# Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells

# A Technology Roadmap to 2025


Developed by National Cell Manufacturing Consortium

February 2016

NIST National Institute of Standards and Technology U.S. Department of Commerce
AMTECH Advanced Manufacturing Technology Consortia
Georgia Research Alliance
Georgia Institute of Technology
Prepared by NEXIGHT GROUP

# Acknowledgements

This roadmap was developed through a public-private partnership under the direction of Greg Dane, Director of the Industry Fellows Program at Georgia Research Alliance; Krishnendu Roy, Robert A. Milton Chair of Biomedical Engineering at Georgia Institute of Technology; and the National Cell Manufacturing Consortium Executive Committee with direct input from industry, academia, clinical facilities, private foundations, and government agencies. Nexight Group supported the overall roadmapping process and prepared this roadmap; Sarah Lichtner, Ross Brindle, and Lindsay Pack are the primary contributors. The cell manufacturing industry experts who made vital contributions through workshop participation, working group support, and roadmap reviews are identified in Appendix B of this report.

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# About this Roadmap

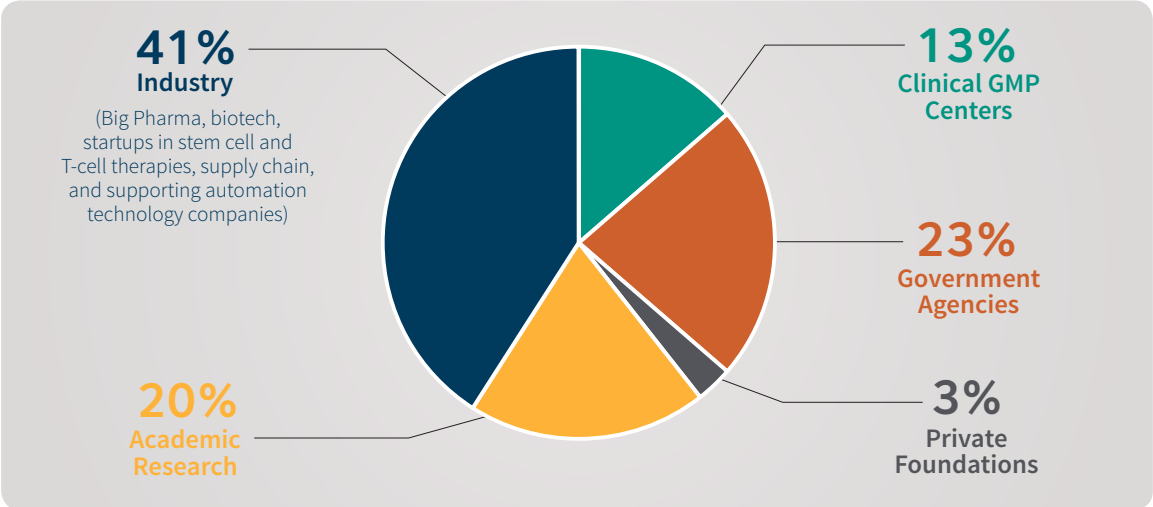
Cell-based therapies—especially stem cell therapies, regenerative medicine, and immunotherapies—and cell-based devices and diagnostics could have significant public health and economic benefits but will require the cost-effective, large-scale, reproducible manufacturing of high-quality cells to realize their potential. Enabling large-scale cell manufacturing calls for resource investments in advanced technologies and techniques that can increase cell production scale and speed while improving quality assurance, reducing manufacturing and product costs, enhancing manufacturing reproducibility and consistency, strengthening information technology security, and increasing treatment efficacy and safety.

The Georgia Research Alliance (GRA) and Georgia Institute of Technology (Georgia Tech) recognized the opportunity to advance innovative technologies and techniques that can overcome current cell manufacturing challenges and support long-term growth of the cell manufacturing industry. Together, GRA and Georgia Tech established the National Cell Manufacturing Consortium (NCMC) and led the development of this roadmap, with funding from the National Institute of Standards and Technology (NIST) Advanced Manufacturing Technology Consortia (AMTech) program. This roadmap identifies challenges that currently constrain cell manufacturing and provides a pathway for developing, advancing, and implementing advanced technologies over the next 10 years to enable large-scale, cost-effective, reproducible manufacturing of high-quality cells.

The development of this roadmap was informed by a variety of stakeholder inputs, built around several highly interactive roadmapping workshops. Nearly 100 cell manufacturing experts came together from more than 60 organizations—including from industry (e.g., Big Pharma, biotech, startups in stem cell and T-cell therapies, supply chain, and supporting automation technology companies), clinical Good Manufacturing Practice (GMP) facilities, academic research, government agencies, and private foundations. During these workshops, participants identified current cell manufacturing challenges and needs, identified and prioritized research and development activities that address these challenges, and defined the vision and mission of the NCMC. The distribution of participants based on organization type is presented in Figure 1.

The priority activities outlined in this roadmap will inform the initiatives of the NCMC, as well

Figure 1. Participating entities by organization type



as the cell manufacturing industry as a whole, academic researchers, public and private funding agencies, and policy makers. The ultimate vision of the NCMC is for the United States to maintain its global prowess as the leading developer of cell manufacturing technologies and manufacturer of cells and for the U.S. to be viewed as the chief authority on cell manufacturing standards and practices worldwide. To achieve this vision, NCMC will work to develop and mature technologies and infrastructure relevant to cell manufacturing; to facilitate regulation, commercialization, and adoption of emerging technologies by the cell manufacturing industry; and to build and train a skilled industry workforce that can sustain continuous industry progress.

## National Cell Manufacturing Consortium (NCMC) Vision

The United States establishes and maintains its global prowess as the leading developer of cell manufacturing technologies and manufacturer of cells and is viewed as the chief authority on cellular manufacturing standards and practices.

### Who Should Read this Roadmap?

This roadmap will be of use to a variety of individuals within and beyond the cell manufacturing community. It is not written solely for **pharmaceutical or biotechnology companies**, but rather for a range of **stakeholders within industry, academia, and government** who are critical to advancing this industry. Achieving large-scale, reproducible production of high-quality therapeutic cells at low cost will require a convergence science approach that brings together clinicians, cell biologists, and immunologists with a wide variety of engineers and scientists—not only bioengineers and chemical engineers who have been classically involved in biomanufacturing, but also electrical and mechanical engineers, computer and data scientists, systems biologists, chemists, physicists, and manufacturing and industrial engineers.

To realize large-scale cell manufacturing, **industry and clinical Good Manufacturing Practice (GMP) centers** must focus on the priority activities outlined in this roadmap to drive the development and implementation of advanced cell manufacturing technologies and techniques. **Academic researchers** must support these efforts by conducting the R&D necessary to bring these life-changing tools and techniques to market. Sensors and automation, big data analytics and machine learning, process engineering and plant design, and systems integration and instrumentation must all be an integral part of the fundamental national strategy to achieve success in industrial-scale cell manufacturing. To inform the efforts of industry scientists and academic researchers, **physicians, biologists, and clinical scientists** must provide the supporting knowledge and design parameters necessary to realize the therapies and treatments that will allow them to improve the lives of millions of people.

In the absence of regulatory buy-in, standardization, social buy-in, and insurance reimbursement, the promises of cell therapies and regenerative medicine will fail to reach their transformative potential. **Government agencies, law makers, regulatory personnel, standards organizations, policy experts, the reimbursement industry, and private foundations** must acknowledge the cell manufacturing industry's areas of priority need, focusing resources in these areas and developing regulations and standards that can facilitate this industry's accelerated growth.

# Executive Summary

Advanced, large-scale manufacturing of high-quality cells has the potential to transform the healthcare industry, improving the health of millions of people while significantly growing the U.S. economy. A coordinated approach to developing and implementing next-generation cell manufacturing technologies is critical to realizing this impact and to securing the United States' lead in this emerging field.

Over the past few decades, cell-based medical technologies have helped treat many patients with cancer, blood disorders, vision disorders, and other ailments. In 2012 alone, these products treated more than 160,000 patients.[1] Though this relatively new industry has been growing significantly—with annual U.S. revenue above $1 billion—its potential is still far from being fully realized.

New and emerging cell-based healthcare products, such as cell therapies, engineered tissues, medical devices, and drug discovery and testing platforms, could help manage and even cure many conditions and diseases that are intractable, chronic, and even terminal today, including cancer, heart failure, paralysis from spinal cord injuries, and autoimmune disorders. Advanced cell-based technologies can help meet the needs of an aging population, accelerate recovery from injuries, and reduce the number of people on transplant lists—currently more than

## What are Cell-Based Medical Technologies?

This roadmap is focused on advancing the manufacturing of cells intended for use in final products, including the following:

**Cell Therapies** — the administration of live cells or genetically altered genes, often via blood transfusions, infusion, or bone marrow transplants, to a patient to replace live cells or repair damaged or diseased cells or tissues

*Emerging products and applications:*

- Cell-based cancer vaccine for metastatic prostate disease
- Spray-on cells for wound healing
- T cell immunotherapy for cancers
- Stem cell therapies for strokes, heart failure, autism, fibrosis, diabetes, and spinal cord injury

**Engineered Tissues** — growth of tissues, (e.g., bone, cartilage, skin, muscle, and organs) from live cells for implantation into a patient to restore, maintain, or improve tissue and organ function

*Emerging products and applications:*

- Ocular, cardiovascular, and neurological tissue regeneration
- Vascular grafts
- Joint cartilage regeneration

**Medical Devices** — devices that measure and monitor cell function, some of which deliver physical, magnetic, electrical, optical, or chemical stimuli to cells to diagnose, control, treat, or prevent disease or to improve sub-optimal cell function

*Emerging products and applications:*

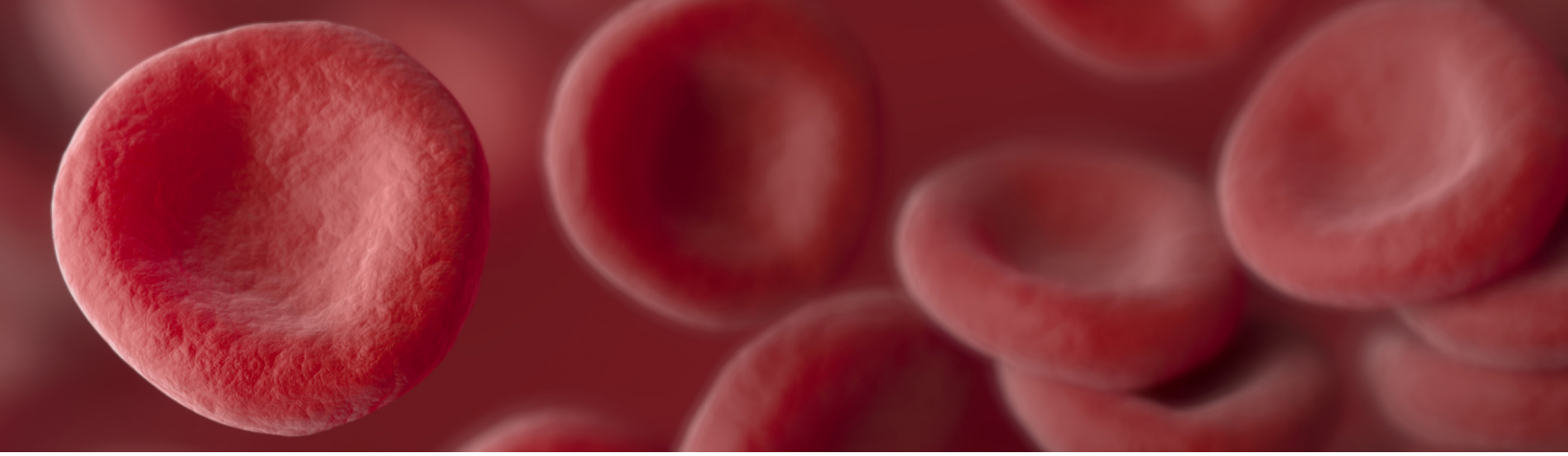
- Hip implants
- Disk repair
- Neural probes

**Drug Discovery and Testing Platforms** — using live cells in pharmaceutical research to study diseases and suboptimal cell function and to test potential treatment compounds in the laboratory for safety and efficacy

*Emerging products and applications:*

- Organ-on-a-chip models that simulate the activities of organs and organ systems

[1] Alliance for Regenerative Medicine, "Promise and Potential," http://alliancerm.org/page/promise-and-potential (accessed December 14, 2015).



120,000.[2] Cell-based technologies could also advance screening platforms for predictive and personalized medicine, allowing earlier treatment of some diseases such as cancer and diabetes, and could facilitate the discovery of safer and more efficient drugs.

Though cells are the building blocks of all of these products, most U.S. investment in this field to date has neglected the advancement of cell manufacturing. Federal agencies—including the National Institutes of Health, Department of Defense, Department of Veterans Affairs, National Science Foundation, Food and Drug Administration, National Nuclear Security Administration, and National Institute of Standards and Technology—invested nearly $3 billion in regenerative medicine from 2012–2014, most of which was focused on basic and clinical research of new therapies.[3] Bringing these new life-changing cell-based medical products to market critically depends on the large-scale, cost-effective, reproducible manufacturing of a variety of cell types.

Through a collaborative, strategic effort as called for in this roadmap and the support of public-private-philanthropic partnerships, the U.S. cell manufacturing industry can lead the advancement of cell manufacturing and enable the increased availability of innovative cell-based technologies. A dedicated translational effort and funding on the order of several hundred million dollars per year—or at least 10%–20% of investments in regenerative medicine—over the next 10 years would greatly accelerate this progress, maintaining the United States' foothold in the industry and its contributions to the entire global cell manufacturing and cell-based products community.

### Definitions: Types of Cells

Cell manufacturing involves the production of a variety of cell types and their derivatives. Though there are commonalities in the manufacturing of each of these cell types, manufacturing processes must be tailored to each specific cell type. This report divides cell types and the activities needed to advance their manufacturing into the following three areas:

**Autologous**—cells harvested, expanded, and later administered to the same patient as a point-of-care cell-based medical product

**Allogeneic**—cells from a donor that are expanded and banked for use in cell-based medical products

**Pluripotent**—unspecialized cells capable of differentiating into a variety of cell types with specialized functions, including muscle cells, red blood cells, or cells of a particular organ

[2] U.S. Department of Health and Human Services, organdonor.gov, "About Donation & Transplantation," http://www.organdonor.gov/about/data.html?gclid=CjwKEAjwjMauBRDH-bOCo56b13wSJABA2-Hv1s_NhRvhrtLt56x6ORHjPBzYJ2b1mlJ6SJu4pN7FYhoCkFnw_wcB (accessed December 14, 2015).

[3] U.S. Government Accountability Office, Regenerative Medicine: Federal Investment, Information Sharing, and Challenges in an Evolving Field, June 2015, http://www.gao.gov/assets/680/670930.pdf.

# Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells: A Strategy Through 2025

For the United States to maintain and secure its strong foothold in the dynamic cell-based technologies industry, multidisciplinary industry stakeholders—including researchers in the fields of biology, chemistry, and physics; equipment producers; cell and product manufacturers; and regulatory officials—must establish a collaborative U.S. cell manufacturing community. By capitalizing on existing expertise, technologies, and process knowledge, the community can streamline its efforts and accelerate progress toward large-scale, cost-effective, reproducible manufacturing of high-quality cells.

This roadmap offers a strategy to guide the cell manufacturing community's efforts over the next 10 years. It combines focused research and development activities with initiatives designed to support and sustain the cell manufacturing industry. In addition to developing and implementing advanced technologies and techniques, the cell manufacturing community must strengthen the industry foundation needed to facilitate the advancement and market penetration of cell-based medical treatments. This strategy to enable large-scale, cost-effective, reproducible manufacturing of high-quality cells is depicted in Figure 2.

The activities included in this roadmap are designated with the cell type—autologous, allogeneic, and pluripotent for the purposes of this report—to which they are targeted, with some activities crosscutting the manufacturing of all of these cell types. The high-priority activities included in this strategy—those with the greatest potential impact on cell manufacturing industry advancement in the next 10 years—are included in Figure 3.

## Develop and Implement Advanced Technologies and Techniques

Current cell manufacturing equipment and methods will not be able to meet the cell production scales needed to realize the potential of advanced medical treatments, devices, and diagnostics. To increase the scale and speed of cell production, the cell manufacturing community must collaborate on developing and maturing innovative technologies and techniques—including culture media and cell storage alternatives, sensors, process models, data analytics, and monitoring and tracking systems. Advancing technologies that can also improve quality assurance, reduce manufacturing and product costs, enhance manufacturing reproducibility and consistency, strengthen information technology security, and increase treatment efficacy will support long-term growth of the industry.

To accelerate technology development and implementation, manufacturers and researchers must work together to identify industry needs and optimize the cell manufacturing technologies and techniques with the greatest potential impact on industry operations. This close collaboration will also facilitate the implementation of these technologies across cell manufacturing facilities, accelerating the time it takes for technologies to move from the laboratory to commercial scale.

## Strengthen the Industry Foundation

Beyond managing the technical aspects of cell processing, storage, and quality control, the cell manufacturing community must also

build a workforce and establish standards and regulations that can sustain long-term industry growth. An effective workforce needs to be capable of not only operating, but continuously improving next-generation cell manufacturing technologies and their associated techniques. At the same time, cell manufacturing standards and regulations must be put into place that encourage innovation and improve manufacturing quality across the value chain. These advances to cell manufacturing are a foundational component of enabling a more robust regenerative medicine supply chain.

Figure 2. Roadmap Strategy

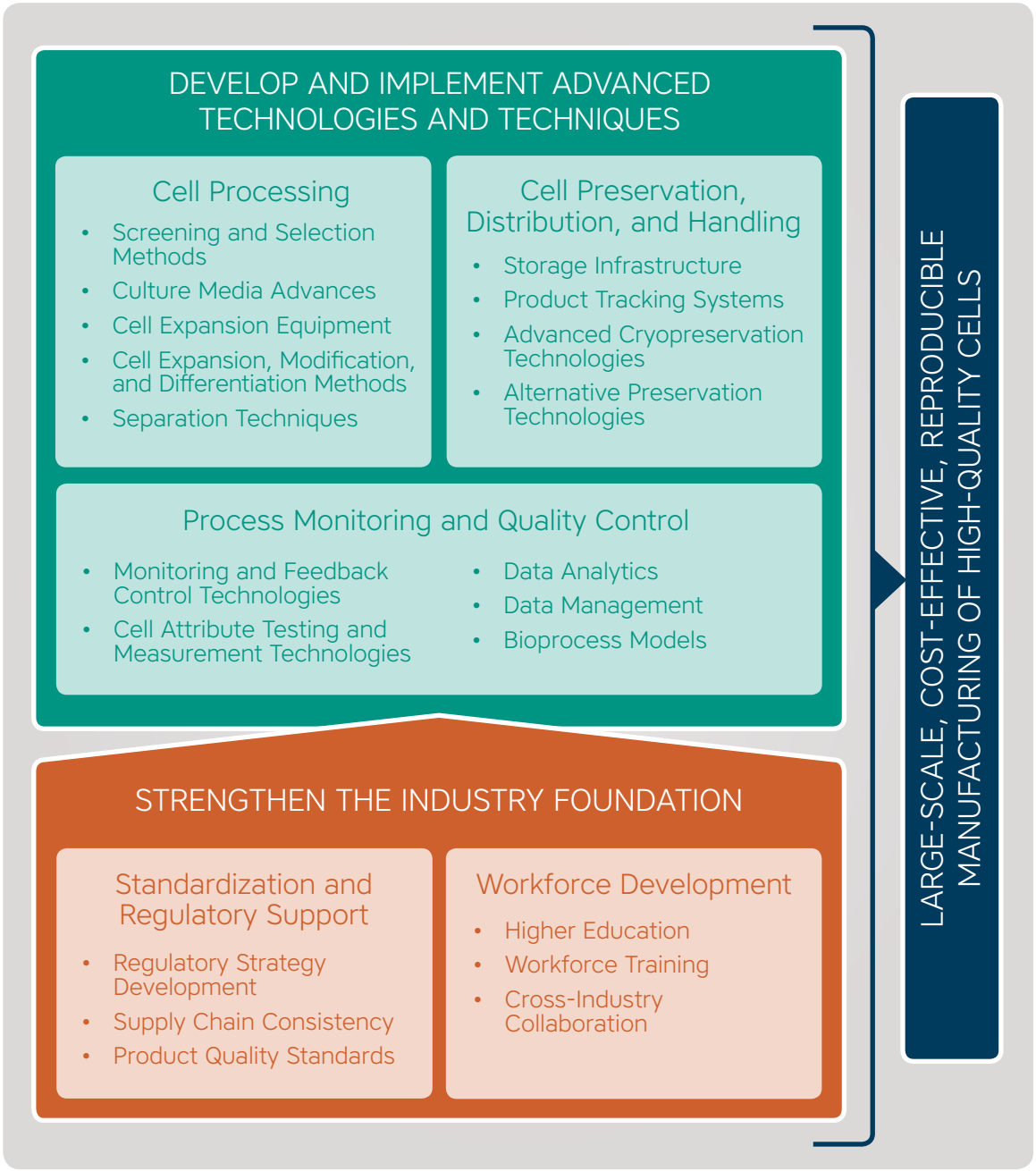


Figure 3. Priority Roadmap Activities

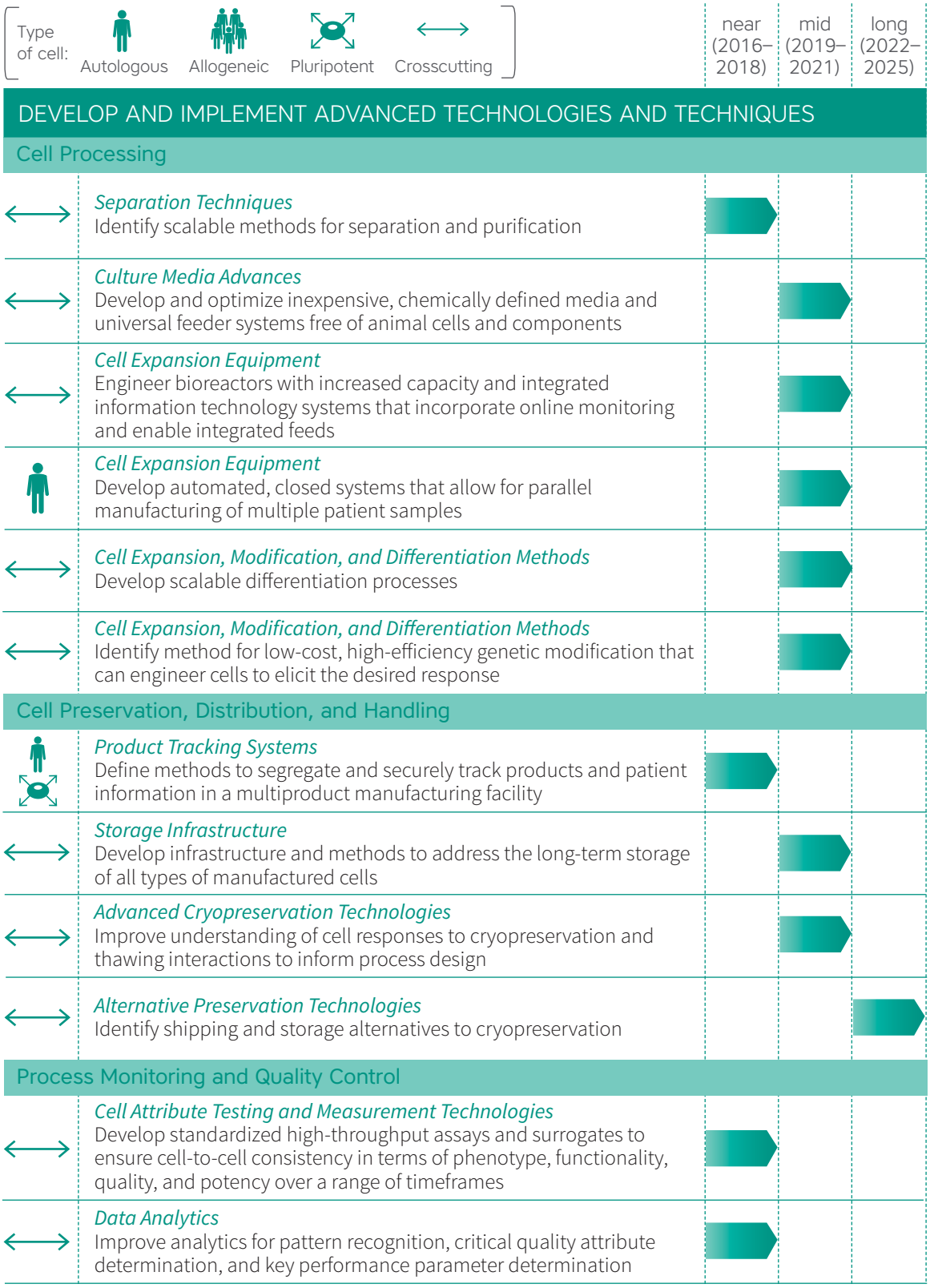
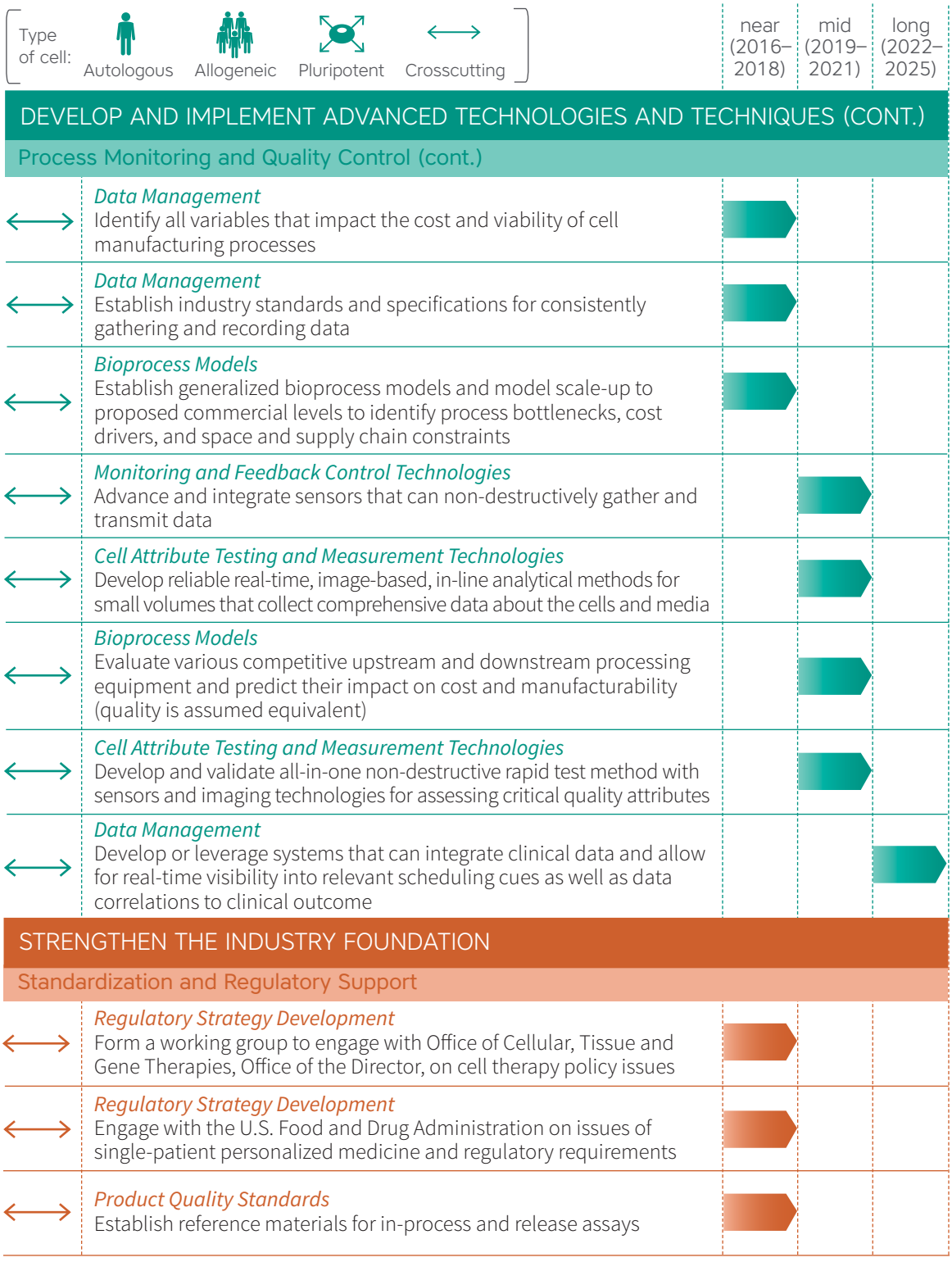


Figure 3. Priority Roadmap Activities (cont.)



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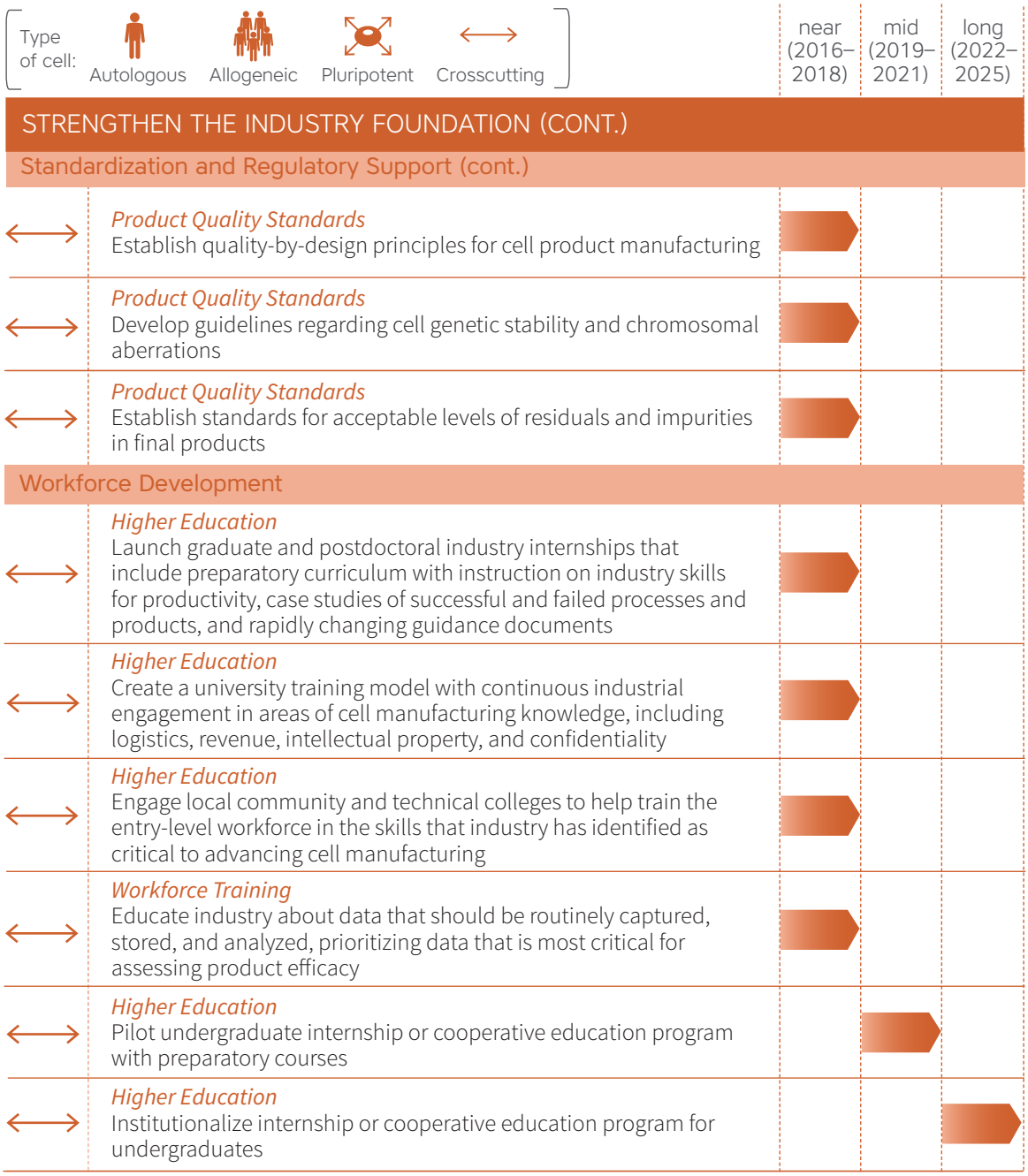

## The Need for U.S. Investment in Cell Manufacturing

Investments in research and development of cell manufacturing technologies and processes, coupled with supporting initiatives to build a skilled workforce and develop industry standards and regulations, could enable the biomanufacturing community to meet intensifying market demands for new cell-based medical treatments. Ultimately, these initiatives will help secure the United States' position as a global leader of state-of-the-art, life-changing therapies.

Large-scale cell manufacturing and the resulting increased commercialization of cell-based products will also accelerate the widespread achievement of several important national goals (outlined on page 9).

## Securing U.S. Competitiveness in an Increasingly Global Market

The United States is currently at the forefront of biomedical research and technology development. International investments in this field, however, are quickly growing, and many countries throughout the world have established national centers to better compete in the growing global industry. Without comparable or greater U.S. investment in cell manufacturing, the United States will no longer be able to secure its lead in this potentially disruptive industry. An overview of some of the key centers currently in operation—including Cell Therapy Catapult (United Kingdom), the Cell Therapy Manufacturing Cooperative Research Centre (Australia), the Center for Commercialisation of Regenerative Medicine (Canada), and the Center for Regenerative Therapies Dresden (Germany)—is provided in the text box on page 10.

Recognizing the need for a focused cell manufacturing effort in the United States, more than 60 organizations—including from industry (e.g., Big Pharma, biotech, startups in stem cell and T-cell therapies, supply chain, and supporting automation technology companies), clinical GMP centers, academic research, government agencies, and private foundations—came together to develop this roadmap. Although U.S. progress can and will be made to address the activities outlined in this roadmap through individual research efforts, a more extensive and coordinated cell manufacturing community, supported by public-private-philanthropic partnerships, will be critical for maximizing U.S. cell manufacturing industry progress.

## Improved health and reduced disease burden

Large-scale cell manufacturing can help bring more effective treatments to market that address the underlying causes of many diseases and conditions rather than only managing their symptoms. These emerging and next-generation cell-based medical products could cure or significantly change the course of diseases, reducing the need for life-long treatments and ultimately improving the quality of life of millions of people.

## Increased competitiveness of U.S. manufacturing

Currently, there are more than 700 companies, ranging from small and medium businesses to multinational corporations, focused on the research and development of cell-based medical products.[4] Increased U.S. investment in cell manufacturing could grow the number of U.S. companies and jobs in this field, building a skilled workforce that can secure the United States' lead in the emerging field of cell-based medical treatments.

## Economic growth

Biotherapeutic companies currently generate nearly $1 billion in revenue from cell-based medical treatments.[5] Large-scale cell manufacturing will enable the scaling up of existing and emerging cell-based products and allow new products to come to market, accelerating the path to growing the industry to a multi-billion-dollar global market in the next decade.[6] The economic growth of the industry will benefit local economies as well, particularly as cell manufacturing expands throughout the United States.

## More affordable healthcare

The United States spends nearly $3 trillion each year on healthcare.[7] Many diseases currently require life-long care and management, creating a significant financial strain to consumers and the government over the course of patients' lives. This economic burden could be reduced by the advancement of large-scale cell manufacturing and the resulting increased availability of cell-based medical treatments that can minimize the need for long-term management of diseases impacting the U.S. population.

## Enhanced national security

The increased availability of novel cell-based medical treatments could enable faster and more effective treatment of military personnel and first responders. Large-scale U.S. cell manufacturing could also help to better accommodate surge demands for cell-based medical treatments in response to emergency incidents—including natural disasters, transportation accidents, exposure to hazardous materials, and terrorist attacks—while reducing the risk of supply disruptions from dependencies on overseas resources.

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[4]Alliance for Regenerative Medicine, "Industry Snapshot: An Expansive and Growing Industry," http://alliancerm.org/page/industry-snapshot (accessed December 14, 2015).
[5]Alliance for Regenerative Medicine, "Promise and Potential," http://alliancerm.org/page/promise-and-potential (accessed December 14, 2015).
[6]C. Mason, D.A. Brindley, E.J. Culme-Seymour, and N.L. Davie, "Cell Therapy Industry: Billion Dollar Global Business with Unlimited Potential," Regen. Med. 6:265-272, May 2011.
[7]Centers for Disease Control and Prevention, "Health Expenditures," http://www.cdc.gov/nchs/fastats/health-expenditures.htm (accessed December 14, 2015).

## International Investments in Cell Manufacturing*

The following international centers are focused on growing each individual nation's contributions to the global cell manufacturing market. The United States must invest comparable or greater resources to establish and maintain its global prowess as the leading developer of cell manufacturing technologies and manufacturer of cells.

**Cell Therapy Catapult – United Kingdom (UK)**

The vision of Cell Therapy Catapult (CTC) is for "the UK to be a global leader in the development, delivery and commercialization of cell therapies, and a place where businesses can start, and confidently grow." The CTC comprises industry, research, and regulatory institutions, who jointly move products into clinical trial; provide technical expertise and infrastructure to manufacture products and deliver them cost effectively; facilitate global and national opportunities for collaboration; and provide business grants and investment financing to advance new products and generate new business propositions. CTC operates on $15 million per year from the UK Technology Strategy Board and $31 million per year from industry and other partner funding.

**Cell Therapy Manufacturing Cooperative Research Centre – Australia**

The Cell Therapy Manufacturing Cooperative Research Centre (CRC) has a mission "to facilitate the cost-effective manufacture and rapid translation of cell therapies into clinical practice." To this end, the CRC develops new treatments and new materials-based manufacturing technologies to treat conditions such as diabetes, chronic wounds, cardiovascular disease, and immune-mediated diseases. CRC comprises industry, research, and government institutions, and operates on a total budget of $43 million in cash and in-kind resources, including $15 million from the Australian Government.

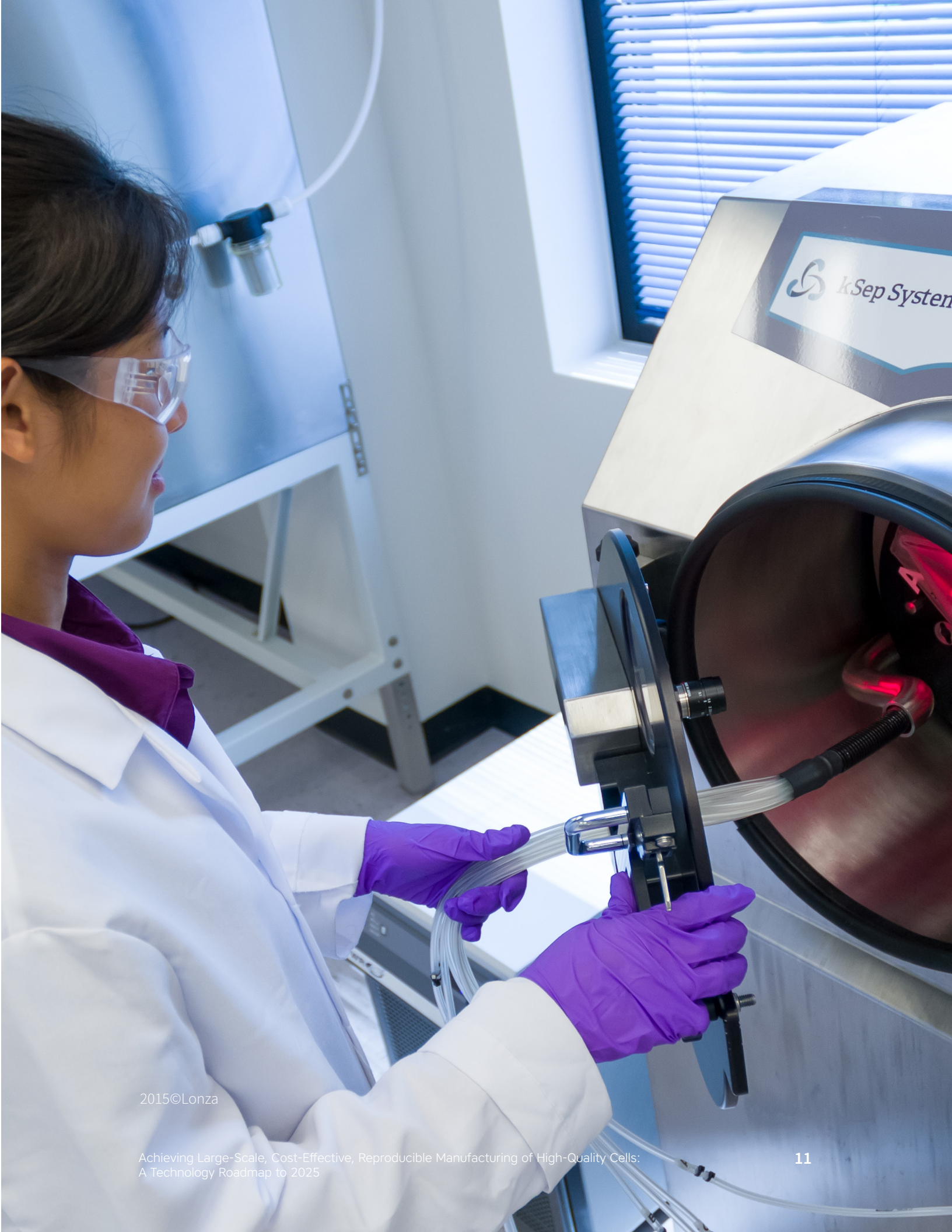
**Center for Commercialisation of Regenerative Medicine – Canada**

The Center for Commercialisation of Regenerative Medicine (CCRM) is a consortium of industry members and research organizations that "supports the development of foundational technologies that accelerate the commercialization of stem cell- and biomaterials-based products and therapies." CCRM conducts work in cell reprogramming and engineering, cell manufacturing, and biomaterials and devices, operating on a 2011–2016 budget of $12 million from the Networks of Centers of Excellence of Canada and $4.8 million from industry and academic partners.

**Center for Regenerative Therapies Dresden – Germany**

The Center for Regenerative Therapies Dresden (CRTD) aims to develop new regenerative therapies. CRTD comprises international and interdisciplinary research groups, who conduct basic and clinical research within four key research areas: hematology/immunology, diabetes, neurodegenerative diseases, and bone regeneration. The CRTD is funded by the German Research Foundation (DFG) as a DFG research center and as a Cluster of Excellence. As a Cluster of Excellence, CRTD receives $6.9 million in funding per year. CRTD scientists also raise third-party funds for their research. Additional funding details are not available.

*Center funding amounts have been converted to U.S. dollars based on October 14, 2015 exchange rates.

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# Cell Processing

Cell processing—the growth of cells in an artificial environment outside of the human body—is a defining part of the cell manufacturing process. Each parameter of cell culturing, including the vessel, media, nutrients, and physicochemical environment, influences the properties that cells require to be effective therapeutically.

The development of new cell-based medical products will demand cell processing technologies and techniques capable of manufacturing cells in greater quantities at greater speeds. However, the materials, space, labor, and time requirements of current methods will prevent existing processes from meeting this growing demand.

To enable large-scale manufacturing of high-quality cells in the next 10 years, the cell manufacturing community must work together to develop, optimize, and implement more cost-effective and efficient cell processing technologies and techniques. Approaches that can also increase the consistency and reliability of cell processing could enhance the quality and efficacy of cell-based products.

# Current Challenges

To realize large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must work to overcome the cell processing challenges that follow.

## Linear nature of existing culture platforms

Most current culture platforms (e.g., planar culture systems or feeder cells) are linear and require additional surface area to manufacture cells in greater quantities. The resulting space constraints, coupled with the substantial culture media and labor requirements of current systems, render existing culturing approaches economically impractical for commercial-scale manufacturing. Additionally, it is difficult to control nutrient gradients across these linear systems to achieve consistent cell characteristics and quality.

## Increased potential for contamination in open-culture settings

In conventional research settings, the current process of dividing cell cultures to enable further proliferation is carried out in open systems where vessels are exposed to the surrounding environment. Every opening of a culture vessel poses the potential for contamination from molds, yeasts, viruses, mycoplasma, and other cell lines. The care taken to maintain sterile environments to reduce this risk is time- and labor-intensive, necessitating the need for innovative closed-system technologies that are sealed from the external environment.

## Difficulty understanding cell complexity

The cell manufacturing community lacks sufficient understanding of the biology and emergent properties of human cells, particularly stem cells and immune cells. Understanding of human cells is further complicated by the fact that cells produced through cell manufacturing differ from those in the body. Because of the inherent complexity of cells, it is difficult to define the needed properties—or the mode of action—for cells to be useful therapeutically or the culture environments and differentiation processes necessary to manufacture cells with these properties.

## High cost, limited supply, and inconsistency of raw materials

Culture media—including growth factors, nutrients, and reagents—are often the most expensive part of the cell manufacturing process. The high cost, as well as the limited supply and shelf life of some raw materials, will prevent existing culture platforms from meeting increased cell production demand. An additional complication is that some media components, particularly animal serums, have batch-to-batch variability, which can reduce cell property consistency and even contaminate cell products.

### Inefficiency of cell separation methods

In many current cell processing systems, cells must be removed from the surface of culturing vessels and separated into new vessels with fresh growth medium for further propagation. When preparing cells for distribution, cells must also be separated from culture media, undifferentiated cells, and other particulates to achieve the cell purity needed for the end product. Current separation processes are inefficient and challenging, particularly because desired cells are often the same size as unwanted particles. Desired cells are also fragile and subject to shear, further adding to the complexity of cell separation.

## Key Initiatives

Addressing these challenges will require coordinated efforts across the cell manufacturing community to develop, optimize, and implement advanced cell processing technologies and techniques. To realize the potential of large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must collaborate on the following key cell processing initiatives: Screening and Selection Methods; Culture Media Advances; Cell Expansion Equipment; Cell Expansion, Modification, and Differentiation Methods; and Separation Techniques. Activities for each of these initiatives are provided in Figure 4, divided into near-term (2016–2018), mid-term (2019–2021), and long-term (2022–2025) time frames.

### Screening and Selection Methods

The therapeutic effectiveness of cell-based treatments, devices, or diagnostic technologies demands the selection of cells with the desired properties for that specific medical product. Current processes for selecting viable, suitable cells can involve extensive trial and error, necessitating the development and optimization of highly automated cell screening and selection methods. Advanced approaches to donor and cell screening, including the use of more sophisticated assays and imaging technologies, could enable cell manufacturers to more quickly, efficiently, and accurately assess and select cells.

### Culture Media Advances

To manufacture lot sizes with trillions of cells, the cell manufacturing community must advance non-linear culture formats, such as suspension cultures, that optimize cellular productivity. Without the need for substrates, microcarriers, or feeder cells, such culture systems could better utilize space, reduce labor requirements, and eliminate what is currently one of the primary cost drivers of cell manufacturing. The cell manufacturing community has the opportunity to develop more chemically defined media alternatives to reduce the risk of contamination from animal materials and overcome the limited availability of clinical-grade sera. Advanced cell culturing formats, lower-cost and more reliable media, and more precise cell passaging could reduce cell processing costs while also maximizing cell yield and quality.

### Cell Expansion Equipment

To support the manufacturing of a variety of new cell-based technologies, next-generation cell expansion equipment must be able to accommodate varying lot sizes and parallel processing of different cell types. Seed trains and bioreactors with parallel processing capabilities could increase manufacturing throughput and shorten processing time, while distributing cost over multiple batches. Advanced cell expansion must also be highly automated and conducted in closed systems that can be monitored and maintained at defined physiochemical levels, resulting in cultures with comparable characteristics

from batch to batch. Closed-system, parallel processing with increased automation is also critical to minimize error and contamination from human interaction with cell products.

## Cell Expansion, Modification, and Differentiation Methods

To more accurately and efficiently differentiate cells with the desired characteristics for a cell-based medical product, the cell manufacturing community must increase its understanding of cell biology. Increased understanding of why cells do what they do—including how they respond to media and environmental conditions, the speed at which they double, and the optimum time to culture them—will enable increased control of cell properties. The industry could also reduce processing times and increase capacity by accelerating the biological speed of cell differentiation (e.g., with the use of complex cell cultures and epigenetics) or reducing cell doubling times. Increasing the speed of expansion and differentiation is particularly important for pluripotent stem cells, which can currently take several months to expand and differentiate, slowing the speed and quantity at which cell-based products are available.

## Separation Techniques

The removal of viable cells from culture media, inactive products, undifferentiated cells, and other particulates is critical to the purity, quality, and safety of cell products. Development of advanced cell separation techniques, particularly for next-generation multi-parameter closed systems, is needed to reduce the labor requirements of both cell reseeding and cell expansion (e.g., detachment from microcarriers and substrates). More efficient separation technologies can also reduce the amount of media and space needed for cell processing.

Figure 4. Cell Processing Priority Activities

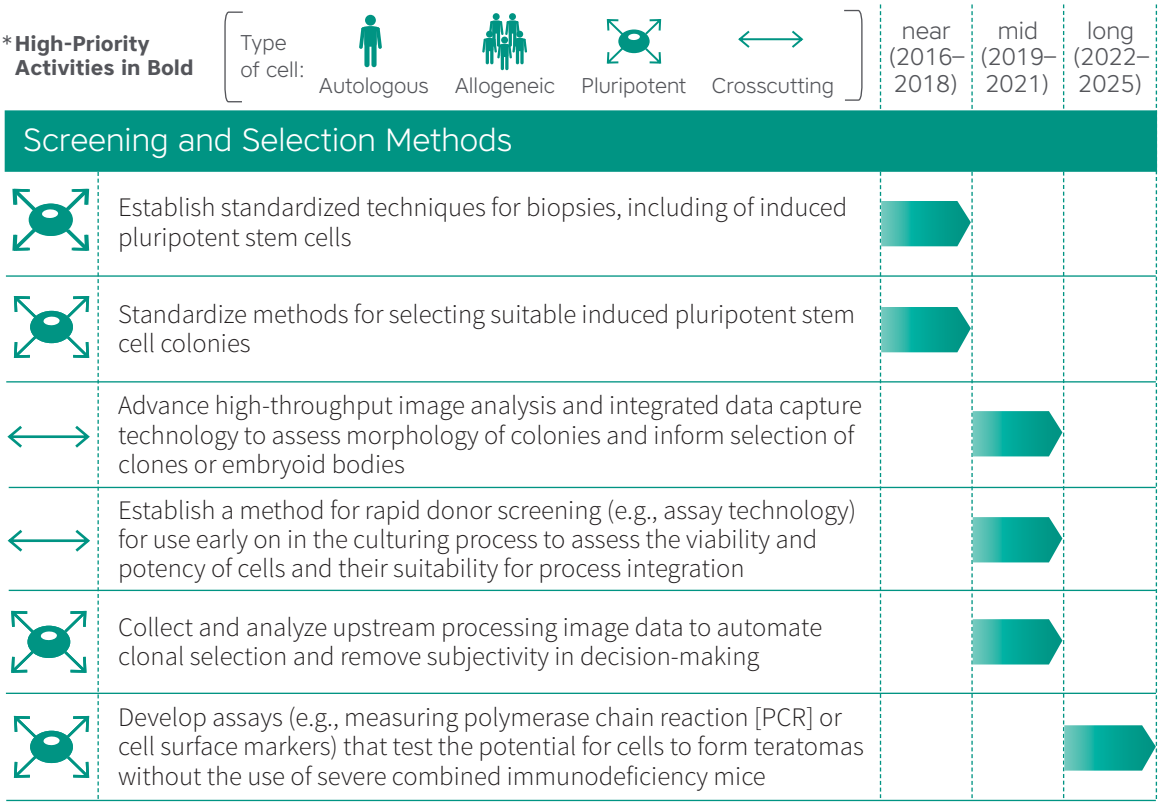
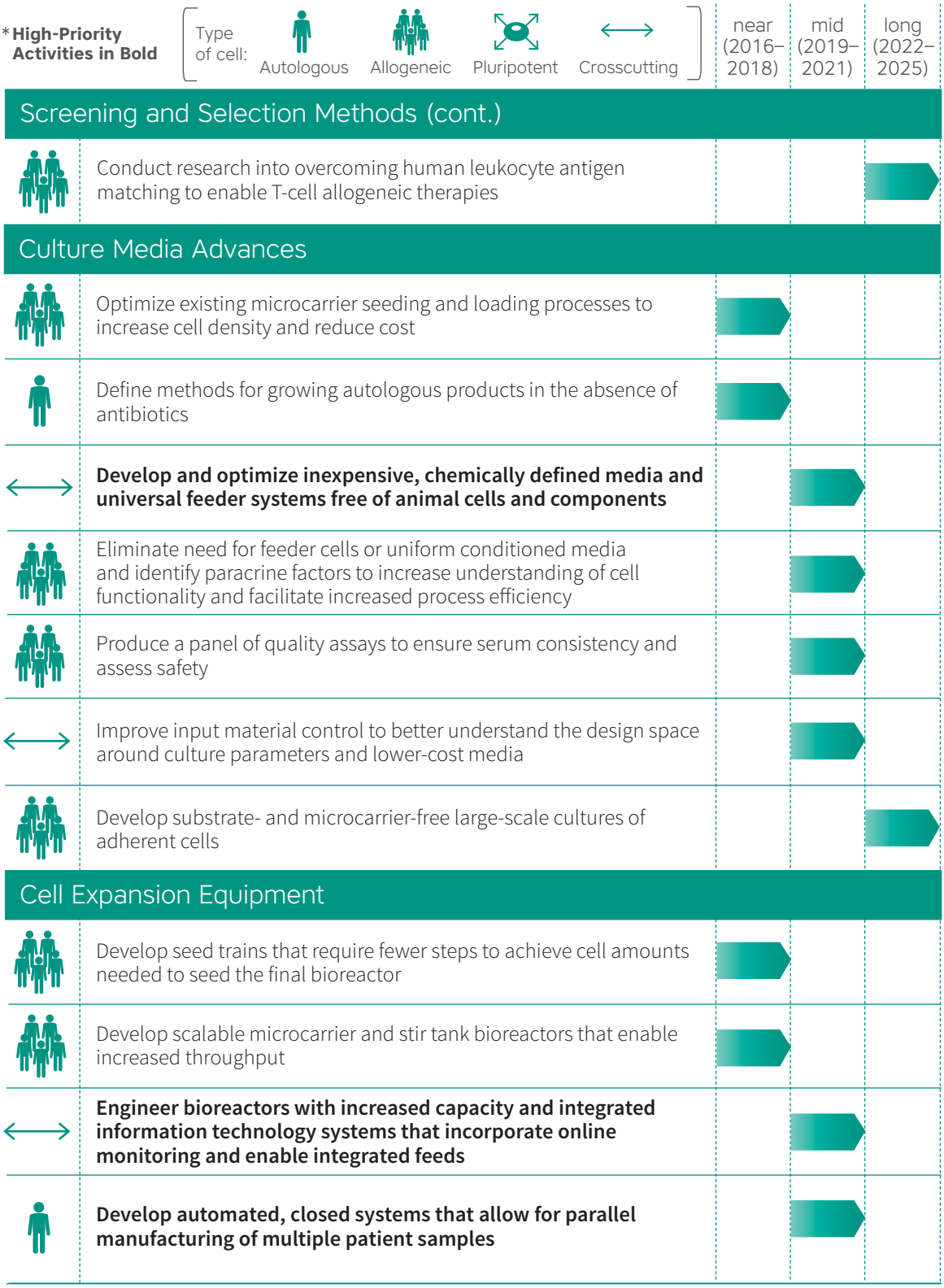


Figure 4. Cell Processing Priority Activities (cont.)



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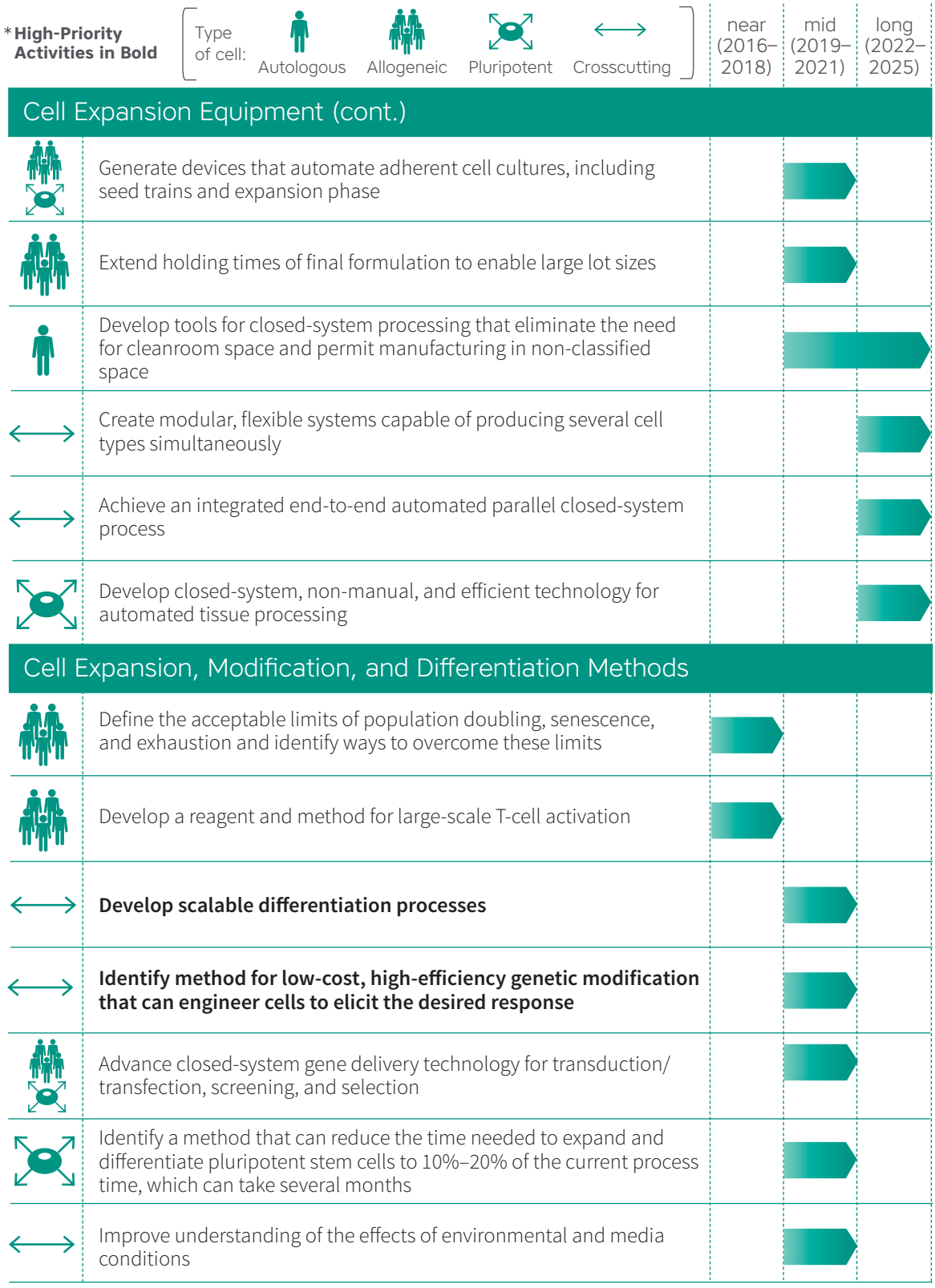

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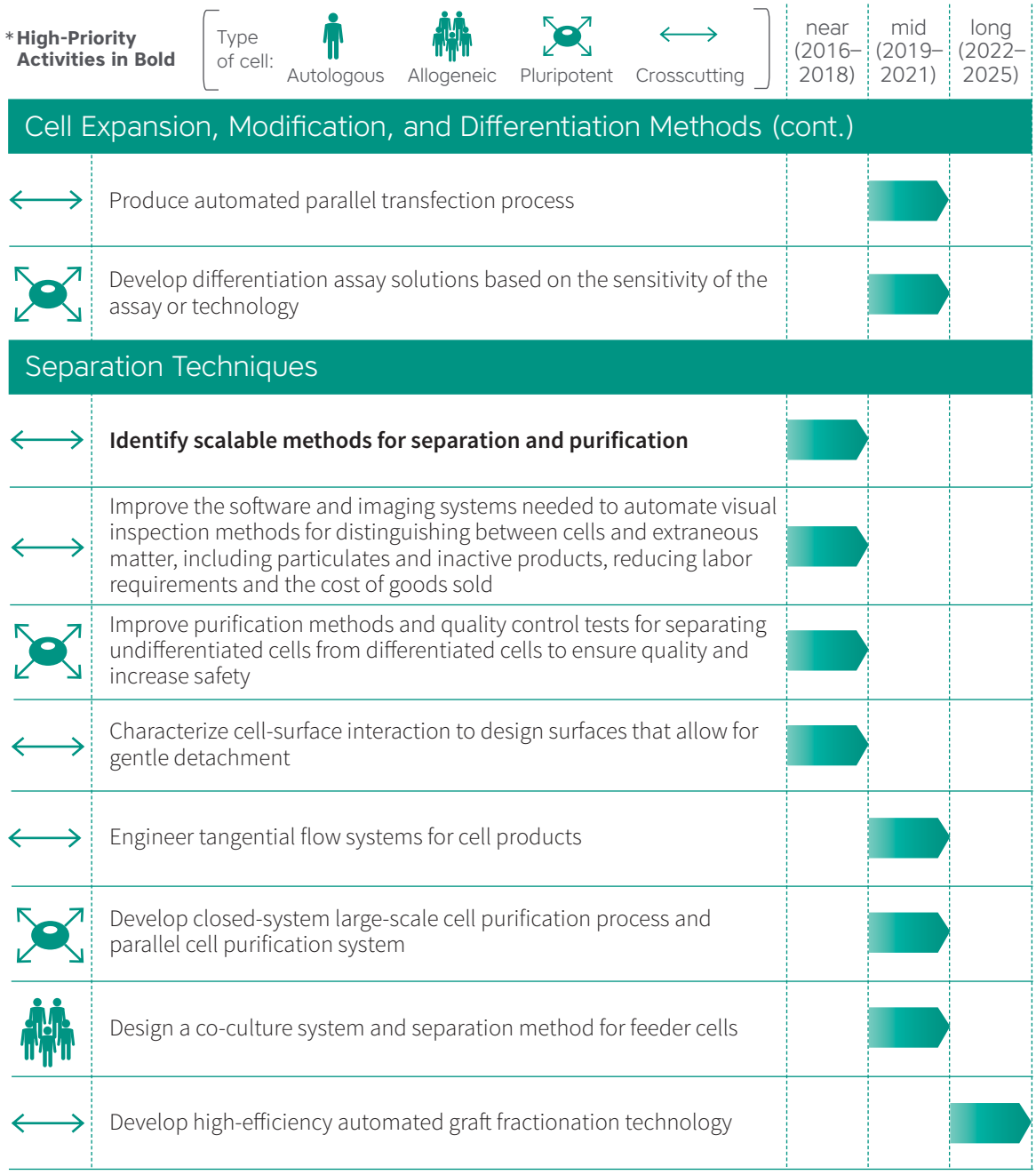



# Cell Preservation, Distribution, and Handling

The care taken to preserve, distribute, and handle cells is critical to cell quality. Current preservation methods, however, are unable to cost effectively ensure the stability of cells at large scales or for long periods of time.

As demand for cell-based medical products grows, reliable storage will be needed to preserve finite cell lines as well as cells that are manufactured in excess of immediate demand. Additionally, to expand the current cell distribution network, the cell manufacturing community must build capabilities to efficiently and cost effectively transport multiple cell types while tracking the workflow of each cell product.

To enable large-scale manufacturing of high-quality cells in the next 10 years, the cell manufacturing community must work together to develop, optimize, and implement more reliable and cost-effective cell preservation, distribution, and handling technologies and techniques. Lower-cost and more reliable approaches that better maintain cell viability and functionality and extend the shelf life of manufactured cells could facilitate the increased availability of high-quality cell-based medical products.

# Current Challenges

To realize large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing industry must work to overcome the cell preservation, distribution, and handling challenges that follow.

## High cost and complex logistics of distribution

The distribution logistics and shipping schedules of cells, both fresh and frozen, are difficult to manage due to the short shelf lives of cells and requirements for carefully controlled environments. As a result, the current cost of cell product distribution is higher than that of the cost of cell manufacturing, particularly for autologous cells that require careful tracking. Shipping a single bag of bone marrow cells at the proper vapor phase, for example, can currently cost thousands of dollars.

## Difficulty scaling storage processes

Current cell storage processes rely on cryopreservation and cold-chain-management equipment. Scaling up these processes is likely to increase incidents of transient warming that can be detrimental to cell quality and viability. Without process advances, the labor, materials, and facility requirements of these processes will also prove cost-prohibitive at larger scales.

## Difficulty maintaining cell characteristics during freezing and thawing

During biopreservation, cell metabolic activity decreases and extracellular ice forms to protect cells. During this process, initiation of molecular stress responses and intracellular ice formation can also cause mechanical breakdown, membrane rupture, or other stresses that interfere with cell survival and recovery. The cell manufacturing industry, however, has limited understanding of cell viability and the functionality of various cell types following preservation and subsequent thawing, making it difficult to preserve cells effectively and consistently.

# Key Initiatives

Addressing these challenges will require coordinated efforts across the cell manufacturing community to develop, optimize, and implement advanced cell preservation, distribution, and handling technologies and techniques. To realize the potential of large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must collaborate on the following key cell preservation, distribution, and handling initiatives: Storage Infrastructure, Product Tracking Systems, Advanced Cryopreservation Technologies, and Alternative Preservation

Technologies. Activities for each of these initiatives are provided in Figure 5, divided into near-term (2016–2018), mid-term (2019–2021), and long-term (2022–2025) time frames.

## Storage Infrastructure

Cell banks, which typically store cells using cryopreservation, maintain valuable backup supplies of cells. Such cell storage helps to mitigate losses of cell integrity from genetic drift, contamination, and processing equipment failures, ensuring the long-term stability of cell lines with the desired critical quality attributes. To establish cell supplies that can meet growing demand for cell-based medical products, the cell manufacturing community must build a more robust and reliable storage infrastructure that accommodates larger quantities of a greater number of cell types.

## Product Tracking Systems

The cell manufacturing industry needs to implement a robust, efficient, automated, real-time bioinformatics-based tracking procedure that records each processing step, tool, and raw material (e.g., nutrient, biologic) used in the manufacturing of a cell product. Tracking the chain of custody could inform process adjustments that can optimize manufacturing processes to facilitate the increased safety, quality, and efficacy of cell-based products. Additionally, a Health Insurance Portability and Accountability Act (HIPAA)-compliant process in which every bag or vial of cells contains a chip with the associated product information will ensure that the correct cells are administered to the correct patient while also keeping patient information secure.

## Advanced Cryopreservation Technologies

To enable large-scale cell manufacturing, the industry needs advanced cryopreservation processes that can cost effectively preserve a greater variety of cells in larger volumes. The cell manufacturing community must work to develop highly automated cryopreservation technologies that facilitate more precise control of freezing and thawing. Increased understanding of the impact of this process on cells could also reduce cell stress and maximize recovery, improve homogeneity of frozen batches, and extend product shelf life to reduce manufacturing cost and waste.

## Alternative Preservation Technologies

Some cell types (e.g., skin cells) do not maintain potency after being frozen, necessitating cell preservation and storage alternatives to cryopreservation. The cell manufacturing community must collaborate on advancing alternative storage methods (e.g., room-storage, hypothermic, and freeze-drying methods) for various batch sizes and cell types that can better maintain cell quality and functionality. Identifying and advancing such alternatives to cryopreservation could increase the flexibility, reliability, and cost effectiveness of cell storage.

Figure 5. Cell Preservation, Distribution, and Handling Priority Activities

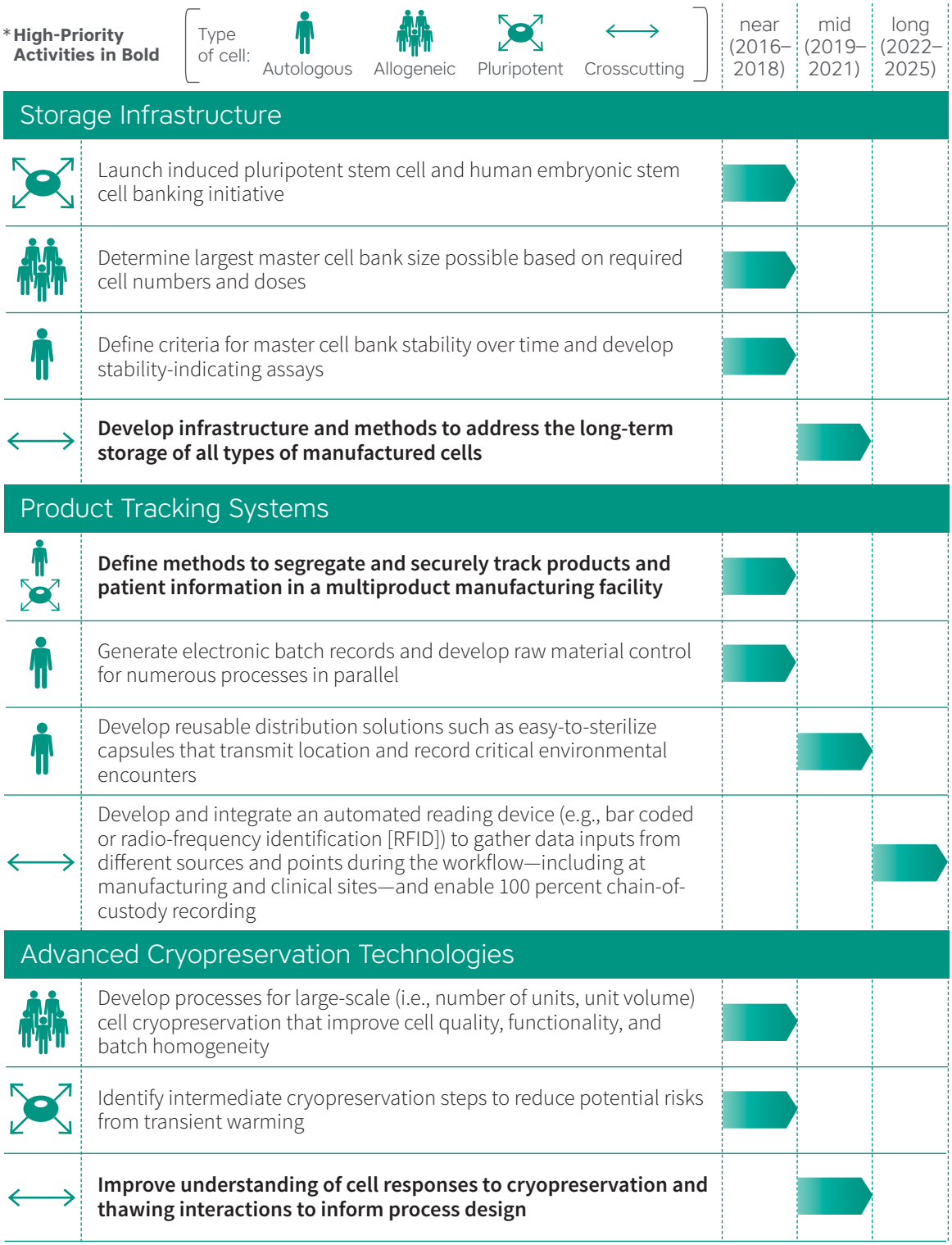
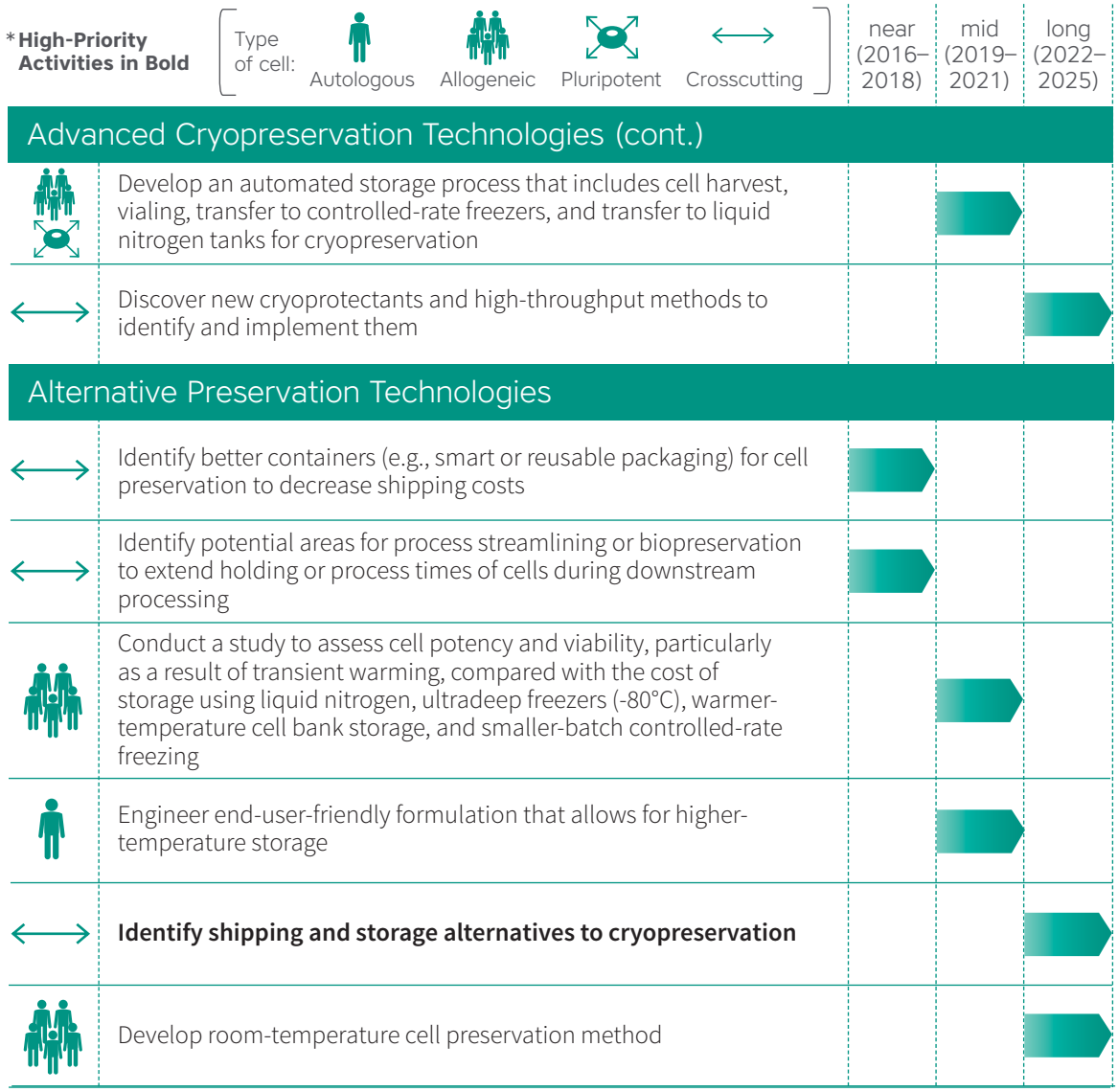
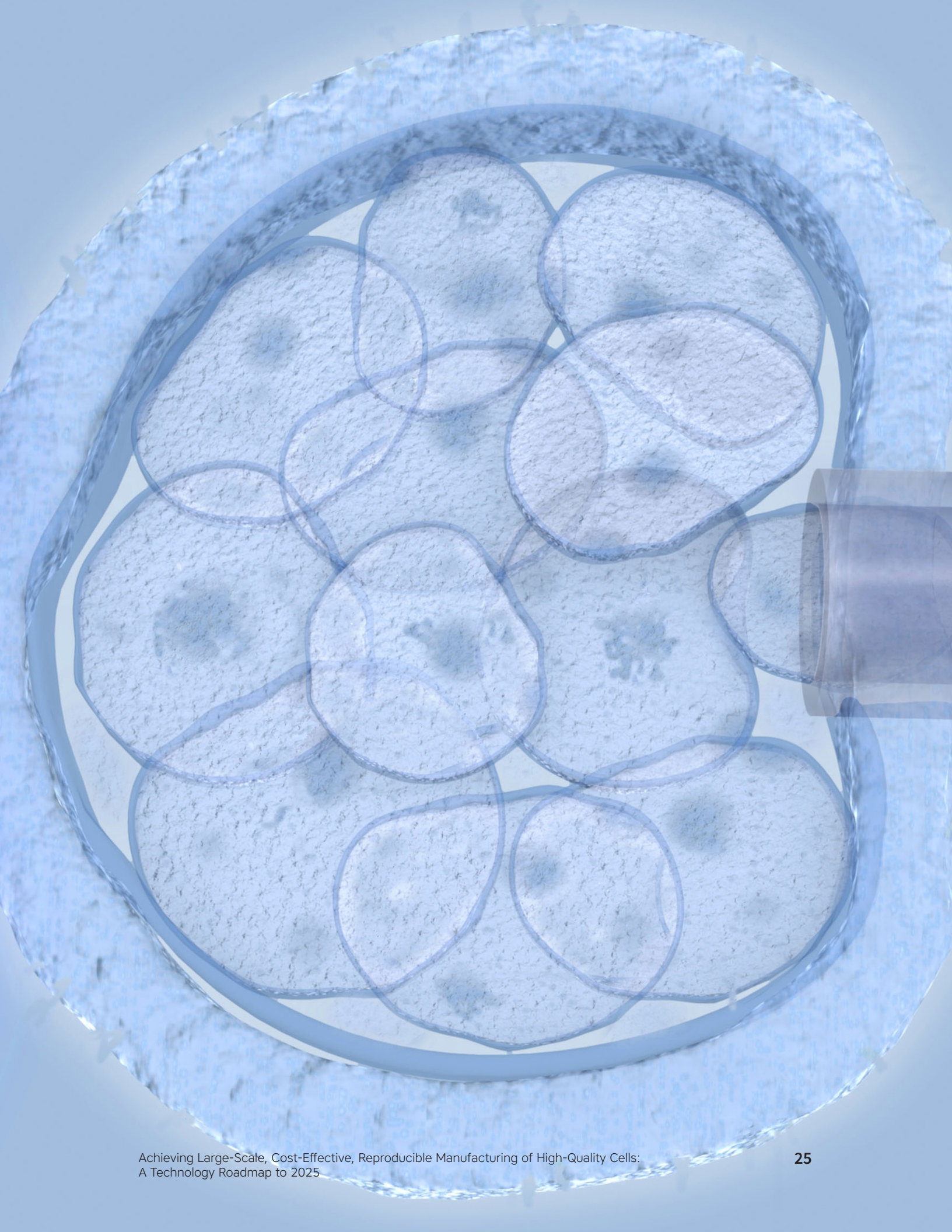


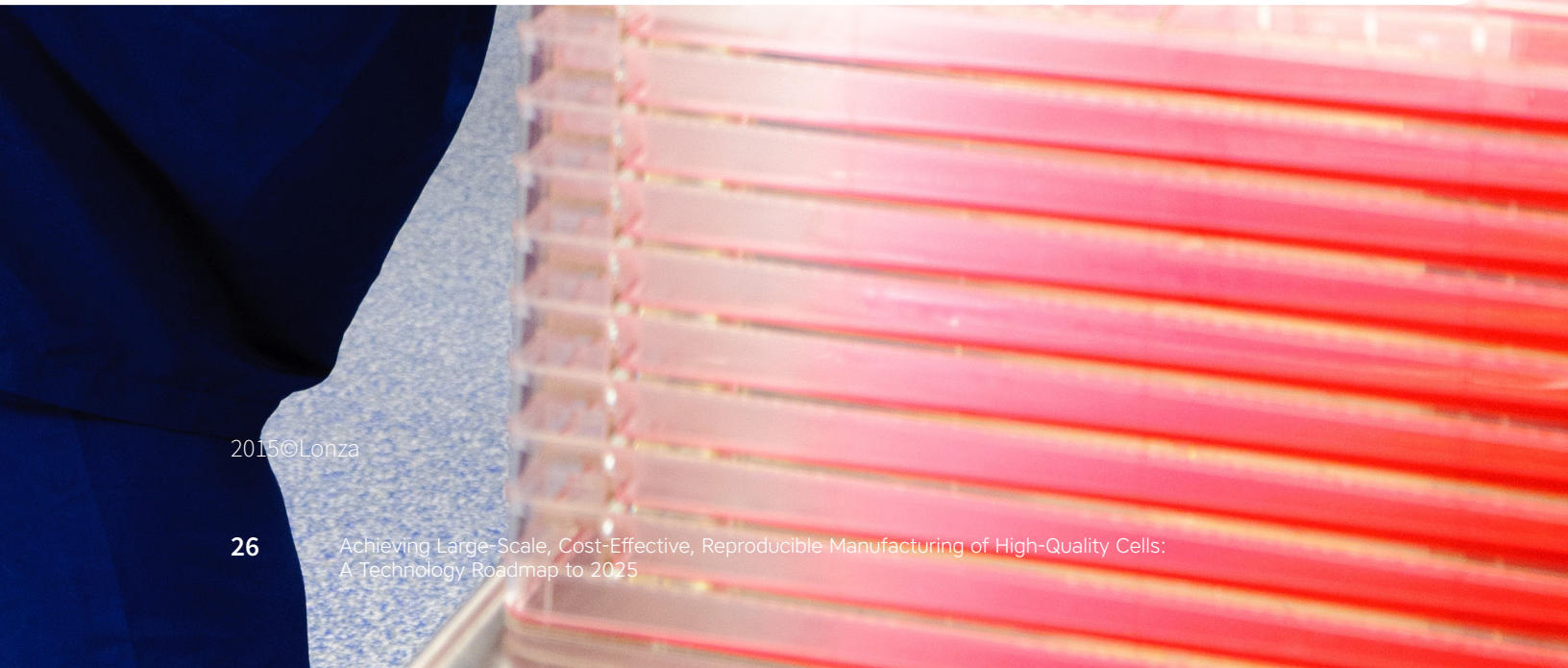
Figure 5. Cell Preservation, Distribution, and Handling Priority Activities





# Process Monitoring and Quality Control

A single process alteration during cell manufacturing could yield cells with properties that deviate from those required for a specific cell-based medical product. More consistent and reliable cell manufacturing processes will be critical to ensure the quality of manufactured cells, particularly as demand for these cells grows.



Sophisticated process simulation, monitoring, and feedback control technologies—such as models, assays, and sensors—could improve the ability to control cell manufacturing processes and increase understanding of the impact of process variations. These advances could also facilitate real-time decision-making and potentially even automated process corrections that would significantly improve process robustness and efficiency.

To enable large-scale manufacturing of high-quality cells in the next 10 years, the cell manufacturing community must work together to develop, optimize, and implement more cost-effective and accurate real-time process monitoring and quality control technologies and techniques. Process monitoring and quality control approaches that can more quickly characterize cells and optimize process parameters could improve the affordability and reliability of cell-based products.

# Current Challenges

To realize large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must work to overcome the process monitoring and quality control challenges that follow.

## Lack of readily available, robust data

Many individual cell manufacturing companies are reluctant to share data due to the competitive nature of the industry. As a result, the cell manufacturing community currently lacks readily available, robust data about cell manufacturing processes and cell products. Without accessible, accurate data, it will be challenging to accelerate process understanding and precisely tailor processes to cost effectively manufacture large quantities of high-quality cells.

## Inability to assess cell viability and characteristics in real time

Alterations to any critical cell characteristics—those that make cells therapeutically active—will render cells useless for their intended application. Yet, the cell manufacturing industry currently lacks sufficient tools to measure cell biomarkers, characterize cells, determine potency, and assess purity in real time to prevent the production of unusable cell products. Cost-effective, large-scale manufacturing will not be possible without the ability to detect and consequently mitigate inconsistencies or issues in cell processing.

## Difficulty identifying and containing the spread of contaminants

One of the primary ways to detect contaminants in cell cultures is through visually inspecting cultures for cloudiness, thin films, or other signs that a culture has been compromised. Using this approach, however, it may take several days after cultures are infected to identify an issue. Other contaminants, including viruses and mycoplasmas, are even more difficult to detect until they achieve much higher densities. By the time contamination is identified, it may have spread more widely throughout the facility, altering cell behavior and function and ruining entire cell lots.

## Insufficient models for bioprocessing

While some manufacturing parameters can be measured and controlled, it is difficult to predict the impact of manufacturing conditions on cell behavior given the variability in both cells and patients. Current models are, therefore, inherently incapable of simulating all relevant bioprocess parameters. The cell manufacturing

community will need sophisticated models and established testing procedures to conduct accelerated stability testing and accurately predict the impact of process variations, including scale-up to larger bioreactors, on cell performance and product cost.

# Key Initiatives

Addressing these challenges will require coordinated efforts across the cell manufacturing community to develop, optimize, and implement advanced process monitoring and quality control technologies and techniques. To realize the potential of large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must collaborate on the following key process monitoring and control initiatives: Monitoring and Feedback Control Technologies, Cell Attribute Testing and Measurement Technologies, Data Analytics, Data Management, and Bioprocess Models. Activities for each of these initiatives are provided in Figure 6, divided into near-term (2016–2018), mid-term (2019–2021), and long-term (2022–2025) time frames.

## Monitoring and Feedback Control Technologies

Monitoring and feedback control technologies could help cell manufacturers more quickly identify and correct processing issues that impact cell quality, potency, purity, or safety. To improve process controls, the cell manufacturing community must collaborate on technologies such as sensors, assays, and imaging systems that can more accurately measure processing conditions like pH, dissolved oxygen, and metabolite accumulation. These technologies can also be leveraged to detect contaminants earlier than current methods, enabling cell manufacturers to contain contamination more quickly to reduce its costly repercussions. In addition to developing better ways to capture process data, the cell manufacturing community must build capabilities for transmitting this data. Developing a centralized, easy-to-operate communications network could facilitate real-time, and even automatic, process adjustments and enable parallel processing of multiple cell types with varying process requirements.

## Cell Attribute Testing and Measurement Technologies

To release cells for distribution, cell manufacturers must define cell critical quality attributes (CQAs)—including cell identity, purity, potency, and safety—that can affect the primary mode of action. The ability to quickly and accurately assess CQAs will require advanced technologies such as assays, sensors, and imaging technologies that can rapidly characterize cells in real time without damaging the cells and reducing the manufacturing yield. The resulting comprehensive in-process cell data would provide the cell manufacturing community with insight into process deficiencies and help predict cell function and efficacy. Ultimately, this ability to ensure cell-to-cell consistency could enable large-scale manufacturing and increase the affordability of end products.

## Data Analytics

To maximize the value of technologies that capture cell manufacturing data, the cell manufacturing industry needs robust systems that can quickly synthesize and interpret this data. Advanced in-line data analytics software and statistical algorithms could correlate data from different sources throughout the manufacturing process and draw meaningful conclusions in real time. This in-process data analysis could facilitate improved decision-making or even self-correcting systems that can increase the cost effectiveness, throughput, and efficiency of cell manufacturing processes

and ultimately drive the manufacturing of higher-quality cells.

## Data Management

Accessibility of robust data, from raw material sourcing to clinical implementation, is critical to better predict and optimize cell manufacturing processes. To maximize the value of existing data, the cell manufacturing community must integrate disparate data from across different companies and databases into more centralized data management systems. Increasing the comprehensiveness of industry data will also require the systematic generation and standardized recording of data for other variables that impact manufacturing costs and cell viability. Systems that can capture multiple data streams from across the manufacturing process and extract data from different sources throughout the cell manufacturing industry will be pivotal in increasing the robustness of data available for modeling and process controls as well as enhancing chain of custody.

## Bioprocess Models

Advanced bioprocess models—including supply chain and cost models—could help the cell manufacturing community more efficiently improve processes and optimize properties of manufactured cells. These models must account for all the factors that could impact the properties and performance of cells and cell products, including the stochastic variability of cells and the inherent variability of cell functionality and cell therapy patients. Models could also more accurately predict manufacturing conditions (e.g., gas exchange, reagent buildups, shear forces, and temperature variations) in larger-scale reactors to reduce the cost and time associated with trial-and-error approaches to scale-up. As models improve, the cell manufacturing community could use them to evaluate the impact of new and emerging technologies and fine-tune manufacturing and supply chain efficiency of more complex cell manufacturing processes.

Figure 6. Process Monitoring and Quality Control Priority Activities

| *High-Priority Activities in Bold | Type of cell: Autologous | Allogeneic | Pluripotent | Crosscutting | near (2016–2018) | mid (2019–2021) | long (2022–2025) |
|---|---|---|---|---|---|---|---|
| **Monitoring and Feedback Control Technologies** | | | | | | | |
| Establish a working group to identify critical manufacturing steps that impact safety, purity, and potency and define acceptable ranges of process variability | | | | ⟷ | ➡ | | |
| Apply smart manufacturing sensors and controls to monitor process conditions (e.g., exposure to high temperatures and humidity) that could impact cell quality | | | | | ➡ | | |
| **Advance and integrate sensors that can non-destructively gather and transmit data** | | | | ⟷ | | ➡ | |
| Produce a single-use sensor for critical process parameters and control points | | | | | | ➡ | |
| Build an easy-to-operate, automated central controller that can accommodate multiple units for parallel processing | | | | | | ➡ | |
| Develop sensor that triggers the biomaterial to change color to demonstrate progress of cultures | | | | ⟷ | | ➡ | |

Figure 6. Process Monitoring and Quality Control Priority Activities (cont.)

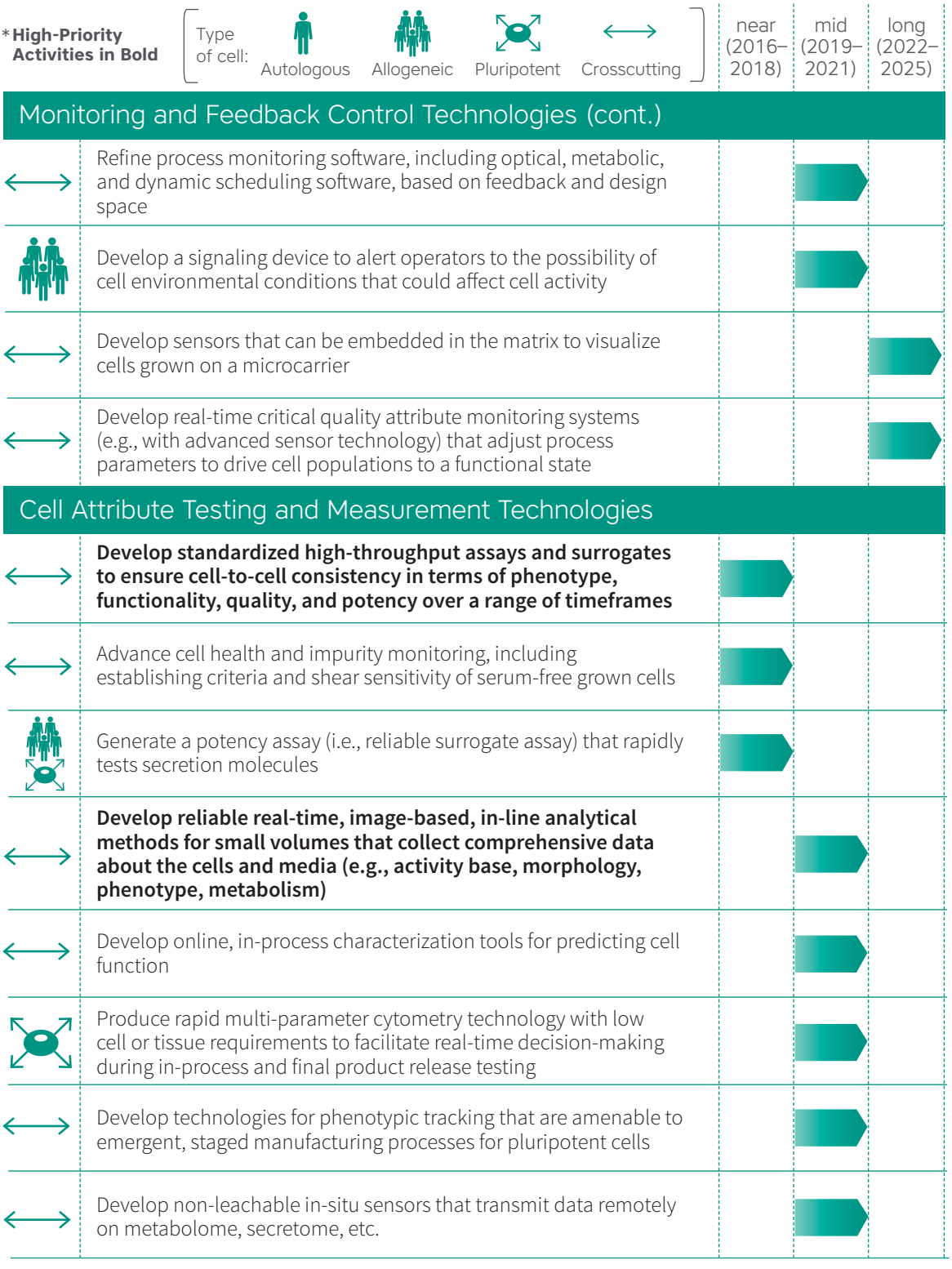


Figure 6. Process Monitoring and Quality Control Priority Activities (cont.)

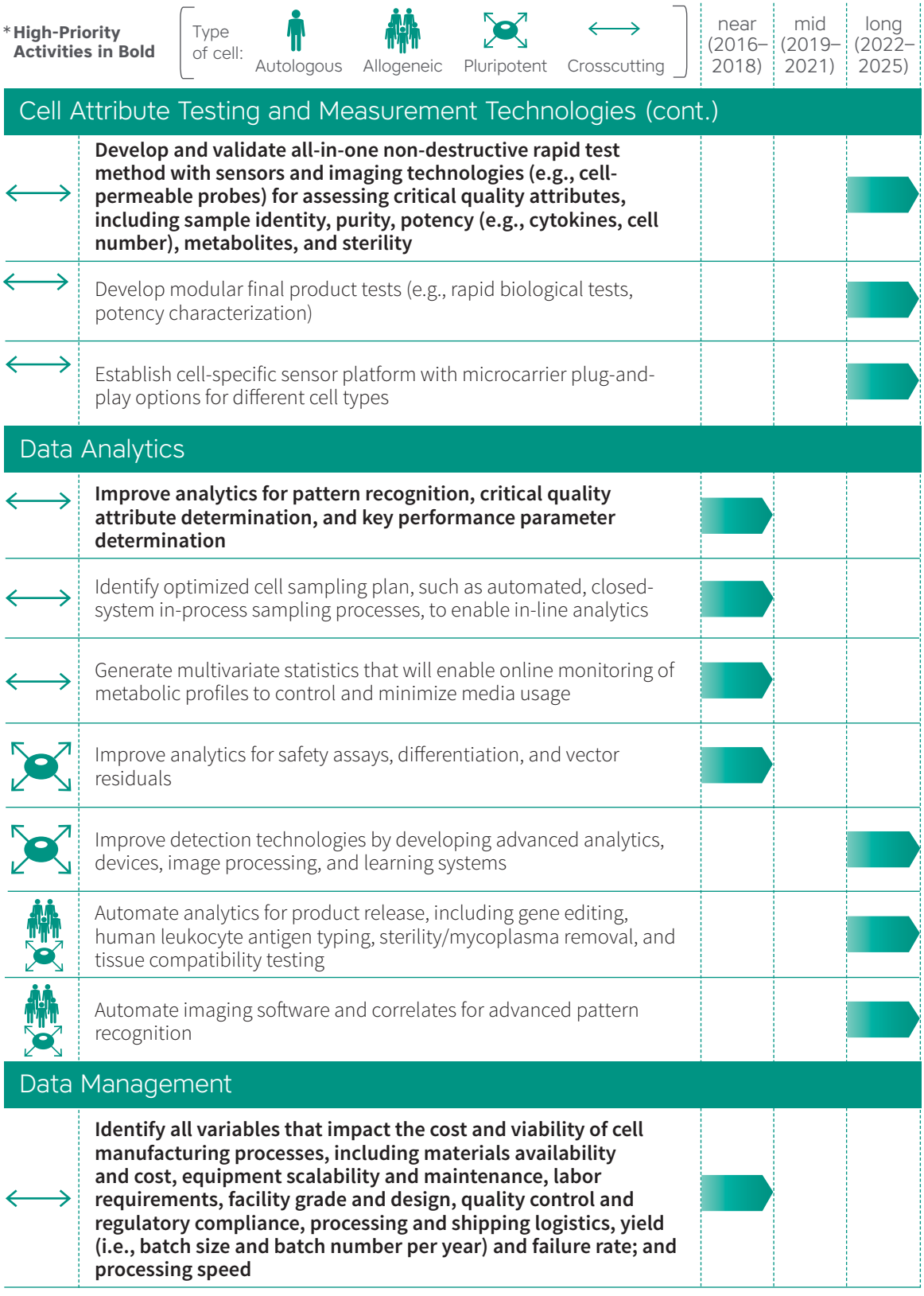


Figure 6. Process Monitoring and Quality Control Priority Activities (cont.)

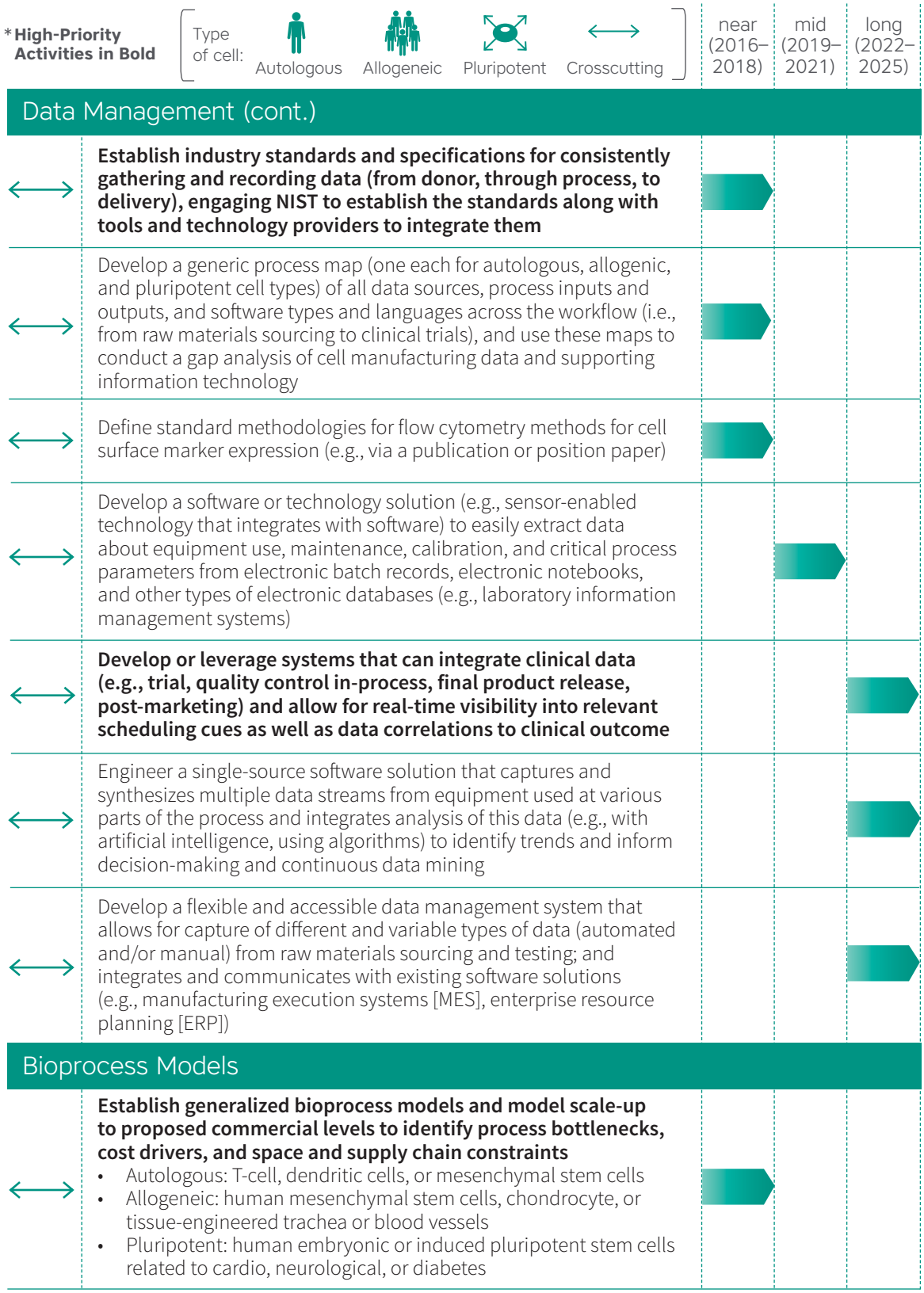
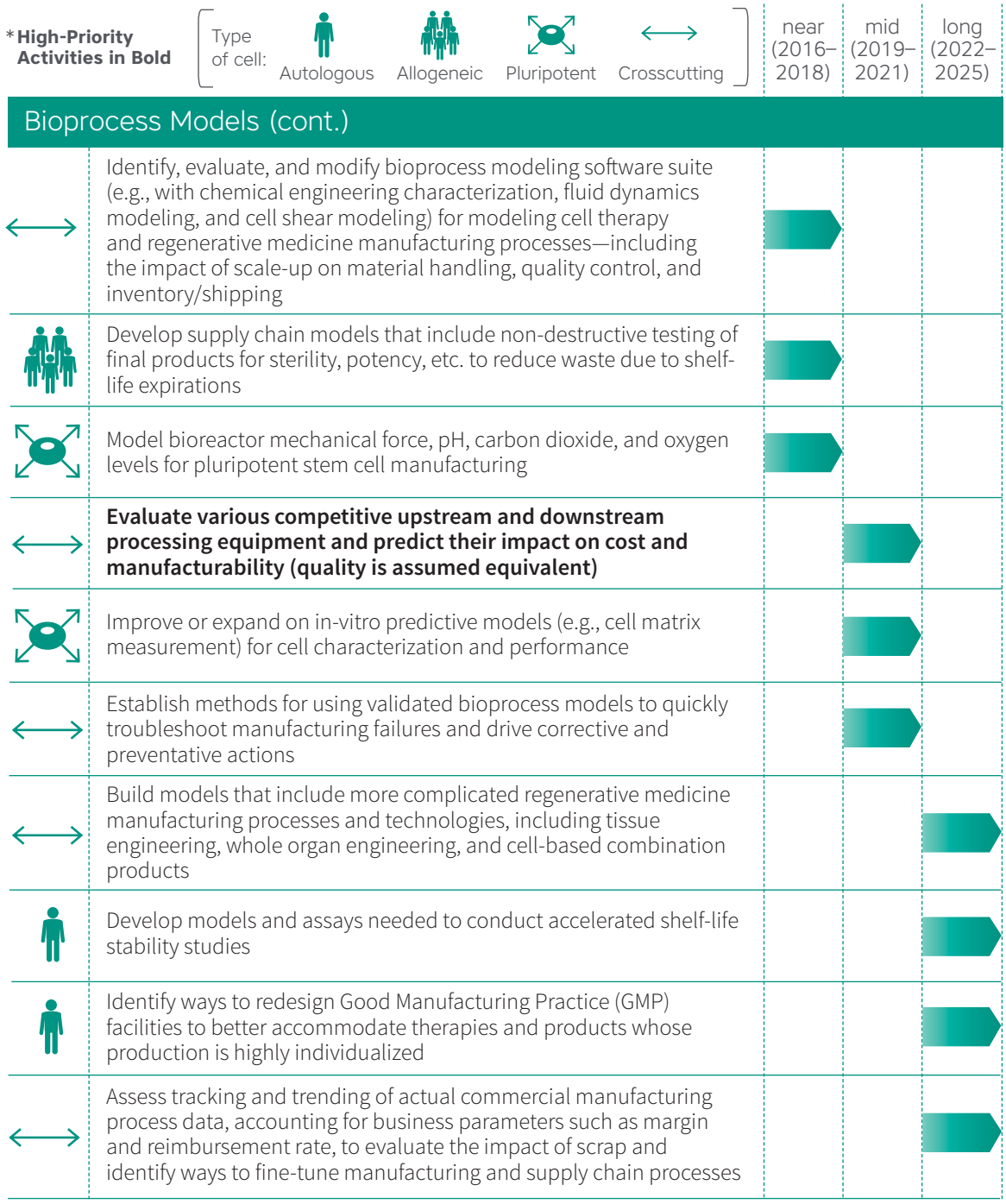


Figure 6. Process Monitoring and Quality Control Priority Activities (cont.)



# Standardization and Regulatory Support

Due to the complexity and constantly evolving nature of the cell manufacturing industry, there is currently a lack of consensus on industry standards. As a result, seemingly similar populations of cells manufactured at different locations could have significantly different properties and modes of action, limiting the industry's ability to predict cell behavior and treatment efficacy.

To improve the consistency and quality of manufactured cells and cell-based products, the cell manufacturing industry must work with regulatory agencies, including the U.S. Food and Drug Administration and other regulators across the global cell manufacturing industry, to define standards and regulations for cell manufacturing processes and cell products. Establishing standards and regulations—including for raw materials, testing procedures, manufacturing processes, and cell product handling—is critical to drive the development of innovative cell products and efficiently move them to commercialization and clinical use.

# Current Challenges

To realize large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must work to overcome the standardization and regulatory challenges that follow.

## Difficulty defining the products of biological processes

In many cases, the cell itself is the product, but cells can also be vehicles to the synthesis of other products, including exosomes, antibodies, vaccines, and cytokines. Regulatory issues are further complicated in the case of combination therapies and other modalities with products that include both regular cells and genetically modified cells or other sophisticated systems. Because of this complexity, it is challenging to develop useful standards and regulations with specific parameters for a given cell type or product while still allowing further innovation.

## Limited support for innovation built into industry standards

To accelerate the growth of cell manufacturing, the regulatory framework must evolve with major industry advances to support long-term technology innovation. Current U.S. cell manufacturing regulations differ from those in other countries, and some industry companies find that U.S. regulations put a greater burden on process and technology innovation. These regulatory differences make it difficult to efficiently move products from early development to commercialization and clinical use, which could impact the United States' ability to maintain its lead in the global cell manufacturing industry.

## Lack of product consistency across the supply chain

Due to concerns about product consistency across the supply chain, many of today's cell manufacturers acquire critical raw materials and equipment from sole source vendors. This dependency increases the risk of supply interruptions and could limit manufacturing throughput and scale, possibly preventing patients from receiving effective and reliable treatments in a timely manner.

# Key Initiatives

To address these challenges and realize the potential of large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must collaborate on the following standardization and regulatory support initiatives: Regulatory Strategy Development, Supply Chain Consistency, and Product Quality Standards. Activities for each of these initiatives are provided in Figure 7, divided into near-term (2016–2018), mid-term (2019–2021), and long-term (2022–2025) time frames.

## Regulatory Strategy Development

Regulations that account for the unique characteristics of cell manufacturing are critical to accelerate innovation of next-generation cell therapies, engineered tissues, medical devices, and drug discovery and testing

platforms. The cell manufacturing industry must coordinate with regulatory agencies—including with the Office of Cellular, Tissue and Gene Therapies (OCTGT); U.S. Food and Drug Administration; Centers for Medicare and Medicaid Services (CMS); and the International Conference on Harmonisation—to formulate a strategy for developing and harmonizing cell manufacturing regulations. Keeping these agencies informed about emerging technologies and techniques will help the cell manufacturing community advocate for regulations that can continuously drive industry advances.

## Supply Chain Consistency

Developing supply chain standards and metrics would help the cell manufacturing industry increase the consistency of materials and process conditions that can impact cell critical quality attributes. To ensure the reliability and quality of raw materials from different suppliers, the industry should establish reference or calibration materials, particularly as the supplier base expands to meet the raw material and supply requirements of the growing cell manufacturing industry. Because manufacturing processes define cell properties, the cell manufacturing industry must also mitigate variations in environmental conditions by developing standards for manufacturing procedures that could impact the quality of manufactured cells, including facility clean room requirements and aseptic techniques to prevent contamination.

## Product Quality Standards

Improved product consistency could allow the cell manufacturing community to more accurately predict patient responses to cell-based products. Increasing standardization of assays and inspection methods for product release and developing reference standards for various cell types could help improve consistency of manufactured cells across companies and facilities. Additionally, purity standards could reduce the amount of inactive product and residuals in final products, increasing the quality and safety of cell-based products.

Figure 7. Standardization and Regulatory Support

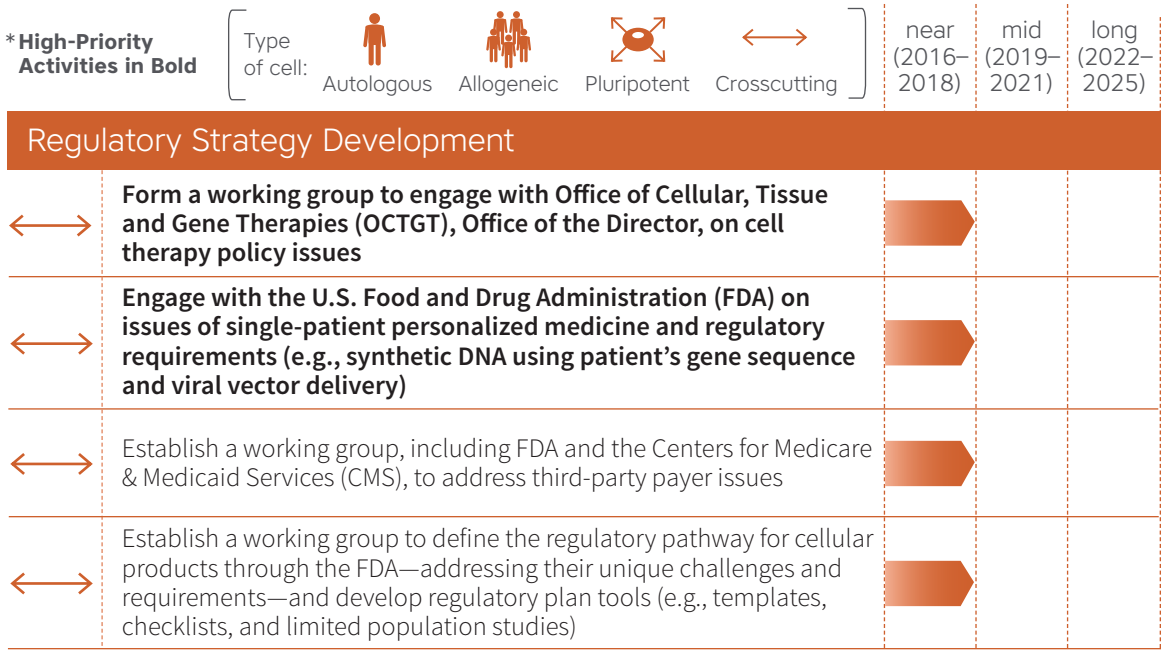


Figure 7. Standardization and Regulatory Support (cont.)

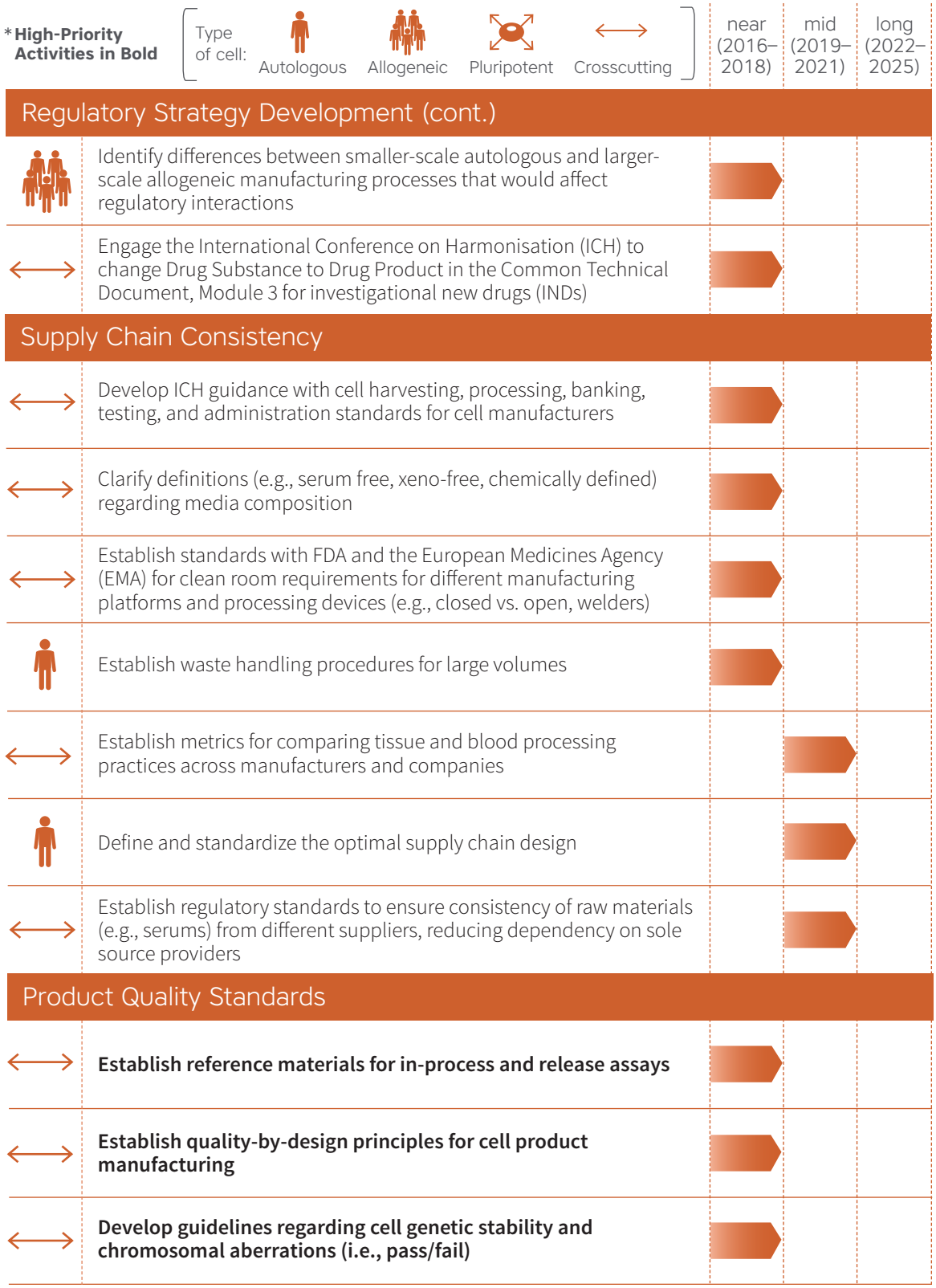
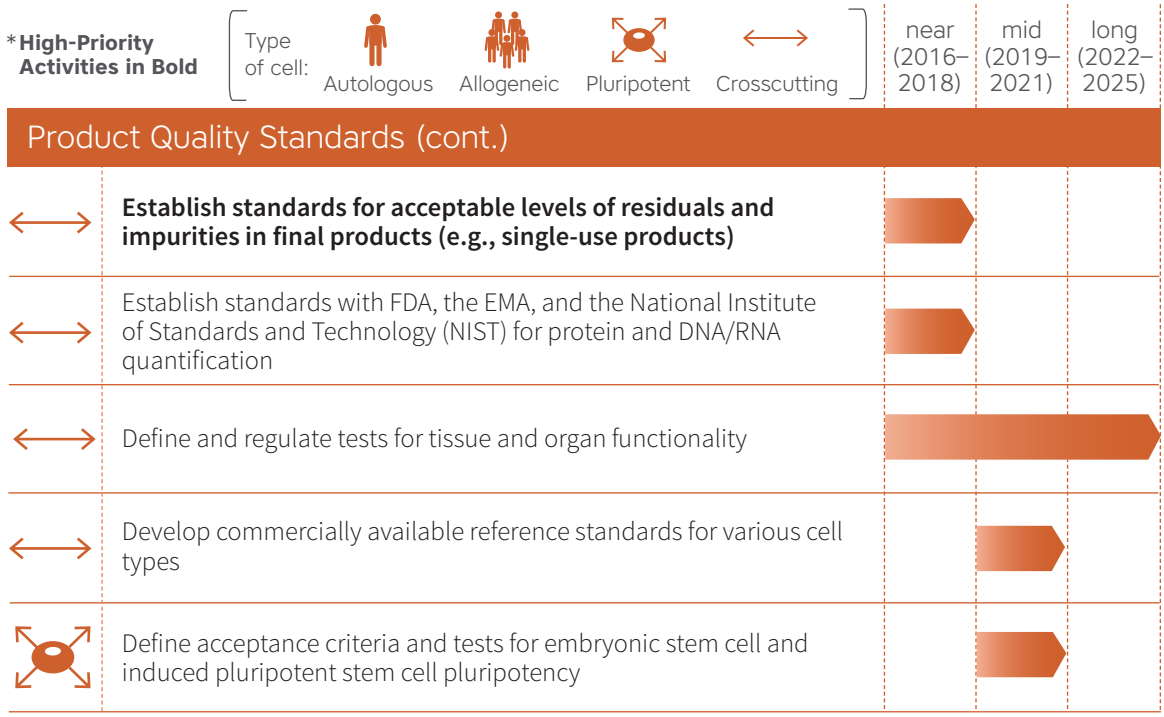
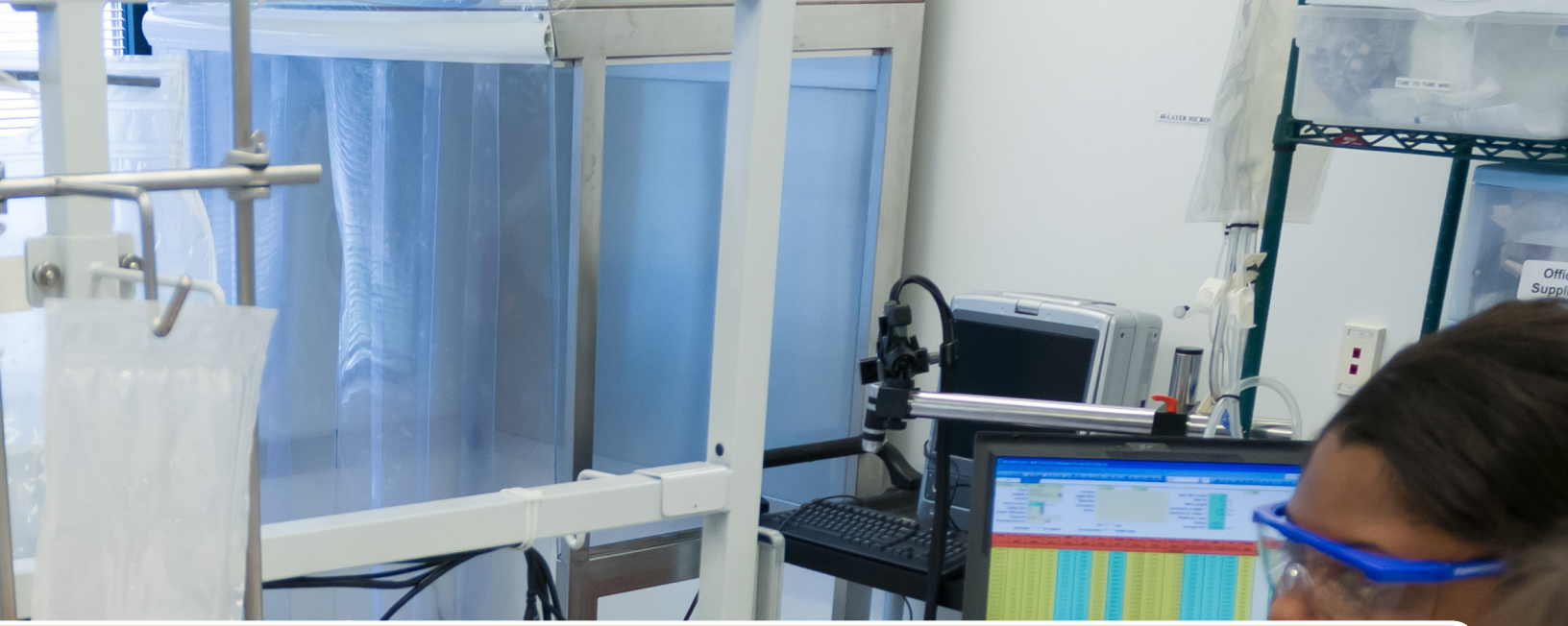


Figure 7. Standardization and Regulatory Support (cont.)





# Workforce Development

Realizing and capitalizing on the benefits of advanced technologies and techniques depends on a highly skilled, multidisciplinary cell manufacturing workforce—with expertise in areas including biological science, engineering, computational modeling, physics, chemistry, mathematics, and statistics.

To strengthen the current workforce, the cell manufacturing community must collaborate with universities and continuing education programs to develop structured training frameworks. Such programs will help attract new talent to the industry and will provide the current workforce with the skills needed to efficiently operate and further improve advanced cell manufacturing technologies and techniques. Additionally, by fostering stronger partnerships across companies, disciplines, and industry segments, the cell manufacturing community can leverage existing expertise to further grow the skillsets, capabilities, and knowledge necessary to meet increasing demand for cell-based medical products.

# Current Challenges

To realize large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must work to overcome the workforce development challenges that follow.

## Inadequate cell manufacturing education programs

Because cell manufacturing is a relatively new multidisciplinary field, there is a lack of robust curricula focused specifically on the field. The constantly evolving nature of the industry also makes it difficult to ensure the relevance and comprehensiveness of undergraduate, masters, doctoral/post-doctoral, and continuing education training programs, limiting the cell manufacturing workforce's ability to maximize value from these programs.

## Limited workforce diversity

The current cell manufacturing community does not have sufficiently broad expertise in fields outside of cell biology, including engineering, computational modeling, physics, chemistry, mathematics, and statistics, with the potential to greatly increase the understanding and efficiency of cell manufacturing processes. The industry also has a limited number of specialists with proficiency in quality and regulatory affairs and in infrastructure protection to move cell manufacturing to commercialization and clinical application.

# Key Initiatives

To address these challenges and realize the potential of large-scale, cost-effective, reproducible manufacturing of high-quality cells, the cell manufacturing community must collaborate on the following workforce development initiatives: Higher Education, Workforce Training, and Cross-Industry Collaboration. Activities for each of these initiatives are provided in Figure 8, divided into near-term (2016–2018), mid-term (2019–2021), and long-term (2022–2025) time frames.

## Higher Education

To grow the future workforce, the cell manufacturing community must invest in higher education activities that attract new graduates to the field and provide them with the skills necessary to sustain industry innovation. It will be critical for educators to continuously engage with industry to inform education programs, updating training content as new technologies, techniques, and regulations emerge. Industry engagement will also ensure that research conducted through undergraduate, graduate, and postdoctoral coursework has industry implications, and will help foster the relationships needed between universities and industry to provide students with hands-on, practical industry internships.

## Workforce Training

The cell manufacturing community must conduct frequent workforce training on emerging topic areas, industry procedures, and cell manufacturing techniques and

technologies to provide the workforce with the knowledge and expertise necessary to implement new manufacturing approaches. Additionally, to ensure that manufacturing knowledge is current across the industry, the cell manufacturing community must formalize a mechanism for transferring legacy knowledge to new members of the expanding workforce. Building a highly skilled workforce could increase cell manufacturing productivity and efficiency, reduce workforce errors, and improve the consistency and quality of manufactured cells and cell-based medical products.

## Cross-Industry Collaboration

To expand the cell manufacturing knowledgebase, the cell manufacturing community must foster stronger partnerships across companies, disciplines, and industry segments. Leveraging expertise and promoting idea exchange from outside of the current cell manufacturing community—including from existing consortia and the additive manufacturing and biotechnology industries—could help the cell manufacturing industry more efficiently and effectively overcome the current challenges of cell manufacturing.

Figure 8. Workforce Development Priority Activities

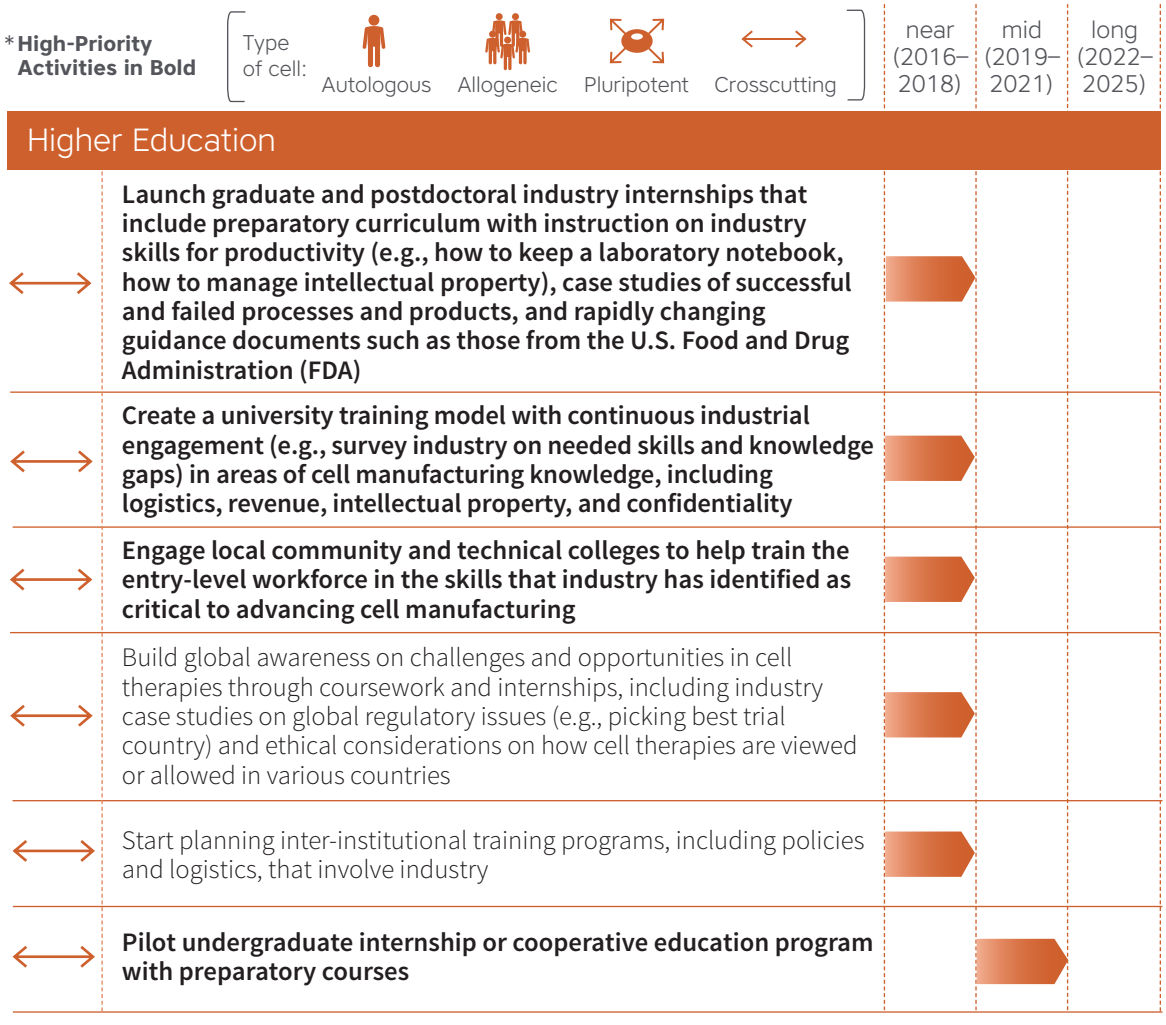


Figure 8. Workforce Development Priority Activities (cont.)

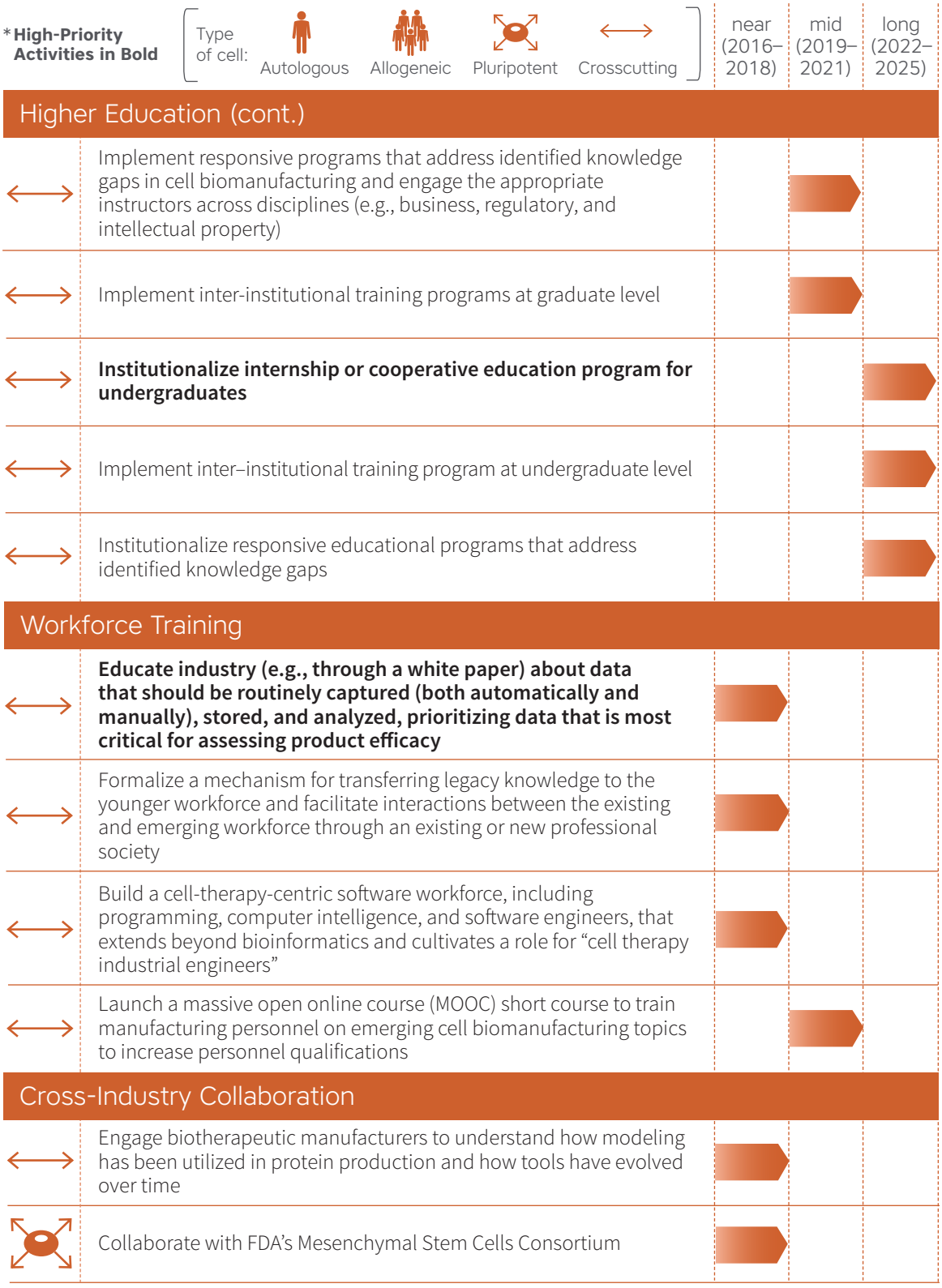
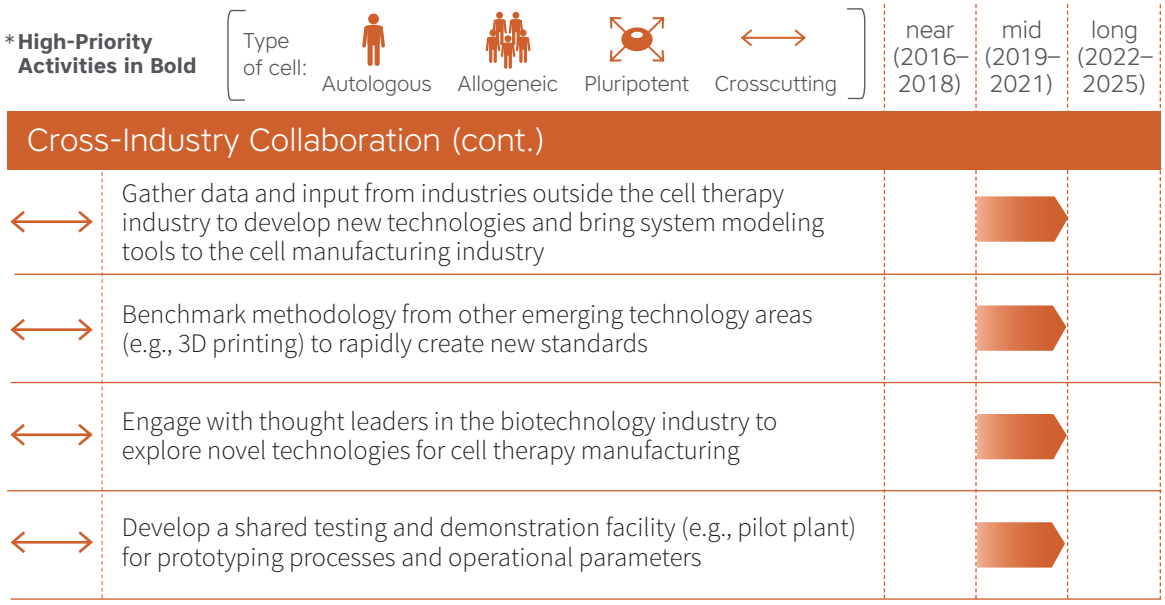


Figure 8. Workforce Development Priority Activities (cont.)



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# The Path Forward

By combining focused research and development activities with initiatives designed to support and sustain the cell manufacturing industry, the cell manufacturing community can facilitate the advancement and market penetration of next-generation cell-based medical products and support the long-term growth and global competitiveness of the U.S. cell manufacturing industry.

Execution of the priority activities within this roadmap will be led by the National Cell Manufacturing Consortium (NCMC), an industry-driven effort aimed at establishing a collaborative public-private partnership between researchers, equipment producers, cell and product manufacturers, regulatory officials, and other relevant stakeholders. This community will accelerate growth of the U.S. cell manufacturing industry more so than individuals or small groups could accomplish working independently. By implementing the priority activities outlined in this roadmap, NCMC can fulfill its mission to develop and mature technologies and infrastructure relevant to cell manufacturing; to facilitate regulation, commercialization, and adoption of emerging technologies by the cell manufacturing industry; and to build and train a skilled industry workforce.

Though NCMC will be operated, in part, through monetary and in-kind support from its members, additional or matched external or federal funding would multiply the impact of the consortium's efforts and ability to pursue a greater number of priority activities in this roadmap. A dedicated translational effort and funding on the order of several hundred million dollars per year for the next 10 years would greatly accelerate U.S. cell manufacturing progress and advance the United States as a global leader of state-of-the-art, life-changing therapies, engineered tissues, medical devices, and drug discovery and testing platforms. Such investments in research and development, coupled with supporting initiatives to build a skilled workforce and develop industry standards and regulations, are critical for enabling the biomanufacturing community to meet intensifying market demands—and potentially grow the industry to a multi-billion-dollar global market in the next decade.[8]

## National Cell Manufacturing Consortium (NCMC) Vision

The United States establishes and maintains its global prowess as the leading developer of cell manufacturing technologies and manufacturer of cells and is viewed as the chief authority on cellular manufacturing standards and practices.

[8]C. Mason, D.A. Brindley, E.J. Culme-Seymour, and N.L. Davie, "Cell Therapy Industry: Billion Dollar Global Business with Unlimited Potential," Regen. Med. 6:265-272, May 2011.

# Appendices

Appendix A: Acronyms and Abbreviations

Appendix B: Roadmap Contributors

# Appendix A: Acronyms and Abbreviations

| | |
|---|---|
| **AMTech** | NIST Advanced Manufacturing Technology Consortia program |
| **CCRM** | Center for Commercialisation of Regenerative Medicine |
| **CMS** | Centers for Medicare & Medicaid Services |
| **CRC** | Cooperative Research Center for Cell Therapy Manufacturing |
| **CRTD** | Center for Regenerative Therapies Dresden |
| **CTC** | Cell Therapy Catapult |
| **CQA** | critical quality attribute |
| **DFG** | Deutsche Forschungsgemeinschaft (German Research Foundation) |
| **DNA** | deoxyribonucleic acid |
| **EMA** | European Medicines Agency |
| **ERP** | enterprise resource planning |
| **FDA** | U.S. Food and Drug Administration |
| **Georgia Tech** | Georgia Institute of Technology |
| **GMP** | Good Manufacturing Practice |
| **GRA** | Georgia Research Alliance |
| **HIPAA** | Health Insurance Portability and Accountability Act |
| **ICH** | International Conference on Harmonisation |
| **IND** | investigational new drugs |
| **MES** | manufacturing execution systems |
| **MOOC** | massive open online course |
| **NCMC** | National Cell Manufacturing Consortium |
| **NIST** | National Institute of Standards and Technology |
| **OCTGT** | Office of Cellular, Tissue and Gene Therapies |
| **PCR** | polymerase chain reaction |
| **R&D** | research and development |
| **RFID** | radio-frequency identification |
| **RNA** | ribonucleic acid |

# Appendix B: Roadmap Contributors

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