THE ALLIANCE FOR
LONGEVITY INITIATIVES

The Multi-Disease Therapeutic Designation

An FDA Pathway for the Shared Biology of Chronic Disease

For inclusion in the PDUFA VIII Reauthorization

Prepared by The Alliance for Longevity Initiatives

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Executive Summary

The Food and Drug Administration has built an expedited drug development apparatus that has, over the past three decades, transformed how American medicine reaches patients. Breakthrough Therapy Designation, Fast Track, Accelerated Approval, Priority Review, and the Regenerative Medicine Advanced Therapy designation together have meaningfully shortened drug development timelines and reshaped the economics of oncology and rare disease. But these pathways share a common architecture: they assume one drug, one disease.

That architecture does not fit a class of investigational therapies now emerging from academic and industry pipelines — geroprotective compounds designed to intervene in the biological mechanisms that drive multiple chronic diseases of aging. Companies developing these therapies must currently navigate separate FDA review divisions for each indication, with inconsistent endpoint expectations and duplicative trial requirements. The result is years of avoidable delay, hundreds of millions in duplicative cost, and a chilling effect on the private investment needed to bring the field to maturity.

This whitepaper proposes the Multi-Disease Therapeutic Designation (MDTD): a new, separate expedited designation under 21 U.S.C. §356, modeled on Congress's creation of RMAT (Regenerative Medicine Advanced Designation) and LPAD (Limited Population Pathway for Antibacterial and Antifungal Drugs) as distinct provisions within the FDA's expedited-program architecture. Under the proposal, a sponsor would qualify for MDTD if its investigational therapy is intended to address biological mechanisms common to two or more serious age-related chronic diseases, and preliminary clinical evidence indicates that the therapy has the potential to address unmet medical needs for those diseases.

The proposal:

- Requires no new appropriations and creates no new office or program.
- Does not lower FDA's safety or efficacy standards for approval.
- Creates a new, RMAT-like expedited designation for multi-disease therapies.
- Carries direct precedent: Congress established Breakthrough Therapy in 2012 (FDASIA) and later added RMAT and LPAD as separate pathways through the 21st Century Cures Act of 2016.

The PDUFA VIII reauthorization — covering FDA fiscal years 2028 through 2032, with technical negotiations concluded in May 2026 and the bill due to Congress by January 2027 — is the natural legislative vehicle.

Chronic conditions drive roughly 90 percent of the nation's $4.9 trillion in annual healthcare spending; nearly half of Medicare beneficiaries live with four or more of them. A regulatory pathway purpose-built for therapies that target the shared biology behind those conditions is not a peripheral reform. It is among the highest-leverage, lowest-cost interventions available to Congress in this reauthorization cycle.

1. The Problem

1.1 The Shared Biology of Aging Drives Most Chronic Disease

For most of the twentieth century, biomedical science treated chronic diseases as discrete entities: cardiovascular disease was a problem of the heart and vasculature, type 2 diabetes a problem of metabolism, Alzheimer's a problem of the brain, cancer a problem of cell-cycle regulation. The institutions of biomedical research —

including the FDA's review divisions — were organized accordingly.

Over the past two decades, geroscience has demonstrated that this organizational logic does not match the underlying biology. The major chronic diseases of aging share a common set of mechanistic drivers — the so-called hallmarks of aging — including genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, dysregulated nutrient sensing, altered intercellular communication, chronic inflammation, and additional hallmarks added in more recent reviews.

These hallmarks interact and amplify one another. Mitochondrial dysfunction generates reactive oxygen species that damage DNA, accelerating genomic instability. Genomic instability triggers cellular senescence, which propagates chronic low-grade inflammation through pro-inflammatory cytokines, which in turn drives vascular damage, insulin resistance, and neurodegeneration. The clinical diseases differ; the upstream biology is convergent.

This understanding has produced a growing class of investigational therapies — geroprotective compounds — that target hallmark biology rather than disease-specific pathology. Senolytic drugs designed to clear senescent cells. mTOR inhibitors that modulate nutrient sensing. NAD+ precursors aimed at mitochondrial function. Metformin, repurposed in the Targeting Aging with Metformin (TAME) trial as the first multi-disease prevention trial designed around shared aging biology. Each of these candidates is being evaluated against multiple chronic disease endpoints simultaneously.

1.2 The Regulatory Architecture Was Built for a Different Era

The FDA's drug review apparatus is organized by indication. The Center for Drug Evaluation and Research operates separate review divisions for cardiology, oncology, endocrinology, neurology, and the other major clinical domains. A sponsor seeking to demonstrate that a drug reduces incidence of cardiovascular disease, type 2 diabetes, and dementia must, today, build three separate development programs, navigate three sets of pre-IND interactions, design three sets of pivotal trials around three sets of endpoints, and submit data to three review divisions that may not share a common framework for interpreting the underlying mechanism of action.

This is not an indictment of the agency. The structure was designed for an era in which drugs were, in fact, developed one disease at a time. It is no longer well-matched to a category of therapies whose central premise is that a single mechanism produces benefits across multiple diseases. The practical consequences are substantial:

- **Duplicative trial cost.** A sponsor pursuing two indications must run two pivotal trial programs, often with overlapping populations and only modestly different endpoints. Total Phase 3 cost can exceed $500 million for a single indication; pursuing two or three multiplies that figure.
- **Endpoint inconsistency.** Different review divisions have developed different expectations for surrogate endpoints, biomarker qualification, and composite outcomes. A trial designed to satisfy cardiology may not fully satisfy endocrinology.
- **Time-to-market delay.** Multi-indication development typically adds three to five years versus a single-indication program, during which patients go untreated and capital sits at risk.
- **Investment aversion.** Venture and pharmaceutical investment requires predictable regulatory pathways.

Where the pathway is unclear, capital flows to indications with cleaner economics — typically narrow oncology or rare disease — at the expense of broad, prevention-oriented programs that target the largest disease burden.

The cost of regulatory ambiguity, in other words, is not borne by sponsors alone. It is borne by patients who do not receive therapies, by Medicare and Medicaid trust funds that absorb the costs of unprevented chronic disease, and by an American biotech sector whose competitive lead in this category is eroding as Chinese, European, and Russian state-backed geroscience programs accelerate.

2. Current Pathways and Why They Do Not Fit

The FDA today offers five expedited programs, summarized in Table 1. None is well-fitted to multi-disease therapies targeting shared biological mechanisms.

Table 1. Existing FDA expedited programs and the proposed MDTD designation.

Program	Statutory basis	Qualifying criterion	Indication scope
Fast Track	FDAMA 1997; FDASIA 2012	Serious condition with unmet medical need	Single indication
Breakthrough Therapy	FDASIA 2012	Serious condition plus preliminary clinical evidence of substantial improvement over available therapy	Single indication
Accelerated Approval	FDAMA 1997; FDORA 2022	Surrogate endpoint reasonably likely to predict clinical benefit	Single indication
Priority Review	PDUFA 1992	Significant improvement in safety or efficacy	Single indication
RMAT	21st Century Cures 2016	Regenerative medicine therapy for serious condition plus preliminary clinical evidence	Single indication
Multi-Disease Therapeutic (proposed)	Proposed new provision within 21 U.S.C. §356 (parallel to RMAT and LPAD)	Therapy targets biological mechanisms common to two or more serious age-related chronic diseases; preliminary clinical evidence indicates potential to address unmet medical needs for those diseases	**Multi-indication**

All five existing programs assume a sponsor is pursuing a defined indication. None contemplates a therapy whose qualifying premise is action across multiple indications. A sponsor of a senolytic drug being evaluated against cardiovascular and renal endpoints simultaneously must today pick one indication as the lead for designation purposes and pursue the others sequentially or in parallel, without the benefit of cross-divisional coordination.

The Multi-Disease Therapeutic Designation (MDTD) is a separate, RMAT-like designation within FDA's expedited-program architecture for therapies whose qualifying premise is action across multiple serious age-related chronic diseases.

3. The Proposal

3.1 Separate Statutory Designation

We propose adding a new Multi-Disease Therapeutic Designation provision within 21 U.S.C. §356, parallel to the separate provisions Congress created for RMAT and LPAD. This structure creates a purpose-built pathway for therapies that target shared mechanisms across multiple serious age-related chronic diseases.

Under the MDTD provision, a drug would qualify if it is intended to address biological mechanisms common to two or more serious age-related chronic diseases, and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for those diseases. Such evidence may include effects on validated clinical endpoints, accepted surrogate endpoints, or qualified aging biomarkers relevant to the diseases addressed.

Drugs qualifying under the MDTD provision would receive designation-specific development benefits modeled on successful expedited-designation tools, including:

- Intensive FDA guidance on efficient drug development beginning as early as Phase 1.
- Senior FDA leadership engagement on novel trial design and endpoint questions.
- Rolling review of application submissions as sections are completed.

Critically, the MDTD provision does not lower the agency's standard for approval. Sponsors must still demonstrate safety and efficacy on the indications pursued. The provision changes how the agency coordinates and engages with a sponsor during development — not what the agency must conclude before approving a drug.

3.2 Qualifying Definitions

"Age-related chronic disease" includes cardiovascular disease, type 2 diabetes, Alzheimer's disease and related dementias, chronic kidney disease, idiopathic pulmonary fibrosis, osteoarthritis, sarcopenia, age-related macular degeneration, and certain cancers — a list to be specified in implementing guidance and updated periodically to reflect scientific consensus.

"Biological mechanisms common to two or more age-related chronic diseases" includes any of the recognized hallmarks of aging — including but not limited to cellular senescence, mitochondrial dysfunction, chronic inflammation, telomere attrition, and dysregulated nutrient sensing — as well as additional shared mechanisms identified in implementing guidance.

"Preliminary clinical evidence" follows an RMAT-style standard: evidence sufficient to indicate that the drug has the potential to address unmet medical needs for the serious age-related chronic diseases at issue. The evidence may come from Phase 1 or early Phase 2 data, supported by mechanistic, preclinical, and translational evidence demonstrating a plausible shared biological mechanism.

3.3 Cross-Divisional Review

The provision directs FDA, on granting an MDTD designation, to constitute a cross-divisional review team with a designated lead division. The lead division coordinates with each relevant review division and assembles a unified set of pre-IND, end-of-Phase-2, and pre-NDA interactions for the sponsor. The objective is a single, coherent development program that satisfies the regulatory requirements of each indication

addressed without duplicative bilateral interactions.

3.4 Additional Provisions

Guidance Directive. FDA shall issue draft guidance within 18 months of enactment on acceptable clinical trial designs and endpoints for multi-disease prevention claims, including composite endpoints, adaptive trial designs, and the qualification of aging biomarkers as surrogate endpoints under the existing Biomarker Qualification Program.

Interagency Coordination. The Director of the National Institute on Aging and the Commissioner of FDA shall establish a joint working group on aging biomarker qualification. The working group shall coordinate with relevant NIH research programs, including the TAME trial infrastructure, ARPA-H's PROSPR program, and the NIA Geroscience Network, to identify candidate biomarkers for qualification.

Congressional Reporting. FDA shall report to the House Energy and Commerce Committee and the Senate Health, Education, Labor, and Pensions Committee within 24 months of enactment, and biennially thereafter, on designation requests received and granted, the progress of guidance development, and recommendations for further statutory or administrative action.

4. The Economic and Strategic Case

4.1 Federal Fiscal Exposure to Chronic Disease

The fiscal stakes are unusually direct. Medicare and Medicaid together cover more than 140 million Americans and account for federal outlays approaching two trillion dollars annually. Their cost trajectory is driven, overwhelmingly, by chronic diseases of aging: cardiovascular disease, type 2 diabetes, Alzheimer's and related dementias, chronic kidney disease, and the major cancers. Chronic conditions, as the CDC reports, drive 90 percent of the nation's $4.9 trillion in annual healthcare spending. Nearly half of Medicare beneficiaries — 45 percent in 2022 — live with four or more chronic conditions simultaneously.

Multi-morbidity is the rule among Medicare beneficiaries, not the exception. Yet drug development — and the regulatory pathway structuring it — proceeds one disease at a time. A drug that reduces the incidence of three chronic conditions across an aging population compounds federal savings in ways that disease-by-disease drug development structurally cannot.

4.2 The Investment Catalyst Case

Congress established Breakthrough Therapy Designation in 2012, and FDA has since received more than 1,600 designation requests and granted more than 600 designations. By March 2026, 374 BTD-designated products had reached approval — a yield rate and a development-time compression unmatched by any prior expedited mechanism. Peer-reviewed analysis finds that the designation has, on average, reduced late-stage development time and meaningfully accelerated private R&D capital flow into the indications where it applies, most prominently oncology and rare disease.

The MDTD provision applies that same investment-catalyst logic to a category of disease burden orders of magnitude larger than rare disease and arguably larger than oncology. The relevant comparison is not the number of designations granted in the first years after enactment — a figure that, like BTD's early years, will

start modest — but the long-run signal it sends to capital: that the FDA recognizes a coherent pathway for multi-disease therapies, that the regulatory clock is calculable, and that the cross-divisional coordination problem has a statutory solution.

4.3 The Longevity Dividend

Independent academic modeling has placed the economic value of delayed aging at meaningful magnitudes. Research by Dana Goldman and colleagues published in Health Affairs estimated that a 20 percent slowing of biological aging would extend life expectancy at 51 by 2.2 years, almost all of those years in good health, with a fiscal value over fifty years of approximately $7.1 trillion — counting only the value of added healthy life, not the additional output of an older, healthier workforce.

These estimates depend on assumptions that will be revisited as data accumulates. But the directional finding is robust across multiple independent analyses: even modest progress against the shared biology of aging produces fiscal returns on a scale that dwarfs the cost of nearly any policy intervention designed to enable it. A procedural reform that improves the regulatory pathway for the therapies targeting that biology has, by any reasonable accounting, exceptionally favorable expected value.

4.4 Competitiveness

The United States is currently the global leader in geroscience research and in the early-stage biotech firms pursuing geroprotective therapies. That lead is real but not assured. China has invested heavily in geroscience infrastructure, including a standardized longevity medicine credential for physicians and growing public-sector research investment. More broadly, other countries are now increasing strategic investment in aging and healthspan science, including large-scale initiatives such as the recently announced multi-billion-dollar commitments in Russia.

The European Union's regulators have begun engaging with multi-disease prevention frameworks through programs such as PRIME. Regulatory clarity — or its absence — is one of the principal variables determining where the next generation of geroprotective drug development is anchored. The MDTD provision is a low-cost, high-leverage tool for ensuring that the next generation is anchored in the United States.

5. Precedent and Legislative Vehicle

5.1 Congress Has Created Pathways Like This Before

The Multi-Disease Therapeutic Designation is not a novel category of legislation. Congress has repeatedly used must-pass legislative vehicles to create or expand FDA expedited designations and pathways when existing structures did not fit an emerging therapeutic category.

The Breakthrough Therapy Designation itself was established by the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), which was the PDUFA V reauthorization. The designation was added through Title IX of that legislation, with statutory criteria worked out in the months preceding enactment by the committees of jurisdiction. There was no new appropriation. There was no new office. The provision became one of the most consequential drug-development reforms of the past three decades.

The Regenerative Medicine Advanced Therapy designation was established by the 21st Century Cures Act

of 2016, signed into law in December of that year. RMAT was a separate procedural reform: it created a new designation for a category of therapies — cell and gene therapies, tissue engineering products — that had not been contemplated when Breakthrough was originally drafted. The Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) was also established by the 21st Century Cures Act as a separate pathway for drugs addressing serious or life-threatening infections in limited populations with unmet needs.

RMAT and LPAD provide the closer statutory analogy for MDTD: Congress identified a gap in the existing architecture and added a targeted provision. The MDTD provision is the next iteration of that pattern for therapies targeting shared biology across multiple serious age-related chronic diseases.

5.2 PDUFA VIII Is the Right Vehicle

The PDUFA VIII reauthorization covers FDA fiscal years 2028 through 2032. FDA-industry technical negotiations concluded on May 15, 2026; the agreed package is moving toward congressional transmittal by the January 2027 statutory deadline, and reauthorization must be enacted by September 30, 2027 to avoid a funding lapse. The bill that ultimately carries the reauthorization will, on historical pattern, also carry substantive policy provisions added by the committees of jurisdiction — House Energy and Commerce and Senate HELP — beyond the FDA-industry technical agreement itself.

The MDTD provision fits that category cleanly. It is a procedural reform within FDA's existing authority and budget, structured as a separate expedited designation. It requires no new appropriation. It sits within the committees' jurisdiction. It has visible bipartisan support through the bipartisan Congressional Longevity Science Caucus. The legislative window for committee work runs from late 2026 through mid-2027. Now is the time to assemble bill text, build endorsement coalitions, and engage the relevant subcommittee staff.

6. Addressing Objections

Several lines of objection are foreseeable. Each can be addressed on the merits.

"This lowers the FDA's standard for approval."

It does not. The provision creates a designation that governs how the agency coordinates and engages with a sponsor during development — not the standard of safety or efficacy required for approval. Sponsors must still demonstrate substantial evidence of effectiveness and an acceptable safety profile on the indications pursued. The MDTD provision is a coordination mechanism, not an approval shortcut.

"FDA lacks the workload capacity to add another designation pathway."

FDA's workload is funded principally through user fees, and the PDUFA VIII technical agreement provides the resource framework for the program's next five years. The MDTD provision creates a separate expedited designation within the existing statutory architecture rather than a new office or program; the marginal workload is the cost of cross-divisional coordination on a modest number of designations annually, which falls well within the existing PDUFA staffing model. The Congressional Reporting provision provides a mechanism for Congress to revisit resourcing if real-world demand exceeds expectations.

"Aging biomarkers are not mature enough to serve as endpoints."

The MDTD provision does not depend on any specific biomarker being qualified as a surrogate endpoint. It permits sponsors to use validated clinical endpoints, surrogate endpoints, or qualified aging biomarkers

— whichever the relevant review divisions determine to be appropriate for the indications addressed. The Interagency Coordination provision and the Guidance Directive accelerate biomarker qualification work, but the designation itself does not wait on it.

"This will produce scope creep — sponsors will claim multi-disease intent on tenuous biological grounds."

The qualifying criteria require preliminary clinical evidence indicating potential to address unmet medical needs, mechanistic plausibility supported by translational data, and indications drawn from a defined list of serious age-related chronic diseases. FDA retains full discretion to deny designation requests that do not meet the criteria, as it does today for other expedited designation requests. The 60-day response window applies to both grants and denials.

"This favors large pharmaceutical companies."

The opposite is true. The cost of navigating multiple review divisions in parallel is precisely the kind of fixed regulatory cost that large incumbents can absorb and emerging biotechs cannot. The MDTD provision lowers that fixed cost. The category of firms with the most to gain — early-stage geroscience biotechs pursuing multi-indication development — is structurally disadvantaged by the current architecture.

7. Conclusion

The chronic diseases of aging are the largest and fastest-growing source of medical cost, disability, and mortality in the United States. They share, to a degree the regulatory architecture does not yet reflect, a common biological substrate. A growing pipeline of investigational therapies is built around that substrate. The single most consequential thing Congress can do — at zero additional cost to the Treasury, within an existing legislative vehicle, on a clear bipartisan footing — is to align the FDA's expedited pathway architecture with the biology those therapies are designed to address.

The Multi-Disease Therapeutic Designation accomplishes that alignment. It creates a new, RMAT-like expedited designation for a category of therapy the current architecture does not fit. It does not weaken FDA's standards. It does not require new appropriations. It carries direct precedent in FDASIA 2012 and, most directly, in the separate RMAT and LPAD provisions added by 21st Century Cures in 2016. It fits the PDUFA VIII reauthorization vehicle cleanly. And it positions the United States to lead — rather than follow — the largest emerging category of drug development in the world.

The Alliance for Longevity Initiatives respectfully urges the House Energy and Commerce Committee, the Senate HELP Committee, and the bipartisan Congressional Longevity Science Caucus to include the Multi-Disease Therapeutic Designation in the PDUFA VIII reauthorization package.

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