July 31, 2024

The Honorable Larry Bucshon, M.D.
2313 Rayburn House Office Building
Washington, DC 20515-1408

The Honorable Diana DeGette
2111 Rayburn House Office Building
Washington, DC 20515-0601

Via Email: cures.rfi@mail.house.gov

Dear Representatives Bucshon and DeGette:

On behalf of the National Center for Advancing Translational Sciences (NCATS) Alliance, a coalition of patient advocates, clinicians, academic medical centers, researchers, and biotechnology companies working to educate the public and policymakers on the important science being advanced by NCATS and ensuring Congress provides NCATS with the necessary funding to deliver on its scientific mission, we write to provide input on how Congress can build on the 21st Century Cures Act and Cures 2.0 to help accelerate patient access to the next generation of life-changing diagnostics, treatments, and cures.

In 2011, Congress established NCATS to accelerate the development of new diagnostics, therapeutics, and cures for common and rare diseases using translational and clinical science. NCATS is the only NIH center or institute charged by Congress with a singular mission to advance translational science to accelerate treatments and cures for all diseases, rare and common, and regardless of which organs or tissues are affected.

The Alliance supports increased federal funding and legislation that will enable NCATS to make rapid advances in the development of new clinical and translational science and technologies to speed the development of safe, effective treatments for diseases that affect tens of millions of Americans and cost the American economy billions of dollars each year. With these objectives in mind, the NCATS Alliance seeks your support for the following policies and proposals to be included in your proposed legislation.

Remove All Clinical Trials Phase 3 Research Restrictions

When Congress created NCATS in 2011, it included a provision in the authorizing legislation that prohibited NCATS from conducting Phase 3 clinical trials. At the time, there were concerns that NCATS Phase 3 trials might compete with biopharmaceutical company trials, and many felt NCATS should instead prioritize earlier stage translational and clinical research. With enactment of the 21st Century Cures Act, Congress modified the statute to allow NCATS to support Phase 3 clinical trials for rare diseases. However, to enroll a clinical trial, NCATS must announce a 120 day public notice period of its intention to determine that no other entity plans to conduct a similar trial. This causes unnecessary delays for vulnerable patient populations for whom time is of the essence. The NCATS Alliance believes the entire Phase 3 limitation is a barrier to fully realizing NCATS's potential in translating scientific discoveries into effective treatments, for both rare and more common diseases where private sector

interest is limited. We are also unaware of any concerns with lifting this prohibition on Phase 3 trials, which other NIH institutes and centers are permitted to conduct.

Expansion of Gene Therapies for Rare Diseases

Building on the successful Platform Vector Gene Therapy (PaVe-GT) and the Bespoke Gene Therapy Consortium (BGTC) programs, the NCATS Alliance supports a new NCAT led initiative to derisk gene therapy development and scale up lower-cost manufacturing to advance more treatments for rare diseases in this quickly evolving field. The PaVe-GT program is making progress towards the goal of streamlining the development and delivery of gene therapies by creating standardized platforms for vector production and clinical testing, thereby accelerating the availability of treatments for rare genetic diseases. Similarly, the Bespoke Gene Therapy Consortium focuses on developing individualized gene therapies tailored to specific patient needs, particularly for those with rare diseases that lack commercial viability. Even with these successes, gene therapies continue to face an uphill battle with barriers in manufacturing, cost, expertise, and regulatory hurdles.

The NCATS Alliance proposes to supercharge these initiatives by consolidating these and other related activities across NIH into a one-stop shop enterprise. NCATS would leverage its leadership in this area to catalyze trans-NIH coordination to provide access to a centralized hub of specialized expertise and infrastructure. To help quickly advance the development and testing of viral-based gene therapies, this program would allow NCATS to undertake limited manufacturing of products for clinical trials in the U.S. and at NIH for rare diseases. NCATS would then seek out industry partners to pursue any successful therapies or future manufacturing expansion to keep up with demand. This will help NCATS address unmet medical needs among small patient populations insufficient to support commercial viability and provide hope for patients with rare conditions. This approach not only fosters innovation but also ensures that groundbreaking therapies reach those who need them most, irrespective of market size. The NCATS Alliance estimates this initiative would require an initial $75 million federal investment.

Reducing Rare Disease Diagnostic Odyssey Through Newborn Screening

Many rare disease patients experience diagnostic odysseys and delayed diagnoses associated with further disease progression, worsening outcomes, and unacceptable and avoidable emotional, health and financial trauma. Drug development and clinical trials still rely on clinical diagnoses despite common agreement that genetic or molecular diagnostics and the inclusion thereof would better define clinical trial cohorts and result in improved clinical trial outcomes. The NCATS Alliance supports allowing NCATS to develop and implement centralized diagnostic resources and standardized diagnostic algorithms. Specifically, we propose enabling NCATS to advance sequencing-based short-read diagnostics followed by long-read sequencing-based second confirmation as a disease agnostic, diagnostic, and clinical trial stratification tool.

Empowering NCATS to advance these systemic infrastructure solutions will permit scaling resources and addressing many rare diseases concurrently. Broad genetic characterization would also improve clinical trials, safeguard against type I errors, and reduce incorrect conclusions that novel therapeutics are ineffective when in fact they are safe and effective subgroups. These efforts have proven extremely beneficial in the neonatal intensive care setting, and similar programs focused on rare disease would generate resources and the needed economies of scale for population wide newborn screening. The Alliance anticipates this initiative would cost $10 million annually.

Cures Acceleration Network

Cures Acceleration Network (CAN) was established as part of the Patient Protection and Affordable Care Act and moved to NCATS to advance the development of high-need cures and address significant barriers within the path from discovery to clinical trials. The authorizing legislation established the CAN Review Board to advise the NCATS Director and make recommendations on new scientific initiatives. The statute requires the Secretary of Health and Human Services (HHS) to appoint 24 CAN board members to represent specified fields. The CAN board must have a quorum of 13 members, excluding ex officio members, to meet. Based on these onerous requirements, the CAN Review Board has not held a meeting since January 2020 because of their inability to reach a quorum. Given the board's important mission, the NCATS Alliance proposes that the CAN Board duties be consolidated within the NCATS Advocacy Council to facilitate these meetings based on a simple majority. Alternatively, Congress could help facilitate these meetings by changing the quorum requirement to a more flexible majority of current members and allowing the Secretary to appoint members with relevant expertise to align with other HHS Advisory Councils.

Further, the authorizing legislation provided NCATS with Other Transactional Authority (OTA) that allows NCATS to expand, modify, and discontinue activities. Only 20 percent of NCATS funds are eligible for OTA. NCATS Alliance proposes to eliminate the arbitrary OTA 20 percent restriction to allow NCATS to unlock the full potential of this authority.

Investing In Novel Alternative Methods and Workforce Training

Novel alternative methods, also sometimes called new approach methods or NAMs, use human cells, tissues, and data to understand human biology, disease states, and therapeutic responses. These NCATS pioneered innovative technologies, including tissue chips and computational models, are recognized by NIH leadership to hold "tremendous promise for helping us better understand fundamental biology to advance human health," while simultaneously providing potential to reduce or replace the use of animals and to "enable research to be done more quickly, by more researchers, and at a more affordable cost." The NCATS Alliance supports an expansion of early-career researcher training grants, fellowship opportunities, and other mechanisms aimed at educating and training the next generation of translational scientists. Support for NCATS to train scientists in NAMs-specific scientific and operational proficiencies would help to modernize health research and get more cures to more patients more quickly.

Further, NAMs incorporate patient and ancestry-specific factors, improving the representativeness and applicability of translational research to all people. In conjunction, support for creating, expanding access to, and incentivizing use of diverse, well-characterized human tissues, cells, and data to employ with NAMs would help ensure social responsibility in these emerging technologies and continue to advance patient-centered health research. Such a program may in turn improve the diversity of the biomedical workforce, a goal for both 21st Century Cures and Cures 2.0, which could further be fostered by requiring applicants to include a Plan for Enhancing Diverse Perspectives, a scored component of proposed research aimed at fostering diversity, inclusivity, and accessibility. The NCATS Alliance believes a new NCATS program aimed at using NAMs to better represent human diversity and understand and address health disparities could be part of NCATS' Tissue Chip Projects and Initiatives. The Alliance anticipates this initiative would cost $10 million annually.

NIH Consolidation Proposals

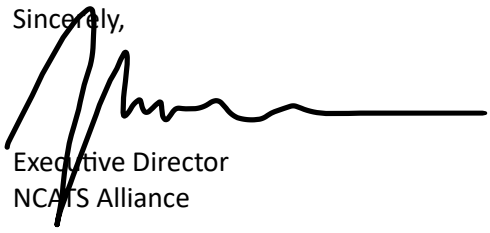
The NCATS Alliance has profound concerns regarding recent efforts to significantly restructure the NIH through the appropriations process without congressional hearings, stakeholder input, and data and analysis to justify these proposed changes. We support a bipartisan, scientifically based, and transparent process to improve and enhance the science supported by the NIH. We urge Congress to consider the experience and expertise of the vast group of stakeholders, including patient advocates, clinicians, academic medical centers, researchers, and life sciences companies, to ensure that any reforms enhance and maintain American preeminence in biomedical research and life sciences and will deliver diagnostics, treatments, and cures to common and rare diseases now and into the future.

Conclusion

Congress recognized the need for improved translational science when it created NCATS in 2011. Despite being seriously under-resourced since its inception, NCATS has made tremendous strides in advancing the translational science and technologies needed to move all biomedical research and development much faster toward effective treatments for rare and common diseases. The NCATS Alliance appreciates the opportunity to provide input as you seek to craft legislation that builds on the 21st Century Cures Act and Cures 2.0. For questions, please contact NCATS Alliance Executive Director, Kevin Brennan at kbrennan@bluebird-strategies.com.

We thank you for your kind attention to these public comments.

Sincerely,



Executive Director
NCATS Alliance