WRITTEN TESTIMONY OF
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Hearing on
"Maintaining America's Leadership in Biomedical Innovation: FDA's Role in Advancing U.S. Drug Development"

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Introduction

Chairman Griffith, Ranking Member DeGette, and Members of the Subcommittee, thank you for the opportunity to submit this testimony. I am Susan Winckler, and I serve as Chief Executive Officer of the Reagan-Udall Foundation for the Food and Drug Administration (the Foundation). I am a pharmacist and an attorney by training, and I have had the privilege of viewing drug development from several vantage points across a thirty-year career — including service as Chief of Staff at the FDA from 2007 to 2009, where I supported both Republican and Democratic Commissioners.

Maintaining America's leadership in biomedical innovation is one of the defining public-health challenges of this decade, and the FDA plays a significant role in addressing that challenge. This testimony draws on select projects from the past year where the Foundation convened the people who develop drugs and run trials. I hope to leave you with confidence in the direction our system

is heading and, more usefully, a clearer picture of the work that remains not only for FDA, but for the broader clinical trials enterprise.

The Foundation is an independent, 501(c)(3) nonprofit organization created by Congress in the FDA Amendments Act of 2007, with the purpose of advancing regulatory science and supporting the FDA's mission.[1] Congress named our organization for President Ronald Reagan and Congressman Morris "Mo" Udall, each of whom lived with an incurable neurodegenerative disease — a reminder that our work is about addressing challenges, accelerating innovation, and improving patients' lives. Consistent with the parameters of our authorizing statute, the Foundation does not engage in regulatory activity nor regulatory decision-making.

I provide this background of our organization's role because it shapes what we can offer this Subcommittee. The Foundation is a convener, not an advocate. We provide a trusted, transparent forum where relevant FDA ecosystem participants—in this case clinical trial sites, clinical research organizations, regulated industry, patient organizations, and regulators—can step above individual product decisions and discussions and engage, with candor, about a topic—in this case the shared challenges, data gaps, and inefficiencies that challenge America's leadership in biomedical innovation. Described another way, we elevate the conversation to a level of common exploration and problem-solving. Efficiencies are gained when parties collaborate rather than each evaluating

[1] The Reagan-Udall Foundation for the FDA is supported by federal funding and private donations. Our operations are partially supported by statutorily-required funding from the U.S. Food and Drug Administration (21 USC Chapter 9, Subchapter VII, Sec. 379dd(n)). All programmatic decisions are our own. We maintain strict oversight through our Board of Directors, which reviews all financial donations over $250 and rejects gifts that pose a conflict of interest or other concern. The Foundation embraces transparency and prioritizes safeguards, including annual reporting to the public, Congress, the FDA, and the IRS. These measures protect against undue influence and ensure independence, accountability, and scientific integrity.

the same problem alone. My testimony is offered in that spirit: a faithful report of what stakeholders have told us, and where they have reached agreement.

Thus, I appear today not to advocate for any specific legislation, but to share what our convenings have surfaced and provide observations useful to the Subcommittee's deliberations.

How These Reports Were Generated

As a component of our activity across FDA's broad jurisdiction, the Foundation assembled stakeholders to explore three distinct areas of drug development: one focused on enhancing early-stage drug development in the U.S., another discussing improvements in large multi-regional clinical trials with a focus in oncology, and a third exploring the gap between patient-relevant and regulatorily-sufficient endpoints in developing products to address rare disease. Each convening involved different participants from the broad FDA ecosystem, and the learnings from each discussion are captured in individual reports. I personally moderated each roundtable discussion and can attest that the participants came to each table with sharply different interests, no shared script, and a willingness to engage with each other constructively. Together, the participants produced dozens of specific, stakeholder-vetted recommendations that serve as an array of potential activities for all in the ecosystem to explore, revise, and pursue.[2] This testimony will capture some areas of alignment between potential activities and recently announced initiatives, and will highlight areas where more might be done.

[2] See page 12 for links to reports referenced in this testimony.

A Foundation for Confidence

When the Department of Health and Human Services released Operation TrialBlazer, a roadmap for maintaining U.S. leadership in early clinical research and development, our team compared each of those three bodies of stakeholder work against the roadmap. Across three separate convenings, we found our report recommendations converge repeatedly and substantively with the direction HHS has charted. That convergence is not coordination; these were independent efforts. When the people who run trials, treat patients, and generate the evidence arrive on their own at the same conclusions as the agency that regulates them, it is a strong signal that the reforms are sound and ready to implement.

To name the strongest alignments briefly: in early-stage development, both our stakeholders and HHS embrace risk-based nonclinical testing and streamlined Phase 1 manufacturing expectations; in improving large, later-stage studies, both prioritize network trial models, single-IRB reliance, and patient-centric trial matching; and finally, our reports and Operation Trialblazer embrace modern adaptive trial designs and fuller use of real-world data. The Subcommittee should take confidence from that agreement. There are opportunities, however, that are not yet pursued and where this Subcommittee holds the tools to drive meaningful change.

A Word on Competitiveness

This hearing rightly frames biomedical innovation as a matter of American leadership. Allow me offer one piece of personal context. In 2007, as FDA Chief of Staff, I led the agency's medical-product negotiations with China's then-State Food and Drug Administration, which produced a bilateral product-safety agreement between the two countries. In that process, I was immersed in the reality that U.S consumers and patients are best served when regulatory authorities collaborate.

At the time, the U.S. was challenging China to enhance their regulatory agility and maturity, to help that country better oversee medical product safety and better harness innovation. Since then, China has done just that: they have developed a stronger and more efficient medical product regulatory system. And thus, China has joined other countries in competing for biomedical innovation, and the U.S. has the opportunity to further improve its performance to nurture that innovation.

I raise this for transparency, not to dwell on, or target, any other country. The Foundation takes no position on trade or geopolitics, and I observe that a durable response to global competition is not to define ourselves against anyone else, but rather to strengthen what we do here, to improve our own operations. Every one of our convenings was, at its core, about that strengthening: how the United States can make its own system faster, clearer, and more capable, so that innovation is developed here because here is the best place to develop it. That is a frame for the Subcommittee to consider: the goal is a stronger American system, and the surest way to lead is to be the best place in the world to bring a therapy from discovery to patients.

Five Themes Where Consensus Runs Deepest

Reading the three convenings together with Operation Trialblazer, five themes recur consistently:

- **Clarity in communication.** Sponsors lose months guessing at FDA's expectations and defaulting to over-conservative data generation, often providing more data than is needed, which takes additional months to gather and analyze. This is especially damaging for smaller, emerging biopharma companies who have little capital to spare and can lead to some promising drug candidates being scrapped before clinical trials can start. Clear, phase-appropriate requirements were the single most cited reform across all three

convenings, and HHS places them first as well. And the FDA could go further: use of the phrase 'clinical hold' to describe the FDA decision to hold an investigational new drug application at the preclinical stage is, not surprisingly, misunderstood by many to mean that actual clinical work has been stopped. When this situation occurs prior to any patient receiving a dose and the action is informational, the descriptor "notice of additional information required" is simply clearer. Further, differences in evidentiary expectations among review divisions at the FDA are often raised as a challenge to product innovation. Sharing the underlying rationale for such differences, particularly the scientific principles driving disparate treatment, can be educational for many product developers and fellow regulators. Extending that such a culture of shared learning to the Agency's application of flexible evidentiary strategies would be an additional innovation acclerant.

- **Reducing duplication.** Single-IRB reliance, reusable regulatory playbooks, computable protocols, and reuse of prior manufacturing knowledge each address redundant effort that adds cost and delay without adding commensurate protection for patients or participants.

  In addition, there is opportunity for regulated industry to consider its role in "over-answering" or borrowing from precedent when unnecessary. As FDA provides greater clarity on what is actually required, industry must review, and apply, that clarity. (See Early-Stage Drug Development Recommendation #12.) Learning forums to share information about pre-IND meetings, IND submission packages, and IND reviews can yield discussion of what has worked, what has not, and where expectations may have shifted.

- **Modern, efficient trial designs.** Master protocols, adaptive and platform trials, and network models appear in every analysis as options to learn more from fewer patients and

less duplicated infrastructure. Doing more with less is essential in oncology and indispensable in rare disease where the patient population may be measured in dozens. Unlocking the potential of network (or hub-and-spoke) models can increase efficiency (and innovation) and allow broader participation of patients in clinical trials. (See Oncology Clinical Trials Recommendation #1)

- **Better use of existing data.** Real-world data, natural history, and patient registries are treated across all three convenings as regulatory assets, with a shared call for clearer, more predictable criteria on when and how such data sources and analysis can support a regulatory decision. Going a step further and pursuing a cross-stakeholder, AI-enabled rare disease knowledge management system could help maximize the impact of this inherently valuable rare data. (See Expanding Regulatory Agility and Evidentiary Integrity in Developing Treatments for Rare Diseases Recommendations #20)
- **An accessible FDA and early engagement.** New consultation channels, contact centers, plain-language resources, and public engagement reflect a shared belief that resolving scientific and regulatory questions early prevents far more costly rework later. A short, well-timed conversation may save a sponsor many months of investment. Broader conversations, where regulators and researchers share their learnings, accelerate the exploration of emerging ideas and, inherently, innovation.

The Work That Remains: Observations Offered for the Subcommittee's Consideration

Candor about alignment requires equal candor about the gaps, because those gaps are where the stakeholder community has completed informative preparatory work. I offer these not as criticism

of Operation Trialblazer, but as a map of where additional effort could accelerate solutions that industry and sites are ready to explore. Several of the not-yet-addressed opportunities identified by our stakeholders share a common feature: they cannot be solved by the FDA alone, and in some cases not by HHS alone. They require resources, statutory clarity, or infrastructure that only Congress can provide. Consistent with the Foundation's role, I offer the following as observations of strong stakeholder consensus— areas the Subcommittee may find worth its attention.

Improving Transparency and Efficiency of the US Clinical Trial Infrastructure

Much of the reform conversation, including Operation Trialblazer, focuses on the regulation of early stages of medical product development: what data an IND requires, how protocols are reviewed, how trials are activated. Those rules matter. But rules and regulations operate on an assumption of physical and human capacity to discharge against those rules. And that capacity is unclear. We do not have a clear, current nationwide picture of where capacity for first-in-human, Phase 1 trials actually resides; we do not have a resource to illustrate which academic medical centers, health systems, and dedicated units can safely and quickly initiate early-phase trials, what specialized capabilities they hold, and how much of that capacity is at risk from staffing shortages and financial strain. If we cannot see our own capacity, we cannot strengthen it, and no amount of regulatory streamlining will compensate for a first-in-human infrastructure that is thinning or non-existent. This challenge extends beyond Phase I trials: trial capacity is unevenly distributed across the country with many patients living far from any trial site. Furthermore, the number of trial sites is declining under financial pressure.[3]

[3] Friedson, Kim, "The Supply of Clinical Trial Sites: Openings, Closings, and Longevity", Milken Institute, September 2025.

A key recommendation from our reports includes building a dedicated network of Phase 1 capable clinical trial sites, including designating first-in-human/Phase I centers of excellence that apply key reforms such as a single IRB and other streamlined site activation processes. (See Early-Stage Drug Development Recommendation #14) Federal funds would clearly enhance such a network while building capacity, disseminating best practices, training the next generation of early-phase investigators, and extending reach into underserved regions. This, in turn, could be part of a national Phase I coordinating strategy.

I want to address one genuine difference in emphasis, because I think it is clarifying rather than concerning. Operation TrialBlazer is structured primarily from a posture of improving competitiveness, with a goal of reversing the trend of investors and sponsors looking overseas to hold their early-phase clinical trials. The Foundation's convenings were animated primarily by the patient: by what patients feel, function, and survive, and by how to reach them faster and more equitably. I do not see these as competing motivations. They are two roads to the same destination. A regulatory system that is faster, clearer, and less duplicative serves to keep innovation onshore and gets therapies to American patients sooner.

Another opportunity to explore is re-thinking the clinical trial structure in discrete disease areas. For example, consider pivoting from screening an individual patient against potential trial participation in a consecutive, trial-centric manner to a truly patient-centric approach. A common, pre-competitive platform that enables patients to be screened for a broad array of trials and referred to the trial(s) that best fit their needs helps patients *and* innovation. (See Oncology Clinical Trials Recommendation #2) The Subcommittee does not have to choose between the competitiveness case and the patient case; the same reforms serve both.

Each report supports the shift to risk-based, phase-appropriate nonclinical and manufacturing requirements, and consistently emphasizes that the value of that shift depends on the FDA finalizing the associated guidance documents so that clarity becomes durable rather than provisional. Stakeholders view the underlying data infrastructure, e.g., electronic health record integration with trial databases, computable protocols, and secure, interoperable real-world data, as the foundation that makes patient-centric enrollment real. Broader data access and connectivity must be paired with a demand for strong cybersecurity.

Finally, some basic operational transformation is needed to improve the efficiency of contracting and budget preparation. Facilitating multiple research sites and product sponsors to agree on essential contracting elements and budget parameters, and to efficiently complete the specific negotiations for each study must become a priority. Patients are waiting while paperwork piles up. (See Oncology Clinical Trials Recommendation #3)

Why Agency Action Alone Will Not Be Enough

Operation Trialblazer may be executed faithfully and yet the US may still fall short; some constraints lie outside the reach of FDA or HHS. The agency can clarify its expectations, streamline its reviews, and modernize its guidance documents — and it should. But it cannot appropriate funds to assess and build Phase 1 capacity. It cannot stand up the physical and human infrastructure on which every reform ultimately depends. Some reforms require change at other HHS operating divisions. Those are the province of Congress and, in places, of CMS and other partners.

That is not a counsel of discouragement. It is the opposite. It means that the reforms with the highest leverage are precisely the ones this Subcommittee is positioned to advance. The user fee

reauthorization now on the horizon is a natural, timely vehicle for several of them. The FDA has done, and is doing, its part.

Conclusion

Let me close with the two points. First, HHS has charted a sound course in Operation TrialBlazer, and the stakeholders who will operate within these reforms have reached, independently, many of the same conclusions. Second, the work that remains presents an opportunity for Congress: assessing and strengthening our national Phase 1 capability, removing the statutory and coverage barriers that keep patients out of trials, and resourcing the infrastructure on which the FDA's reforms. The surest way to maintain America's leadership in biomedical innovation is to build — deliberately, and with the tools that reside in this chamber — the strongest system for developing therapies anywhere in the world.

The Reagan-Udall Foundation will continue to do what Congress created us to do: convene the ecosystem, surface the shared challenges, and translate complex questions into terms that patients, developers, and policymakers can all engage. We stand ready to support this Subcommittee and the FDA in that work. Thank you, and I welcome your questions.

Links to Reports cited in this written statement:

1. Improving Oncology Multi-Regional Clinical Trials (https://reaganudall.org/publications/improving-oncology-multi-regional-clinical-trials)
2. Recommendations for Expanding Regulatory Agility and Evidentiary Integrity in Developing Treatments for Rare Diseases (https://reaganudall.org/publications/recommendations-expanding-regulatory-agility-and-evidentiary-integrity-developing)
3. Enhancing Early-Stage Drug Development in the United States (https://reaganudall.org/publications/enhancing-early-stage-drug-development-united-states)

Addendum to Winckler Testimony, July 15, 2026

Compilations of Recommendations to Reports by the Reagan-Udall Foundation for the FDA

1. Improving Oncology Multi-Regional Clinical Trials

Improving Oncology Site Activation, Enrollment & Study Start Up Timelines Is Imperative – Especially in the U.S.							
Solutions	**Collaborators**						**Time**
	Regulators	**Clinical Trial Sponsors**	**Clinical Trial Sites & Organiza-tions**	**Clinical Research Groups**	**Patient Groups**	**Medical Research Groups**	**Short,- Mid-, or Long-Term Endeavor**
Recommendation #1: Unlock the Potential of Network Approaches							
Collectively define specifics of operational and regulatory compliance processes for network approaches, ideally harmonized with international standards	✓ (FDA, ICH)	✓	✓	✓			
Recommendation #2: Improve Enrollment and Study Start Up Timelines by Advancing More Patient-Centric, Rather Than Trial-Centric, Approaches							
Improve Referral and Screening Processes							
Develop pre-competitive platform approaches to enable patients to be screened for a broad array of trials and referred to the trial(s) that best fit their needs		✓	✓	✓	✓	✓	
Build More Opportunities to Enroll in Oncology Clinical Trials							
Develop and promote policies and best practices that enable sites with little to no experience to build clinical trial capacity	✓ (FDA)	✓	✓	✓			
Clarify regulatory policies and remove barriers to the effective deployment of tools that support decentralized approaches such as remote monitoring and in-home data collection	✓ (FDA , ICH)	✓	✓	✓	✓		
Explore pre-competitive approaches to support sustainable long-term community engagement and educational models that enable patients and families to better locate and evaluate clinical trial opportunities		✓	✓	✓	✓	✓	

Time Endeavors: Short-Term Mid-Term Long-Term

Improving Oncology Site Activation, Enrollment & Study Start Up Timelines Is Imperative – Especially in the U.S.

Solutions	Collaborators						Time
	Regulators	Clinical Trial Sponsors	Clinical Trial Sites & Organiza-tions	Clinical Research Groups	Patient Groups	Medical Research Groups	Short,- Mid-, or Long-Term Endeavor
Reduce Patient and Family Financial Burdens							
Promote policies that reduce financial burdens on patients and advocate for the removal of statutes that prohibit or limit trial sponsors' ability to reduce patient burdens	✓ *Federal and state policy leaders (some solutions may require statutory changes)	✓	✓	✓	✓	✓	
Recommendation #3: Explore Common Budget and Contract Processes for U.S. Trial Sites							
Develop base-line budget and contracting processes for U.S. clinical trials and establish an iterative process for publishing case studies and capturing data about how best to manage site budget and contract variabilities		✓	✓	✓			
Develop data-driven processes for clinical trial costs and how to structure budgets		✓	✓	✓			
Develop and implement streamlined payment processes		✓	✓	✓			
Develop a framework that promotes best practices and enables widespread adoption of AI and platform approaches to streamline clinical trial budget and contract processes		✓	✓	✓			
Develop common compensation for physician referrals and physician participation in clinical trials (*e.g.*, reimbursement for time spent and execution of specific tasks)		✓	✓	✓			
Develop multi-sponsor and site budget and contract templates		✓	✓	✓			
Develop actionable recommendations for building collective resources and funding for site budget and contract needs, including outsourcing certain functions		✓	✓	✓			

Improving Oncology Site Activation, Enrollment & Study Start Up Timelines Is Imperative – Especially in the U.S.

Solutions	Collaborators						Time
	Regulators	Clinical Trial Sponsors	Clinical Trial Sites & Organiza-tions	Clinical Research Groups	Patient Groups	Medical Research Groups	Short,- Mid-, or Long-Term Endeavor
Recommendation #4: Ensure Utilization and Deployment of Technology Yield Benefits							
Develop an industry-wide approach to site technology demands, such as a framework for determining when sites may select/use their own vendors/technology resources or when deploying a specifically requested technology is required		✓	✓	✓			
Recommendation #5: Align on Training Needs and Minimize Duplicative Activities							
Construct collective, or at least aligned, training requirements to minimize duplicative clinical trial site activities		✓	✓	✓			

Importance of Global Harmonization of Science-Based Approaches to Clinical Trial Representativeness Targets and Generalizability Analyses

Solutions	Collaborators						Time
	Regulators	Clinical Trial Sponsors	Clinical Trial Sites & Organiza-tions	Clinical Research Groups	Patient Groups	Medical Research Groups	Short,- Mid-, or Long-Term Endeavor
Recommendation A: Develop Scientific Principles for Representativeness Requirements and Adapt for Disease-Specific Application							
Define scientific principles for representative requirements and statistical and data quality principles to drive analyses of safety and effectiveness in trials with patients from different countries and different racial and ethnic groups that include activities to provide context for specific diseases	✓ (FDA , ICH)	✓			✓	✓	(Active Clinical Trials) Mid-term (Future Clinical Trials
Develop processes that enable timely inspections aligned with other clinical research requirements	✓ (FDA)	✓	✓				(Active Clinical Trials) Mid-term (Future Clinical Trials)
Recommendation B: Manage Heterogenous and Continuously Evolving Standard of Care by Articulating Contextualized Regulator/Researcher Understandings for Discrete Cancer Areas							
Develop and advance regulatory understandings about how to address evolving and varying standards of care for oncology patients in MRCTs that consider clinical context/discrete disease area, patients' needs, and operational feasibility	✓	✓			✓	✓	(Active Clinical Trials) Mid-term (Future Clinical Trials)

2. Recommendations from Expanding Regulatory Agility and Evidentiary Integrity in Developing Treatments for Rare Diseases

Table 1. Topics, Challenges, and Recommendations

Developing Regulatorily-Acceptable Patient-Relevant Endpoints				
Recommendations	**Challenges**	**Next Steps***	**Product**	**Stakeholders**
1. Enable Mutual Recognition of Endpoint Qualifications	• Misaligned Validation and Qualification Timelines with Patient Need • The Precedent Paradox That Limits Acceptance of Novel Approaches	FDA and key regulatory agencies collaborate with sponsors to develop processes for mutual recognition agreements	Mutual recognition agreements, data sharing platform that enables collaborative work between multi-regional regulatory authorities and sponsors	FDA, regulated industry, EMA, other key regulatory authorities
2. Establish Fit-for-Purpose Tiered Pathways for Patient-Relevant Endpoint and Biomarker Qualification	• The Precedent Paradox • Translation Gaps Between High-Level Principles and Real-World Operational Needs • Lack of Clarity on Pathways for Developing and Using Disease-Agnostic Endpoints and Measurement Tools	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Frameworks published by FDA	FDA, ICH, regulated industry, patient organizations, medical researchers
3. Advance Methodological Approaches for Patient Relevant Endpoints	• The Precedent Paradox • Translation Gaps Between High-Level Principles and Real-World Operational Needs • Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework (and potential guidance) published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, patient organizations (specifically including patients and caregivers), medical researchers, clinical research organizations
4. Collaboratively Explore and Promote Best Practices for Video- and Sensor-based Functional Assessments	• Translation Gaps Between High-Level Principles and Real-World Operational Needs	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, patient organizations, clinical research organizations, medical researchers
5. Establish Stakeholder/FDA Consultations for Rare Disease Endpoint Development	• Misaligned Validation and Qualification Timelines with Patient Need • The Precedent Paradox • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	FDA publication of new meeting mechanism and/or FAQ on best practices for scheduling and preparing for a dedicated rare disease endpoint meeting	FDA, regulated industry, patient organizations
6. Align Evidentiary Thresholds for Slowly Progressive Diseases	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers

7. Develop and Implement Training Programs on Data Collection for Patients and Caregivers	• Translation Gaps Between Principles and Operational Realities	Training program development for patient experience data reporting and collection	Training program deployed to clinical sites and to patient organization; patient organization to deploy training programs to patients and caregivers	Regulated industry, medical researchers, patient organizations, contract research organizations
8. Enable Use of Endpoint Triangulation and Composite Endpoints	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Endpoint Triangulation and Composite Endpoint Uncertainty	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers
9. Expand FDA Grants to Advance Composite Endpoint Methodological Approaches	• The Precedent Paradox • Endpoint Triangulation and Composite Endpoint Uncertainty	FDA to expand/prioritize funding	Grants provided; publication of funded studies	FDA
10. Support Development and Use of Disease-Agnostic Endpoints and Tools	• Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoint and Measurement Tool Development	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Inclusion in frameworks, case studies and peer reviewed publication for recommendations to: enable use of endpoint triangulation and composite endpoints; develop alignment on evidentiary thresholds for slowly progressive diseases; collectively explore, develop and disseminate methodological approaches for patient relevant endpoints; advance regulatory understandings for use of patient experience data to support endpoint acceptance; develop and enable fit-for-purpose tiered patient-relevant endpoint qualification; and establish stakeholder–FDA rare disease endpoint consultations	FDA, ICH, regulated industry, patient organizations, medical researchers
11. Establish Incentives for Large-Scale, Pre-Competitive Disease-Agnostic Data Collaboration	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Statutory and regulatory incentive proposals	FDA, regulated industry, medical researchers, patient organizations, data scientists
12. Create Function-Based, Domain-Driven Endpoint Libraries	• Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	A publicly available, government housed or government-adjacent, domain-based endpoint library	FDA, regulated industry, medical researchers, patient organizations

Optimizing Patient Perspective and Natural History Data Collection and Use

Recommendations	Challenges	Next Steps*	Product	Stakeholders
13. **Advance Best Practices for Responsible Rare Disease Data Sharing**	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, EMA/global regulators, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies
14. **Create Tiered Approaches for Natural History and Registry Data Acceptability**	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies
15. **Clarify Evidentiary Requirements for Utilizing Legacy Registry Data**	• The Precedent Paradox • Translation Gap Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies

Advancing Shared Understandings of Evidentiary Expectations and Regulatory Requirements

Recommendations	Challenges	Next Steps*	Product	Stakeholders
16. **Promote Shared Understandings of Scientific Principles Supporting Flexible Evidentiary Strategies**	• Lack of Clarity on Scientific Principles Driving Different Evidentiary Expectations and Regulatory Requirements	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Frameworks updated and/or published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers
17. **Enable Early Identification and Resolution of Issues for Novel Endpoints and Trial Designs**	• Lack of Clarity on Scientific Principles Driving Different Evidentiary Expectations and Regulatory Requirements	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Rare disease meeting best practices or guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers (including statisticians), patient organizations

18. Enable Rare Disease Clinical Trials to Learn and Adapt More Effectively	• Successfully Incorporating Learnings Generated During a Clinical Trial	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Best practices and/or framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers (including statisticians)
19. Define Evidentiary Thresholds for Rare Disease Second- and Third-Line 3rd Line Treatments	• Successfully Incorporating Learnings Generated During a Clinical Trial	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers

Improving Cross-Stakeholder Knowledge Management

Recommendations	Challenges	Next Steps*	Product	Stakeholders
20. Build a Cross-Stakeholder, AI-Enabled, Rare Disease Knowledge Management System	• Difficulty Translating Siloed Knowledge Management Improvements into Broader Public Benefit	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	A publicly available, easily searchable, government housed (or government-adjacent), AI-enabled rare disease knowledge management system	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies

* **Bold and Purple Text = Potential Reagan-Udall Foundation for the FDA Led Activity**

3. Enhancing Early-Stage Drug Development in the United States

Consolidated Recommendations and Solutions

SOLUTIONS	STAKEHOLDER LEADS
Modernizing IND Requirements and Processes	
Recommendation #1: Adopt Risk-Proportionate IND Submission Requirements and Triage Review Processes	
a) Develop specific recommendations for risk-proportionate IND submission requirements and triaged review processes. Efforts could include: i. Developing and implementing risk-proportionate IND review timeline (e.g., 14-day IND review for well-characterized platforms, simple formulations, microdosing, exploratory INDs). ii. Developing and implementing a triaged IND classification based on drug risk vs. subject risk that determines the level of submission requirements and reviewer time. iii. Establishing principles and developing modality specific guidance that describes what data are required for low-, medium-, higher-risk INDs. iv. Developing FDA internal training and standard operating procedures (SOP) about how to triage FDA reviewer time based on need. b) Establish a dedicated first-in-human (FIH) specialist review unit at FDA for novel-modality or high-risk INDs, consolidating expertise currently distributed across multiple divisions. c) Invest in a specialized FIH-review workforce at FDA that delivers clear, consistent, and modality-aware early-phase regulatory expectations, reducing variable cross-division feedback.	**FDA:** Generate guidance documents; implementation of review, training, and organization reforms **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #2: Advance Rolling IND Submissions	
a) Adopt a modular, rolling IND review pathway: a sequential nonclinical package and Phase-appropriate CMC data package enabling first-cohort dosing. Elements of the pilot could explore: i. Cases where FIH dosing could proceed based on non-GLP studies and GMP-like materials. ii. An Investigator Brochure (and draft study reports) to enable start of FIH plus SEND datasets submitted at a later date.	**FDA:** Develop and implement new pathway(s) implementation **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #3: Modernize Nonclinical Requirements and Practices	
a) Develop dose selection scientific principles that take into consideration disease severity and distinguishes first-in-healthy-humans needs from first-in-patient needs. b) Refine Project Optimus implementation through greater use of model-informed drug development (MIDD) and population PK modeling to optimize dose selection and escalation and address data gaps. c) Convene meetings among regulators, biopharmaceutical companies, CROs, and medical researchers to discuss how to advance the utilization of New Approach Methodologies (NAMs) and create a pathway for sponsors to secure endorsement to use a single species toxicology study including reliance on nonclinical platform data that can be carried forward to future IND submissions. This effort should include development and implementation of FDA internal training programs exploring a review posture in which applications are presumed adequate with in vitro/comparative biology data unless reviewers provide scientific rationale for an animal study and provide insight on which species is most predictive. The substance of these trainings may be strengthened with input from external experts. d) Formalize a structured pharm-tox reviewer rotation program across FDA divisions and centers to cross-pollinate risk-tolerance frameworks.	**FDA:** Develop and implement principles, rotation program **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations
Recommendation #4: Update and Streamline Chemistry, Manufacturing and Controls (CMC) Requirements	
a) Expand the January 2026 CBER CMC flexibility announcement into formal guidance covering cell and gene therapies, explicitly clarifying that cGMP under 21 CFR Part 211 is not required before Phase 2 or Phase 3, and extend analogous flexibility to other modalities when supported by risk-benefit determination. b) Streamline CMC content required for certain Phase 1 trials to allow short-term or accelerated CMC stability data with a scientifically justified shelf-life covering only the clinical dosing period, paired with a sponsor commitment to continue stability testing during the trial. This could be modeled after Belgium's Phase 1 CMC submission model. c) Issue a formal policy statement on cross-regional comparator characterization, enabling sponsors to rely on drug characterization accepted by EMA or other ICH regulators. d) Establish a risk-based pathway to waive or streamline routine Phase 1 CMC submission and review for defined categories, including: (i) products manufactured using well-established platforms or with extensive prior sponsor experience with analogous FDA submissions; (ii) products for serious, life-threatening, ultra-rare, or N-of-1 conditions; (iii) very low-risk study designs such as microdosing studies and exploratory INDs; and (iv) simple formulations using known excipients and standard manufacturing processes (e.g., immediate-release oral tablets, aqueous solutions). e) Routinely publish an anonymized list of common CMC deficiencies and remediation pathways.	**FDA:** Publish policy, guidance and top 10 list; implement new pathway **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #5: Clarify Required IND Data	
a) Publish updated, modality-specific guidance and case studies clarifying minimum IND data expectations for Phase 1 INDs by scenario (e.g., small molecule, oligonucleotide, oncology, viral vector, cell therapy). b) Develop Q&A-style or decision-tree guidance tools that supplement narrative guidance documents, allowing sponsors to arrive at a transparent articulation of minimum CMC and nonclinical package requirements for their specific Phase 1 study based on modality, therapeutic area, prior human data, and study design.	**FDA:** Develop and publish guidance, case study and decision-tree publications **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #6: Improve "Safe-to-Proceed" and "Clinical Hold" Communications	
a) Establish "Safe-to-Proceed" coordinated processes within FDA including: i. Consistent, timely notifications across all review divisions within the 30-day statutory period. ii. Written rationale on all clinical holds that identify the deficiency, the regulatory basis, and the recommended resolution path. b) Reframe 30-day IND notification terminology for pre-dosing actions where no patient has been dosed and the action is informational from "clinical hold" to "notice of additional information required."	**FDA:** Develop and implement new processes and communications, organizational reform **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #7: Enable Greater Use of a Phase 1 Clinical Trial Notification (CTN) Pathway	
a) Develop and implement FDA's proposed Clinical Trial Notification pathway for certain Phase 1 trials.	**FDA:** Develop and implement pathway **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Modernizing Phase 1 Clinical Trials and Tools	
Recommendation #8: Enable Use of Innovative Clinical Trial Designs	
a) Review and update innovative clinical trial design guidance and develop accompanying FAQs that: i. Provide early-phase-specific examples for Bayesian adaptive dose-escalation, seamless Phase 1/2 designs, and biomarker-stratified expansion cohorts. ii. Permit adaptive Phase 1 designs to allow modifications to dose range, escalation increment, indication focus, and therapy line based on emerging clinical data—without protocol amendment but operating under pre-specified guardrails. b) Modernize Form FDA 1572 to reflect decentralized-element trial models and facilitate state-level alignment on telehealth-delivered research activities.	**FDA:** Develop and issue new documents **Collaborators on Substance:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #9: Increase Inclusion of Patient Perspectives in Early-Stage Drug Development	
a) Develop a review matrix that documents when patient perspectives were used to inform toxicology requirements.	**FDA:** Develop and publish review matrix **Collaborators** Biopharmaceutical companies
Recommendation #10: Develop Artificial Intelligence (AI) Enabled Sponsor-Facing Decision Support Tools	
a) Develop a meeting series for FDA and stakeholders to collaborate on developing and implementing knowledge management initiatives that can serve as the basis for the development of AI-enabled sponsor-facing decision support tools.	**Reagan-Udall Foundation for the FDA:** Develop and implement meeting series **Collaborators:** Biopharmaceutical companies, FDA; medical researchers, patient organizations
Optimizing FDA–Sponsor Early-Stage Engagements and Processes	
Recommendation #11: Enhance Pre-IND Meeting and IND Review Best Practices	
a) Standardize pre-IND meeting outputs to produce three documented conclusions: (i) required; (ii) optional but potentially helpful; and (iii) unnecessary for the proposed initial study. Treat pre-IND alignment on specific elements (e.g., inclusion/exclusion criteria) as commitments the IND review will not revisit without written justification. b) Pilot an IND-stage sponsor "safe-to-proceed checkbox" enabling sponsors to elect minimum-comment Phase 1 safety review, deferring forward-looking protocol, endpoint, and development-strategy feedback to later meetings; FDA's clinical hold, safety reporting, and inspection authorities fully preserved. c) Pilot an iterative, weekly Australian-style engagement model for pre-IND and IND-stage interactions. This effort could be supported by updating and reviving the Target Product Profile (TPP) as a sponsor-facing tool rather than a binding guidance designed to support a more iterative engagement model that surfaces assumptions earlier and provokes structured dialogue before formal IND submission.	**FDA:** Develop and implement approach **Collaborators on Substance:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #12: Capture IND Regulatory Decision-Making Trends	
a) Support stakeholder efforts to capture evidence and identify trends of consistent or differing feedback on distinct IND topics, such as BIO's BRIDGE platform, designed to capture regulatory trend data from sponsors describing their interactions with the FDA. b) Convene disease-area or modality-specific shared learning forums (e.g., rare disease, chronic disease, gene therapy) to share information about pre-IND meetings, IND submission packages, and IND reviews and discuss what has worked, what has not, and where expectations have shifted. c) Encourage FDA to develop internal mechanisms to capture trends of consistent or differing feedback on specific IND related topics and cross-pollinate learnings.	**Reagan-Udall Foundation for the FDA:** Institute meeting series **FDA:** Implement internal trend/ knowledge management **Collaborators:** Collect trend data and platform development
Recommendation #13: Incentivize Fit-for-Purpose IND Submissions and Engagements	
a) Develop incentives for high-quality, appropriately scoped IND submissions. For example, FDA should develop best-practice templates and Pre-IND checklists that, when followed, provide the sponsor reasonable assurance that regulatory expectations have been met, and IND-stage changes would be limited to instances of emerging safety or scientific knowledge. b) Establish an expedited pre-IND pathway for U.S. biotech sponsors developing truly novel modalities or molecule types, modeled on EMA's PRIME early-entry program.	**FDA:** Implement meeting reform and new pathway implementation **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Building a Streamlined and Dedicated U.S. Phase 1 Infrastructure as Part of a National Clinical Trial Infrastructure and Coordinating Strategy	
Recommendation #14: Build and Fund a Dedicated Network of Phase 1 Capable Clinical Trial Sites	
a) Direct NIH and FDA to develop and/or designate FIH/Phase 1 centers of excellence, including using a single IRB process and other streamlined site activation processes. b) Provide federal funds to support a national Phase 1 clinical trial infrastructure.	**FDA and NIH** **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #15: Create a National Phase 1 Coordinating Strategy (as part of an overall National Clinical Trial Strategy)	
a) Create a National Phase 1 Coordinating Strategy. The strategy should include: i. Establishing a National Biotechnology Coordination Office. ii. Jointly publishing a U.S. Life Sciences Competitiveness Roadmap with explicit benchmarks by NIH and the FDA. iii. Formally designating the U.S. life sciences industry as a national treasure that defines clinical trial infrastructure as a critical national infrastructure, enabling cross-agency resource allocation and sustained capital investment consistent with other strategically significant sectors. iv. Commissioning and annually maintaining a national Phase 1 clinical trial site inventory capturing site type, modality capability, activation and enrollment metrics, workforce composition, and continuity of trial activity. v. Creating a nation-wide communication campaign on the value of early-phase trial participation paired with expanding community-practitioner education about clinical trial opportunities. vi. Continuing investment in NIH basic research funding. vii. Developing of a competency/certification framework for research nurses, coordinators, and pharmacists (with loan-repayment incentives). viii. Developing a centralized investigator database consolidating investigator credentials, training records, and site qualifications to eliminate duplicative sponsor-specific training. *NOTE: These solutions should be part of an overall national clinical trial infrastructure and coordinating strategy.*	**FDA and NIH** **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #16: Streamline IRB and Site Activation Processes	
a) Finalize single-IRB rule. b) Develop a national strategy to support single and centralized IRB capacity needs including: i. Requiring an sIRB process. ii. Developing enhanced Phase 1 IRBs that could be used as an outside sIRB authority. iii. Creating a pool of FDA certified regulatory auditors who could augment centralized IRB processes at clinical trial sites by providing technical CMC/safety seals of approval. iv. Embedding FDA subject-matter experts within major academic medical centers to support centralized IRB processes at clinical trial sites. c) Pilot a hybrid FDA-IRB parallel-review model with FDA to focus on scientific sufficiency and safety and IRB focus on trial protocol, informed consent, and ethical considerations, both of which are completed on an agreed-upon parallel timeline rather than the current sequential approach. d) Develop standardized informed consent templates for Phase 1 studies to reduce site-by-site consent negotiation delays. e) Extend financial and career incentives to clinician-investigators (e.g., reimbursement for time spent and execution of specific tasks). (See Box 1.) f) Expand rural and underserved Phase 1 access via academic satellite locations and hub-and-spoke models with limited but defined FIH/FIP capabilities (e.g., lower-risk/less-complex studies).	**FDA:** Finalize sIRB rule, implement parallel-review model **FDA and NIH:** Implement national sIRB capacity and strategies **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations **Biopharmaceutical Companies and Clinical Trial Sites:** Develop standardized templates and hub-and-spoke models **Stakeholders:** Advocate for financial incentives and clinical trial reimbursement reforms **Trial Sites:** Develop standardized templates and hub-and-spoke models **Biopharmaceutical Companies and Clinical:** Advocate for financial incentives and clinical trial reimbursement reforms
Mitigating Litigation Risk for Phase 1 Clinical Trial Sites	
Recommendation #17: Explore Safe Harbors and Insurance Reforms for FIH and Phase 1 Trials	
a) Explore federal safe harbors for Phase 1 clinical research sites and examine insurance coverage practices for potential reforms that would help mitigate litigation risks.	**Congress:** Enact safe harbor and master insurance laws **Collaborators:** FDA, NIH, Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations