towards the creation or expansion of programs that support a vibrant domestic biomanufacturing ecosystem, as informed by the strategy developed pursuant to subsection (a) of this section:

(i) the NSF shall expand its existing Regional Innovation Engine program to advance emerging technologies, including biotechnology;

(ii) the Department of Commerce shall address challenges in biomanufacturing supply chains and related biotechnology development infrastructure;

(iii) the Department of Defense shall incentivize the expansion of domestic, flexible industrial biomanufacturing capacity for a wide range of materials that can be used to make a diversity of products for the defense supply chain; and

(iv) the Department of Energy shall support research to accelerate bioenergy and bioproduct science advances, to accelerate biotechnology and bioinformatics tool development, and to reduce the hurdles to commercialization, including through incentivizing the engineering scale-up of promising biotechnologies and the expansion of biomanufacturing capacity.

(c) Within 1 year of the date of this order, the Secretary of Agriculture, in consultation with the heads of appropriate agencies as determined by the Secretary, shall submit a plan to the President, through the APNSA and the APEP, to support the resilience of the United States biomass supply chain for domestic biomanufacturing and biobased product manufacturing, while also advancing food security, environmental sustainability, and the needs of underserved communities. This plan shall include programs to encourage climate-smart production and

use of domestic biomass, along with budget estimates, including accounting for funds appropriated for Fiscal Year (FY) 2022 and proposed in the President's FY 2023 Budget.

(d) Within 180 days of the date of this order, the Secretary of Homeland Security, in coordination with the heads of appropriate agencies as determined by the Secretary, shall:

(i) provide the APNSA with vulnerability assessments of the critical infrastructure and national critical functions associated with the bioeconomy, including cyber, physical, and systemic risks, and recommendations to secure and make resilient these components of our infrastructure and economy; and

(ii) enhance coordination with industry on threat information sharing, vulnerability disclosure, and risk mitigation for cybersecurity and infrastructure risks to the United States bioeconomy, including risks to biological data and related physical and digital infrastructure and devices. This coordination shall be informed in part by the assessments described in subsection (d)(i) of this section.

Sec. 6. Biobased Products Procurement. (a) Consistent with the requirements of 7 U.S.C. 8102, within 1 year of the date of this order, procuring agencies as defined in 7 U.S.C. 8102(a)(1)(A) that have not yet established a biobased procurement program as described in 7 U.S.C. 8102(a)(2) shall establish such a program.

(b) Procuring agencies shall require that, within 2 years of the date of this order, all appropriate staff (including contracting officers, purchase card managers, and purchase card holders) complete training on biobased product purchasing. The Office of Federal Procurement Policy, within OMB, in cooperation with the Secretary of Agriculture, shall provide training materials for procuring agencies.

(c) Within 180 days of the date of this order and annually thereafter, procuring agencies shall report previous fiscal year spending to the Director of OMB on the following:

(i) the number and dollar value of contracts entered into during the previous fiscal year that include the direct procurement of biobased products;

(ii) the number of service and construction (including renovations) contracts entered into during the previous fiscal year that include language on the use of biobased products; and

(iii) the types and dollar values of biobased products actually used by contractors in carrying out service and construction (including renovations) contracts during the previous fiscal year.

(d) The requirements in subsection (c) of this section shall not apply to purchase card transactions and other "[a]ctions not reported" to the Federal Procurement Data System pursuant to 48 CFR 4.606(c).

(e) Within 1 year of the date of this order and annually thereafter, the Director of OMB shall publish information on biobased procurement resulting from the data collected under subsection (c) of this section and information reported under 7 U.S.C. 8102, along with other related information, and shall use scorecards or similar systems to encourage increased biobased purchasing.

(f) Within 1 year of the date of this order and annually thereafter, procuring agencies shall report to the Secretary of Agriculture specific categories of biobased products that are unavailable to meet their procurement needs, along with desired performance standards for currently unavailable products and other relevant specifications. The Secretary of Agriculture shall publish this information annually. When new categories of biobased products become commercially available, the Secretary of Agriculture shall designate new product categories for preferred Federal procurement, as prescribed by 7 U.S.C. 8102.

(g) Procuring agencies shall strive to increase by 2025 the amount of biobased product obligations or the number or dollar value of biobased-only contracts, as reflected in the information described in subsection (c) of this section, and as appropriate and consistent with applicable law.

Sec. 7. Biotechnology and Biomanufacturing Workforce. (a) The United States Government shall expand training and education opportunities for all Americans in biotechnology and biomanufacturing. To support this objective, within 200 days of the date of this order, the Secretary of Commerce, the Secretary of Labor, the Secretary of Education, the APDP, the Director of OSTP, and the Director of NSF shall produce and make publicly available a plan to coordinate and use relevant Federal education and training programs, while also recommending new efforts to promote multi-disciplinary education programs. This plan shall promote the implementation of formal and informal education and training (such as opportunities at technical schools and certificate programs), career and technical education, and expanded career pathways into existing degree programs for biotechnology and biomanufacturing. This plan shall also include a focused discussion of Historically Black Colleges and Universities, Tribal Colleges and Universities, and Minority Serving Institutions and the extent to which agencies can use existing statutory authorities to promote racial and gender equity and support underserved communities, consistent with the policy established in Executive Order 13985. Finally, this plan shall account for funds appropriated for FY 2022 and proposed in the President's FY 2023 Budget.

(b) Within 2 years of the date of this order, agencies that support relevant Federal education and training programs as described in subsection (a) of this section shall report to the President through the APNSA, in coordination with the Director of OMB, the ADPD, and the Director of OSTP, on measures taken and resources allocated to enhance workforce development pursuant to the plan described in subsection (a) of this section.

Sec. 8. Biotechnology Regulation Clarity and Efficiency. Advances in biotechnology are rapidly altering the product landscape. The complexity of the current regulatory system for biotechnology products can be confusing and create challenges for businesses to navigate. To improve the clarity and efficiency of the regulatory process for biotechnology products, and to enable products that further the societal goals identified in section 3 of this order, the Secretary of Agriculture, the Administrator of the Environmental Protection Agency, and the Commissioner of Food and Drugs, in coordination with the Director of OMB, the ADPD, and the Director of OSTP, shall:

(a) within 180 days of the date of this order, identify areas of ambiguity, gaps, or uncertainties in the January 2017 Update to the Coordinated Framework for the Regulation of Biotechnology or in the policy changes made pursuant to Executive Order 13874 of June 11, 2019 (Modernizing the Regulatory Framework for Agricultural Biotechnology Products), including by engaging with developers and external stakeholders, and through horizon scanning for novel products of biotechnology;

(b) within 100 days of completing the task in subsection (a) of this section, provide to the general public plain-language information regarding the regulatory roles, responsibilities, and processes of each agency, including which agency or agencies are responsible for oversight of different types of products developed with biotechnology, with case studies, as appropriate;

(c) within 280 days of the date of this order, provide a plan to the Director of OMB, the ADPD, and the Director of OSTP with processes and timelines to implement regulatory reform, including identification of the regulations and guidance documents that can be updated, streamlined, or clarified; and identification of potential new guidance or regulations, where needed;

(d) within 1 year of the date of this order, build on the Unified Website for Biotechnology Regulation developed pursuant to Executive Order 13874 by including on the website the information developed under subsection (b) of this section, and by enabling developers of biotechnology products to submit inquiries about a particular product and promptly receive a single, coordinated response that provides, to the extent practicable, information and, when

appropriate, informal guidance regarding the process that the developers must follow for Federal regulatory review; and

(e) within 1 year of the date of this order, and annually thereafter for a period of 3 years, provide an update regarding progress in implementing this section to the Director of OMB, the United States Trade Representative (USTR), the APNSA, the ADPD, and the Director of OSTP. Each 1-year update shall identify any gaps in statutory authority that should be addressed to improve the clarity and efficiency of the regulatory process for biotechnology products, and shall recommend additional executive actions and legislative proposals to achieve such goals.

Sec. 9. Reducing Risk by Advancing Biosafety and Biosecurity. (a) The United States Government shall launch a Biosafety and Biosecurity Innovation Initiative, which shall seek to reduce biological risks associated with advances in biotechnology, biomanufacturing, and the bioeconomy. Through the Biosafety and Biosecurity Innovation Initiative — which shall be established by the Secretary of HHS, in coordination with the heads of other relevant agencies as determined by the Secretary — agencies that fund, conduct, or sponsor life sciences research shall implement the following actions, as appropriate and consistent with applicable law:

(i) support, as a priority, investments in applied biosafety research and innovations in biosecurity to reduce biological risk throughout the biotechnology R&D and biomanufacturing lifecycles; and

(ii) use Federal investments in biotechnology and biomanufacturing to incentivize and enhance biosafety and biosecurity practices and best practices throughout the United States and international research enterprises.

(b) Within 180 days of the date of this order, the Secretary of HHS and the Secretary of Homeland Security, in coordination with agencies that fund, conduct, or sponsor life sciences research, shall produce a plan for biosafety and biosecurity for the bioeconomy, including recommendations to:

(i) enhance applied biosafety research and bolster innovations in biosecurity to reduce risk throughout the biotechnology R&D and biomanufacturing lifecycles; and

(ii) use Federal investments in biological sciences, biotechnology, and biomanufacturing to enhance biosafety and biosecurity best practices throughout the bioeconomy R&D enterprise.

(c) Within 1 year of the date of this order, agencies that fund, conduct, or sponsor life sciences research shall report to the APNSA, through the Assistant to the President and Homeland Security Advisor, on efforts to achieve the objectives described in subsection (a) of this section.

Sec. 10. Measuring the Bioeconomy. (a) Within 90 days of the date of this order, the Secretary of Commerce, through the Director of NIST, shall, in consultation with other agencies as determined by the Director, industry, and other stakeholders, as appropriate, create and make publicly available a lexicon for the bioeconomy, with consideration of relevant domestic and international definitions and with the goal of assisting in the development of measurements and measurement methods for the bioeconomy that support uses such as economic measurement, risk assessments, and the application of machine learning and other artificial intelligence tools.

(b) The Chief Statistician of the United States, in coordination with the Secretary of Agriculture, the Secretary of Commerce, the Director of NSF, and the heads of other appropriate agencies as determined by the Chief Statistician, shall improve and enhance Federal statistical data collection designed to characterize the economic value of the United States bioeconomy, with a focus on the contribution of biotechnology to the bioeconomy. This effort shall include:

(i) within 180 days of the date of this order, assessing, through the Department of Commerce's Bureau of Economic Analysis, the feasibility, scope, and costs of developing a national measurement of the economic contributions of the bioeconomy, and, in particular, the contributions of biotechnology to the bioeconomy, including recommendations and a plan for next steps regarding whether development of such a measurement should be pursued; and

(ii) within 120 days of the date of this order, establishing an Interagency Technical Working Group (ITWG), chaired by the Chief Statistician of the United States, which shall include representatives of the Department of Agriculture, the Department of Commerce, OSTP, the NSF, and other appropriate agencies as determined by the Chief Statistician of the United States.

(A) Within 1 year of the date of this order, the ITWG shall recommend bioeconomy-related revisions to the North American Industry Classification System (NAICS) and the North American Product Classification System (NAPCS) to the Economic Classification Policy Committee. In 2026, the ITWG shall initiate a review process of the 2023 recommendations and update the recommendations, as appropriate, to provide input to the 2027 NAICS and NAPCS revision processes.

(B) Within 18 months of the date of this order, the ITWG shall provide a report to the Chief Statistician of the United States describing the Federal statistical collections of information that take advantage of bioeconomy-related NAICS and NAPCS codes, and shall include recommendations to implement any bioeconomy-related changes as part of the 2022 revisions

of the NAICS and NAPCS. As part of its work, the ITWG shall consult with external stakeholders.

Sec. 11. Assessing Threats to the United States Bioeconomy. (a) The Director of National Intelligence (DNI) shall lead a comprehensive interagency assessment of ongoing, emerging, and future threats to United States national security from foreign adversaries against the bioeconomy and from foreign adversary development and application of biotechnology and biomanufacturing, including acquisition of United States capabilities, technologies, and biological data. As part of this effort, the DNI shall work closely with the Department of Defense to assess technical applications of biotechnology and biomanufacturing that could be misused by a foreign adversary for military purposes or that could otherwise pose a risk to the United States. In support of these objectives, the DNI shall identify elements of the bioeconomy of highest concern and establish processes to support ongoing threat identification and impact assessments.

(b) Within 240 days of the date of this order, the DNI shall provide classified assessments to the APNSA related to:

(i) threats to United States national and economic security posed by foreign adversary development and application of biomanufacturing; and

(ii) foreign adversary means of, and intended usages related to, acquisition of United States biotechnologies, biological data, and proprietary or precompetitive information.

(c) Within 120 days of receiving the DNI's assessments, the APNSA shall coordinate with the heads of relevant agencies as determined through the NSM-2 process to develop and finalize a plan to mitigate risks to the United States bioeconomy, based upon the threat identification and impact assessments described in subsection (a) of this section, the vulnerability assessments described in section 5(d) of this order, and other relevant assessments or information. The plan shall identify where executive action, regulatory action, technology protection, or statutory authorities are needed to mitigate these risks in order to support the technology leadership and economic competitiveness of the United States bioeconomy.

(d) The United States Government contracts with a variety of providers to support its functioning, including by contracting for services related to the bioeconomy. It is important that these contracts are awarded according to full and open competition, as consistent with the Competition in Contracting Act of 1984 (Public Law 98-369, 98 Stat. 1175). In accordance with these objectives, and within 1 year of the date of this order, the Director of OSTP, in coordination with the Secretary of Defense, the Attorney General, the Secretary of HHS, the

Secretary of Energy, the Secretary of Homeland Security, the DNI, the Administrator of NASA, and the Administrator of General Services, shall review the national security implications of existing requirements related to Federal procurement — including requirements contained in the Federal Acquisition Regulation (FAR) and the Defense Federal Acquisition Regulation Supplement — and shall recommend updates to those requirements to the FAR Council, the Director of OMB, and the heads of other appropriate agencies as determined through the NSM-2 process. The recommendations shall aim to standardize pre-award data collection to enable due diligence review of conflict of interest; conflict of commitment; foreign ownership, control, or influence; or other potential national security concerns. The recommendations shall also include legislative proposals, as relevant.

(e) The Director of OMB shall issue a management memorandum to agencies, or take other appropriate action, to provide generalized guidance based on the recommendations received pursuant to subsection (d) of this section.

Sec. 12. International Engagement. (a) The Department of State and other agencies that engage with international partners as part of their missions shall undertake the following actions with foreign partners, as appropriate and consistent with applicable law — with a specific focus on developing countries, international organizations, and nongovernmental entities — to promote and protect both the United States and global bioeconomies:

(i) enhance cooperation, including joint research projects and expert exchanges, on biotechnology R&D, especially in genomics;

(ii) encourage regulatory cooperation and the adoption of best practices to evaluate and promote innovative products, with an emphasis on those practices and products that support sustainability and climate objectives;

(iii) develop joint training arrangements and initiatives to support bioeconomy jobs in the United States;

(iv) work to promote the open sharing of scientific data, including genetic sequence data, to the greatest extent possible in accordance with applicable law and policy, while seeking to ensure that any applicable access and benefit-sharing mechanisms do not hinder the rapid and sustainable development of innovative products and biotechnologies;

(v) conduct horizon scanning to anticipate threats to the global bioeconomy, including national security threats from foreign adversaries acquiring sensitive technologies or data, or

disrupting essential bio-related supply chains, and to identify opportunities to address those threats;

(vi) engage allies and partners to address shared national security threats;

(vii) develop, and work to promote and implement, biosafety and biosecurity best practices, tools, and resources bilaterally and multilaterally to facilitate appropriate oversight for life sciences, dual-use research of concern, and research involving potentially pandemic and other high-consequence pathogens, and to enhance sound risk management of biotechnology- and biomanufacturing-related R&D globally; and

(viii) explore how to align international classifications of biomanufactured products, as appropriate, to measure the value of those products to both the United States and global bioeconomies.

(b) Within 180 days of the date of this order, the Secretary of State, in coordination with the USTR and the heads of other agencies as determined by the Secretary, as appropriate, shall submit to the APNSA a plan to support the objectives described in subsection (a) of this section with foreign partners, international organizations, and nongovernmental entities.

Sec. 13. Definitions. For purposes of this order:

(a) The term "agency" has the meaning given that term by 44 U.S.C. 3502(1).

(b) The term "biotechnology" means technology that applies to or is enabled by life sciences innovation or product development.

(c) The term "biomanufacturing" means the use of biological systems to develop products, tools, and processes at commercial scale.

(d) The term "bioeconomy" means economic activity derived from the life sciences, particularly in the areas of biotechnology and biomanufacturing, and includes industries, products, services, and the workforce.

(e) The term "biological data" means the information, including associated descriptors, derived from the structure, function, or process of a biological system(s) that is measured, collected, or aggregated for analysis.

(f) The term "biomass" means any material of biological origin that is available on a renewable or recurring basis. Examples of biomass include plants, trees, algae, and waste material such as

crop residue, wood waste, animal waste and byproducts, food waste, and yard waste.

(g) The term "biobased product" has the meaning given that term in 7 U.S.C. 8101(4).

(h) The term "bioenergy" means energy derived in whole or in significant part from biomass.

(i) The term "multiomic information" refers to combined information derived from data, analysis, and interpretation of multiple omics measurement technologies to identify or analyze the roles, relationships, and functions of biomolecules (including nucleic acids, proteins, and metabolites) that make up a cell or cellular system. Omics are disciplines in biology that include genomics, transcriptomics, proteomics, and metabolomics.

(j) The term "key R&D areas" includes fundamental R&D of emerging biotechnologies, including engineering biology; predictive engineering of complex biological systems, including the designing, building, testing, and modeling of entire living cells, cell components, or cellular systems; quantitative and theory-driven multi-disciplinary research to maximize convergence with other enabling technologies; and regulatory science, including the development of new information, criteria, tools, models, and approaches to inform and assist regulatory decision-making. These R&D priorities should be coupled with advances in predictive modeling, data analytics, artificial intelligence, bioinformatics, high-performance and other advanced computing systems, metrology and data-driven standards, and other non-life science enabling technologies.

(k) The terms "equity" and "underserved communities" have the meanings given those terms by sections 2(a) and 2(b) of Executive Order 13985.

(l) The term "Tribal Colleges and Universities" has the meaning given that term by section 5(e) of Executive Order 14049 of October 11, 2021 (White House Initiative on Advancing Educational Equity, Excellence, and Economic Opportunity for Native Americans and Strengthening Tribal Colleges and Universities).

(m) The term "Historically Black Colleges and Universities" has the meaning given that term by section 4(b) of Executive Order 14041 of September 3, 2021 (White House Initiative on Advancing Educational Equity, Excellence, and Economic Opportunity Through Historically Black Colleges and Universities).

(n) The term "minority serving institution" has the meaning given that term by 38 U.S.C. 3698(f)(4).

(o) The term "foreign adversary" has the meaning given that term by section 3(b) of Executive Order 14034 of June 9, 2021 (Protecting Americans' Sensitive Data From Foreign Adversaries).

(p) The term "life sciences" means all sciences that study or use living organisms, viruses, or their products, including all disciplines of biology and all applications of the biological sciences (including biotechnology, genomics, proteomics, bioinformatics, and pharmaceutical and biomedical research and techniques), but excluding scientific studies associated with radioactive materials or toxic chemicals that are not of biological origin or synthetic analogues of toxins.

Sec. 14. General Provisions. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of OMB relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

JOSEPH R. BIDEN JR.

THE WHITE HOUSE,
September 12, 2022.

Therapies of the state

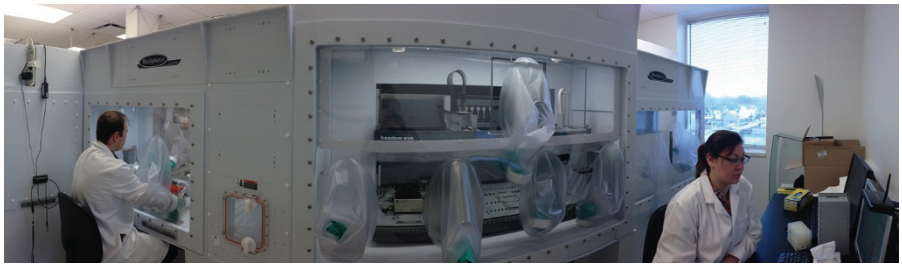
Beth Schachter

What can governmental agencies do to lower the risk of cell therapies and the enterprises commercializing them?

Interest in cell-based medicine has grown steadily in the past couple of decades (**Fig. 1**). Until recently, however, that interest has been largely academic. Big pharma and venture capitalists, for the most part, have steered clear of cell therapies emerging out of academic laboratories.

For one thing, big pharma's business model is very different from what is needed to translate cell therapies into practice. The pharma model involves mass manufacturing of products that can be stored in warehouses and distributed through pharmacies to large markets of patients. Cell therapies, on the other hand, may be highly individualized, are incompletely characterized, are expensive to produce, have a short shelf life and onerous supply chain, must be transplanted into patients by skilled healthcare workers and have complex regulatory requirements. These challenges, along with a dearth of cell-therapy successes, have kept away investors, too[1].

And yet, as knowledge advances about the basic biology of cellular reprogramming, differentiation and maturation, new techniques have been introduced that are capable of handling and characterizing cells with more sophistication and sensitivity. At the same time, expertise and experience grows in testing these treatments in humans (almost 100 cell therapies are now in clinical trials according to the Alliance for Regenerative Medicine[2]). Consequently, certain sectors of the healthcare industry are beginning to take note. General Electric Healthcare (GE Healthcare, Buckinghamshire, UK), for example, which started moving into the cell therapy space about seven years ago, has been playing an increasing role as a technology enabler—developing processes and equipment that cell-therapy companies could use to manufacture cells in an automated, highly regulated environment.



"X-Evo Instrument" at the National Center for Regenerative Medicine's OH-Alive Platform for robotic media preparation and automated cell culture. Source: National Center for Regenerative Medicine, Cleveland, Ohio.

GE Healthcare's chief scientist, Stephen Minger, feels that although the field is progressing in many respects, companies can't build the industry on their own. Nor can research institutes and hospitals. "Government involvement is going to be absolutely crucial to translate these efforts from small, early-scale, phase 1 trials through phase 3 and, ultimately, to authorized therapies. And then the scales [of potential industry growth] are absolutely enormous," says Minger.

This sentiment is shared by many stakeholders around the globe, and government-sponsored programs to support the development of cell-based therapies have emerged in several regions (**Table 1** and **Fig. 2**). Here we examine three of them, the California Institute for Regenerative Medicine (CIRM) in the United States, the Centre for Commercialization of Regenerative Medicine (CCRM) in Canada and the Cell Therapy Catapult in the United Kingdom. They are at different stages of life, the CIRM being the oldest and best funded with the Catapult at the other end of the spectrum, having been founded less than two years ago. In different ways, though, all of them are aiming to de-risk the perilous process of advancing cell therapies that show potential in animal studies through human testing to commercialization (**Box 1**).

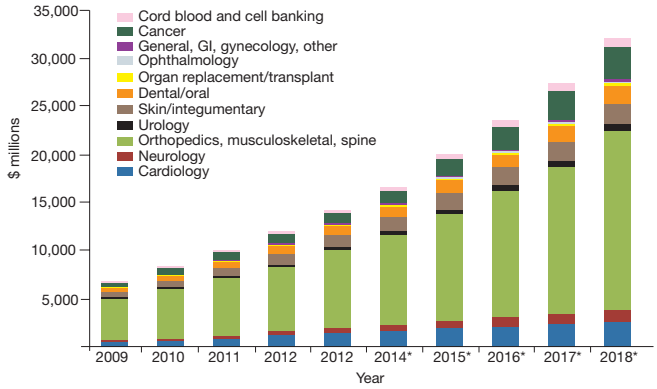


Figure 1 Global tissue engineering market. *projected. Source: MedMarket Diligence.

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Box 1 Something completely different: The New York Stem Cell Foundation

Public charities can work more nimbly than government-run operations; all that's needed is a powerhouse fund-raiser. The New York Stem Cell Foundation (NYSCF) and its founding CEO Susan Solomon provide ample evidence to support that notion. Solomon, who has experience starting businesses and a son with type 1 diabetes, sensed that stem cell therapies held the potential for curing chronic diseases such as diabetes. And so, she created a nonprofit to actualize that potential.

Conceived in 2005, NYSCF has a multifaceted program that funds extramural research and training, conducts research in its own facilities, and now will become a source of cell lines (iPSCs) for the stem cell community to use.

One of the first NYSCF programs established fellowships for the training of young investigators in stem cell science to ensure that a whole generation of investigators was not lost because of US federal restrictions on human embryonic stem cell research. NYSCF offered postdoctoral fellowships for individuals to train in laboratories throughout the United States. The program has now evolved to include funds for junior faculty members to set up their laboratories. Importantly, that money cannot be used to replace startup funds from the scientist's institution.

Another early role for NYSCF was as safe haven for high-risk research that could not be done in federally funded academic institutions. The first such example, and indeed, the project that motivated NYSCF to set up its own laboratory, aimed to use somatic cell nuclear transfer as a step in developing a treatment for type 1 diabetes. The research, a Harvard-Columbia collaboration, needed to be done in a laboratory that received no NIH funding and in a state in which the donors could be compensated for their effort. The NYSCF fulfilled that requirement and provided laboratory space and some of the research funding.

NYSCF also supports iPSC technology through extramural and in-house programs. To accelerate the generation of iPSC lines, which is usually a labor-intensive and time-consuming process, NYSCF in-house researchers constructed an automated, roboticized system, the NYSCF Global Stem Cell Array, which can produce iPSCs from individual patients and controls for disease modeling or for therapeutic applications.

The New York Stem Cell Foundation

Date founded	2005
Location	New York
Funding and source	$120 million, raised from public and private sources
Duration	Ongoing
Facilities	10,000-ft² laboratory; Good Manufacturing Practices facility planned
Staff/governance	60 in-house staff/nonprofit, CEO, Board of Directors

The risks

Because cells are highly sensitive to their microenvironment, a cell product depends exquisitely on the process used to manufacture it. Controlling the inherent heterogeneity of cell populations, scaling up production to treat large numbers of patients in clinical trials and beyond, and assuring the stability of cell products during distribution through the supply chain all pose thorny technical challenges. Any of these issues can easily affect the safety or efficacy of a cell product, increasing the risk that the product will not gain regulatory approval. Moreover, regulators have relatively little experience with pluripotent cell–derived therapies in particular but even with cell therapy in general—which spans a wide variety of cell types, routes of administration, end points and the like. Hence, uncertainty about regulatory requirements for products using cells exists.

In addition to the regulatory risk, there is risk surrounding intellectual property (IP); what aspects of a cellular therapy are patentable in the first place and how impenetrable and fragmented is the patent thicket for licensing?

And finally, there is reimbursement risk; who will pay for the product and how much will they pay? Cell Therapy Catapult's chief business officer, Matthew Durdy, says that this should be part of the calculus from the earliest stages. "[Building the industry] is not about the product. It's about a conversation held at some point in the future between a product salesperson and a potential buyer. What information does the potential buyer need? What product specifications would be needed to enable the transaction?" From the seller's perspective, these questions can be answered by calculating risks and then finding ways to mitigate them, Durdy says. Although the three public programs discussed here have different structures, different levels of involvement and types of resources, and different missions, they all see risk reduction as crucial to the success of their programs.

The Centre for the Commercialization of Regenerative Medicine

The CCRM stands alone in building an industry component into the structure of its program. According to CCRM board chair and founder and managing partner at Proteus Venture Partners (Palo Alto, CA, USA), Greg Bonfiglio, regenerative-medicine translational centers in the United States lack a direct link to industry. He believes that a key component of the CCRM is the industry consortium, which to date has 24 full and 10 associate members, ranging from Canadian small-to-medium–sized enterprises to giant international healthcare firms, including GE Healthcare and Pfizer. Most full members pay a yearly fee for a variety of services or as an advance against co-development projects. Small pre-revenue Canadian companies may have the fee deferred on a case-by-case basis.

Consortium participation gives its members specific IP privileges (**Box 2**) along with access to the scientific expertise and laboratory resources at CCRM's academic institutions. According to Jennifer Moody, CCRM's director of commercialization and licensing, consortium members can co-develop projects with CCRM; such projects are leveraged with CCRM money. "So, potentially, companies can come to us and work with us on projects, and they really will only have to put up 50% of the funds compared [with] doing the work on their own," Moody says.

In addition to industry, CCRM has academic partners, all of whom originate from the Canadian Stem Cell Network, which was set up by the government in 2001 to catalyze the translation of stem cell research. Michael May, CCRM's founding CEO, says that the

Centre for Commercialization of Regenerative Medicine

Date founded	2011
Location	Toronto
Funding and source	$16-million federal grant, $14 million from industry and academic partners
Duration	Five years, renewable for another five years
Facilities	6,000-ft² laboratory; Good Manufacturing Practices facility planned
Staff/governance	24 in-house staff/13-member board of stakeholders

Box 2 Managing intellectual property

IP gets dealt with differently at the three agencies. These differences stem both from the structural differences between the organizations, as well as cultural differences among the countries in which they operate.

The CIRM owns almost none of the IP that comes from the programs it funds. Instead, it has revenue-sharing requirements for grantees that differ, depending upon whether the grantee is a nonprofit or for-profit entity. Currently, for a CIRM-funded nonprofit, CIRM and the grantee will each take a share of what the nonprofit makes along the way. The nonprofit would exercise diligence in outlining its inventions, including whatever clinical data might be collected with CIRM funds. Then, depending on the portion of the amount contributed by CIRM, CIRM would get a specified percentage of the revenue. The amount CIRM gets is capped at 9 × the amount of the award, unless the product becomes a blockbuster. In that case, CIRM gets 1% of the revenue. Currently, in the arrangement with for-profit grantees, CIRM would share in the net commercial revenues that arise in whole or in part from the CIRM-funded project, a rate of 0.1% per $1 million of the award, which includes the 9 × cap as well.

CCRM has an agreement with its academic members that any IP comes to CCRM for a first look and evaluation. This gives the universities access to sector-specific expertise and a direct line to industry input through CCRM's industry consortium. Licensing agreements are standard—negotiated with each institution individually, and revenues are not pooled between members, according to CCRM's Jennifer Moody.

With respect to companies, Moody said, full members of the industry consortium have first rights to look at IP coming through CCRM. In addition, they also have the opportunity to join co-development projects with CCRM that are leveraged with CCRM money.

The Cell Therapy Catapult is primarily tasked with growing the UK cell therapy industry, rather than generating maximum financial value from its IP. As a result, it takes a flexible approach to IP with its collaborations, making sure it's clear what pre-existing IP each party has (the background IP), and agreeing upfront how to deal with any IP generated during the course of the collaboration (foreground IP). The Cell Therapy Catapult strives to make sure that any IP it owns or has an option to access as a result of work with partners is as available to the rest of the cell therapy community as possible, at the same time ensuring commercial partners have full freedom to operate and pursue their strategies.

network, comprising over 100 researchers from 27 institutions, "created a wonderful culture of collaboration among the stem cell scientists in Canada, and got them, after ten years or so, to buy into the idea that they were ready to commercialize and translate their discoveries."

May explains how the process works: "New inventions within the academic partner institutions get disclosed to CCRM for our evaluation." And this is where the in-house staff plays a key role. "Although we receive those disclosures, what we're building is a proactive engagement of the academics in the community. We talk to them, we tell them what we know about the market, we try to spark invention, we look at their inventions," he says.

The in-house, Toronto-based staff has its own 6,000-square-foot facility with equipment, not unlike that of a startup. There they can do benchwork and evaluate technologies to accelerate and drive commercialization. In-house research effort has three major themes: cell manufacturing, cell reprogramming and engineering, and biomaterials and devices.

CCRM works with its academic partners both in developing technologies to out-license to industry and in bundling technologies to create companies. Regenerative medicine is a multidisciplinary effort, which can require pulling together pieces of IP and technology from different places, explains Bonfiglio. This is particularly true of startups, where an academic working on a particular technology may be missing a key component needed to translate it into a useful product. The CCRM model involves looking around the world for complementary pieces of IP and technology and bundling them together in a way that accelerates the commercialization of products. Such bundling, May argues, will create a new kind of enterprise, "with not one invention with one inventor and one company, but where we create companies strategically, as opposed to reactively to inventions being created in the community."

One example of technology bundling that resulted in company formation is a CCRM-supported program to expand blood cells for transplantation. The cell-expansion technology involves IP pooled from several sources—a bioprocess developed by Peter Zandstra at the University of Toronto, matched with a small molecule from Guy Sauvageau's laboratory and the Institute for Research in Immunology and Cancer at the University of Montreal. The bioprocess stabilizes the culture system by providing nutrients on demand and diluting negative regulators of cell growth, while the small molecule promotes expansion of the cells without the loss of stem cell function. Moody further explains, "this blood cell expansion requires a closed-system device to make it clinically amenable, and we are working with industry partners to generate that device."

In the program's two and a half years of existence, it's been able to accomplish a lot, according to Bonfiglio. "That model that Mike [CEO May] has built for moving technologies through this valley of death and into a place where they can be funded by traditional sources like venture is an excellent model. I think you're going to find other translation centers emulate it," he says. And Bonfiglio has helped to make this happen; The New York Blood Center announced in late June the creation of a new translational center, with $50 million in funding from Proteus Ventures, which will use the CCRM model to develop next-generation synthetic blood products.

The California Institute for Regenerative Medicine

CIRM is the oldest and by far the best-funded public program dedicated to regenerative medicine. Hatched during the dark days (for human embryonic stem–cell researchers) of the George W. Bush presidency, when the field was restrained by an executive order limiting the use and derivation of human embryonic stem cells, the institute was voted into existence by the California electorate in 2004 by means of Proposition 71. Since 2007 (the agency was tied up in legal challenges for several years), the CIRM has given out over $1.3 billion through several grant programs—Tool and Technologies, Early Translation, and Disease Teams, to name three with a bent toward translation—to individual researchers, trainees, research programs and infrastructure projects.

Now in the second half of its decade-long life with but $400–500 million left to distribute, the institute shows signs of transitioning from its initial emphasis on basic research

Table 1 Government-sponsored stem cell programs

Program name	Year established	Source of funds	Annual budget ($ millions)	Program duration (years)	Facilities	Staff/governance
New York Stem Cell Science Program (NYSTEM)	2007	State taxpayer dollars	~40	≥11	None	Three full-time staff/Empire State Stem Cell Board
Connecticut Stem Cell Research Fund	2005	State taxpayer dollars	10	10	None	17-member advisory committee chaired by the Commissioner of Public Health
National Center for Regenerative Medicine (Ohio)	2003	Federal, state, foundation and philanthropic	0.50	11	OH-Alive (automated cell culture optimization platform), Cellular Therapies Integrated Services (clinical cell production), and Pluripotent Stem Cell Facility (iPS line deriving and training)	Seven-person staff and five member board of governors representing participating institutions
Maryland Stem Cell Research Fund	2006	State taxpayer dollars	10.4 for 2015	Ongoing	None	Three-person administrative staff and Maryland Stem Cell Research Commission
Global Stem Cell and Regenerative Medicine Acceleration Center (Korea)	2007	Six ministries	47	Ongoing	Korean Stem Cell Registry and bank (81 domestic, 21 imported), funding for National Center for Stem Cells and Regenerative Medicine	Ten full-time staff
Berlin-Brandenburg Center for Regenerative Therapies (BCTR)	2006	German Federal Registry of Education and Research; the states of Berlin and Brandenburg, Charité - Universitätsmedizin Berlin, Helmholtz Zentrum Geesthacht	~10	Ongoing	GMP facilities for ATMP and clean room for factor release testing. Interdisciplinary translation center aiming to enhance endogenous regeneration by cells, biomaterials and factors to develop and implement innovative therapies and products	250 in-house staff
Stem Cells Australia	2011	Australian Research Council Special Research Initiative	21	7	Core facilities located around the country	Eight-person administrative team
Research Center Network for Realization of Regenerative Medicine (Japan)	2013	Ministry of Education, Culture, Sports, Science and Technology	1,090	10	1 core center (core center for iPS cell research), 29 projects	Not available
Project for Realization of Regenerative Medicine (II) (Japan)	2008–2012	Ministry of Education, Culture, Sports, Science and Technology	800	5	4 core centers (core center for iPS cell research), 1 cord blood bank (for research), 5 projects	Not available
Project for Realization of Regenerative Medicine (I) (Japan)	2003–2007	Ministry of Education, Culture, Sports, Science and Technology	112	5	None	Not available

and infrastructure to a range of efforts directed at translation. Already, CIRM has approved more than $45 million for funding the Strategic Partnerships, in which funds are awarded for projects that are able to attract private investment. The CIRM has awarded a $16-million grant to Cellular Dynamics (Madison, WI, USA) for creating a bank of induced pluripotent stem cells (iPSCs) from 3,000 individuals with a range of diseases that can serve as the basis for disease modeling, and target and drug discovery. At the same time, the CIRM granted $10 million to the Coriell Institute for Medical Research (Camden, NJ, USA) for creating a biorepository for storing these and other cell lines.

A major new effort at de-risking the cell-therapy enterprise is the CIRM's Alpha Stem Cell Clinics Network, five clinical trial centers based at or near California medical centers that have ongoing clinical trial programs. The Alpha Clinics aim to turn the running of cell-based therapy clinical trials into a routine endeavor.

And finally and perhaps most importantly, the CIRM selected a biotech industry veteran, C. Randal (Randy) Mills, to lead it in the final days of this first round of funding. (Whether there will be a second round of funding from the state or some other source remains to be seen.) Mills served as CEO of Osiris Therapeutics, the first company to bring a stem cell drug to market—Prochymal (remestemcel-L), which has conditional approval in Canada and New Zealand, for treating acute graft-versus-host disease in children.

According to CIRM's senior vice president

The California Institute of Regenerative Medicine

Date founded	2004
Location	San Francisco (administrative offices)
Funding and source	$3 billion from state-issued bonds
Duration	Ten years
Facilities	None
Staff/governance	50 staff/29-member governing board of stakeholders

of R&D, Ellen Feigal, CIRM, from the outset, has funded types of R&D that historically have had difficulty raising external capital because they were deemed too risky because of scientific, technological or regulatory uncertainty. For example, the biotech company Viacyte (San Diego) was an early recipient of CIRM funding in a project that paired the company with Jeffrey Bluestone, a diabetes researcher at University of California, San Francisco. The team wanted to explore creating an implantable device that could serve as an insulin delivery system for people with type 1 diabetes. "This is an approach that hasn't been attempted before and without our support would almost certainly not have reached this stage now. No VC [venture capitalist] or [big pharma company] wanted to invest in something that was so dramatically different from any other approach until they saw evidence it worked," says Feigal. The team is preparing for a clinical trial later this year, and has attracted money from the Juvenile Diabetes Research Foundation (New York) and Johnson & Johnson (New Brunswick, NJ, USA).

In developing this extensive program, the CIRM has, in a sense, been standing in for the National Institutes of Health (NIH). It has also been taking the role that venture capital might have assumed, had the US government given the go-ahead on human embryonic stem cells, thereby building a robust preclinical/translational research program. As Bonfiglio puts it, "CIRM galvanized the industry, putting regenerative medicine on the map, both in terms of what the politicians and the lay people saw and in terms of maintaining scientific training in that arena."

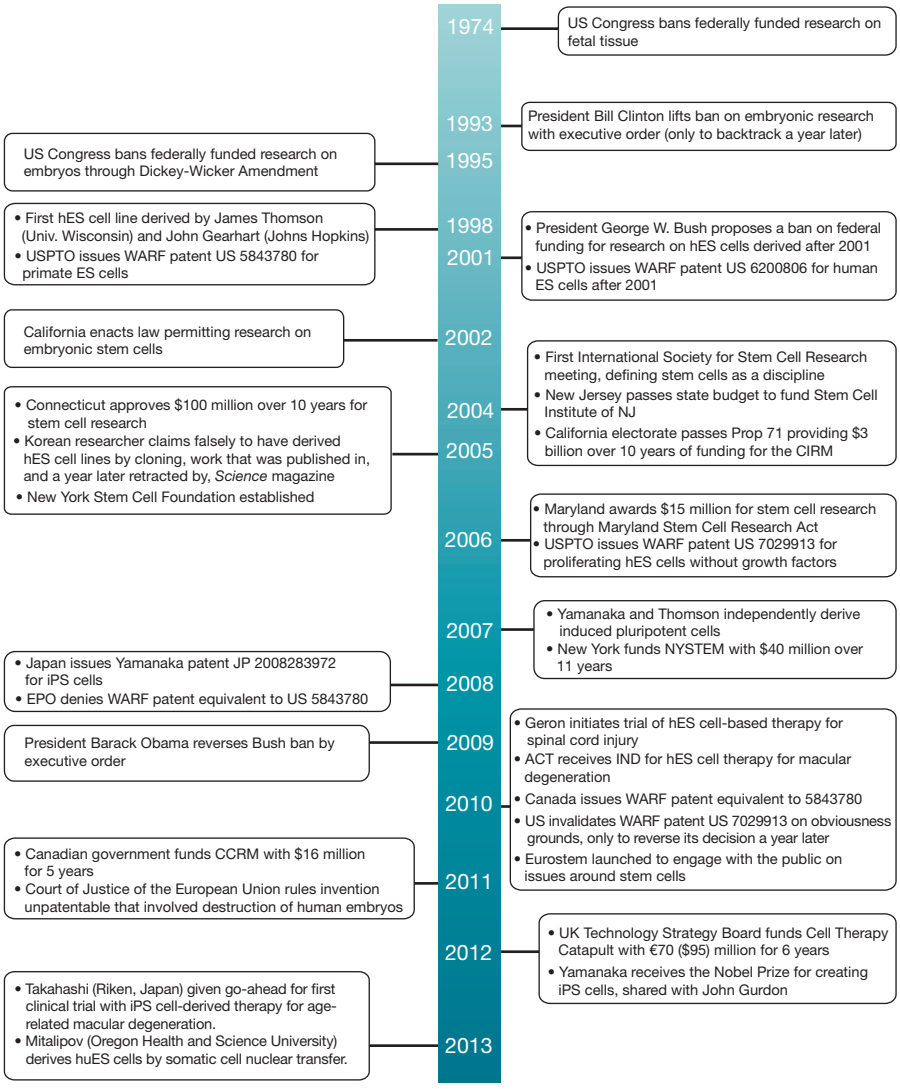

Figure 2 Timeline of seminal events in cell therapy R&D. hES cell, human embryonic stem cell; USPTO, US Patent and Trademark Office; WARF, Wisconsin Alumni Research Foundation; NYSTEM, New York State Stem Cell Science; EPO, European Patent Office; ACT, Advanced Cell Therapy; IND, investigational new drug; iPS cell, induced pluripotent stem cell.

Cell Therapy Catapult

The UK, like Canada and California, houses much of the world's top-flight cell therapy research. But those in UK biotech recognize that they have missed opportunities in the past to interest entrepreneurs and investors in turning their basic research into commercial ventures. Monoclonal antibody therapy provides an example. The key initial discoveries were made in the United Kingdom. But, as Natalie Mount, Catapults' chief clinical officer explains, the infrastructure to finance and develop those biologics just didn't exist, "so a lot of that left the UK and it went out to the United States and Asia, and our share, the UK's share of that industry, is very, very small."

Cell Therapy Catapult opened its doors in 2012, one of seven Catapults, centers of excellence set up by UK's Technology Strategy Board—the only one in life sciences. Cell therapy was chosen as the first biomedical-science Catapult, Mount explains, because of unmet medical needs, combined with the UK's strong science base in that area. Also there was the recognition that "developing and producing cell therapies is complex," Mount adds. "Whilst there are some cell therapies which are now gaining approval, it's a challenging area to work in because it's not a traditional approach." The Cell Therapy Catapult's goal is to build a £10 ($17)-billion industry within the United Kingdom.

What distinguishes the Cell Therapy Catapult from the other translational centers is its emphasis on forward thinking. Their staff of 70 people, who have expertise in both assay development and process development, help therapy developers optimize processes early on, whether it involves scaling up or scaling out. This means that from the start the developer has a process suitable for the large volumes needed for market. "And so, a lot of the

Cell Therapy Catapult

Date founded	2012
Location	Guy's Hospital, London
Funding and source	€70 ($95) million from UK Technology Strategy Board
Duration	Six years
Facilities	1,200 m^2 of modular laboratories; Good Manufacturing Practices facility
Staff/governance	>70 in-house staff/seven member board of stakeholders

process development risk is taken out because it's no longer such an unknown. That's a huge change. This can take one to two million dollars to do," Durdy says.

To do this, the Cell Therapy Catapult has set up modular laboratories, with facilities designed to mimic manufacturing suites. This enables projects to go from laboratory scale to commercial scale, using the pilot process development expertise.

Another risk is reimbursement. Durdy notes that during development, such factors as product efficacy and competition cannot be known. But some things can be planned for sooner rather than later, and planning helps to develop product profiles on which to gather the necessary data—not just the scientific, efficacy and clinical trials data, but the reimbursement data, the economic data, the data that builds your case. Then, says Durdy, "when you go to the payer, you have a rock-solid business case for why they should buy the product." And that can reduce the risk of not getting paid.

It's still early days for Catapult, and it may be experiencing some growing pains, says cell therapy consultant Lee Buchler. Like CCRM, there is real infrastructure involved, yet the details of the translational model are not exactly clear, he says. "They're not a funding agency, not just an incubator and they're not a fee for services, as companies bring in their own people. So perhaps the best way to think about them is as a hybrid between just providing space and a CMO [contract manufacturing organization]."

Peering into the future

What each of these programs brings to the field is more than just money. A critical element of each of them is the access that their participants have to expertise and, in some cases, to needed facilities. At this juncture it's not clear how long government funding will be needed or wanted. The CIRM will reach the end of its funding in the next few years, and they have yet to reveal, if they even know, what their plans are for continuing to serve the high-powered research community that they have essentially created in California. Meanwhile, CCRM and Cell Therapy Catapult both have the possibility of renewing their funding for a second term, which seems likely and necessary given the uphill struggle still in attracting money from venture capitalists or even pharma. Many pharma companies give lip service to cell-based therapies, but with a few exceptions—Pfizer (New York), which did shut down its regenerative medicine program after only three years, now is working with CCRM—have not made a serious effort.

Also not clear is how each of the governments will assess the success or failure of these programs. How will governments know when the time is right to wean the programs from public monies? Will they consider job creation, the number of companies spun out, or launching successful products in the marketplace? Given the complexity of cell therapies and regulatory uncertainty, none of these things may happen for decades. Perhaps a better measure is whether any of the companies created gets traction with big pharma. That might indicate that the commercial promise of these therapies is finally evident.

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The U.S. Bioeconomy: Charting a Course for a Resilient and Competitive Future

A Bioeconomy Strategy

APRIL 2022

SCHMIDT FUTURES

Illustrative Case Studies

1. Protecting Vulnerable Species with Sugar, Yeast, and an Engineering Biology Platform Technology
2. Building a Network of Pilot Biomanufacturing Facilities
3. Repurposing to Power the Bioeconomy
4. Future Biobased Feedstocks
5. Advancing the Bioeconomy by Sharing Resources and Knowledge
6. Illustrating the Complex Regulatory Ecosystem
7. Local, State, and Federal Financing Models That Can Incentivize Biomanufacturing

CASE STUDY 1

Protecting Vulnerable Species with Sugar, Yeast, and an Engineering Biology Platform Technology

Key Takeaways

- Platform technologies provide flexibility and versatility
- Federal funding for process development and scaling played a critical role
- Biobased production from renewable resources can protect threatened and endangered species

In 2004, armed with a grant from the Bill and Melinda Gates Foundation, researchers at Amyris, then a year-old, fledgling biotech company with a novel engineering biology technology, set out to develop an efficient process for producing artemisinin. At the time, obtaining this key ingredient in the first-line therapy for malaria depended on the unpredictable harvest of sweet wormwood and the expensive process for extracting small amounts of artemisinin present in the plant's leaves. By 2006, company scientists had engineered brewer's yeast to produce a chemical called artemisinic acid that could be easily converted into artemisinin, and in 2008 Amyris handed the technology free of charge to the French pharmaceutical company Sanofi, which began commercial production of artemisinin in 2013.

Though the demand for artemisinin produced in this manner never met expectations, in part because of a dramatic fall in the price of artemisinin, the work put into enabling its production by yeast has not gone for naught. Artemisinin and artemisinic acid belong to a family of naturally occurring chemicals called terpenoids or isoprenoids that have many uses in pharmaceuticals, personal care products, and liquid fuels. Through the long and involved process of inserting 13 genes into yeast to produce commercial-scale quantities of artemisinic acid—those involved estimated it took approximately 150 person-years[61]—Amyris scientists learned how to add the necessary genes to yeast and produce another terpenoid known as farnesene that opened the door to producing a wide range of terpenoids. The result was a versatile, engineering biology platform technology for converting sugar from sugarcane into high-value personal care and pharmaceutical products.

Farnesene, it turns out, is a precursor molecule that with a bit of clean chemistry can be converted to other natural ingredients that Amyris produces, as well as to farnesane, which can be used as diesel and jet fuel. Though the company explored becoming a producer of biofuels, going so far as to build a production facility in Brazil to capitalize on its extensive sugarcane to ethanol infrastructure, it realized that instead of becoming a minor player in the small margin liquid fuels industry, it could use its engineering biology platform to produce high-value, high-margin fine chemicals.

One of the first such products was squalane, a common ingredient in skin care products thanks to its moisturizing and anti-aging properties. The problem with squalane, and its naturally

occurring precursor squalene, is that its major source was the liver of deep sea sharks. By one estimate, 2.7 million deep sea sharks were harvested in 2012 alone to meet the cosmetics industry's need for squalane.[62] Today, Amyris's biobased squalane produced from sugarcane accounts for 70 percent of the world's market, with the company estimating that sugarcane grown on approximately 170 acres, or one-fifth the size of Central Park, is saving two to three million sharks a year.[63] Squalene, the precursor to squalane, also has important uses, particularly as an immune-boosting component of the mRNA vaccines developed to fight COVID-19, as well as other vaccines.

Today, in addition to squalane and squalene, Amyris has taken 11 different terpenoids to scale—another two dozen are in active development—and even has its own line of what it calls its clean beauty and health brands based on the products of its engineering biology platform. One of its products, manool, was traditionally obtained from fallen Manoao pine trees, an endangered species native to New Zealand. Manool is a key ingredient used to make woody, amber notes in the fragrance industry. Another, a sandalwood-like oil called santalol, replaces the need to cut down sandalwood trees, a threatened species. The company has even developed an unrelated process to convert discarded sugarcane ashes into cosmetic-grade silica, which is usually obtained from non-renewable sand dredging, which requires significant energy consumption and emits large amounts of carbon dioxide.

In addition to illustrating the value of developing a versatile platform technology, Amyris's story is notable for a few other reasons relevant to the strategic plan outlined in this report. The first is the important role that federal funding played in enabling the company to take its technology to commercial scale. Two grants from DARPA helped the company accelerate the time to market for any new molecule it produced via fermentation, while multiple grants from DOE helped the company optimize the conversion of cellulosic feedstocks to molecules such as farnesene via fermentation.

This story also illustrates the importance of selecting appropriate markets to serve with biobased products created from renewal biomass feedstocks: in this case, the company's decision to use its renewable, biobased processes to become a leading producer of high-value products for the growing consumer market for "clean" personal care products, rather than a niche producer of liquid fuels. Finally, the company's continued success depends, at least in part, on its ability to hire well-trained process engineers and computer scientists.

CASE STUDY 2

Building a Network of Pilot Biomanufaturing Facilities[64]

Key Takeaways

- A network of pilot-scale biomanufacturing facilities, located strategically to take advantage of regional sources of biomass, local post-secondary training programs, and opportunities for equitable economic development, would give the nascent U.S. bioeconomy a competitive edge and drive product commercialization
- A shortage of pilot-scale facilities is inhibiting transition of bio-based products from the laboratory scale to commercial markets

Modern biotechnology tools, including those from engineering biology, struggle to break into commercial manufacturing. To realize the promise of industrial biomanufacturing for economic impact and sustainability, the United States needs a concerted, strategic push to catalyze the creation of a pilot-scale infrastructure to transition biomanufacturing processes from laboratory research to economic opportunity and manufacturing jobs. Indeed, realizing the promise of industrial-scale biomanufacturing would open the door to a distributed, resilient network for biobased chemical manufacturing, bringing jobs and opportunities to local communities and securing a domestic supply chain.

At a high level, biological synthesis and manufacturing of industrial chemicals occurs in three developmental phases:

1. Proof of concept, in which companies develop a biobased system to synthesize a chemical of interest at a scale of milligrams to grams in bioreactors that typically are 100 liters or smaller. As a result of increasing public and private investments in engineering biology, companies can make almost any chemical in a predictable and reliable manner at this scale.
2. Pilot-scale development and product testing, during which companies work out the biomanufacturing and downstream processes capable of producing kilogram quantities of a chemical that potential end users can assess in terms of performance characteristics or comparability to existing industrial chemicals.
3. Commercialization, which is when companies take a pilot-scale process and transition it to a relevant commercial production scale of often 100,000 liters or more. Several U.S. biomanufacturing companies have significant infrastructure at this scale, but this infrastructure is largely inaccessible to small- and medium-sized enterprises to access a consequence of the relatively small number of publicly available pilot-scale production facilities in the United States that would enable these companies to complete phase 2.

Developing a substantial pilot-scale infrastructure aims to solve a major roadblock at the second of these steps. Typically, a company is not able to validate a potential product, whether produced via biomanufacturing or traditional chemical manufacturing, until it can produce on the order of a kilogram for testing. Today, however, a company with a biobased product finds itself in a Catch-22 situation: To get to that kilogram, it may need to use larger-scale equipment in the 1,000-to 5,000-litter range because the yield of its product is low given that it has not yet optimized the bioproduction process, which also requires working with larger-scale equipment. However, existing facilities operating at that scale are hesitant to take on an unproven or inefficient process because it fails to meet their benchmarks for cost recovery.

That first kilogram is also the most expensive to make—in large part because scaling a biobased production process is less predictable and thus more challenging and time-consuming than scaling a traditional chemistry-based process. As a result, it can be too expensive for a fledgling industrial biotechnology company and its investors to take a risk on a product that may not make it to market. This holds back innovation and possible market entry and is driven in part by the lack of access to infrastructure to do that work in a speedy and cost-efficient way.

The challenge today, then, is to de-risk the economic model of offering pilot-scale manufacturing as a service so that companies will no longer be forced to use the small number of those facilities available on a for-service basis in Europe and Mexico to get through the pilot phase of development. While the cost of a single pilot production facility may only be $75-100 million, the return on investment for private capital has not been proven, so companies that wanted to build pilot-scale manufacturing facilities, either for their own process development activities or to make them available as a fee-for-service business for others, may not be able to recover their investment. The solution to this problem—one that would accelerate the transition from promising laboratory technologies to commercial output—is for the United States to invest in a networked, pilot-scale infrastructure in a manner that enables early-stage technology development efforts to conduct the scale-up work needed to justify subsequent investments in a robust infrastructure for high-volume domestic production of bioproducts.

Fully realizing the potential of the nascent U.S. biomanufacturing industry, one that would support regional and equitable economic development, requires the nation to invest on the order of $750 million to $1.2 billion to build an integrated network of 10 to 12 pilot-scale biomanufacturing facilities. These facilities should be located strategically to take advantage of regional sources of biomass, foster the growth of a biomanufacturing workforce, and promote equitable economic development. A substantial federal investment to support the bulk of the capital expenditures and 24-month runways for operational expenses should catalyze state and possibly private sector partnerships to share the cost of establishing the facilities as a non-profit network.

These facilities, once established, can be self sustaining via facility user fees, with any excess revenue funneled back into research and development to continually strengthen the network's capabilities. The federal government took one step in this direction when it created BioMADE, the new Bioindustrial Manufacturing Innovation Institute,[65] but this is a modest investment that excluded infrastructure and will not come close to meeting the demand for a U.S.-based pilot-scale infrastructure. In that regard, one only needs to look at BioBase Europe, which is currently the gold standard for biomanufacturing pilot facilities and is catalyzing the growth of a European biomanufacturing industry. A series of infrastructure grants from the European Commission helped establish this pioneering network.

Facilities in the proposed U.S. network could specialize based on several factors as a means of covering the different aspects of producing the wide range of chemicals that biomanufacturing has the potential to produce.

- Proximity to regional feedstocks, such as corn stover in Iowa, sugar beets in Montana, switchgrass in Virginia, pine forest residue in Georgia, almond hulls in California's Central Valley, and others
- Product class, given that biomanufacturing can create a wide array of products that often have different scaling and post-production needs
- Biomanufacturing methods, in which facilities could specialize on a particular production technique, such as aerobic versus anaerobic versus solid-state fermentation, non-fermentation or cell-free systems, or different types of purification or downstream processing
- Specific workforce development components

An optimal model for these facilities would be for them to operate as a single non-profit network that a single entity, such as BioMADE, owns and operates for the good of the industry. Such a model would allow for robust coordination across the network and provide broad benefits to industry members if facilities are differentiated. It would also allow for income pooling to reduce individual facility risk, greater opportunities to reinvest excess income back into biomanufacturing innovation, and consistency across the ecosystem of diversified facilities. As the map below illustrates, the overlap of regional sources of biomass, post-secondary training programs, and opportunities for equitable economic development provides ample opportunities for locating the individual facilities in the network across the nation.

Once established, this infrastructure would rapidly increase the number, value, quality, and diversity of biobased products reaching the market. Facilities can, and should, also focus on being a locus of bio-innovation in their communities—spurring investment and innovation. There are several benefits of having this capability in the United States:

1. The global supply of such facilities is far too low to meet the demand and international competition for using the limited number of these facilities could freeze out U.S.-based companies.
2. These facilities would be part of the nation's innovation pipeline and proximity often matters to build an innovation ecosystem. If one of the objectives is to catalyze a robust biomanufacturing pipeline, co-locating facilities with U.S. innovators, a trained workforce, and a ready source of biomass as feedstock will accelerate the maturation of that ecosystem.
3. While these facilities are primarily about scale-up to get to a larger commercial scale, they are still *manufacturing* facilities. As the COVID-19 pandemic has shown, fragile global supply chains can be disrupted and the ability to pivot domestic manufacturing capabilities is crucial. These facilities, which would be funded through public and private investment, can be thought of as a national network on "warm standby" that would be able to respond to national or regional emergencies or disruptions to the supply chain, as occurred when massive flooding accompanying Hurricane Harvey in 2017 and record-setting cold in 2021 shut down refining operations.
4. Biomanufacturing has the opportunity to provide value-added materials with unique properties. Some of these properties may be used to strengthen national security, and domestic development and production is important for those specific objectives.

CASE STUDY 3

Repurposing to Power the Bioeconomy

Key Takeaways

- Abandoned petrochemical and corn-to-ethanol plants can be repurposed for bioproduction of chemicals and food protein made from sustainable biomass
- Repurposing existing facilities can power equitable regional economic development and job growth and enable reskilling of people to fill good-paying bioeconomy jobs

One of the promising aspects of continuing to develop the U.S. bioeconomy is the opportunity to convert existing corn-to-ethanol and surplus petrochemical facilities into bioproduction facilities. In fact, several companies are already doing just that, and the result is not only turning an unproductive asset into a productive one, but creating economic growth and jobs in parts of the country that could use a boost.

For example, Solugen has converted an abandoned petrochemical plant in Stafford, TX, into a facility that uses "cell-free" bioproduction processes with enzymes to produce 10,000 metric tons of specialty chemicals a year. Solugen's first product was hydrogen peroxide, an industrial chemical that is usually made with natural gas as a feedstock in a process that requires high heat, generates hazardous waste products, and is energy intensive. In contrast, the feedstock for Solugen's enzyme-based process is corn syrup produced by wet mills in Iowa, a commodity that has seen a falloff in demand in recent years. The process, which does not involve fermentation, operates at low heat, uses much less energy, and produces no waste. The company has since developed other enzyme-based processes to produce chemicals used in water treatment applications and to harden concrete, with others in development.

In addition, Solugen not only repurposed an abandoned facility, as well as equipment once used to make candy, but it also retrained former petrochemical refinery workers to operate the reengineered facility. Rather than expand this existing facility as it grows its product offerings, the company plans to repurpose unused facilities around the country to create a distributed network of plants that will help grow regional economies and reduce transportation-associated emissions.

Overseas in Italy, Novamont, a producer of bioplastics, is using a process developed by Genomatica, a San Diego-based biological engineering company, to produce 30,000 tons a year of 1,4-butanediol, a key chemical used to make biodegradable and compostable products such as fruit and vegetables bags, mulch film and coffee capsules, as well as biodegradable lubricants and greases, biobased ingredients for the cosmetics industry, and most recently, sustainable biocide preservatives. The company's processes all use sustainable biomass processed in industrial sites that were decommissioned or no longer competitive. One of Novamont's corporate goals is to reinvigorate regional economies in Italy and to do so using regional biomass produced in a manner that protects soil health and helps soil regenerate.

Back in the United States, Superbrewed Food has turned an abandoned corn-to-ethanol plant in rural Minnesota into a facility that produces food-quality protein using micro-organisms found in the human gut. The company's first product was a sustainable fish feed, and subsequent products include cream cheese, cheddar cheese, and mozzarella cheese made from its cultured plant-based protein. The Minnesota facility will eventually be able to deliver 40 million gallons worth of plant protein-based milk from the microbial cultured protein.

In the same vein, Nature's Fynd is using fungi that grow naturally in Yellowstone National Park, and originally discovered as part of a NASA-sponsored project, to produce food-grade protein from renewable and sustainable biomass. This process, which relies on a proprietary liquid-air interface fermentation technology that is easily scalable, takes place in a facility built in the historic but abandoned Union Stockyards on Chicago's South Side. The company has made a practice of hiring and training residents from the local community, yet another example of providing new purposes for facilities and new careers for people as part of the growing bioeconomy.

CASE STUDY 4

Future Biobased Feedstocks

Key Takeaways

- A future circular U.S. bioeconomy depends on an ability to efficiently use waste biogenic carbon
- Sustainable biomass has the potential to serve as the feedstock for U.S. chemical production
- More research is needed to address the technical challenges of converting most biomass into desired bioproducts

Imagine a future where a plane carrying flame retardant to drop on a forest fire is powered by fuel derived from forest slash generated by forest fire prevention programs. That future is not out of reach should the nation's efforts to convert sustainable biomass into feedstocks for aviation fuel and chemical production come to fruition.

The 2016 Billion-Ton Report states that the United States has the capacity to produce a billion tons of sustainable biomass annually without affecting food production for domestic consumption or export or leading to deforestation or land degradation.[66] If fully utilized, those billion tons could be used by a thriving bioeconomy to generate 25 percent of the nation's liquid transportation fuels and 50 billion pounds of biobased chemicals, as well as cut carbon dioxide emissions by 450 million tons and support 1.1 million U.S. jobs.

All biomass contains sugars, and sugars can be converted to a variety of chemicals, including ethanol, a "first generation" renewable fuel produced from the fermentation of corn that is included in 98 percent of U.S. gasoline. Indeed, the successful conversion of plant-based sugars into a variety of chemicals, not just ethanol, from corn and sugarcane has been advancing steadily. In fact, an estimated 20 percent of chemical production now comes from biomass rather than petroleum.

Unfortunately, releasing the sugars tied up in cellulose, a major structural component of all plants, is not as easy as liberating it from corn kernels, sugar cane, or sugar beets. Nor is it easy to release the useful chemicals known as aromatic compounds, from lignin, a complex polymer that serves as the other major structural component of plants. To accomplish that task, researchers are working—with some success—to harness the natural ability of many microorganisms to break down cellulose and lignin into their constituent sugars and aromatic compounds. Making this challenge more difficult, particularly if the goal is to use the wide variety of plant-based waste materials and post-consumer wastes, is the heterogeneity of the residues left after harvesting crops, processing food, or turning trees into lumber and paper, which will require more than one approach to liberating those sugars for further processing and biomass refineries that can handle heterogeneous materials.

Once research solves that challenge—and that should be possible using the tools of molecular and engineering biology—biomass can be converted into what are called platform

chemicals that are then used to produce a variety of industrially important chemicals. Platform chemicals produced today via conversion of petroleum feedstocks include levulinic acid, furfurals, sugar alcohols, lactic acid, succinic acid, phenols, olefins, and terpenoids (see the Amyris case study for all the uses of terpenoids). The vision for a circular bioeconomy rests on the idea of converting biomass into chemicals that are then used to make materials that would eventually, when their useful lifetime has ended, serve as another source of biomass for conversion into fuels and chemicals. U.S. biotechnology leadership provides a promising foundation for a future strategic renewable feedstocks research effort with significant potential to open the door to converting the carbon that exists in plants to the carbon we can use sustainably.

CASE STUDY 5

Advancing the Bioeconomy by Sharing Resources and Knowledge

Key Takeaways

- Sharing resources can maximize the use of existing infrastructure and be a force multiplier for expertise and knowledge
- Resource and knowledge sharing can reduce the time to move novel products from the lab to the marketplace

The world-leading U.S. biobased research infrastructure continues to produce the discoveries needed to power the nation's resilient, competitive bioeconomy, but translation of those discoveries into the commercial processes that lead to economic activity and bioeconomy jobs is lagging. Having a network of pilot plant facilities, as discussed elsewhere in this report, is a necessary step for catalyzing the translation of those processes that require fermentation, but it is not sufficient to unleash the bioeconomy's full potential unless successes at the pilot stage can then transition to commercial-scale production. This is where government-incentivized public-private partnerships can play an important role.

Economically viable commercial-scale production requires several inter-connected and mutually reinforcing capabilities:

- Available fermentation capacity of at least 100,000 liters to achieve economy of scale
- An experienced process engineering team to take it from pilot scale to commercial scale
- A robust industrial production organism
- Fermentation capacity suitable for making a variety of products. Anaerobic tanks used to make ethanol and beer, for example, are abundant but limited in the types of products they can produce. Tanks with oxygenation are required to make proteins and many other products
- Downstream processing capability is required to purify the fermentation products
- Formulation and blending capabilities to make liquid and solid products
- Cost-effective sanitation protocols to avoid contamination
- Special precautions for making food-grade products
- Regulatory expertise to bring products to market
- A supply chain to deliver the finished product
- Commercial route to market

Developing these capabilities takes time and financial resources that very few startup companies possess. While venture capital, the traditional source of funding, sees the enormous potential payoff from a vibrant U.S. bioeconomy, investors are reluctant to put up funds at the necessary scale, having been burned during the advanced biofuels wave of capital-intensive

investments that failed to generate expected returns. One avenue that a startup can take is to find a contract manufacturer to produce their product, but contract manufacturers are in high-demand and access to their capacity is limited. In addition, contract manufacturers only manufacture—they do not provide regulatory expertise, a supply chain, or a commercial route to market, nor will they work to optimize the production process.

Government-incentivized public-private partnerships with established players can address this problem without requiring every company to invest in physical infrastructure. Currently, there are two fermentation-based industries with production know-how and excess capacity—breweries nationwide and wet-mill ethanol plants in the Midwest—that are looking to use their excess capacity to produce new, high value-added products but may need additional investments in equipment to produce and purify other products. Now imagine if the federal government were to provide funds for these facilities to upgrade their infrastructure so that they could serve as commercial-scale manufacturers in exchange for providing those services at a cost that a startup could bear and which venture capital would find attractive. Such a partnership could also include a provision that these facilities would serve as part of a national network on "warm standby" that would be able to respond to national or regional emergencies or disruptions to supply chains of various types.

There are also established firms, particularly those that use biobased and bio-enabled processes to produce fine chemicals such as flavors and fragrances and food products, who may also have available capacity. In that case, a public-private partnership could provide funds to reserve a certain percentage of the firm's capacity for use by a company looking to scale their production process. The startup might also contract with the established firm to provide other services, such as process refinement, downstream processing, and even supply chain and marketing services, though there are intellectual property issues, such as who owns the rights to any improvements the established firm might develop.

Information Sharing

In addition to sharing of physical assets, knowledge sharing would also fuel the bioeconomy, especially in the case of precompetitive knowledge that could inform bioprocess development and reduce the need for every research group, whether in academia or industry, to reinvent the wheel every time it attempted to transition a process to the pilot scale. Academic investigators, for example, neither study bioprocesses at scale, nor publish extensively in this field. In addition, there is currently no incentive to publish failed studies or lessons thereby learned. These unfortunate realities have led to decades of substantial repetition of failed experiments in the community as a whole, resulting in significant knowledge gaps and a waste of resources that could be better applied toward further derisking scale-up.

One solution, proposed by staff at the Advanced Biofuels and Bioproducts Process Development Unit (ABPDU) at Lawrence Berkeley National Laboratory, a non-profit process development unit funded by DOE, would be to develop a responsive learning/artificial intelligence platform technology that researchers could use to predict the outcomes of fermentation and downstream recovery and purification experiments based on the collective experience and learnings of the research community and input from experts in the field (Figure CS5-1). Non-proprietary data to power the system would come initially from ABPDU's process development experience, and the database—and the accuracy of its predicted outcomes—would grow as researchers who use the system volunteer to contribute precompetitive

experimental details and outcome data. The system would include a web-based tool for users to input their experimental plans and receive experimental guidance to avoid common pitfalls and maximize resources (Figure CS5-2).

Aside from sharing knowledge to benefit process development, this system would also enable early career scientists and engineers to learn about process development without having to perform actual experiments. In essence, this system would be creating an ever-evolving reference source that would benefit the entire bioeconomy.

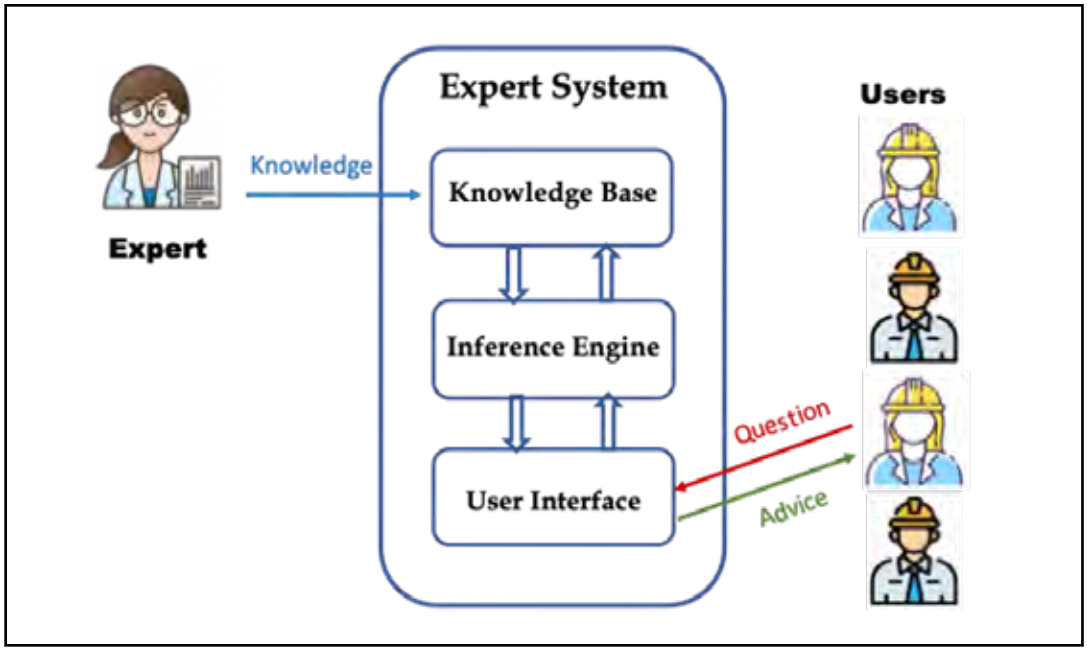

FIGURE CS5-1
A data-sharing, inference-based system allows expert knowledge to scale to many users. *Credit* Deepti Tanjore, ABPDU

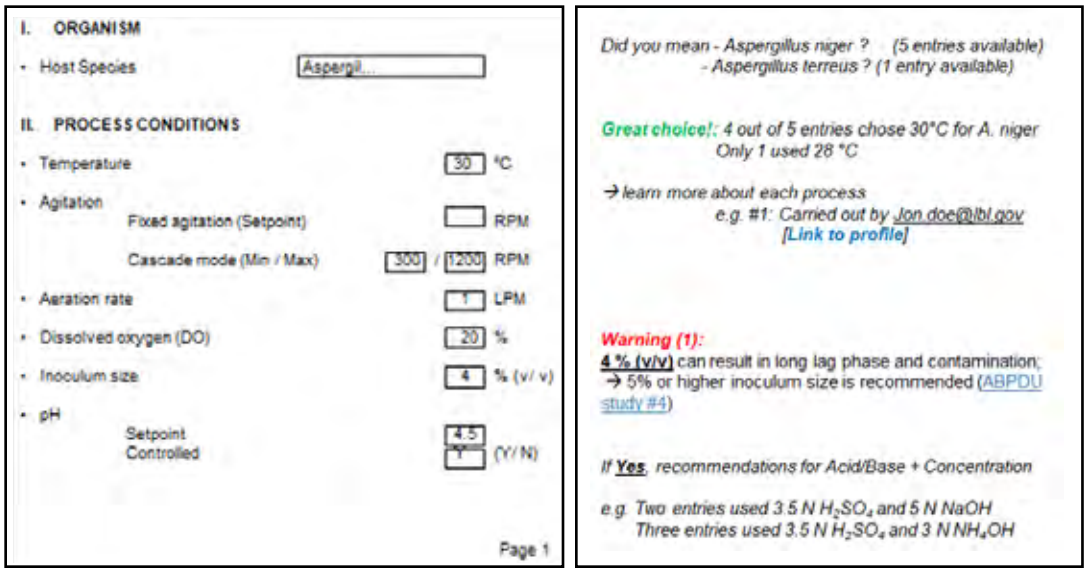

FIGURE CS5-2
An example of the form users would fill in and advice the system would generate. *Credit* J.P. Prahl, ABPDU; Deepti Tanjore, ABPDU

CASE STUDY 6

Illustrating the Complex Regulatory Ecosystem

Key Takeaways

- Many bioeconomy products must receive approval from multiple regulatory agencies before they can reach the market
- In complex, multi-agency regulatory assessments, companies have to submit different sets of data to each agency
- Time to market for a novel product of biotechnology can be long

The regulatory ecosystem for products of biotechnology is complex, fragmented, and time-consuming, with EPA, FDA, and USDA each being responsible for certain aspects of regulating the products of biotechnology. There are many challenges that the developers of bioeconomy products face in getting their products approved for commercial use. As shown previously in Table 3 the three regulatory agencies play a role in bringing a bioeconomy product to market. Table CS6-1 contains information on the products selected for this case study, including the name of the product developer/manufacturer, the product's current market status, and a brief description of the product and its significance as a regulated bioengineered product. The table also delineates a timeline of major regulatory decisions related to each product, though it is not a complete timeline of every regulatory decision that was made on the product. The timelines were compiled using publicly available literature and information collected from databases maintained by EPA, FDA, and USDA. Forthcoming regulatory decisions are labeled as TBD. Regulatory decisions that have been made but whose dates could not be found are labeled with N/A. It is clear from the available data that "first-in-kind" products of biotechnology can have a complex path and long time to market.

TABLE CS6-1 — EXAMPLE PRODUCTS AND THE TIMELINE OF MAJOR REGULATORY DECISIONS This table contains information on the products selected for the case study, including name of the product developer/manufacturer, the product's current market status, and a brief description of the product and its significance as a regulated bioengineered product. The table also delineates a timeline of major regulatory decisions related to each product (note that it is not a complete timeline of every regulatory decision that has been made on the product). The timelines were compiled using publicly available literature and information collected from databases maintained by the EPA, the FDA, and the USDA. Regulatory decisions that are forthcoming are labeled as TBD. Regulatory decisions that have been made but whose dates could not be found are labeled with N/A.
Credit Sifang Chen, postdoctoral fellow, Engineering Biology Research Consortium

Table CS6-1 Example products and the timeline of major regulatory decisions.

Product	TIMELINE OF MAJOR REGULATORY DECISIONS
Blight Fungus Resistant American Chestnut *SUNY ESF* *Market status: under development* Genetically engineered (GE) blight-resistant chestnut trees developed using an oxidate oxidase-encoding gene from wheat; the first transgenic trees being considered for restoration use.	**2020:** SUNY ESF submits Petition for Nonregulated Status. **2023:** USDA anticipates publishing a final decision on the petition. **TBD:** EPA will review environmental safety and interactions with the blight fungus. **TBD:** FDA will review blight-resistant chestnut for nutritional safety since both people and animals use chestnuts as food.
AquAdvantage Salmon *Aquatic Bounty Technologies* *Market status: on the market* GE Atlantic salmon developed for faster growth; the first GE animal intended for human consumption.	**1995:** ABT requests an Investigational New Animal Drug exemption from FDA to pursue the development of AquAdvantage Salmon. **2015:** FDA releases Environmental Assessment and Finding of No Significant Impact approving AquAdvantage Salmon application.
Pivot Bio PROVEN *Pivot Bio* *Market status: on the market* GE diazotrophic microbes that enable biological nitrogen fixation for corn; the first commercial biofertilizer for cereal crops.	**2019:** Pivot Bio inquires the USDA on the regulatory status of the product. **2020:** USDA confirms that it does not consider the diazotrophic bacteria, as described by Pivot Bio, to be regulated as a plant pest. **N/A:** EPA determines the product falls under the soil amendment category and are therefore regulated by individual states.
TransFerm Yield+ *Mascoma* *Market status: on the market* GE strain of yeast that expresses glucoamylase enzyme, developed to improve the efficiency of ethanol fuel production from liquefied grains.	**2019:** FDA receives GRAS notice from Mascoma **2020:** FDA completes evaluation of Mascoma's GRAS notice **N/A:** TransFerm Yield+ meets the review requirements via completion of a Microbial Commercial Activity Notice.
Rainbow Papaya *Cornell University, University of Hawaii* *Market status: on the market* GE papaya cultivar with resistance to papaya ringspot virus; the first commercialized transgenic fruit crop.	**Feb, 1996:** University of Hawaii and Cornell University submit to USDA a Petition for Determination of Nonregulated Status. **May, 1996:** USDA approves Petition for Determination of Nonregulated Status. **Jan, 1997:** University of Hawaii and Cornell University submit to the FDA a safety and nutritional assessment. **Sep, 1997:** FDA concludes consultation on transgenic virus resistant papaya.

Table CS6-1 Example products and the timeline of major regulatory decisions (cont).

Product	TIMELINE OF MAJOR REGULATORY DECISIONS
SmartStax Pro RNAi Pest Control *Monsanto* *Market status: under development* GE corn seeds developed using Ribonucleic acid interference (RNAi) technology to control corn rootworm; the first time RNAi technology has been used against this insect.	**Oct, 2013:** Monsanto submits Petition for Determination of Nonregulated Status to USDA. **Nov, 2013:** Monsanto submits to FDA a safety and nutritional assessment. **Oct, 2014:** FDA completes evaluation of Monsanto's submission to determine any safety or regulatory issues with respect to its use in food or feed. **Oct, 2015:** USDA approves Petition for Determination of Nonregulated Status. **Jun, 2017:** EPA issues notices of pesticide registration for SmartStax products.
UPSIDE Chicken *UPSDIE Foods (f/k/a Memphis Meat)* *Market status: under development* Chicken meat developed from cultured animal cells; the first cultured meat product intended for sale in the US.	**Mar, 2019:** FDA and USDA publish MOU stating FDA will oversee collection and growth of cultured cells, and USDA will oversee processing of those cells into meat products and product labeling. **N/A:** Pre-market consultation process with FDA to evaluate the production process and produced biological material. **N/A:** After pre-market consultation, FDA to conduct routine inspections of cell banks and facilities. **N/A:** USDA to carry out inspections at establishments where cells derived from livestock and poultry are harvested.
EVERY ClearEgg *The EVERY Company (f/k/a Clara Foods)* *Market status: on the market* Egg white proteins cultivated from GE yeast; the first bio-identical egg product intended for sale in the US.	**Mar, 2019:** FDA and Clara Foods hold pre-submission (GRAS notice) meeting. **Sep, 2020:** FDA receives Clara Foods' GRAS notice submission. **Sep, 2021:** FDA completes evaluation of Clara Foods' GRAS notice submission.

CASE STUDY 7

Local, State, and Federal Financing Models that Can Incentivize Manufacturing

Key Takeaway

- All levels of government can craft financial incentives to enable the growth of a national bioeconomy with an emphasis on regional economic development

With leadership of the $4-plus trillion global bioeconomy at stake, it behooves local, state, and federal governments to provide the necessary financial incentives to help address the barriers to creating a vibrant, resilient U.S. bioeconomy and rise to challenge of global competition in this advanced technology space. Providing such incentives for nascent technology-based industries is not unprecedented. Thanks in large part to early federal investment in computer research and development, the United States is home to globally dominant information technology companies. Local, state, and federal investments and incentives have also enabled the United States to become the world leader in the biomedical sector.

Local and state governments are not new to the incentive game, as they routinely offer companies billions of dollars in fiscal incentives, including cash grants, rebates, and tax credits, to entice them to relocate, expand, or stay in a specific locality. According to a Brookings Institute report, local and state economic development incentives range between $45 and $90 billion annually.[67] The city of Vacaville, CA, for example, provided seed funding in 2020 that helped establish the California Biomanufacturing Center, a 501(c)(3) non-profit organization supporting industry development and workforce training in partnership with Solano Community College and the University of California at Davis. This initiative is part of the city's plan to establish a series of manufacturing centers of excellence in highly specialized segments of innovative industries, including bioproduction of chemical products, materials, and fuels, for the purposes of economic development. As part of this program, the city has created a new zoning paradigm to simplify and facilitate desirable biotechnology investments with the biomanufacturing center, and it provides a central point of contact for reviewing all new biotechnology-related projects that process land-use applications within 100 days of submission. Previously, Vacaville provided a 10-year property tax rebate to entice Genentech to build a manufacturing facility in the city.

In 2019, the citizens of Oklahoma City approved a $71 million investment in the city's innovation district, which includes bioscience companies. The investment includes funds to encourage further development for minority-owned small businesses, better connectivity in and around the district, and the construction of an "Innovation Hall" to serve as a central place to facilitate activities that will grow the city's innovation economy. The city was also awarded a American Rescue Plan grant that will go toward investing in biotechnology-focused infrastructure and workforce training.

Another city with big plans to be a biomanufacturing center, albeit in the biomedical space, is New York. In 2021, the city announced plans to invest $38 million in biotechnology centers at four institutions in the city. Montefiore Medical Center, for example, will use $13

million to create a biomanufacturing operation focused on cell, gene, and antibody therapy production for both early-stage and established companies.

At the state level, the Federal Reserve Bank of San Francisco estimated in 2014 that financial incentives from state governments have boosted biotechnology jobs overall in states that offered incentives and generated sizable effects in local service sectors. In general, states have used research and development tax credits, which provide a credit against a business's income taxes that is proportional to its expenditures on qualified research and development and biotechnology-specific subsidies. Biotech-specific tax credits have included tax credits on investment or job creation by biotech companies, sales and use tax exemptions for purchasing equipment used in biotech activity, low-interest loans to biotech startups, and lump sum grants to biotech companies.

California, for example, provides a special incentive for biobased production facilities through a 6 percent income tax credit for "special purpose buildings" and a property tax provision that allows companies to depreciate biotechnology equipment more rapidly. Kansas has used grants from NSF and strategic investments to establish the Center for Environmentally Beneficial Catalysis at the University of Kansas as a center focused on converting biomass—Kansas has the fourth largest amount of biomass—into chemicals. The state believes that its investment will create thousands of jobs in rural communities and generate billions of dollars in economic activity. Outside of biomanufacturing, Michigan used tax incentives totaling $780 million for advanced battery manufacturing and research to land four advanced battery production facilities worth a total of $1.7 billion that will employ several thousand workers. GM and Ultium Cells, for example, received a $600 million grant, Ultium was granted a $158 million tax break, and the local utility and surrounding township received $66.1 million to upgrade infrastructure at the site of the planned production facility.

At the federal level, the federal R&D credit rewards companies that create and improve products involving technical uncertainty and a process of experimentation, and biomanufacturing companies are prime candidates for claiming this benefit. The Commerce Department's Build to Scale program manages a portfolio of grant competitions that further technology-based economic development initiatives that accelerate high-quality job growth, create more economic opportunities, and support the future of the next generation of industry leading companies.

In terms of national financial support for biomanufacturing, Europe provides several examples from which the United States can learn. The Pilots4U program, funded by the Biobased Industries Joint Undertaking under the European Union's Horizon 2020 Research and Innovation Programme, is a platform that mapped all open-access pilot- and multipurpose demo-infrastructures across Europe that are open to all companies and research institutes. Its purpose is to create a visible and easily accessible network that will support the development of a thriving bioeconomy. While the initial public funding for the project itself ended, the database of facilities is still operating and searchable.[68] Pilots4U also conducted a gap analysis and European industry survey to identify the infrastructure and expertise required from open-access centers and built a business case to address the identified gaps. Europe has also established the European Network for Pilot Production Facilities and Innovation Hubs (EPPN), akin to the network of pilot facilities this document has proposed creating in the United States. The European Commission provided €195 million in funding to establish this network of 24 facilities and develop a digital ecosystem to serve as an interactive marketplace for its members. EPPN also serves as a single entry point for any user to access pilot facilities and services across Europe and early-stage access to intelligence on more efficient development processes.