Advancing the U.S. Bioeconomy and Revitalizing a Historic Manufacturing Area[1,2] By Establishing Global Leadership in Biofabrication through the ReGen Valley Tech Hub

More than 6 in 10 Americans live with at least one chronic health condition[3]; disadvantaged populations face disproportionate healthcare access barriers and socioeconomic burden[4]; and U.S. health outcomes trail other developed countries despite the highest per capita spend on the globe[5]. Chronic illness results in billions in lost productivity each year, even as rising health care costs approach one fifth of U.S. GDP. Moreover, the endpoint of chronic illness is organ failure, and the U.S. supply of donor transplants egregiously short of need and inequitably distributed, 17 Americans die each day waiting for a transplant[6]. The human impact of this status quo is stunning in its own right, but poor population health also threatens national security – draining economic resources[5], harming military readiness[7], and deepening reliance on a precarious global supply chain and medical products manufactured abroad[8].

The potential to manufacture curative regenerative medicine therapies and achieve transformational impact in the lives of Americans has been known to academia, industry, medicine, and government for decades[9]. This field, known as biofabrication, combines engineering, biology, advanced manufacturing, robotics, automation, regulatory, data science, and medical expertise. However, attempted commercialization of even the most promising technologies has fallen short due to fragmentation between these disciplines, inconsistent and expensive manual manufacturing approaches, and fluctuations in both funding and financial objectives of investors[10]. For example, products from Organogenesis and Advanced Tissue Sciences raised early expectations and millions in investment but failed to translate to clinical impact and market success due to manufacturing and regulatory challenges. Without an entity operating in the public interest, creating common process and platform enabling technologies, standards, and policies, intellectual property from failed startups moved to foreign countries. America cannot afford to become reliant on overseas manufacturing as we have in other industries of national security importance (e.g., semiconductors). In 2016, the U.S. Department of Defense (DoD) selected the Advantaged Regenerative Manufacturing Institute (ARMI) and invested in its BioFabUSA program to solve these challenges.

ARMI, the lead organization setting forth the Manchester-Nashua Metropolitan Statistical Area (ReGen Valley) Case for Designation on behalf of a diverse and deeply connected Consortium, is a member-based nonprofit founded to overcome barriers in the biofabrication industry and propel the U.S. to global leadership. ARMI's mission-centered, cross-disciplinary, unifying approach, bolstered by the expertise of nearly 200 government, industry, and academic members and broad State, municipal, and community support, is advancing new regenerative therapies through cutting-edge manufacturing techniques, while also building the biofabrication industry's workforce. Companies are working in ReGen Valley to produce therapies such as heart disease, end stage renal failure, diabetes, arthritis, and traumatic injury, develop enabling manufacturing and supply chain technologies, and fund these innovations.

This progress, made possible by the commitment of public and private entities represented in the ReGen Valley Consortium (the *Consortium*), has fueled early economic revitalization in the region and positioned it for rapid growth. The foundation of transformative impact and global competitiveness is already solid in ReGen Valley (enhanced by its proximity to, yet separation from, the Boston/Cambridge area), but more investment is needed now to accelerate the progress made to date and enable the U.S. to compete with other nations racing to lead[9,11]. At present, certain resources necessary for growth

With Tech Hub funding, in 10 years, ReGen Valley will represent at least 10% of global market share ($6B) with a pipeline of cost-effective curative therapies available to all who need them, thereby reducing U.S. annual health care costs by 10x and serving as the center of global exports. On the solid foundation in ReGen Valley, this funding will propel the U.S. to leadership in biofabrication and enabling technology while cutting in half the number of families in Manchester below current poverty levels (14.2%) and the out-migration of talent (70%) from Nashua.

in ReGen Valley – revitalized commercial space, wraparound startup support, and workforce development program capacity, among others, are not keeping pace with demand and the prospect of startup failure and intellectual property loss looms large. By way of example, the BioFab Startup Lab, an incubator launched with BBBRC funding, received 3x the applicants it can accommodate before even advertising its services. Manchester-Nashua is also a region with growing diversity, including immigrant and refugee communities whose vibrancy and resiliency are essential to a thriving, globally competitive region. However, infrastructure and community supports like affordable housing, transportation, and childcare need investment to overcome historical underrepresentation and fuel inclusive economic growth. Consortium members are currently working in tightly-knit teams to solve these challenges. Designation as a Tech Hub with follow-on funding is essential to coalesce these efforts and catalyze the region's evolution from a biotechnology epicenter into a global competitor, lift community prosperity for generations, and seal U.S. leadership in biofabrication.

1) Technology-based potential of the region for global competitiveness

Despite medical advances, chronic illness remains an enormous strain on families and communities. Heart disease, kidney disease, and diabetes cost the nation millions of lives and more than $690B annually[5], and the problem is set to worsen due in large part to the aging population and increased sedentary lifestyle. Globally, the market for biofabricated medical products is $15B and projected to reach $62B by 2033[11]. ReGen Valley capturing a conservative 10% of the global market represents a $6B opportunity – and a revolution in health care.

Despite this enormous need, U.S. biofabrication was a fractured, nascent collection of university-developed biological advances without a solid commercial path forward[10] when, 7 years ago, the Obama Administration determined that a Manufacturing USA Institute was the catalyst needed to finally advance the industry. Building on a foundation of nearly $175M in investment from DoD, the U.S. Department of Health and Human Services (HHS), and most recently EDA's Build Back Better Regional Challenge (BBBRC), state, municipal and state entities have executed economic policy measures, biofabrication-targeted tax incentives, and active investment to drive business development and talent retention. As a result, startups like PRO Therapeutics (PRO-T), Organamet Bio, and Safi Biotherapeutics have decided to grow in Manchester. International startups such as Allarta Life Science and multinational corporations such as United Therapeutics Lung Bio and 3D Systems have established a commercial base and workforce in ReGen Valley. Further, global leaders like Microsoft and Consortium member Rockwell Automation are invested in this region, dedicating resources and technology on the evidence-based premise that ReGen Valley is the epicenter of this new American industry. Finally, enabling technology companies such as Advanced Solutions Life Sciences (ASLS) and Merrimack Manufacturing as well as chronic disease care companies such as Sequel Medical Technologies are furthering the growth in ReGen Valley, illustrating the broad economic benefits a nationally-focused Manufacturing USA program like BioFabUSA can bring to its local community.

The biofabrication industry is at the intersection of two primary key technology focus areas (KFTAs): (1) biotechnology, medical technology, genomics and synthetic biology; and (2) robotics, automation, and advanced manufacturing. Machine learning and autonomy are also critical areas of innovation needed for cost-efficiency and scale, especially for advanced manufacturing and related supply chain technologies. ReGen Valley is uniquely home to all of the essential disciplines required for this industry. BioFab Foundries, a 25,000ft^2 state-of-the-art development facility on ARMI's campus funded by DoD, supports the manufacture of pre-clinical and early clinical products. Through the BBBRC award, ARMI is developing a new 80,000ft^2 facility to support later-stage clinical and commercial production, adjacent to a new 26,000ft^2 workforce and training facility, both targeted for 2024 completion. Deeply-connected academic partners, including the Community College System of New Hampshire – home to ApprenticeshipNH, are also co-developing biofabrication curriculum. The University of New Hampshire (UNH), a flagship research university and EPSCoR program with a strong presence in the Manchester Millyard, is working with Consortium members to build curriculum for

professional degree programs such as engineering, data analytics, and computer science, alongside regional engineering powerhouses Dartmouth and UMass Lowell, a Minority Serving Institution.

2) Role of the Private Sector

Thriving private sector activity is a key asset of ReGen Valley. Dean Kamen, Chair of ARMI's Board of Directors, has been investing in the area for decades, creating DEKA Research & Development Corp - a mission-driven company with nearly 1,000 engineers, and FIRST- a U.S.-based global STEM education nonprofit bringing robotics to millions of youth each year. DEKA has contributed $30M in cost share (engineering services and administrative support) to kick-start the formation of ReGen Valley. On this foundation, Rockwell Automation opened a Customer Demonstration Center on ARMI's campus and provided $10M in manufacturing software, training, consulting, and equipment to build automation infrastructure and train the next generation biofabrication workforce. The company is also a key partner in the development of a BBBRC-funded Registered Apprenticeship Program (RAP), has permanent personnel in Manchester, and is committed to providing ongoing resources to grow the industry. Local investment by United Therapeutics has grown from a single lab to an 88,000 ft^2 building dedicated to the manufacture of the company's 3D-printed lungs, creating jobs and increased demand for skilled workers. Companies outside the region like Microsoft Health see potential as well. They selected ARMI for early access to their AI-based Science Engine to help speed the pace of innovation.

As private-sector firms increasingly invest in this ecosystem, a dense concentration of biofabrication-related companies has formed around the Millyard. For example, Consortium member ASLS provides innovative robotics solutions from offices immediately adjacent to cell-based therapy developers, the BioFab Startup Lab, and ARMI workforce development facilities. ASLS also participates on BioFabUSA's Leadership Advisory Council and mentors startups in the ecosystem. ProKidney is working with ARMI to automate the manufacture of their renal therapy, shown in late-stage clinical trials to delay the need for dialysis by up to three years[13]. They see ReGen Valley as an ideal location to build out automated manufacturing, creating 1000's of jobs and hiring local talent as demand for their product grows post FDA-approval. Merrimack Manufacturing, a local advanced manufacturing company, launched in the Manchester Millyard several years ago and will support 15 Registered Apprentices in 2024 and anticipates doubling its workforce in the next 2 years. VitroLabs will build advanced manufacturing facilities here and create hundreds of good jobs (*see support letters*).

3) Regional Coordination and Partnerships

Another essential element ensuring ReGen Valley's success is the region's dedicated focus on biofabrication. The NextGen Manchester Resiliency Council, formed on a foundation of long-standing partnership, is guiding BBBRC efforts to ensure the benefits of the biofabrication industry are realized in the local community. While BBBRC funding is enabling critical infrastructure, baseline startup support, and important workforce diversity initiatives, more is urgently needed to foster commercial and workforce growth and engage diverse entrepreneurs. Commercial demand now, intensifying with industry growth, is beyond the capacity of one city alone; the Cities of Manchester and Nashua are unified in their commitment to the Consortium. As the largest and most diverse in NH, the Cities are longstanding collaborators on regional economic development. Strong City and State engagement also ensures local investment complements potential Federal investment, as exemplified by the City of Manchester's $25M RAISE grant to connect low income workers with jobs and training[14], the Community Loan Fund's planned $20M investment in affordable housing, and the Community Development Finance Authority's leadership on childcare access and annual investment of $15M in complementary projects.

Consortium Members	Primary Role
Dartmouth, MCC, SNHU, UMass Lowell (MSI), UNH	Institutions of Higher Ed
Manchester, Nashua, NH BEA	State and local government
Advanced Solutions Life Sciences, ARMI (Lead), DEKA, Catholic Medical Center, Merrimack Manufacturing, NH Hospital Alliance, Rockwell Automation, Safi Biotherapeutics, VitroLabs	Tech/Innovation/Manufacturing Industry
NextGen Manchester Resiliency Council, Southern NH Planning Commission, Business Finance Authority	Economic Development Orgs
NH AFL-CIO, NH Building, Construction and Trades Council	Labor and Workforce Training Orgs
Manchester School District	Elementary/secondary/career and technical schools
FIRST Robotics NH, Business Association for People of Color	STEM and entrepreneur diversity
Granite YMCA	Economic stability, opportunity
Amoskeag Ventures	Venture Development Organization
Community Loan Fund, NH CDFA	Underserved communities economic development

Figure 1: ReGen Valley Consortium

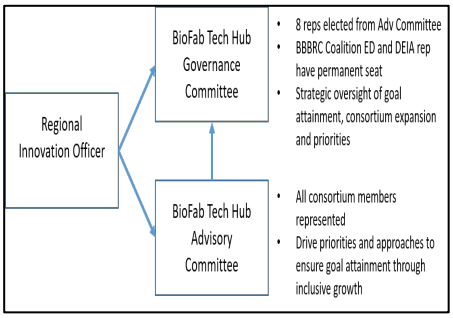

Figure 2: Consortium governance

As a non-profit, member-based organization, ARMI has led successful collaboration across government entities, industry, and academia since 2016. More than 6 years of sustained engagement and lessons learned has led to effective, rigorous governance structures and excellence in incorporating multiple stakeholder perspectives. Building on this experience and incorporating BBBRC governance, the 29 members of the Consortium will establish a dedicated structure for the ReGen Valley Tech Hub *(Fig 2)*. Consortium members represent 14 of 18 categories set forth in the NOFO and have articulated ongoing actions and concrete commitments in the enclosed letters of support. A foundational tenet of the Consortium will be to engage community voices in governance, including Unions, underrepresented workers, new Americans, and minority-owned businesses. The Regional Innovation Officer will be Julie Lenzer, ARMI's Chief Innovation Officer, who is a serial entrepreneur with over a decade of experience leading technology-based ecosystem development.

4) Equity and Diversity

In the early history of Manchester-Nashua, the manufacturing industry played a crucial role in diversifying the area's population and economic base[15]. Today, this area is growing anew, proving the value of early investments in biofabrication and foreshadowing the future of ReGen Valley[1]. However, while the Millyard is an economic center, the broader City of Manchester experiences persistent poverty and is home to historically disadvantaged communities. The Millyard and surrounding neighborhoods cover just a few square miles yet hold 30,000 people, including thousands of immigrants and refugees[16,17]. 14.2% of residents live below the poverty level. *Fig 3*[18] demonstrates that while past efforts have driven inclusive growth in the Millyard (*green*), adjacent areas need investment to drive access to good jobs (*yellow and red*).

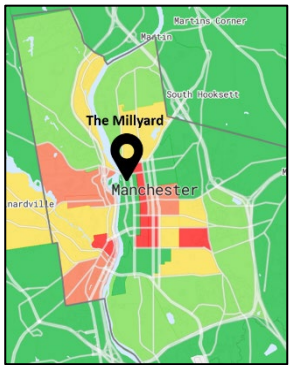

Figure 3: Manchester Inclusive Growth Scores

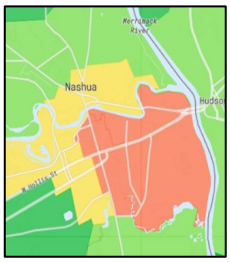

Figure 4: Nashua Inclusive Growth Scores

Recognizing these challenges, the BBBRC coalition focused the grant's largest programmatic element on engaging disadvantaged communities through entities like SNHU's Center for New Americans, the Granite YMCA, and a Transit Equity Study. While this was an important start, significant funding is needed to scale workforce inclusion programs, implement transit recommendations, and ensure community infrastructure is designed for equitable access to good jobs. The City of Nashua faces similar challenges, with pockets of the population experiencing poverty and the added strain of 70% out-migration of talent to the Boston area. Offering commercial space and becoming the home of companies creating jobs in biofabrication will enable Nashua to develop and retain talent while additional funding will help ensure this growth is equitable.

At a national level, efforts to alleviate U.S. healthcare disparities have achieved insufficient progress to date. By engaging the wisdom of the people most impacted, the Consortium will drive better health outcomes for underrepresented and rural communities. Building on action by members such as the Business Association for People of Color and the Community Loan Fund, the Consortium will design for, measure, and manage to gains in equity across all goals and deliverables The NH Hospital Association and UNH extension program will specifically assist the Consortium in connecting with rural communities.

5) Composition and capacity of the regional workforce

The current workforce in ReGen Valley has a 94.4% high school graduation rate; 41.4% obtain a Bachelor's degree or beyond[19]. Of those who pursue a degree program, 60% leave the state to do so (*highest in the nation*), and many never return[21]. Consortium members are already focused

on retention, offering skill-building options and driving a pipeline of talent into post-secondary programs - both community colleges and universities - that lead to good jobs. Consortium members have created industry-informed, stackable curricula, delivered from middle school through degree programs. ARMI's BioTrek, a project-based biofabrication and entrepreneurship program for high school students, reached more than 1,000 students across ReGen Valley this past year and is set to double in 2024, preparing them to pursue certificate, apprenticeship, and degree programs. Connectivity with community youth organizations including FIRST NH's planned bio-focused programs provides important youth engagement paths. Multiple BBBRC workforce programs are also set to launch, including a mobile lab and STEM camps, as well as Department of Labor-approved Registered Apprenticeship Programs in biofabrication and advanced manufacturing. While an effective model is in place, these programs need funding to rapidly scale an inclusive pipeline of talent. Consortium members AFL-CIO and the Building Construction and Trades Council will ensure Good Job Principals and labor management practices are centered in workforce programming.

6) Innovative "lab to market" approaches

Even with the significant technical advancement in the last several years, biofabrication needs investment to realize the industry's full potential. The manufacturing, regulatory, and quality expertise provided by ARMI provides a solid foundation for advancing biofabrication-related therapies and enabling technology startups to market while the BBBRC-funded BioFab Startup Lab fills business gaps. Demand, however, already outpaces available capacity. Since founding the BioFab Startup Lab in early 2023, promising companies exceed by 3x the available capacity and an influx of companies seeking to found or grow in ReGen Valley need resources.

Companies like PRO-T – seeking to commercialize a regenerative graft for rotator cuff repair, and RyTek Bio – seeking to commercialize a sensor that non-destructively monitors cell viability, need automation, scaled manufacturing, regulatory and reimbursement strategies, and business support. Translational funding is required to mitigate risk and draw investment.

Recognizing the criticality of U.S. leadership in health technology, HHS also funded a separate international incubator in Manchester for Israeli companies to establish a U.S. commercial base. Of the companies in the first two HHS-ARMI "HealthTech Hub" cohorts launched in 2023, half intend to establish their U.S. presence in ReGen Valley.

Capital is the urgent and primary challenge for both U.S. and international companies in this industry, and support for innovators to transition from expensive bespoke prototypes to commercial products must scale. The State, through its recent *Life Sciences Industry Strategy*, is developing industry grants and policies to support biofabrication startups. With mounting manufacturing and regulatory wins, long-time collaborator, life sciences investor, and former J&J executive launched Consortium member Amoskeag Ventures and committed to raising a several hundred million dollar fund in the coming months. Still, ReGen Valley's concentration of promising companies exceeds available resources. Federal investment is essential to keep these groundbreaking technologies in the U.S.

7) Impact on economic and national security of the United States

Without infrastructure and urgent investment to support translation, critical intellectual property in biofabrication will continue to default to foreign interests or, as with CAR-T therapies, be cost-prohibitive and fail to reach those most in need[10, 22]. The moment is now to ensure biofabrication does not repeat the path of the semiconductor industry, with U.S. dependence on our own breakthrough technology manufactured offshore[23]. Moreover, poor U.S. population health threatens the strength of our defense forces, tears the fabric of our communities, and stifles growth. America cannot lose the race for the biofabrication industry and deepen these threats. We must act to ensure this new American industry thrives here, equitably protects American lives, and contributes to a vibrant national economy for all.

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