REAGAN-UDALL FOUNDATION FOR THE FDA

Affecting the Aging Trajectory:

Regulatory Constructs for Gerotherapeutic Drug, Biologic & Device Development

Public Meeting Summary

July 2026

ARPA-H & XPRIZE Foundation provided funding for this meeting

REAGAN-UDALL FOUNDATION FOR THE FDA

About the Reagan-Udall Foundation for the FDA

The Reagan-Udall Foundation for the FDA is an independent 501(c)(3) created by Congress to advance the mission of the FDA to modernize product development, accelerate innovation, and enhance product safety. The Foundation works to advance regulatory science, support development and dissemination of reliable information, and facilitate engagement and information exchange.

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Executive Summary

Advances in geroscience, the study of the biological mechanisms that drive age-induced health decline, have intensified interest in whether interventions targeting aging biology might extend healthspan, delay multiple chronic diseases, and help older individuals retain function longer. However, no FDA-approved pathway currently exists for an aging indication, and key questions remain about what endpoints, populations, and regulatory constructs could credibly support development in this area. These questions have become increasingly timely as large translational efforts such as XPRIZE Healthspan, a $101 million USD global competition designed to accelerate development of aging-targeting therapeutics, and ARPA-H's PROSPR program, a new $144 million USD government investment in infrastructure, endpoint development, and early testing of healthspan interventions, begin generating data.

To begin this important conversation, the Reagan-Udall Foundation for the FDA, in collaboration with ARPA-H and XPRIZE Healthspan convened a public meeting on May 27, 2026 titled "Affecting the Aging Trajectory: Regulatory Constructs for Gerotherapeutic Drug, Biologic, and Device Development." The meeting brought together regulators, geroscience researchers, clinicians, trialists, funders, and product sponsors to examine whether and how FDA-regulated products might be developed to preserve function, reduce age-related decline, and extend healthspan.

The meeting focused on a central challenge: aging is a major risk factor for many chronic diseases, yet there is no FDA-approved indication for aging itself and no validated aging biomarker or accepted regulatory endpoint for gerotherapeutic claims. Participants explored possible alternatives, including frailty related measures, all-cause mortality, disability-free survival, multimorbidity endpoints, adult health curves, and intrinsic capacity as a multi-domain functional framework.

Several themes emerged. Speakers broadly agreed that healthspan is more meaningful than lifespan alone for patients and society, even though lifespan is easier to conceptualize and measure. Many participants emphasized that functional outcomes, how people feel, function, or survive, are currently more compelling anchors for clinical development than molecular aging biomarkers alone. The meeting demonstrated that evidence generation is already underway through foundational investments by NIH's National Institute on Aging, Hevolution Foundation, and others, now moved to urgency by large-scale initiatives such as XPRIZE Healthspan and ARPA-H's PROSPR program, both of which are testing interventions and building infrastructure for endpoint development, biomarker discovery, and longitudinal follow-up.

Participants also acknowledged major unresolved issues and areas where there is a lack of consensus. Some speakers strongly advocated for multi-domain functional constructs such as intrinsic capacity, while others questioned whether composite measures are sufficiently interpretable or convincing and urged greater attention to mortality, disability, or condition-specific endpoints. Participants also differed on how close the field is to translational readiness, with some emphasizing promising evidence from repurposed drugs and active trials, and others underscoring the continuing absence of settled regulatory constructs.

The meeting also highlighted the scale of current investment and activity. Speakers described rapid growth in federal and philanthropic support, candidate gerotherapeutic interventions, and increasing sponsor interest in age-related disease, frailty, immune, metabolic, and functional indications.

FDA participants and former FDA staff emphasized that the agency has mechanisms for engagement and that progress will depend on specific sponsor proposals, not just conceptual discussion. Existing tools (Investigational New Drug application meetings, biomarker qualification programs, clinical outcome assessment development, and disease-focused pathways) can support near-term movement, even in the absence of a direct aging indication.

Overall, the meeting reflected a field that is scientifically active, increasingly translational, and still, regulatorily emerging. It clarified both the momentum in geroscience and the work still required to define measurable, clinically meaningful, and practical pathways for gerotherapeutics development.

Introduction and Opening Remarks

Susan Winckler, Chief Executive Officer of the Reagan-Udall Foundation for the FDA, opened the meeting by framing it as a public forum for shared learning across sectors rather than a venue for policy setting or product-specific regulatory decision-making. She emphasized that the Foundation's role was to convene diverse perspectives to explore how geroscience might intersect with regulatory science and noted that the day's discussion was intended to help inform thinking rather than establish formal regulatory policy.

Opening FDA Perspective

The opening FDA framing was provided by Dr. Steven Kozlowski, Chief Scientist in the Office of the Commissioner. Kozlowski began the meeting within a long history of efforts to alter aging, then turned to present-day regulatory reality. He emphasized that aging is a major driver of chronic disease, yet there are no interventions with regulatory approval for an aging indication, and no aging biomarker has achieved validated or reasonably likely surrogate endpoint status.

> "The outcome most meaningful to patients and with the highest societal impact would be healthspan, not lifespan."
>
> DR. STEVEN KOZLOWSKI, FDA

Kozlowski also referenced the previously proposed TAME (Targeting Aging with Metformin) trial, noting that he was part of a meeting where FDA discussed its multimorbidity-prevention framework with investigators in 2015 [1]. This provided useful context for the day by demonstrating that FDA engagement with aging-related concepts is not entirely new, even as the field's scientific and translational activity has expanded significantly.

A notable conceptual element of his remarks was the question of whether aging might have a Spearman "g factor," a shared general factor analogous to the one proposed in cognition research. This framing introduced the possibility that aging might be reflected across correlated functional domains and helped set up a later discussion of intrinsic capacity and multi-domain endpoint frameworks.

Kozlowski stressed that while molecular aging markers remain valuable for exploratory use, functional outcomes are closer to what matters to patients. He maintained that measures such as mobility, strength, cognition, frailty, and related constructs may be better aligned with patient benefit than molecular signals alone. This emphasis on patient-relevant function became one of the strongest recurring themes of the meeting.

The Healthspan Imperative: Geroscience, Federal and Private Sector Investment, and the Evidence Base

The first session illustrated why geroscience is gaining momentum and why both public and private stakeholders are increasingly investing in healthspan-oriented development. Speakers described aging not simply as a background condition of life but as a biologically meaningful driver of vulnerability across multiple chronic diseases. The case was made that extending lifespan without addressing the burden of chronic disease leaves societies with a widening gap between years lived and years lived well.

James Appleby, Chief Executive Officer of the Gerontological Society of America, opened the session by reframing how aging should be understood. While public discussion often centers on the cost and consequence of an aging population, he emphasized that aging itself is a blessing, not a disease. The aim is not to resist aging, but to help people age in healthier ways and maintain their independence for as long as possible. Appleby distinguished between geriatric medicine, which focuses on the care of persons over 65, and geroscience. He suggested that insights from geroscience may eventually make it possible to target aging at a molecular level, delaying the onset of multiple chronic diseases simultaneously. He described this as a pivotal moment for the field. In his view, years of rapid progress since the founding of the NIH Geroscience Interest Group in 2012 have brought geroscience to a stage where action is both possible and necessary (Figure 1). With populations aging in the United States and globally, he stressed that the implications reach far beyond individual health, affecting broader societal and economic wellbeing. In his view, the opportunity now is to translate advances in aging biology into practical strategies that help people stay healthier for longer. At the same time, he urged caution in how these advances are described. Although some biological processes may be reversible at the molecular level, he suggested that phrases such as slowing or delaying aging are often more accurate and scientifically grounded than claims about reversing aging at the level of the person or population.

> "The country that enables their citizens to thrive, to fully engage, to be productive as they reach advanced age will reap enormous benefits."
>
> MR. JAMES APPLEBY, GERONTOLOGICAL SOCIETY OF AMERICA

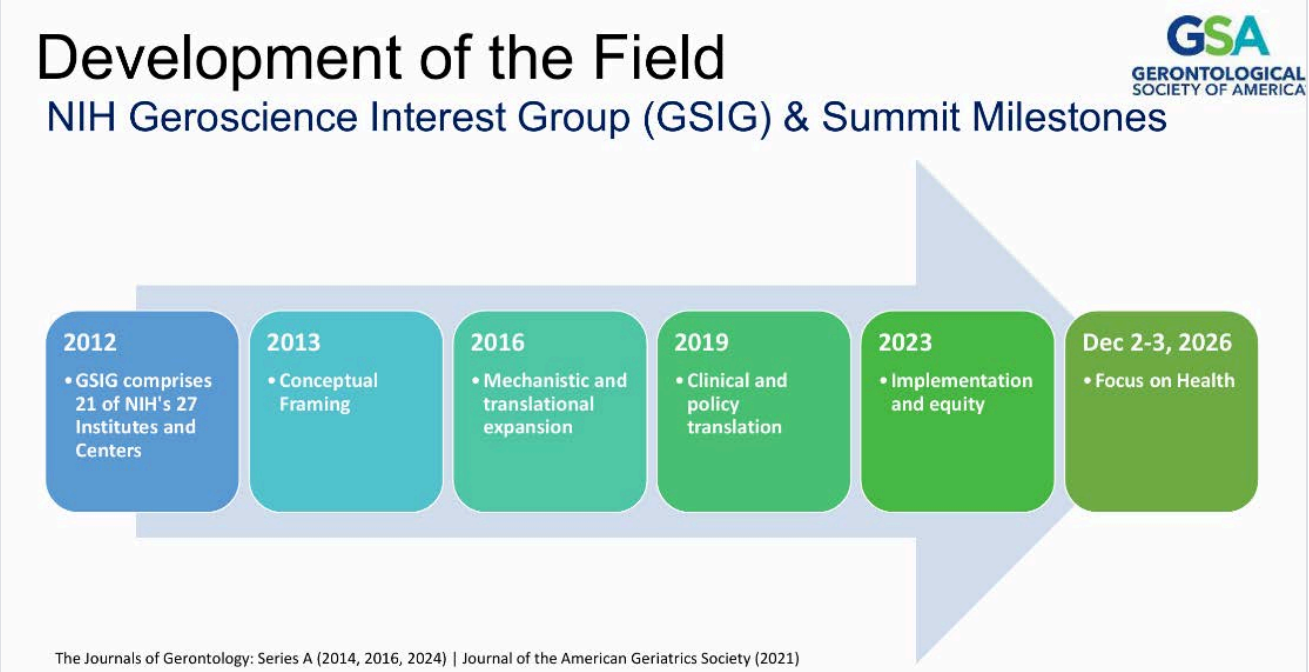

FIGURE 1. Representation of the major milestones since the founding of the NIH Geroscience Interest Group in 2012.

William Greene, Chief Investment Officer of Hevolution Foundation, framed the issue in economic and translational terms. He described the healthspan gap as a global challenge, with people living longer but often spending many additional years with multiple chronic diseases. Hevolution's role, as he described it, is to catalyze the field through funding discovery science, support for company formation, and strategic investment in infrastructure needed to move healthspan-oriented interventions into clinical testing.

Jamie Justice, Executive Director of XPRIZE Healthspan, described XPRIZE as both a competition and an evidence-generation platform designed to answer a basic translational question: if an intervention can improve how people age, how would the field know? She emphasized that this question is no longer theoretical. XPRIZE Healthspan is a $101 million award program within a broader $157 million effort, supported by approximately 20 sponsors, and, at the time of the meeting in DC, attracted 789 registered teams from 73 countries. In May 2026, 65 finals applicants with early-stage human trial data had advanced in the process, with at least 10 teams expected to move into one-year clinical trials this year. Justice highlighted both the urgency and the breadth of the work now underway, noting that the 2025 stage of competition includes candidate drugs, various biologics, devices, multimodal interventions, and functional foods, all aimed at improving healthspan-related outcomes (Figure 2). She also stressed that the competition is building centralized resources, including shared data infrastructure, coordinated laboratory support, and biobanking, with the goal of creating a durable evidence base for future biomarker development, endpoint refinement, and regulatory engagement.

> "The science is developing. It is maturing. We do have now some medicines and therapeutics that are ready for testing in humans."
>
> **DR. JAMIE JUSTICE, XPRIZE FOUNDATION**

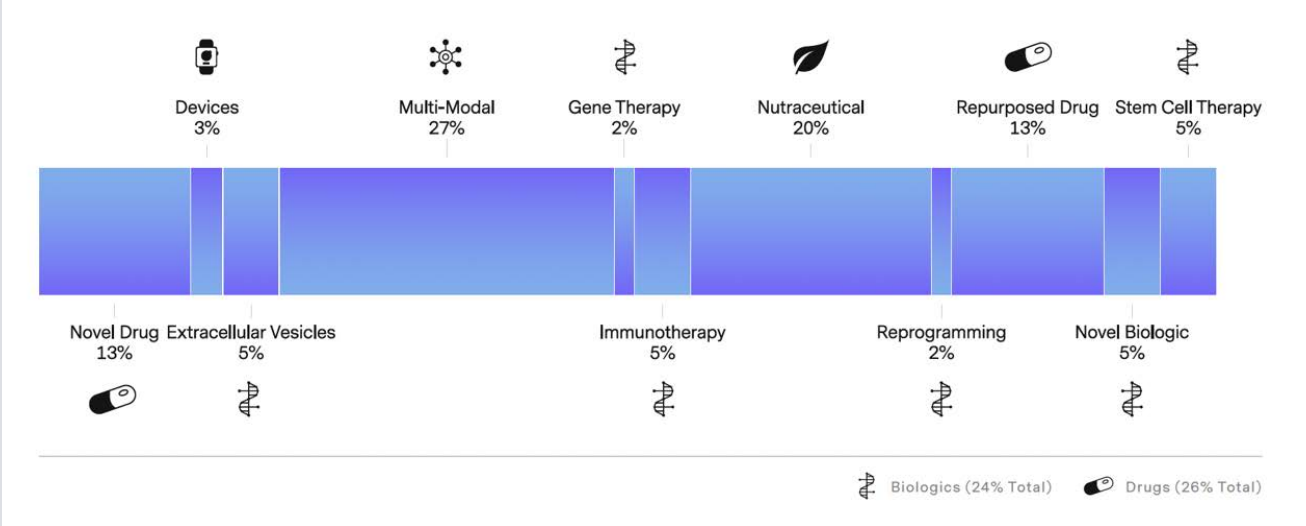

FIGURE 2. An example of the breadth of approaches from XPRIZE Healthspan candidate gerotherapeutics, which span FDA regulatory centers.

Andrew Brack, Program Manager in ARPA-H's Proactive Health Office, described the PROSPR program as ARPA-H's first major initiative focused directly on healthspan and framed it as a signal that the field is ready for acceleration. He emphasized that ARPA-H is not supporting aging research as a distant aspiration, but is investing in work intended to make gerotherapeutics development practically executable. With up to $144 million committed across seven teams, PROSPR is building the infrastructure needed to test whether healthspan-focused interventions can be measured, interpreted, and ultimately advanced toward regulatory use. Brack underscored that active teams are already moving toward formal FDA touchpoints, including work on intrinsic capacity-based clinical outcome assessments, at-home measurement tools, repurposed therapeutics, and next-generation interventions. In his framing, the urgency of the effort lies not only in the scale of the aging population, but in the fact that the field now has sufficient scientific, technical, and organizational momentum to begin generating the evidence needed to support real development pathways.

> "PROSPR will identify predictive and intervenable surrogates of hard endpoints to test therapeutics targeting aging directly in clinical trials."
>
> **DR. ANDREW BRACK, ARPA-H**

This session established that geroscience is no longer a niche scientific discussion. It is supported by demographic need, economic rationale, substantial philanthropic and federal investment, and a translational ecosystem actively moving toward clinical testing.

Landmark Evidence: What Aging Trials Have Taught Us

Although the regulatory path is still evolving, aging-related and geroscience-informed trials are not new. Speakers in this session examined what prior work has shown about candidate therapeutics, the strengths and weaknesses of different endpoint strategies, and the practical challenges of bringing these concepts into clinical development.

Nir Barzilai, Director of the Institute for Aging Research at Albert Einstein College of Medicine observed that aging biology itself drives chronic disease and should be targeted before overt disease develops. He used the hallmarks of aging as a mechanistic framework and then moved toward a more practical question: what should count as a true gerotherapeutic? To address that, he presented a structured, 12-point scoring preclinical and clinical evidence framework for evaluating existing interventions and highlighted several existing drug classes (SGLT2 inhibitors, metformin, GLP-1 receptor agonists, and bisphosphonates) that he felt may already demonstrate broad aging-related relevance. For example, SGLT2 inhibitors achieved a 12-point score, driven in part by ~40% reductions in mortality and up to 35-65% reduction in major adverse events such as hospitalizations and chronic disease progressions. He proposed that some of these therapies should be studied more directly for aging-related development.

> "Having an index, (deficit accumulation or frailty outcome)...provides coverage across all the age-related problems that one might have."
>
> **DR. STEPHEN KRITCHEVSKY, WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE**

Stephen Kritchevsky, Toby R. Alligood Endowed Professor in Geroscience at Wake Forest University School of Medicine, reviewed efforts such as TAME, frailty-oriented frameworks, and deficit accumulation models (Figure 3). He emphasized that geroscience continues to push against a biomedical system still largely organized around single diseases and disease-specific risk factors. He described several candidate endpoint families, including multimorbidity accrual, disability-free survival, frailty and deficit accumulation, mobility and cognitive decline, and biomarker-based strategies. Kritchevsky reasoned that a deficit accumulation index is ideal because it is responsive regardless of which age-related disease or conditions arise, and he pointed to the LOOK AHEAD study where the lifestyle intervention changed the index during the active intervention, years 1-8, and persisted an additional 8-years later [2]. He also noted the difficulty of moving from broad enthusiasm for geroscience to agreement on specific endpoints that are feasible, interpretable, and approvable.

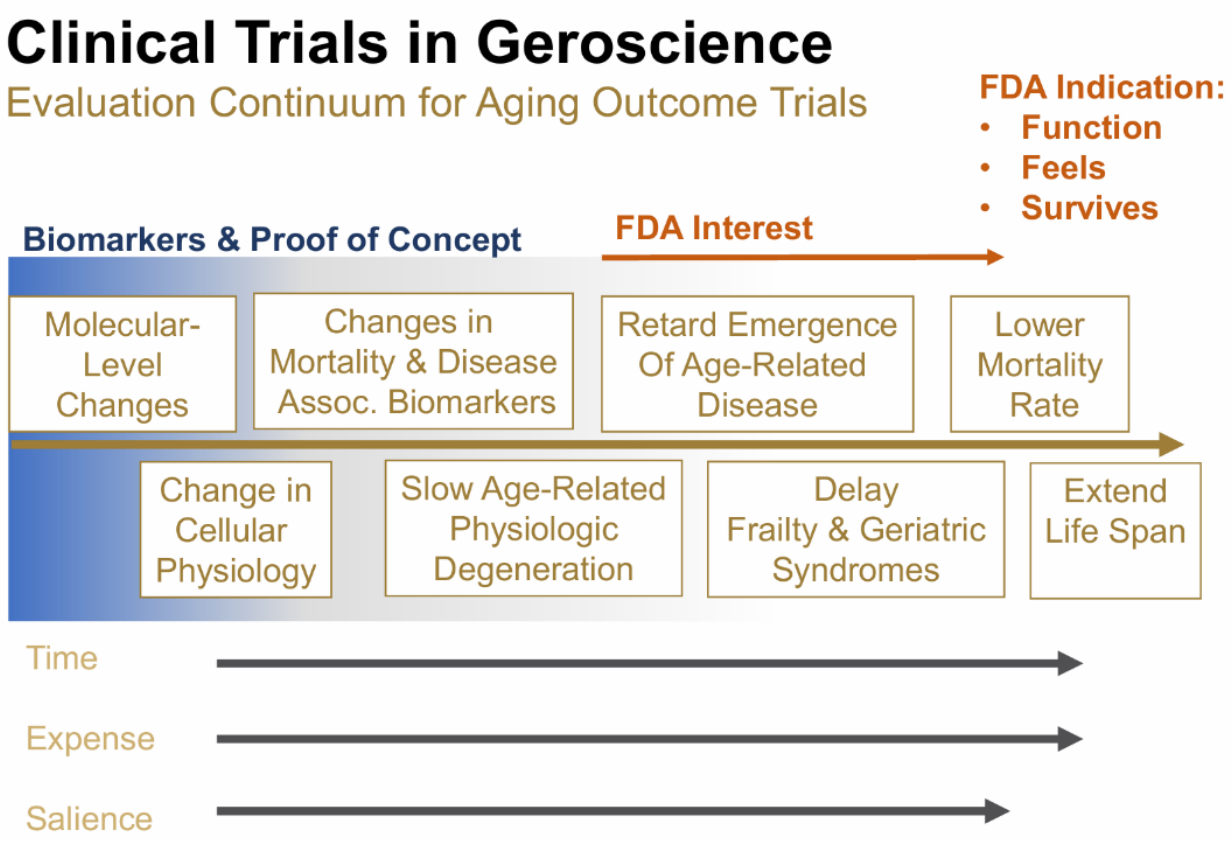

Figure 3. Dr. Kritchevsky presented the various types of geroscience outcomes on a continuum of increasing FDA interest, demonstrating that the most attractive are also the most expensive and lengthy.

Joan Mannick, Chief Medical Officer at Altos Labs, presented low-dose mTOR inhibitors as a case study in how an intervention targeting aging biology might first be advanced through a specific functional domain: immune function in older adults. She described studies showing improved influenza vaccine response, fewer respiratory infections, and upregulation of antiviral pathways under certain dosing conditions. At the same time, she noted that a later trial using symptom-based respiratory endpoints did not succeed, in part because the endpoint captured a broad set of respiratory symptoms that were not always specific to laboratory-confirmed infection and was therefore difficult to interpret consistently. Her talk illustrated how promising biology can be undermined when the chosen clinical endpoint is not specific enough to distinguish meaningful treatment effects from background variability in a medically complex older population.

Eric Morgen, Co-founder and Chief Operating Officer of BioAge Labs, described the current approach that companies must take for gerotherapeutic development: a disease-first development strategy, in which therapies targeting aging biology are advanced first through recognized disease indications while retaining broader healthspan ambitions. He argued that given the length of time it takes for a drug to go through clinical trials for multiple sequential approvals, and the prohibitive cost of long, large prevention-type trials to show healthspan extension, this paradigm fails to capture the vast majority of clinical value and financial return for a gerotherapeutic. His conclusion was that gerotherapeutics are massively under-incentivized relative to their potential societal benefits. He also discussed a policy concept associated with the Kitalys Institute that would create a more direct healthspan-oriented pathway to fix the incentives. The drafted legislative framework would provide a pathway for therapies, drugs, or biologics aimed at addressing or preempting two or more age-related or chronic diseases, a tiered, conditional market access or provisional approval system, and "fit-for-purpose" and step-up evidentiary standards. This was presented as a conceptual future mechanism rather than existing regulatory policy.

> "Clinical development on drugs for aging actually is under-incentivized dramatically relative to the potential."
>
> DR. ERIC MORGEN, BIOAGE LABS

This session showed that aging-related development already has translational anchors, including existing human outcome data, multimorbidity and frailty frameworks, and concrete domain-specific examples such as immune function. It also reinforced that endpoint selection remains one of the most significant unresolved barriers in the field.

Toward Regulatory Constructs: Intrinsic Capacity, Mortality, and Multi-Domain Endpoints

Focusing on how aging-related changes might be measured in ways that are clinically meaningful, practically feasible, and potentially relevant to regulatory development, this session is where the clearest disagreements emerged.

David Allison, Chief of Nutrition and Director of the USDA Children's Nutrition Research Center at Baylor College of Medicine challenged the field to be more careful about what it claims to measure. He noted that statements such as "aging is a disease" are social judgements rather than scientific claims and warned that the field should be wary of leaning too heavily on composites which are often poorly defined and may be unconvincing if they can be endlessly recombined or reinterpreted. While admitting that lifespan studies are limited by the practical concerns of the very lengthy trials they require, he maintained that lifespan remains the most credible endpoint (Figure 4). He described work in his lab with rodent models where very large cohorts, but shorter mortality rate studies (noting how many animals died during a certain period) corresponded well to lifespan studies (that wait for the death of the majority of animals). Allison reasoned that human studies of mortality rate, could similarly signify lifespan outcome changes given enough participants, allowing a more defined endpoint than composites, while being shorter in duration than a traditional lifespan study.

Endpoint	Strength	Limitation
Total mortality	Directly measures survival Clinically meaningful	Rare → requires large, long trials Mixes different causes of death
Disability-free survival	Patient-relevant (function + quality of life)	Hard to define consistently Can change over time
Specific diseases	Measurable; regulatory relevance	Does not reflect overall aging One disease ≠ whole system
Multimorbidity	Reflects multiple age-related conditions	Depends on which conditions are included
Frailty (Indices/ Phenotype)	Captures overall aging/vulnerability	No standard measure May be insensitive to change

FIGURE 4. David Allison's summary of the strengths and weaknesses of various endpoints that could be used in geroscience trials.

John Beard, Irene Diamond Professor at Columbia University Mailman School of Public Health, offered a different perspective: that current measures such as overt disease, disability, and mortality often occur too late in the life course to be ideal endpoints for detecting and intervening on aging-related changes early. He presented intrinsic capacity as a multi-domain construct encompassing cognition, locomotion, sensory function, psychological function, and vitality domains, and suggested that it may eventually support the creation of adult health curves analogous to pediatric growth curves. He showed data demonstrating that in multiple large population-based studies, intrinsic capacity declines with age and predicted future mortality and care dependence, regardless of multimorbidity, age, and socio-economic status. He highlighted the use of intrinsic capacity in global studies and the existing ICD code for age-related decline in intrinsic capacity as a signal of its successful use, but also acknowledged that work remains to be done to formalize practical and sensitive measures for use in regulatory-grade clinical trials.

Kelly Anderson, Scientific Engineering and Technical Advisor at ARPA-H, described the results of an ARPA-H convened consensus effort focused on whether and how intrinsic capacity might be used in geroscience trials. She explained that the meeting brought together a multidisciplinary group of key opinion leaders with expertise spanning geriatrics, geroscience, clinical trials, biostatistics, industry, and regulation. Importantly, the group included both supporters and skeptics of intrinsic capacity as an endpoint framework, and most participants had prior experience using one or more related measures in human studies. Anderson emphasized that the group did not conclude that intrinsic capacity is ready as a validated surrogate endpoint or universal primary endpoint. Instead, the consensus position was that intrinsic capacity should be treated as a concept for a function-based, multi-domain clinical outcome framework that requires disciplined testing. The group favored a near-term approach centered on domain-specific measures rather than a single global score, with particular attention to community-dwelling older adults experiencing early decline but not yet advanced disability. Anderson described a proposed Version 1 framework that includes core measures for each intrinsic capacity domain, with the goal of improving consistency across studies and generating the evidence needed for future regulatory discussions (Figure 5). She framed this as a practical starting point: not a final answer but a way to move the field from conceptual interest in intrinsic capacity toward disciplined, comparable, and trial-ready use.

CORE IC TRIAL BATTERY V1.0

DOMAIN	MINIMUM CORE MEASURES
Locomotor	Gait speed; SPPB (continuous preferred)
Cognitive	MoCA + processing speed/executive task
Psychological	Depression + anxiety/distress measure
Sensory	Visual acuity + hearing assessment
Vitality	Candidate measures such as grip strength, respiratory function, appetite/nutrition, fatigue/energy

FIGURE 5. The measures determined to be most practical for assessing intrinsic capacity now in geroscience trials according to the ARPA-H-led consensus meeting participants.

Nicholas Schork, Research Director, Longevity and Precision Medicine, HonorHealth Research Institute, focused on the idea that gerotherapeutics development may require new trial methods and analytic strategies in addition to new endpoints. He stated that if aging-related interventions are expected to produce heterogeneous, multi-domain effects across individuals, then the field should not rely exclusively on conventional large parallel-group trial designs built around single outcomes. Instead, he advocated for approaches that can better capture variation in response and more directly test whether an intervention is producing clinically meaningful change across multiple dimensions. He emphasized the value of defining response thresholds in advance, so that trials can distinguish responders from non-responders in ways that are both clinically interpretable and statistically useful.

He also highlighted single-case experimental designs, or N-of-1 approaches aggregated across individuals, as one possible way to generate richer information about how different people respond to an intervention. In addition, he drew attention to the emerging concept of real-time clinical trials, in which accumulating data can be used to support earlier decisions about whether a study is showing sufficient evidence of response. More broadly, Schork urged the field to take advantage of newer statistical and digital approaches to build a more flexible and responsive clinical trial paradigm, rather than forcing gerotherapeutics questions into development models designed for narrower and more uniform disease settings.

This session made clear that the clinical trial design for gerotherapeutics trials is still being debated, mirroring the complexity of aging biology itself. While intrinsic capacity is emerging as a promising framework for some participants, it is not yet a settled standard. The value of the session lies not in producing consensus, but in surfacing the real scientific and conceptual disagreements, particularly between which endpoints would be best for gerotherapeutics trials, that will need to be resolved through further evidence generation.

XPRIZE Healthspan and ARPA-H PROSPR Awardees: Evidence Building Now

Shifting from conceptual discussion to active development programs, this session illustrated that the field is already building evidence in humans through a range of coordinated efforts across XPRIZE and ARPA-H's PROSPR.

Among the XPRIZE Healthspan finalists, David Brown of Stealth BioTherapeutics, presented work from the "Mitochondrial All-Stars" team focused on elamipretide, a mitochondria-targeting peptide already approved for an ultra-rare disease. He described data from an open-label Phase 2A study evaluating outcomes such as knee extensor strength, six-minute walk, and cognition, and emphasized the role of mitochondrial dysfunction as a possible driver of aging-related decline. Zahi Fayad, representing Mount Sinai's "NYC-VITA 2030" team, described a multimodal intervention combining exercise, spermidine, and rapamycin. He framed the approach around inflammatory and macrophage-related biology and outlined a 12-month, 200 participant trial design incorporating functional and biomarker measures. Blake Rasmussen, from the UT San Antonio Barshop Institute, presented an early-stage device-based, low frequency ultrasound approach, including published preclinical mouse data and an ongoing first-in-human pilot study.

Among the ARPA-H PROSPR awardees, Brianna Stubbs, representing a Stanford/Buck Institute team, described a detailed regulatory and infrastructure plan involving an in-clinic intrinsic capacity clinical outcome assessment, a computational PROSPR intrinsic capacity score anchored to long-term outcomes, and an at-home testing kit intended for the FDA de novo classification pathway. James Peyer of Cambrian Bio, described work on a selective mTORC1 inhibitor and emphasized both mechanistic and phenotypic biomarker strategies, as well as what he characterized as a metabolic shortcut to preventative development through existing obesity-related regulatory precedent. George Kuchel of the UConn Center on Aging, part of the University of Rochester team, and in partnership with Brown and the University of Texas Galveston, together with Transposon, presented their plan to repurpose reverse transcriptase inhibitors from HIV treatment to target LINE-1 retrotransposon activity as a possible aging-related mechanism.

TABLE 1 · AWARDEE PROGRAMS AT A GLANCE

TEAM	PROPOSED TRIAL FOCUS	KEY ENDPOINTS OR MEASURES	DEVELOPMENT STAGE
XPRIZE / David Brown, Stealth BioTherapeutics	Elamipretide, a mitochondria-targeting peptide intended to improve mitochondrial function and bioenergetics	Knee extensor strength, six-minute walk, cognition; safety and tolerability	Open-label Phase 2A study completed; finalist application submitted for longer placebo-controlled trial
XPRIZE / Zahi Fayad, Mount Sinai	Combined exercise, spermidine, and rapamycin; designed to target inflammatory and macrophage-related aging biology	VO2 max, cognitive processing speed, immune function measures, additional secondary functional & biomarker endpoints	Finalist trial design described; 12-month, 200-participant study planned
XPRIZE / Blake Rasmussen, UT San Antonio Barshop Institute	Low-frequency ultrasound intended to influence senescence-related biology and improve physical function and lifespan-related measures	Physical function testing, cognition, DNA methylation age, senescence-associated markers, body composition and strength measures	Preclinical lifespan-extension data published; first-in-human pilot ongoing
ARPA-H/PROSPR / Brianna Stubbs, Stanford, Buck Institute and collaborators	Development of an intrinsic capacity score suite and at-home intrinsic capacity test kit for broad healthspan measurement	PROSPR – Intrinsic Capacity (updated during the PROSPR program)	Program underway; FDA COA submission initiated; decentralized studies planned
ARPA-H/PROSPR / Cambrian Bio, James Peyer	TOR-101, a selective mTORC1 inhibitor intended to preserve geroprotective effects while avoiding mTORC2-associated immunosuppression	PROSPR – Intrinsic Capacity (updated during the PROSPR program)	Preclinical / translational development underway
ARPA-H/PROSPR / George Kuchel, UConn Center on Aging, University of Rochester	Censavudine (TPN-101), a reverse transcriptase inhibitor repurposed from HIV research to target LINE-1 retrotransposon activity	PROSPR – Intrinsic Capacity (updated during the PROSPR program)	Preclinical / translational development underway

These examples demonstrated that the field is actively testing interventions in humans, generating real-world multi-domain datasets, and building infrastructure that could support future regulatory engagement. They also underscored that the candidate product space is diverse, spanning drugs, devices, biologics, and multimodal approaches.

Regulatory Landscape: What Pathways Exist and What Constructs Are Needed

In this session, former FDA officials and FDA voices discussed how existing regulatory tools might be applied in the gerotherapeutics space and where the principal uncertainties remain.

Former FDA personnel Sandra Kweder and Alexander Fleming emphasized that familiar regulatory questions still apply. They stressed the importance of clearly defining the indication, identifying the target population, understanding the benefit-risk profile, selecting endpoints that can support labeling, and determining how long a therapy must be used and with what safety consequences. Kweder made the point that although "well-tolerated" may be acceptable for certain disease-targeting drugs, that sentiment is not enough for gerotherapeutics, especially when therapies may be used chronically or preventatively in generally healthy people where risk tolerance is lower. Further, it was noted that there is a considerable lack of regulatory clarity around chronic interventions in general, which gerotherapeutics might need for lifelong efficacy.

Fleming highlighted the fact that FDA has engaged with some of these questions before, citing prior TAME-related discussions, earlier public comments from former Director of the Center for Drug Evaluation and Research at the FDA, Janet Woodcock, and former FDA Commissioner, Robert Califf's invitation for the field to propose specific endpoints. Current FDA participants reinforced that the agency already has multiple mechanisms for engagement, including IND meetings, qualification pathways, clinical outcome assessment development, and disease-specific review interactions.

The discussion also underscored the need to distinguish among exploratory biomarkers, target-engagement markers, and surrogate endpoints intended to support approval. It was noted that biomarkers and clinical outcome assessments can be developed for defined contexts of use, but such development still requires specificity regarding population, intervention, and intended claim. Fleming offered that intrinsic capacity is attractive due to the face validity of the functional endpoints the comprise this composite, such as the ability to walk further, while noting that programs like PROSPR are needed to validate these measures. Fleming expressed skepticism that mortality or formal lifespan endpoints are likely to be practical in the near term, while Kweder indicated that she was not sure she agreed, citing earlier opinions by David Allison.

Overall, the session clarified that FDA has tools that can be used now, but progress will depend on specific sponsor proposals, clear contexts of use, and continued evidence generation.

TABLE 2 · EXISTING PATHWAYS AND HOW THEY MIGHT BE USED

PATHWAY	POTENTIAL USE	KEY CONSIDERATIONS
Sponsor-specific FDA engagement (e.g., pre-IND / IND meetings)	Discussion of a specific product, proposed indication, study population, dose, trial design, safety, and endpoints	Best suited when sponsor has a therapeutic candidate and focused questions, rather than a broad conceptual idea.
General FDA engagement (critical path–type discussions, etc.)	Discuss cross-cutting scientific or methods issues, that extend beyond one product	Useful when the issue is broader than a single sponsor program. Informs general thinking, not product-specific direction.
Clinical Outcome Assessment (COA) development / qualification	Develop patient-relevant functional measures, that could be used across trials	Requires concept of interest, context of use, evidence that assessment is meaningful, reliable, and validated in the intended population.
Biomarker development and qualification	Use of biomarkers for enrichment, risk stratification, pharmacodynamic readouts, mechanistic support, or surrogate development	Requires defined biomarker, specific context of use, analytical validation, and evidence linking the biomarker to meaningful clinical outcomes. Surrogate use requires a much higher evidentiary bar.
Exploratory or target-engagement biomarker use within trials	Collection of biomarker data to show target engagement, support mechanism, refine dose selection, or generate hypotheses	Practical near-term use of biomarkers. Can be incorporated into many trials even when biomarkers are not yet validated for regulatory decision-making.
Disease-first or syndrome-based development pathways	Development through recognized diseases or age-related syndromes such as obesity, frailty, sarcopenia, immune decline, or other defined conditions	Requires recognized clinical framework, defined population, acceptable endpoints, and a standard benefit-risk assessment. May serve as a stepping-stone toward broader healthspan goals.
Accelerated approval–type thinking in narrower conditions	Use of earlier endpoints in serious age-related conditions or syndromes where a meaningful clinical need exists	Would require a condition, endpoint rationale, safety data, and a path for confirmatory evidence. Not yet an established route for gerotherapeutics.

Industry Perspectives: What is Needed from FDA to Bring Gerotherapeutics to Market

This session examined the sponsor perspective on entering the gerotherapeutics space. Panelists described real interest in the field, but also a familiar set of practical questions about development strategy, evidence expectations, and regulatory clarity.

Panelists included Joshua Diamond of GSK, David Glass of Regeneron, Jill Lee of Novo Nordisk, and Evan Mills of Olink, part of Thermo Fisher. Together, they described the scientific appeal of the field and the uncertainty that still surrounds the path to approval.

> "I think the government could get involved more proactively to really get a well-powered approvable set of biomarkers that could have real value for the field."
>
> DR. EVAN MILLS, OLINK, PART OF THERMO FISHER

Sponsors raised questions about what target indication should be pursued, how to distinguish pathologic from physiologic aging, what endpoints would be acceptable, how to justify long-term safety in preventative populations, and how to select dose when the outcomes of interest may take years to emerge.

Several panelists also emphasized that the field needs stronger and more practical outcome frameworks. Glass expressed that the field may sometimes undervalue direct biologic effects that are already clearly meaningful. Using age-related muscle loss as an example, he questioned whether preserving muscle mass might itself be sufficient evidence of benefit in some settings and criticized six-minute walk test as a noisy and motivation-sensitive endpoint. Diamond drew on frailty and transplant experience to highlight how difficult it can be to agree even within narrower clinical communities on what constitutes the right measure of decline. Lee pointed to prediabetes as an analogy for a clinically meaningful but regulatorily unsettled intermediate state. Mills raised the question of whether future biomarker regulation might eventually accommodate algorithmic, multi-marker, or AI-aggregated outputs rather than only traditional reductionist approaches.

> "There has to be some sort of agreed, harmonized way that we're collecting the data, measuring the data... all shooting for the same endpoints or biomarkers."
>
> DR. JILL LEE, NOVO NORDISK

The panel also identified areas where collaboration might be useful, including shared longitudinal datasets, endpoint harmonization, home-and digital-based measures, and biomarker development. Participants also acknowledged that real-world sponsor incentives may limit the extent of precompetitive data sharing.

This session reinforced that industry interest in gerotherapeutics exists, but stronger progress will likely require clearer endpoint expectations, more mature evidence frameworks, and infrastructure that reduces uncertainty while still allowing sponsor-specific development.

Next Steps to Designing Workable Regulatory Constructs for Gerotherapeutics

The closing discussion brought together current FDA staff (Jeffrey Siegel, Office Director in CDER, Lisa Yanoff, Deputy Director in CDER, and Justin Penzenstadler, Acting Associate Director in CDER), former regulators, ARPA-H, XPRIZE, and industry participants, who helped ground the conversation in the practical realities of development and review. FDA panelists emphasized that the agency is prepared to engage, but that progress will depend on specific, well-defined proposals. Rather than waiting for a perfect or universally accepted framework, they encouraged sponsors and other developers to come forward with a defined product, a defined population, a proposed endpoint strategy, and focused questions tied to the stage of development. They also underscored that existing mechanisms for engagement already exist, including sponsor-specific meetings, review-division interactions, and qualification pathways, and that these can be used now.

> "It's people who don't want to be patients that we're ultimately working for."
>
> **DR. ALEXANDER FLEMING, KITALYS INSTITUTE**

FDA participants drew clear distinctions among different kinds of tools and evidence. Functional measures that directly capture how patients feel or function were discussed as especially attractive because they may be more immediately meaningful and may require less inferential work than biomarkers. Biomarkers were described as important but more dependent on context of use and longer-term validation. FDA participants also reinforced that safety, dose selection, and manufacturing considerations remain essential parts of development in this space, just as in any other area. The discussion also included a useful note of realism from Lisa Yanoff, who acknowledged the appeal of shared longitudinal datasets and precompetitive collaboration, but cautioned that such data sharing can be difficult in practice. Her observation served as a reminder that while shared infrastructure is often described as a major need for the field, the incentives and operational realities of sponsor participation may complicate how easily such resources can be built and sustained.

> "When you measure things that are face-valid 'feels, functions, and survives', there's much less validation that is needed. As you consider developing IC, that should be your prime directive."
>
> DR. JUSTIN PENZENSTADLER, CDER, FDA

Beyond these FDA perspectives, the closing discussion highlighted several practical next steps. Jamie Justice made two explicit requests. First, she called for a formal multi-stakeholder convening to define the evidentiary requirements for an approvable non-disease indication related to aging, with participation that includes international perspectives as well as patient and consumer voice. Second, she called for an FDA workshop focused specifically on clinically meaningful, multi-domain functional endpoints, so that the evidentiary foundation for such endpoints can begin to be built while data are still being generated rather than after development programs are underway. Justice also referenced a preliminary, modified Delphi consensus survey, where early results from XPRIZE's global advisors, judges, and contestants suggests that many of them favor function-based, non-disease-oriented approaches, with endpoints centered on immune aging, physical function or mobility, and cognitive function, as well as intrinsic capacity or related constructs as frameworks, while many opposed mortality as a primary endpoint and epigenetic clocks as a single biomarker. Justice emphasized that these observations were not ready to serve as formal field consensus, but that they anticipate a formal version with additional experts also included, to be available in the coming months.

Another concrete next step idea came from Justin Penzenstadler, who noted that ICH E19, the guideline on selective safety data collection, may be underutilized in this area. He suggested that for repurposed drugs with already established safety profiles, this approach could support leaner safety data packages and help reduce the logistical and cost burden of gerotherapeutic development. Andrew Brack suggested that frailty could serve as a near-term stepping-stone indication within more familiar regulatory structures. FDA participants and former regulators pointed to earlier examples, such as bone mineral density in osteoporosis and non-invasive markers in MASH, as illustrations of how qualification pathways can mature when paired with clear clinical development need. Alexander Fleming also recommended that, over time, these questions may benefit from discussion in an ICH context given their likely global relevance.

The closing session suggested that the next phase of work should be both practical and iterative. The strongest message was that progress is likely to come from combining sponsor-specific development efforts with broader evidence-building around functional outcomes, biomarkers, and trial methods. The involvement of current FDA participants made clear that the agency is open to engagement now, while also reinforcing that the burden remains on the field to bring forward specific, scientifically credible proposals.

Summary

This meeting demonstrated that geroscience is no longer merely conceptual. It is now supported by substantial investment, active clinical development, coordinated evidence-generation programs, and increasingly detailed regulatory engagement. At the same time, the field still lacks a direct aging indication, a validated healthspan surrogate, and settled consensus on the best outcome frameworks for development.

Several themes recurred throughout the day. Healthspan was consistently presented as more meaningful than lifespan alone. Functional outcomes currently provide the clearest bridge between aging biology and patient benefit. Specific sponsor-regulator engagement was repeatedly emphasized as essential. Shared infrastructure, especially longitudinal data, endpoint harmonization, and remote or at-home measurement tools, was described as increasingly important to accelerate progress.

Just as importantly, the meeting showed that the field is still working through real disagreements, about composites, mortality, collaboration, and how close the science is to practical readiness. Preserving those disagreements is important to accurately reflect the meeting as one of shared learning rather than settled consensus. Overall, the meeting advanced the discussion by clarifying both the opportunities and the unresolved questions that will guide future gerotherapeutics development.

APPENDIX A

Meeting Agenda

Affecting the Aging Trajectory: Regulatory Constructs for Gerotherapeutic Drug, Biologic, and Device Development

Wednesday, May 27, 2026 · 10am – 4pm (eastern) · Hybrid Public Meeting

10am

Welcome & Opening Remarks

Susan C. Winckler, RPh, Esq., CEO, Reagan-Udall Foundation for the FDA
Steven Kozlowski, MD, Chief Scientist, Office of the Chief Scientist, Office of the Commissioner, FDA

10:20am

The Healthspan Imperative: Geroscience, Federal and Private Sector Investment, and the Evidence Base

- James Appleby, BSPharm, MPH, Chief Executive Officer, Gerontological Society of America
- William Greene, MD, Chief Investment Officer, Hevolution Foundation
- Jamie Justice, PhD, Executive Director, XPRIZE Healthspan, XPRIZE Foundation
- Andrew Brack, PhD, Program Manager, PROactive Health Office, ARPA-H

10:45am

Landmark Evidence: What Aging Trials Have Taught Us About Endpoints, Populations, and Feasibility

- Nir Barzilai, MD, Director, Institute for Aging Research, Albert Einstein College of Medicine, President of the Academy of Geroscience
- Stephen B. Kritchevsky, PhD, Professor, Gerontology and Geriatrics Internal Medicine, Wake Forest University School of Medicine
- Joan Mannick, MD, Chief Medical Officer, Altos Labs
- Eric Morgen, MD, MPH, FRCPC, Chief Operating Officer, BioAge Labs

11:30am

Toward Regulatory Constructs: Intrinsic Capacity, Adult Health Curves, and Multi-Domain Endpoints

- David B. Allison, PhD, Chief of Nutrition and Director, USDA Children's Nutrition Research Center, Baylor College of Medicine
- John Beard, MBBS, PhD, Irene Diamond Professor, Columbia University Mailman School of Public Health
- Kelly Anderson, PhD, Scientific Engineering and Technical Advisor, ARPA-H
- Nicholas Schork, PhD, Director, Quantitative Medicine & Systems Biology, HonorHealth Research Institute

12:15pm

Lunch

1:05pm

XPRIZE Healthspan and ARPA-H PROSPR Awardees: Evidence Being Built at Scale

Introductions by Justice and Brack

XPRIZE HEALTHSPAN PRESENTERS

- David A. Brown, PhD, Chief Scientific Officer, Stealth BioTherapeutics
- Zahi A. Fayad, PhD, Lucy G. Moses Professor of Medical Imaging and Bioengineering, Icahn School of Medicine, Mount Sinai
- Blake B. Rasmussen, PhD, Professor and Chair, UT San Antonio Long School of Medicine

ARPA-H PROSPR PRESENTERS

- Brianna Stubbs, PhD, Director of Translational Science, Buck Institute for Research on Aging
- James Peyer, PhD, Founder & CEO, Cambrian Bio
- George A. Kuchel, MD, CM, FRCP, Director, UConn Center on Aging, University of Connecticut

2:05pm

Regulatory Landscape: What Pathways Exist, Where They Break Down, and What Constructs Are Needed

- Sandra Kweder, MD, Principal, Drug and Biological Sciences, Eliquent
- G. Alexander (Zan) Fleming, MD, President, Kitalys Institute

2:25pm

Industry Perspectives: What Product Sponsors Need from FDA to Bring Gerotherapeutics to Market

- Joshua Diamond, MD, MSCE, Medical Director Clinical Development, Respiratory Early Pipeline Unit, GSK
- David J. Glass, MD, Vice President, Research, Aging/Age-Related Disorders, Regeneron
- Jill Lee, JD, Senior Director, Regulatory Policy & Intelligence, Novo Nordisk
- Cindy Lawley, PhD, Senior Director, Population Health and Scientific Strategy, Olink, part of Thermo Fisher Scientific

3:05pm

Next Steps to Designing Workable Regulatory Constructs for Gerotherapeutics

- Andrew Brack, PhD, Program Manager, PROactive Health Office, ARPA-H
- G. Alexander (Zan) Fleming, MD, President, Kitalys Institute
- Jamie Justice, PhD, Executive Director, XPRIZE Healthspan, XPRIZE Foundation
- Jill Lee, JD, Senior Director, Regulatory Policy & Intelligence, Novo Nordisk
- Justin Penzenstadler, PharmD, Acting Associate Director, Office of Cardiology, Hematology, Endocrinology, and Nephrology, Office of New Drugs, CDER, FDA
- Jeffrey Siegel, MD, Office Director, Office of Drug Evaluation Sciences, Office of New Drugs, CDER, FDA
- Lisa Yanoff, MD, Deputy Director, Office of Cardiology, Hematology, Endocrinology, and Nephrology, Office of New Drugs, CDER, FDA

3:55pm

Closing Remarks

4pm

Adjourn

ARPA-H and XPRIZE Foundation provided funding for this meeting.

APPENDIX B

References

[1] N. Barzilai, J. Crandall, S. Kritchevsky and M. Espeland, "Metformin as a Tool to Target Aging," *Cell Metabolism*, pp. 1060-1065, 2016.

[2] U. C. S. F. E. S. H. H. P. A. B. T. E. M. Evans JK, "Long-term Impact of a 10-Year Intensive Lifestyle Intervention on a Deficit Accumulation Frailty Index: Action for Health in Diabetes Trial.," *J Gerontol A Biol Sci Med S*, 2023.

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