CASA–Bio
Catalyzing Across Sectors to Advance the Bioeconomy

Delivery on Target: Transforming Vaccines and Biologics Delivery

Coordinated advancements in delivery systems for vaccines and biologics for humans and animals will enhance U.S. preparedness for emerging health threats, improve global health outcomes, and foster innovation in biotechnology, public health, and agriculture.

Debra Auguste, Northeastern University
Catherine Fromen, University of Delaware
Marian Gindy, Merck
Daniel Heller, Memorial Sloan Kettering Cancer Center
Abigail Koppes, Northeastern University
Jonathan Lovell, University at Buffalo – State University of New York
Scott McVey, University of Nebraska-Lincoln
Juliane Nguyen, University of North Carolina at Chapel Hill
Daniel Reker, Duke University
Nadine Rouphael, Emory University
Anita Shukla, Brown University
Junghae Suh, Biogen

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Executive Summary

Need

The past decade has seen a revolution in new vaccines and biologics, such as nucleic acids, proteins, and drug combinations. However, these new molecular tools are often failing to make an impact in the healthcare and agriculture spaces. This is especially true for respiratory diseases, which represent a significant healthcare and agricultural burden in the form of infectious diseases (influenza, bovine respiratory disease [BRD], COVID-19, *etc.*) and chronic conditions. For instance, the total cost of the seasonal flu is estimated to be $87 billion per year,[1] which includes direct medical costs as well as lost productivity due to absenteeism and mortality; the estimated annual cost for BRD in the U.S. can exceed $1 billion due to treatment, lost production, and mortality.[2] The economic burden of respiratory diseases can be reduced by advancing therapies with improved delivery that prevent or target these diseases.

Goals

- **We need to target medicines and vaccines to the place in the body where they are needed.** These new molecules often cannot be delivered on their own; they often need a delivery system to help them reach the right organ in the body, overcoming the body's natural defenses designed to block foreign substances. In the case of respiratory diseases, drugs can navigate from the airway through an aerosol, or from the bloodstream through an injection; each route provides distinct advantages but requires more development.
- **We need testing approaches that are faster, smarter, and cheaper.** We have limited tools to predict how well a new vaccine or therapeutic will work across different animal species and in humans. This severely limits the translation and adoption of new modalities.
- **We need new biomanufacturing paradigms.** These new technologies require manufacturing practices that can make thermostable formulations that can maintain their effectiveness across a broader temperature range.

Deliverables

Our long-term goal is to develop resilient technologies and infrastructure capable of addressing complex healthcare challenges across both human and agricultural sectors, ultimately enhancing the quality of life in our communities. This initiative proposes deliverables that will revolutionize respiratory disease treatment by establishing cutting-edge, tissue-targeting injectable systems, advancing needle-free vaccine technologies, and validating new testing modalities using immune-predictive tissue models and simulations. In addition, by expediting biomanufacturing of thermostable vaccines and biologics and launching a powerful public-private consortium, we will fast-track the delivery of life-saving innovations from the lab to the global community.

An investment of $1 billion dollars over the next five years in U.S. research and infrastructure will streamline therapeutic development and enhance our preparedness against emerging threats. This will stimulate the U.S. bioeconomy, improve U.S. healthcare and agriculture systems, and strengthen national security. Investing in new health and veterinary care technologies is vital, but transforming how we bring these technical innovations to market is game-changing. By streamlining the drug development pipeline, we can not only safeguard human and agricultural health, but also unlock vast economic opportunities and boost workforce productivity.

Motivation

Safeguarding both human and animal health is essential for economic and national security. Our healthcare system is critical to the stability of our economy. Yet, illness costs Americans $575 billion annually in lost productivity, diminishing income and purchasing power.[3] When our workforce is sidelined by sickness, it affects all aspects of life, including national security. The COVID-19 pandemic, which resulted in the tragic loss of millions of lives, caused an estimated $16 trillion in lost productivity,[3] highlighting the immense impact on our health, agricultural supply chains, and communities. There are also 400 million people worldwide experiencing disabling Long COVID, highlighting the need for preventative therapeutics.[4]

Animal agriculture, which sustains American and global food security, is equally vulnerable. Disruptions in agricultural supply chains can devastate herds and flocks, threatening the livelihoods of farmers and ranchers while straining national food supplies. Bovine respiratory diseases already cost nearly $1 billion per year in North America; a potential outbreak of African swine fever could result in catastrophic losses of up to $80 billion.[5]

Healthcare for humans and animals share a common challenge: the need for improved therapeutics (treatments for diseases) and prophylactic vaccines (preventative measures). Emerging biological tools hold immense potential to treat, cure, and prevent a wide range of diseases that impact our community and agricultural health. Over the past few decades, we have seen remarkable progress in the capabilities of nucleic acids, gene-editing technologies, and designer antibodies. Many of these breakthroughs have already been translated into highly effective, FDA approved products, such as COVID-19 vaccines and cell-targeted immune therapies. However, despite these advancements, the full potential of these biological tools has yet to be realized for many complex diseases, including cystic fibrosis in humans, polymicrobial infections in animals, and respiratory infections in both humans and animals.

Delivering new therapies is challenging because the body's natural defenses often block them. Drugs injected into the bloodstream are cleared by the liver, while oral or inhaled therapies struggle to penetrate barriers like the lungs' mucosal lining. Each delivery method has unique obstacles that need to be overcome.

To unlock the true potential of these therapies, we need to precisely target medicines and vaccines to the organs where they are most needed. Developing targeted drug delivery methods offers significant advantages. For instance, in the case of the lung, drugs administered via the bloodstream can access its vast surface area, providing a rapid means of treating airway inflammation. Delivering vaccines through the airway mimics natural respiratory infection pathways, engaging the resident immune cells and resulting in more effective immune responses, better protection, and reduced transmission. While the lung is a compelling example, this need for targeted delivery also applies to all organs.

Although some progress has been made, the field is hampered by a lack of predictive tools to gauge the performance of new delivery technologies in early development. This leads us to the second major challenge: **We need faster, smarter, and more cost-effective testing approaches.** Our current tools are inadequate for predicting how well a new vaccine or therapy will perform across different animal species or in humans. While specific biological barriers are shared between species, critical differences exist, particularly in immune responses. This makes it difficult to design broadly applicable solutions and often results in one-off approaches. Predicting immune response is crucial, as it directly influences safety

testing and vaccine efficacy. Without accurate immune response prediction, we cannot effectively forecast how a therapy will behave, severely limiting the development, translation, and adoption of new modalities.

Even if we overcome these delivery challenges with innovative technologies, the complexity of these molecules and their innovative carriers requires specialized manufacturing processes. This leads us to the third challenge: **We need new biomanufacturing strategies that enable the rapid and cost-effective production of thermostable vaccines and biologics.**

Addressing these three challenges will profoundly and positively impact advancing the next generation of biologically derived vaccines and therapies. By improving targeted delivery methods, we can enhance the effectiveness of treatments and vaccines, leading to better outcomes and reduced healthcare costs for humans and animals. Streamlining testing processes will accelerate the development timeline for new therapies, enabling faster responses to emerging health threats and minimizing the time needed to deliver effective treatments. Moreover, innovative biomanufacturing approaches can democratize access to advanced therapies, making them more widely available and affordable, ultimately transforming healthcare delivery on a global scale. Together, these advancements will improve health outcomes, strengthen public health systems, and enhance resilience against future challenges.

Vision and Key Deliverables

Our overall vision is to build robust technologies and infrastructure to enable delivery solutions for emerging vaccines and biologics for human and agriculture needs. The 5-year vision centers on building critical technologies for respiratory diseases as a starting point, because they represent a heavy burden on U.S. healthcare for humans and animals. The following deliverables are recommended:

- Establish a tissue-targeting, injectable delivery system for respiratory diseases
- Advance needle-free vaccine technologies
- Validate immune-predictive lab models and computer simulations
- Expedite biomanufacturing of thermostable vaccines and biologics
- Launch a public-private consortium for technology translation

While these efforts target respiratory diseases initially, the advancements made will directly translate into broader approaches for delivering therapies to other organs. The tools and technologies developed, such as targeted delivery systems and immune-predictive models, will be adaptable to other complex conditions affecting the liver, heart, brain, and more. Enhanced biomanufacturing capabilities will create scalable solutions for a wide range of biologics, ensuring rapid and efficient production of future therapies. Furthermore, public-private partnerships established for technology development will provide a strong foundation for tackling other significant challenges in healthcare and agriculture, driving innovation and collaboration across sectors.

An investment of $1 billion dollars over the next five years in research and infrastructure will streamline our ability to bring new vaccines and biologics to market, which will safeguard our communities and agriculture from the spread of communicable respiratory diseases and enhance our preparedness against emerging threats. This will stimulate the U.S. bioeconomy, improve U.S. healthcare and agriculture systems, and strengthen national security.

Deliverable 1: Establish a tissue-targeting, injectable delivery system for respiratory diseases

Complex therapies, such as mRNA and gene-editing tools, show promise in treating diseases at the molecular level. However, the body's defenses (e.g., liver filtering) prevent many therapies from reaching the intended target organs. To address this challenge, new drug delivery technologies must be developed to ensure therapies can bypass defensive barriers and reach specific organs.

We propose starting with a new, improved nanoparticle design specifically for targeting the lungs. This could help stop respiratory infections like bovine respiratory disease (BRD), porcine reproductive and respiratory syndrome (PRRS), influenza, and respiratory coronaviruses, and treat conditions such as pneumonia or cystic fibrosis using gene-editing tools. By developing lung-targeting technologies, we will also gain valuable insights into how to target other organs. This will lead to better therapies for a variety of diseases and across different species.

A key challenge is developing systems that can deliver therapies directly to the target area while avoiding the liver. Currently, these systems are created using a trial-and-error method, which is inefficient, expensive, and often unsuccessful. Most manufacturers use a one-size-fits-all approach for drug delivery, but different therapies need customized systems to be safe and effective. Although many studies have examined how nanoparticles are distributed in the body, we still don't fully understand how their composition impacts the overall treatment outcome.

We need a new approach to designing nanoparticles that are customized for specific therapies. By using advancements in artificial intelligence (AI) and machine learning (ML), we can create systems that improve nanoparticle chemistry, making it easier to target the right organ. AI and ML can help us design nanoparticles that better circumvent the body's defenses and reach their intended destination. This will replace current trial-and-error processes by allowing us to use data-driven models to find the best solutions more efficiently.

<u>Milestones</u>

To achieve a working prototype, we need to develop nanoparticles that shield therapies from the body's natural filtering processes and targeting mechanisms that enable accumulation in the desired organ. Lung targeted drug delivery could be derived from mixing and matching of nanoparticle constituents, targeting-mechanisms, and therapies to create therapeutics with optimal safety and effectiveness. Characterization of the delivery system's physical properties, accumulation in each organ, and ability to gain entry into cells would create a database of needed information. AI/ML could then create customized solutions for a specific treatment, which then could be tested in biologically relevant systems.

More data will lead to better solutions. Similar to how a car's navigation system relies on traffic data to find the best route to your destination, sharing experimental data will help researchers determine the nanoparticle chemistry to build a novel targeted delivery system. AI/ML holds potential to provide guidance, but to achieve this, we need collaboration across different organizations and projects to establish clear data standards and guidelines for sharing information. This will be crucial for allowing researchers to contribute to and gain access to large, shared repositories of data that is compatible for all users. Combining AI/ML for prediction with state-of-the-art experimental techniques for testing and validating will help generate the most useful data, improving our ability to design the best delivery systems.

Impact

The use of AI and ML will accelerate the development of new therapies by tailoring the delivery specifically for the cargo and the disease. This will expand the number of targeted drug delivery systems that can be used for vaccines and therapeutics. AI/ML methods may enable the design of delivery systems for individual patient needs, including rare cancers and genetic diseases, and different animal species' needs. Achieving effective targeted delivery will enhance therapeutic efficacy and reduce the side-effects of drugs. New, advanced therapeutics will drive economic growth by fostering innovation, creating jobs, and reducing healthcare and agriculture costs.

Deliverable 2: Advance needle-free, aerosol vaccine technologies

Needle-based vaccines face several logistical challenges, such as requiring cold storage and specialized healthcare provider training. They also generate biohazardous waste and carry the risk of needle injuries. Biologically, these vaccines may be less effective at stimulating protective immune responses in mucosal areas like the lungs or gut, which are crucial for defending against respiratory and gastrointestinal diseases. Additionally, they can produce weak immune responses for certain pathogens and populations, often needing multiple doses over a lifetime. These issues reduce vaccine accessibility, affordability, and effectiveness, especially in low-resource settings.

Creating modular, needle-free vaccine technologies to combat diseases caused by bacteria, viruses, parasites, and fungi across different species would be a major breakthrough. This is especially important for zoonotic infections—diseases that spread between animals and humans, like coronaviruses and influenza—which pose significant threats to both human and animal health and have the potential to trigger future pandemics.

A major breakthrough in vaccination lies in needle-free strategies. Aerosol or droplet delivery, including sprays for animals, could greatly boost vaccination rates by offering an alternative to needles. Tablet-based or feed-based options also provide efficient, needle-free solutions. These methods trigger immune responses directly at the site of entry, stimulating mucosal antibodies and cellular defenses. This not only protects individuals but also helps reduce transmission within communities. Needle-free methods can combine vaccines targeting gastrointestinal or respiratory pathogens, like coronaviruses, RSV, influenza, and pertussis. Aerosol delivery is particularly useful for emerging diseases. Recent respiratory outbreaks, such as H1N1 and COVID-19, could have benefitted from faster responses with inhaled vaccines, thanks to their ease of administration. This approach would be particularly advantageous for populations where intramuscular injections are challenging, including children, the elderly, immunocompromised individuals, the undernourished, those with obesity, and people with bleeding disorders.

Milestones

A strategic shift is needed to incentivize research communities to design effective, non-injectable delivery systems. The use of oral and aerosol vaccine delivery methods are needed as they are tailored for specific pathogens (e.g., oral for enteric pathogens and intranasal/aerosol for respiratory infections). These technologies must show enhanced durability compared to injections, incorporate strategies that utilize universal antigens and various adjuvants, while also ensuring sustained release and an acceptable safety profile.

There is a significant need to develop technologies that can utilize a plug-and-play design, where antigens can be swapped out for different variants or for use in different animals. While beneficial to current vaccine platforms, this is critical for next generation non-injectable approaches. To make this

happen, we need more foundational research to better understand species-specific immunology, mechanisms that underlie the immune response, and interactions between each species and the components of the vaccine.

Impact

The successful implementation of a needle-free vaccine technology would bring transformative benefits to several key populations. It would greatly aid those with needle aversion, including children and approximately a quarter of adults, by offering non-invasive delivery options. Healthcare and veterinary workers would benefit from a reduced risk of needle injuries, enhancing safety in these professions. In low-resource settings, where access to trained healthcare providers is limited and maintaining cold chains or managing sharp waste is challenging, a needle-free technology would offer a more practical solution. Additionally, during outbreaks, self-administration could be implemented for infection control, enabling faster, broader immunization. Finally, for farm animals, such a technology would enable cost-efficient mass vaccination, reducing the burden and financial repercussions of disease in agricultural systems.

Deliverable 3: Validate immune-predictive lab models and computer simulations

Current screening methods for drug delivery technologies often fall short in predicting how they will perform in the body, especially regarding immune and toxicity responses. Simplified cell cultures and animal models fail to capture the complexity of whole-body interactions and frequently don't predict responses in humans or other species, posing a significant challenge to drug and vaccine development.

Creating a robust, predictive lung testbed early on would help identify safe and effective vaccine and therapeutic candidates, leading to more informed investment decisions. These testbeds would evaluate respiratory disease progression and the performance of new delivery technologies that are delivered from the airway or bloodstream. Improved testing methods would streamline drug and vaccine development, making the process faster, more cost-effective, and enhancing both safety and efficacy. Tailoring technologies to target specific organs, like the lung, allows for more efficient resource use, speeding up the path from discovery to approval.

Advanced three-dimensional models, such as a Microphysiological System (MPS) or organ-on-a-chip systems, offer a promising alternative to traditional preclinical testing methods. These lab-grown models replicate the environment of human or animal organs using cells from the target species, allowing for more accurate studies of organ function and disease mechanisms, especially immune responses, which can vary between species. By mimicking natural biological processes, an MPS provides deeper insights into drug efficacy and safety. The FDA already permits and encourages MPS as an alternative to traditional cell cultures and animal models for drug safety testing.

Digital twins, virtual replicas of biological systems, are emerging as powerful tools to improve predictions of immune responses and other biological interactions. Similar to Virtual Reality, these computational models use vast amounts of animal- and patient-specific data to simulate how a drug or vaccine will behave in the body. By creating dynamic, adaptable models, digital twins can predict immune reactions, efficacy, tolerance, and optimal dosing across individuals or species. Like MPS, they address the limitations of traditional preclinical testing, offering a data-driven approach to better understand therapeutic safety and effectiveness before clinical trials.

Focusing on the lung as a model organ holds great promise for advancing MPS and digital twin technologies, enhancing their ability to predict drug delivery outcomes. The lung's complexity--spanning various length scales, intricate mucosal surfaces, and dynamic movements--poses challenges for accurately modeling how aerosolized vaccines travel through airways and interact with the mucosal barrier, blood, and immune cells. Developing robust lung models will lead to major breakthroughs in predicting organ-specific responses across species, revolutionizing the creation of more effective therapies and delivery methods.

Milestones

To enable the widespread and accepted use of MPS and digital twins, we need to invest in fundamental research to understand species-specific immune responses in the lung to new drug delivery technologies. This foundational knowledge will be critical in developing cross-species MPS and digital twins that can support cells from human and animal origins, accurately mimicking organ functions. Such insights will ensure that the models can effectively replicate the complex interactions within the lung, which will be vital for predicting therapeutic outcomes in living beings.

A validated lung MPS must accurately replicate mucosal surfaces, air flow and blood flow, architecture, and immune responses using species-specific cells. The construction should prioritize fabrication methods that enable high-throughput production, global distribution, automated control, and minimal handling to ensure consistency and scalability. Standardization efforts led by the FDA and USDA are essential for establishing clear evaluation protocols for healthy and diseased organs across various species. Validation of this technology will concentrate ideally on capturing the complete immune response of the studied species to the aerosolized vaccine, thereby enhancing its predictive capabilities for evaluating new drug delivery systems in real-world applications.

An analogous lung digital twin should be informed by high-quality data necessary to effectively train AI/ML-based models. In addition to population-based data where available, high-quality data derived from the lung-on-a-chip MPS technology should be incorporated, enabling it to simulate real-time responses to drug delivery systems and other stimuli. Integrating a model that connects with the lung model to provide data on systemic immune responses would be highly valuable. Collaborative efforts to develop standardized protocols for data collection, device instrumentation, and sharing are crucial, as these can address the obstacles that AI/ML methods currently face, such as the lack of agreeable benchmarks.

Impact

Together, lung MPS and digital twins could revolutionize how we assess the immune response to new technologies, ultimately accelerating the path to drug and vaccine approval by minimizing risk. A set of validated lung models would support the success of the first two deliverables, leading to robust injectable and inhalable technologies that can localize complex biologics to the lung to treat and prevent a host of respiratory diseases. New treatments will have a greater potential for safety and efficacy in the target population. Furthermore, these approaches will enable a rapid response to emerging biosecurity threats and could be ideal for assessing “species jumping” disease emergence.

Deliverable 4: Expedite biomanufacturing of thermostable vaccines and biologics delivery

The World Health Organization estimates that up to 50% of vaccines globally are wasted each year[5], primarily due to disruptions in the cold chain, resulting in billions of dollars in losses annually. To tackle this problem, there is a critical need for thermostable formulations that can maintain their effectiveness

across a broader temperature range. Developing these formulations would simplify the storage and transportation of vaccines and biologics, ensuring they remain viable for distribution to more people and animals, even in remote or resource-limited areas. This advancement could greatly enhance health outcomes by making vaccines and treatments more accessible and reliable.

Common methods for improving the storage and transport of therapeutics include freeze-drying, which converts liquid formulations into powder. However, the potential inactivation of active components during this process highlights the need for alternative stabilization methods. Cryoprotectants, such as starch and sugar molecules, have shown promise in safeguarding vaccine antigens and adjuvants from inactivation while enhancing the stability of biologics during freeze-drying. Biomineralization is a newer and less explored approach for vaccine protection. This technique involves using specialized materials, like a combination of metals and organic substances, to coat and safeguard the critical components of vaccines. Despite their potential, only a few of these techniques have advanced to clinical trials.

Efficiently developing thermostable vaccines and biologics delivery systems will require optimizing both formulation and manufacturing processes. Techniques such as spray drying, freeze drying, and encapsulation must be integrated with cryoprotectants, biomineralization, stabilizing adjuvants, and protein engineering to ensure the stability and effectiveness of vaccines and therapeutics under various temperature conditions. Thermostability in manufacturing is vital as it guarantees that vaccines and therapeutics remain safe and effective, even when exposed to temperature fluctuations, particularly in settings where reliable cold storage is unavailable.

Milestones

To transform the vaccine and biologics space, there is a need for innovative manufacturing processes that enhance vaccine and therapeutic stability. Thermostable vaccines and biologics are advantageous because they do not require refrigeration, making them easier and cheaper to distribute, especially in remote areas. This means they can maintain their potency despite temperature changes, reducing waste and ensuring effectiveness.

Therefore, it is crucial to develop new manufacturing processes, freeze-drying techniques, cryoprotectants, and materials that can effectively protect vaccines and therapeutics from external temperature fluctuations and other environmental factors. Furthermore, comprehensive studies are required to understand the long-term stability and efficacy of these new formulations under various conditions. These studies will help identify the most effective methods and materials for maintaining vaccine and therapeutic potency and safety. By investing in this research, we can ensure that vaccines and therapeutics remain effective throughout their shelf life, ultimately improving health outcomes and agricultural health.

Impact

Developing thermostable vaccines and therapeutics will revolutionize medical treatment delivery by allowing for safe and effective administration methods, including nasal, aerosol inhalation, oral, injectable, and transdermal. This flexibility enhances accessibility, especially in remote areas, reduces costs by eliminating the need for refrigeration, and improves patient compliance by offering needle-free options. Additionally, it enables rapid deployment during emergencies and reduces waste due to spoilage, ultimately improving global health outcomes.

Deliverable 5. Launch a public-private consortium for technology translation

Next-generation biomedicines are ushering in a new era of precision medicine for both humans and animals. However, many promising technologies remain stuck in the early stages of exploratory research, lacking the critical data needed to progress to clinical testing. This bottleneck delays the development of potentially life-saving therapeutics and vaccines. Public-private partnerships (PPPs) can help address this challenge by combining intellectual, financial, and infrastructural resources from both sectors. This collaboration can accelerate the transition of innovative technologies from concept to clinical application while mitigating financial and technical risks. We propose a PPP network aimed at exploring new delivery methods for biologics, which will facilitate extensive testing of the most promising medicines in terms of efficacy, safety, manufacturability, and stability.

Consider a small biotech company that has developed a promising new aerosol vaccine but lacks the resources to test it on a large scale. Through the proposed PPP, the company partners with a large pharmaceutical firm and a government agency (e.g., the NIH, FDA, or USDA). The pharmaceutical firm provides access to advanced manufacturing facilities, while the government agency offers regulatory guidance and access to clinical trial networks. Together, they expedite the development and testing process, allowing the vaccine to move from research to widespread use in less time than the company would have achieved alone.

A clearly defined scope for the PPP will foster synergistic partnerships. Academia, industry, government, and non-profit organizations each have distinct priorities and incentives for participating in a public-private partnership. Large companies will gain access to new technological advances tested in collaboration with research arms of government agencies, while small companies and academic institutions will benefit from reducing the risks associated with their novel medicines.

Supporting vaccine development is essential, especially in areas where infrastructure and profitability are significant barriers. Many vaccine candidates, particularly those targeting diseases affecting low-income or resource-limited regions, often struggle to reach advanced development stages due to the high costs associated with research, production, and distribution. Pharmaceutical companies may deprioritize vaccines for diseases that aren't considered highly profitable, leaving critical public health needs unmet. Additionally, the lack of manufacturing infrastructure hampers the ability to scale up production and maintain vaccine supply chains. By addressing these challenges, we can ensure the development of vaccines for underserved populations, improve global health outcomes, and prevent future outbreaks.

Milestones

The role of the PPP is to develop shared resources, including knowledge and infrastructure. The PPP will engage stakeholders to bridge the public and private sectors. Large pharmaceutical and biotechnology companies with significant resources and a vested interest in drug delivery technologies are essential to attract small to medium industry members and academics. The PPP leadership must understand both the public and private partners' needs and perspectives. Academics and start-ups participating in the PPP must be open to learning about industrial drug discovery and development processes. Government partners from relevant agencies will be critical, and non-profit partners can help amplify efforts.

A number of shared services and resources are needed including legal for contracts and intellectual property, project management support, drug discovery expertise and capabilities, preclinical pharmacology, scale-up and manufacturing, chemistry, manufacturing, and controls (CMC) strategy,

regulatory standards, animal care facilities, start-up incubator space, data storage and management systems, executive team and steering committee for governance and oversight, and advisory boards.

A focus on relationship building across all PPP members is vital. Industry partners will be hesitant to share proprietary knowledge, whereas academic partners will want to protect their rights to publish. Clear communication, established guidelines, and shared expectations amongst stakeholders are important to timelines, deliverables, patents, dissemination of results, and definitions of success.

A goal should be to invest in a robust peer review and investment process to add new technologies on a rolling basis. The PPP will assist in activities that support translation, including: evaluation of safety and therapeutic efficacy, small-scale manufacturability, material analytical assays, and quality controls. A review process will be needed at different stages of development to identify if milestones are met and whether the project should advance to the next stage. Applicants should participate in educational programs offered by the PPP to obtain training in drug discovery and development. A hallmark of the PPP will be to engage regulatory agencies at early stages to increase chances for approval. The success of the PPP is measured in the ability to improve and expedite the time-to-market process.

Impact

The proposed public-private consortium represents a significant opportunity to accelerate the development of therapeutics and address the existing bottlenecks hindering their clinical translation. By fostering collaboration, streamlining processes, and providing essential resources, the consortium can stimulate innovation, drive economic growth, and ultimately improve global health outcomes for both humans and animals.

Cross-Cutting Opportunities

The development pipeline for new vaccines and biologics delivery is lengthy and requires substantial investment from experts across various fields. This initiative emphasizes the urgent need for partnerships that extend beyond the conventional boundaries of universities, hospitals, industry, manufacturing facilities, farms, and government agencies. Success hinges on creating forums that encourage active collaboration among stakeholders to facilitate streamlined drug development and implementation.

Translating academic research into scalable manufacturing processes demands specialized knowledge and expertise. Successful scale-up requires technology transfer to experienced industrial partners or hiring experts in process engineering and regulatory compliance to address the knowledge gap. We must develop capabilities for scaled-up manufacturing that utilize new technologies and distributed manufacturing while maintaining quality standards. Additionally, researchers need training in designing, validating, and scaling the production of therapeutics and MPS.

Creating biomanufacturing training in academic settings is key to bridging the gap between lab research and large-scale production. By fostering early awareness and expertise in vaccine and biologics development, we can ensure a smoother transition from research to manufacturing. This alignment between academic innovation and industrial capabilities will accelerate the development and distribution of vaccines and biologics while preparing the next-generation workforce.

New technologies and manufacturing practices also require investments in workforce training to build a pipeline of skilled factory and healthcare workers. It is essential to equip people to operate advanced

biomanufacturing plants using cutting-edge analytical tools to ensure product safety and efficacy. Additionally, practitioners and regulators need education on new delivery methods and their applications.

Training researchers in computational methods is vital for generating the comprehensive open-source data required for AI/ML. The lack of uniform controls, standardized assays, and standardized endpoint metrics renders the available data incompatible with AI/ML. As a result, researchers often rely on smaller datasets leading to inaccurate predictions. Establishing robust open-source data that showcases the performance of various drug delivery formulations in a standardized format would significantly advance the development of new targeted therapies. Likewise, data will be useful in building a digital twin of the lung, which needs to be validated using relevant biological experiments.

In addition to data on delivery systems, a deeper understanding of comparative biology would enable us to investigate the effects of targeted delivery across various species. For instance, we need insights into how results from mouse testing can be applied to pigs, cows, or humans. Creating digital twins for each species could offer valuable data to assist researchers. The overarching goal would be to streamline labor-intensive and costly testing processes while identifying new and promising drug delivery candidates.

Expected Outcomes and Conclusions

This initiative describes five 5-year deliverables aimed at catalyzing the growth of lung-targeted delivery of vaccines and biologics from inception to market. These deliverables focus on identifying new delivery systems for specific organs, enhancing testing methods to screen the best therapeutic candidates, advancing manufacturing processes to ensure the safety and efficacy of selected candidates, and facilitating the translation of these therapeutics to the community. Progress in any of these areas could significantly impact healthcare and agricultural outcomes and costs. Each deliverable is designed to accelerate the research and development pipeline, reducing the time from discovery to market.

A $1 billion investment will lead to rapid growth in the U.S. bioeconomy by achieving the following goals:

- **Accelerated vaccine and biologics development and commercialization:** Streamlining the path from innovation to market will require collaborations that share data, expertise, and resources, including science-based adaptation of regulatory processes and novel manufacturing infrastructure.
- **Synergy between agricultural and human health:** By addressing both human and agricultural populations, new therapies will enhance One Health goals by addressing public, animal, and environmental health, recognizing the critical interdependencies between these sectors.
- **Rapid adaptation to emergencies:** Flexible biomanufacturing systems will allow for swift responses to emerging public health threats, such as pandemics or new disease outbreaks, enabling manufacturers to quickly adjust production for various vaccines or therapies and reducing time delays associated with developmental processes.
- **Job creation:** Innovation in biopharmaceuticals will create new jobs, with each therapeutic potentially generating between 500 and 5,000 positions.[8] A skilled workforce will need training in the discovery, translation, and application of new technologies.

Authorship and Acknowledgements

This report was written by:
Debra Auguste, Northeastern University; Catherine Fromen, University of Delaware; Marian Gindy, Merck; Daniel Heller, Memorial Sloan Kettering Cancer Center; Abigail Koppes, Northeastern University; Jonathan Lovell, University at Buffalo – The State University of New York; Scott McVey, University of Nebraska-Lincoln; Juliane Nguyen, University of North Carolina at Chapel Hill; Danel Reker, Duke University; Nadine Rouphael, Emory University; Anita Shukla, Brown University; and Junghae Suh, Biogen.

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