

## THE ALLIANCE FOR LONGEVITY INITIATIVES

# The Advanced Approval Pathway for Longevity Medicines (AAPLM)

Improving incentives for drugs that treat disease by targeting the mechanisms of aging

## **Executive summary**

Aging is the primary driver of chronic diseases that impair and kill millions of Americans each year. Drugs that target aging represent a powerful approach to treating these diseases, improving quality of life, reducing healthcare costs, and extending our economically productive lives. Despite the impressive progress being made in longevity biotech, the field remains under-incentivized relative to its immense potential benefits, highlighting the need for systemic changes that encourage businesses to develop medicines based on longevity science.

The proposed Advanced Approval Pathway for Longevity Medicines (AAPLM) aims to align economic incentives with the transformative health improvements that these breakthrough therapies can offer. The AAPLM's three core provisions, which mirror existing incentive programs established in other areas, will encourage investment in the field, increase financial incentives, and facilitate clinical development of novel drugs for diseases with significant unmet medical needs—all without imposing additional costs on taxpayers.

- 1) The <u>special approval track</u> offers a faster pathway to drug approval for longevity medicines, bringing them to patients more rapidly and accelerating profitability.
- 2) The <u>priority review voucher system</u> rewards sponsors who receive approval for a longevity medicine by granting expedited FDA review for a future drug, conferring a competitive advantage for the sponsor. Alternatively, vouchers can also be sold to, effectively transferring financial resources from established industry players to innovative companies focused on developing longevity medicines.
- 3) <u>Indication-by-indication patent term extensions</u> will be granted for each clinically approved longevity medicine, incentivizing companies to develop drugs not only for an initially selected disease, but also for broader approval to treat multiple chronic diseases of aging.

By promoting the development and approval of groundbreaking longevity medicines, the AAPLM has potential to improve individual health and autonomy, reduce healthcare costs, and generate substantial social and economic gains. Healthy aging benefits not only older individuals but also governments, insurers, employers, investors, and entrepreneurs, making it an essential policy for the future of healthcare and society as a whole.

## Aging: The primary driver of chronic disease

An overwhelming majority of Americans die of chronic diseases, typically after years of suffering and large expenditures of healthcare resources. These chronic diseases are driven by the underlying process of biological aging, and risk of developing these chronic diseases rises exponentially with age. Chronological age is the primary risk factor for the top nine causes of non-accidental death in the United States: heart disease, cancers, COVID-19, stroke, respiratory illnesses, Alzheimer's, diabetes, and kidney disorders.<sup>1</sup>

Collectively, these conditions cause the deaths of millions of Americans each year and impose enormous financial burdens on patients, their families, and our healthcare systems. More than 877,500 Americans die of heart disease or stroke every year, costing the healthcare system \$216 billion. Cancers are responsible for another 600,000 annual deaths, with costs predicted to surpass \$240 billion by 2030. Medical costs and lost productivity due to diabetes exceed \$327 billion. Chronic health conditions require ongoing medical care and treatment, incurring \$3.7 trillion in annual healthcare spending.<sup>2</sup> In addition, many older adults require intensive and specialized care, including long-term nursing care, putting additional financial pressure on the healthcare system and entitlement programs such as Medicare. For example, the cost of caring for the 5.7 million Americans with Alzheimer's disease, the sixth leading cause of death in the US, was \$305 billion in 2020, and is projected to exceed \$1 trillion by 2030.<sup>3</sup>

Over the past century, average longevity in the US increased by more than 30 years, due in large part to advances in medical care and technology. However, our healthspan—the amount of time we live free of disease—has increased more slowly. As a result, although we are living longer, we spend more years (and a growing proportion of our lives) in poor health, with the average American living 15 years with one or more serious illnesses.<sup>4</sup> As the proportion of older adults in the population grows, the impact of aging on the health of Americans and the demands placed on the US healthcare system will only become greater with time.

<sup>&</sup>lt;sup>1</sup> CDC stats on the leading causes of death in the United States

<sup>&</sup>lt;sup>2</sup> CDC stats on the social and economic costs of chronic disease

<sup>&</sup>lt;sup>3</sup> Alzheimer's disease - fact sheet

<sup>4</sup>https://publichealth.wustl.edu/heatlhspan-is-more-important-than-lifespan-so-why-dont-more-people-know-about-it/

Our current paradigm of chronic medical care is unsustainable, as it focuses on mitigating the progression of individual chronic diseases after they have arisen, with far less effort devoted to effectively curing or preventing these illnesses. This approach has led to escalating healthcare costs, impaired quality of life for patients, and increased use of healthcare resources. It is therefore essential that federal regulatory policy support a shift in the biotech and pharmaceutical industry towards developing medicines that address the root cause of chronic disease — the biological process of aging itself. By incentivizing the development of drugs that can treat or even entirely prevent multiple chronic diseases simultaneously, we can create a more sustainable and effective healthcare system that significantly improves the quality of life for Americans.

### Longevity medicine: Treating disease by targeting the mechanisms of aging

Although taxpayer-supported scientists and the pharmaceutical industry spend billions of dollars each year researching and developing therapies for individual age-related diseases, aging itself has long been considered inevitable and unalterable. This assumption is reflected in our national funding priorities, with less than 1% of the NIH budget devoted to studying the fundamental biological processes associated with aging.<sup>5,6</sup>

Notwithstanding modest federal support for research in this area, our knowledge of the biology of aging (geroscience) has accelerated in recent years, converging with advances in technology to place us at a unique position in history: the ability to treat disease by intervening in the aging process is within our reach. Studies conducted over the past two decades have demonstrated that it is possible to directly alter the biology of aging, and revealed small-molecule drugs that slow aging and extend the adult lifespan of laboratory mice by 20% or more.<sup>7,8</sup> Importantly, the compounds that slow aging in experimental animals almost always delay the onset of multiple age-associated diseases, increasing healthspan as well as lifespan.

Researchers of aging leverage such findings to understand how the biological processes of aging promote disease, and then apply that understanding to delay the onset and progression of

<sup>&</sup>lt;sup>5</sup> https://www.nia.nih.gov/about/budget/fiscal-year-2022-budget

<sup>&</sup>lt;sup>6</sup> https://www.nih.gov/about-nih/what-we-do/budget

<sup>&</sup>lt;sup>7</sup> https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344944/

<sup>8</sup> https://www.michiganmedicine.org/health-lab/new-drug-slows-aging-mice-what-about-us

age-associated health problems. The promise of this approach is commonly expressed as the "geroscience hypothesis": As people live longer, a growing proportion of our population suffer from more than one age-related condition. Because aging is the primary driver of chronic diseases, therapies that directly target aging physiology or reduce the rate of aging could alleviate, cure, or prevent multiple chronic diseases. Such interventions have the potential to dramatically decrease both mortality and healthcare costs, likely to a greater extent than even the complete cure of any one disease, while alleviating suffering and improving quality of life — revolutionizing healthcare for all Americans.

Inspired by these findings and our growing understanding of how human beings age, biotech companies have embarked on the mission of creating medicines that combat aging as a root cause of chronic disease. The therapies these companies seek to develop are termed "longevity medicines," so called because they are based on the science of longevity. The intent of these medicines is not to extend lifespan per se but to modulate the biological processes underpinning healthy longevity, extending the years of healthy lifespan (healthspan) while shortening years of sickness.

Dozens of longevity biotech companies have been founded over the past decade, and capital is entering the emerging sector at an accelerating pace, with \$5 billion committed in 2022 alone, demonstrating that investors understand the value proposition of longevity medicine.

## Incentives to develop longevity medicines are insufficient

Despite these promising trends, the incentives to develop longevity medicines do not adequately reflect the societal benefit of these therapeutics or the financial risks faced by the companies involved in developing them. Within the current US (and global) regulatory paradigm, new drugs must be evaluated for their efficacy in treating specific medical conditions. By contrast (as described above in our discussion of the geroscience hypothesis) medicines targeting the process of aging will have positive effects on multiple tissues and organs within the body, and therefore have the potential to treat, delay, or entirely prevent multiple age-associated diseases. Thus, the benefit of longevity medicines has the potential to improve the health of older Americans, national economic productivity, and healthcare costs far beyond the indications for which they

are initially approved (and can hence be legally marketed). To remedy this mismatch, policymakers should seek to align financial incentives to encourage development of such therapeutics after taking into account a full assessment of their societal benefits.

In order for the full benefit of a particular longevity medicine to be realized, the sponsoring company must pursue approval for additional disease indications, expanding the number of people who can receive the medication and creating a body of clinical research establishing the full range of conditions for which the drug is beneficial, to guide evidence-based use of the drug. Because clinical trials are expensive, and each additional approval takes many years to achieve, current patent term limitations drastically limit the incentive for a company to pursue approvals in a variety of diseases, even if the drug will be extremely beneficial in all of those diseases. This also leads to a much smaller financial value being placed on drugs with the potential to treat many diseases, making them less likely to be developed in the first place. The Inflation Reduction Act of 2022 has exacerbated this problem by establishing a price negotiation clock of 9–13 years that starts ticking at initial market authorization, after which the drug is likely subject to price controls.

The limited period of increasing profitability, between the time that a drug can actually start to be marketed and either patent expiration or legislated price reduction, may incentivize sponsors to wait until they have the evidence package for the broadest conceivable patient population, rather than entering the market as rapidly as possible with narrow indications and expanding applications of the drug over time with post-approval clinical development. This strategy would negatively affect patients in two ways: delaying patient access to the drug and limiting the number of indications approved (and thus the patient population served by the drug).

Conversely, it is impractical and expensive to develop a drug in many indications simultaneously. Moreover, this approach concentrates cost for all indications at the outset, in the absence of any initial clinical trial success that would derisk future development. Therefore, drugs with the potential to be approved for multiple diseases are likely to be valued in regard to

\_

<sup>&</sup>lt;sup>9</sup> https://www.zs.com/insights/inflation-reduction-act-what-biopharma-needs-to-know

only the first one or two indications for which they could be applied – and consequently undervalued, or not selected for development in the first place.

Expanded patent protection could help to alleviate financial risk facing companies in the longevity biotech sector and further the national interest in promoting development of longevity medicines.

## Solution: The Advanced Approval Pathway for Longevity Medicines

To address these issues and help Americans realize these benefits, we propose that policymakers create the Advanced Approval Pathway for Longevity Medicines (AAPLM). AAPLM confers three major benefits on sponsors seeking approval of drugs in this category:

- 1) a <u>special approval track</u> for longevity medicines that facilitates communication between regulators and drug sponsors;
- 2) a <u>transferable priority review voucher</u> granted to companies who obtain approval for an eligible longevity medicine; and
- 3) indication-by-indication <u>extension of patent terms</u>, ensuring that companies have sufficient financial incentive to obtain multiple approvals to achieve broad application of their products.

We will describe the rationale and implementation of each provision after defining the criteria for eligibility in AAPLM.

#### Special approval track: RMAT as a template

The 21st Century Cures Act, signed into law in 2016, created the Regenerative Medicine Advanced Therapy (RMAT) designation. RMAT is intended to accelerate the development of regenerative medicine by granting qualifying efforts special status during review by FDA. Eligible therapies receive several benefits: (1) Fast Track designation, which grants the drug's sponsor more frequent meetings and written correspondence with FDA, as well as a "rolling review" under which the sponsor may submit to the FDA completed sections of the drug's New Drug Application (NDA) as they become available. By contrast, under conventional review, FDA does not evaluate an NDA until it has been submitted in its entirety. (2) Breakthrough

<sup>&</sup>lt;sup>10</sup> RMAT overview provided by FDA

<u>Therapy designation</u>, which, in addition to the benefits of Fast Track, grants heightened FDA guidance and organizational commitment from senior managers at FDA.<sup>11</sup> (3) Engagement between FDA and the drug's sponsor to facilitate accelerated approval, which if granted allows evaluation on the basis of surrogate or intermediate endpoints or data from a relatively limited number of sites.

AAPLM will create a special regulatory track for longevity medicines that grants these same benefits (Fast Track designation, Breakthrough Therapy designation, and review for accelerated approval). Eligibility for the program would be determined similarly to the RMAT, although reoriented towards longevity medicines, as follows:

- 1) The drug must be a <u>longevity medicine</u> (see next section, *Which Medicines Will be Eligible?*)
- 2) The drug is intended to treat, modify, cure, or prevent a <u>life-threatening or life-altering</u> <u>disease</u> or condition; and
- 3) Preliminary clinical evidence indicates that the drug has the potential to address an <u>unmet</u> medical need for such a disease or condition, i.e., either no treatment currently exists or available treatments are inadequate.

Participation in the AAPLM regulatory track would speed specific aspects of the approval process, shortening time to market and profitability. The provisions aimed at promoting communication between sponsors and regulators would also yield important benefits. In focus group discussions with the Alliance for Longevity Initiatives (A4LI), leaders from geroscience research and longevity biotech identified the lack of frequent and clear communication with regulators as the primary "informal" factor hindering progress in the industry. Specifically, they contended that contact with regulators was inconsistent in tone and content, creating uncertainty about how their clinical strategies might be evaluated. Lack of confidence about the regulatory landscape for longevity medicine hinders strategic development of clinical assets, and could discourage entry into the sector by incumbents. By strengthening communication channels between innovators and regulators, the special regulatory track would encourage clinical

\_

<sup>&</sup>lt;sup>11</sup> Overview of FDA's various accelerated review pathways

development of longevity medicines by reassuring sponsors that their clinical strategies were designed optimally to maximize the chances for approval.

#### Which Medicines Will be Eligible?

To ensure that the program promotes the most innovative longevity medicines while excluding efforts that are already being pursued by conventional biopharma and adequately incentivized under the status quo, it is essential to establish a clear and rational basis for determining whether a therapy is a longevity medicine. However, this is more challenging than in the example of RMAT, the template for the special approval track. RMAT designates a regenerative medicine as a "cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product" — in other words, designation is made based on the origins, manufacture, and physical nature of the product. By contrast, such straightforward classification is not possible for longevity medicines, which could include therapeutic modalities ranging from small molecules to biologics to cell therapies. The criterion of "unmet need" enumerated in the previous section is helpful in this regard, as it rules out drugs under development for indications already targeted by multiple medications; however, it is also important to define longevity medicines affirmatively as well as by exclusion.

Here we propose several potential standards for designating a therapeutic as a longevity medicine. Because of the diversity of valid potential approaches, these are expressed as desirable features of a drug development effort rather than necessary or sufficient conditions for inclusion in the program: Drugs meeting a greater proportion of these standards would be prioritized more highly for participation. Ultimately, it would be up to FDA to determine how best to implement these guidelines in order to achieve the goals of the program.

Note that because of the enormous potential benefits of these therapies, we wish to both enable biotech startups founded with the mission of creating new longevity medicines and to encourage healthcare and pharmaceutical industry incumbents to repurpose, commit, and mobilize their resources towards the development of longevity medicine. Therefore, our proposed standards focus primarily on the pharmacodynamic properties of the drug in question, and secondarily features of its sponsor, including the company's mission, vision, and intent.

- 1) The drug acts through a <u>fundamental mechanism of aging</u>, rather than simply treating the manifestations of a specific age-related disease. The sponsor could provide evidence, either through preclinical studies or other research, that the mechanism is directly linked to the biology of aging or impacts a known aging process. For example, a drug that boosted anticancer surveillance by rejuvenating the immune system (and thus prevented multiple cancers) would be considered favorably, whereas a medication that directly inhibited the growth of prostate cancer cells would not, even though both are anticancer drugs.
- 2) The sponsor is pursuing a <u>broader clinical strategy to apply the drug to one or more age-associated conditions</u> beyond the indication for which initial approval is sought. For example, consider a drug with the potential to prevent or reverse age-related muscle atrophy, a condition associated with a wide range of disease states. The sponsor might plan to seek initial approval by performing a trial for a narrow indication such as clinical illness myopathy in ICU patients, but intend to subsequently develop the same medication for common age-related conditions driven by muscle aging, such as sarcopenia and frailty. The sponsor could provide a clear demonstration of their intent by collecting data relevant to the broader clinical strategy in early-phase trials for the initially selected indications.
- 3) The drug has a conceivable <u>application in preventive medicine</u>. This provision is largely intended to distinguish true longevity medicines from therapies whose sole or primary purpose is to treat a disease that has already arisen, and that it would be unreasonable to administer to a healthy person. Returning again to the example of anticancer drugs: Although cancers are diseases of aging, it would be inappropriate to prescribe most anti-cancer drugs preventively, both because of the lack of biological rationale for prevention and because adverse events would outweigh any preventive benefit. Accordingly, traditional anti-cancer drugs would not qualify for eligibility as longevity medicines.
- 4) The sponsor has obtained clinical evidence, through trials or observational studies, that the drug is effective in <u>improving biomarkers of aging</u> or reducing the risk of age-related disease. The existence of such data would demonstrate the potential of the drug to exert beneficial effects on multiple age-related conditions, a key property of longevity medicines.

5) The company has an <u>aging-focused mission statement</u> that emphasizes their focus on addressing the aging process and improving healthy longevity, demonstrating their commitment to the field and their intent to develop therapeutics consistent with the goals of the program.

By promoting drug development aligned with these guidelines, the AAPLM would encourage both new and incumbent companies to focus on clinical strategies most suited to realizing the benefit of longevity medicine.

#### Transferable priority review vouchers

Over the past decade, three priority review voucher programs have been established to promote development of drugs in neglected or urgent areas: tropical diseases, <sup>12</sup> rare pediatric diseases, <sup>13</sup> and material threat medical countermeasures. <sup>14</sup> We propose that companies who receive approval for medicines eligible for the AAPLM program, based on the guidelines described above, be granted transferable priority review vouchers modeled after these programs. When redeemed, a voucher grants the right to expedited FDA review of a future drug. In the case of the programs established to date, this faster review period is 6 months (vs the standard review period of approximately 10 months). The vouchers are transferable and may be sold by the qualifying sponsor to another entity, who may redeem it for a product of their own.

Accelerated review is valuable to companies for two main reasons: first, because it brings forward the time when the sponsor receives revenue from their future product, and second, because it may allow the sponsor to bring their product to market before a competitor, potentially allowing the drug to be established as a standard of care for an unmet need and thus yielding a long-term advantage.

The ability of companies in the AAPLM program to redeem vouchers on behalf of their own future products would address a concern raised in A4LI's focus group discussion with geroscience and longevity biotech leaders, namely that the status quo regulatory framework does

<sup>&</sup>lt;sup>12</sup> Overview of FDA's tropical disease priority review program

<sup>&</sup>lt;sup>13</sup> Overview of FDA's pediatric disease priority review program

<sup>14</sup> Industry guidance on FDA's material threat countermeasure priority review program

not adequately reflect the urgency with which our society should be developing longevity medicines. Specifically, the current system is designed to evaluate and approve drugs that target individual diseases in people who are already sick, whereas longevity medicines will have the potential to simultaneously prevent and/or treat diverse diseases. Regulatory policy should recognize the benefits of longevity medicines by giving them priority in the approval process.

However, a voucher conferring accelerated review may be even more important because of its direct monetary value. The vouchers will be transferable, enabling sponsors receiving the vouchers to sell these assets to other entities that desire accelerated approval for their own products. In this regard, a salient feature of the program is that the vouchers can be redeemed for a drug targeting any disease, and are not restricted to longevity medicines. Accordingly, the potential buyers for the vouchers include all of biopharma, and the market value of these assets is quite large: for example, sale prices of vouchers from the Rare Pediatric Disease program have ranged between \$67 million and \$350 million.<sup>15</sup> Voucher sales could thus serve to transfer financial resources from large, well-capitalized industry incumbents seeking rapid approval of conventional drugs to smaller, newer companies focused on the mission of developing longevity medicines, to the mutual benefit of both types of companies. This would provide a mechanism to rapidly and non-dilutively recapitalize after the long and expensive clinical trial process for a recently approved therapy. In addition to financially incentivizing the formation of longevity-focused companies and subsidizing their ongoing clinical development, the vouchers could incentivize well-established players to focus on longevity medicines themselves, driving further progress in the field.

By improving the risk-adjusted rate of return on drug development in this important area, the voucher program should both stimulate investment in biotech startups founded on a thesis of longevity medicine and encourage incumbent companies to pursue such clinical strategies — at no cost to taxpayers

#### Indication-by-indication patent extension

5 1

<sup>15</sup> https://www.kidsvcancer.org/priority-review-vouchers/

By granting market exclusivity, patents incentivize innovation by allowing innovators to recoup their investments. In drug development, these investments are large, and patent expiry quickly leads to generic competition that erodes up to 90% of a drug's profitability. However, because the patent clock begins ticking early in the drug development process, which can take five to ten years, the effective duration of a patent is well below the number of years nominally covered by its protection. Accordingly, patent term extensions (PTEs) are extremely useful for incentivizing companies to develop drugs that are commercially risky, especially those that have a long time horizon to greatest profitability. This will be of particular interest in the case of longevity medicines, whose greatest benefits will be realized after undergoing prolonged clinical trials to validate efficacy and obtaining multiple rounds of approval, first for narrow indications for which they are initially marketed and subsequently for broader age-related conditions.

Patent extension doctrine for pharmaceuticals dates back to the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Act). Title II of this law, which provides the terms and conditions under which patent term extension (PTE) can be granted to a drug, was intended to allow sponsors to increase the amount of time during which their drug would have both approval for marketing and market exclusivity. The provision protects drug innovators in two major ways. First, for a 5-year period after a drug is approved for marketing, other manufacturers are prohibited from referencing the IND in order to support a generic competitor product; consequently, FDA will not approve a generic version of the drug during this period, enforcing market exclusivity. Second, the life of a patent may be extended by the amount of time required for FDA review, preventing the regulatory process from eroding the term of a patent.

Although it has been valuable for the broader biopharmaceutical industry, PTE under Hatch-Waxman is not an optimal fit for longevity medicines and their associated clinical strategies because its protections apply almost exclusively to new chemical entities, and extensions are rarely granted to novel uses of parent compounds. As a result, Hatch-Waxman PTE is unable to accommodate one of longevity medicine's most salient unique features: because these therapeutics will yield their fullest benefit when applied to multiple chronic diseases, the

<sup>16</sup>https://www.pharmamanufacturing.com/home/article/11316935/mitigating-the-fall-profitability-beyond-the-blockb uster

<sup>&</sup>lt;sup>17</sup> https://www.alacrita.com/whitepapers/pharmaceutical-patent-term-extension-an-overview

the sponsor of such a drug must pursue a series of costly, time-consuming approvals for novel applications of the same chemical entity while the remaining patent life for the parent compound dwindles.

To address this issue, we propose to extend the Hatch-Waxman protections to longevity medicines on an indication-by-indication basis, extending the existing patent(s) for a given chemical entity by up to 5 years (as in Hatch-Waxman) and granting 5 years of regulatory exclusivity when the sponsor obtains a new clinical approval for that compound, preventing manufacturers of generic compounds from referencing the IND or subsequent trial data for the same period. By extending patent protection and blocking generic competition as sponsors continue to invest in broader applications of longevity medicines, AAPLM will ensure that companies are incentivized to develop these drugs to yield the greatest potential benefit.

#### **Conclusion: Unlocking the Longevity Dividend**

Aging is the primary driver of the chronic diseases that disable and kill Americans as we grow older. Targeting the mechanisms of aging represents a powerful approach for developing drugs to treat these conditions. Although a new generation of biotech companies has begun to adopt this approach, with the past few years seeing explosive growth in the longevity sector, the field is markedly under-incentivized relative to the potential benefit to Americans,

Conceived to address this core problem, the Advanced Approval Pathway for Longevity Medicines (AAPLM) provides a suite of solutions that will help this nascent sector overcome status quo barriers. The program's core components - the special approval track, the priority review voucher system, and indication-by-indication patent extension - emulate or extend existing templates for promoting drug development that have an established record of success.

Collectively, these provisions would promote the flow of capital into the field, increase financial incentives to create drugs aimed at the fundamental biology of aging, and ultimately accelerate approval and clinical deployment of novel drugs for chronic diseases with enormous unmet medical need. Importantly, the program would achieve these goals at negligible cost to taxpayers. Longevity medicines have the potential to revolutionize our broken healthcare system, which

currently only focuses on treating diseases once patients are already sick. By targeting the underlying mechanisms of aging, a single drug could potentially treat, delay, or even prevent multiple chronic diseases, providing enormous benefits to patients and reducing healthcare costs. The AAPLM would incentivize development of these transformative therapies, bringing us closer to a healthcare system that emphasizes disease prevention and healthy longevity.

Drugs that treat, delay, or prevent diseases of aging have the potential to dramatically improve Americans' healthy lifespan. In addition to the individual health benefits, there is also a strong social and economic case for promoting investment and activity in this field. Longevity medicine will have major impacts not only on the health status of individuals and the healthcare system, but also on society more broadly. The social and economic gains resulting from successful efforts to treat chronic disease by targeting the mechanisms of aging are seen as being potentially tremendous, and have been termed the "longevity dividend." <sup>18</sup> Increasing healthy life will enable individuals to remain vibrant contributing members of society for a much longer period. Healthy people are not only more independent and happier, but they are more likely to participate in the labor force and more productive when they do<sup>19</sup>, with each one-year increase in working lifespan predicted to drive a 1% increase in GDP (corresponding to \$260 billion per year in the US)<sup>20</sup>. These economic benefits would be further amplified by delayed onset and reduced severity of chronic diseases, which are currently associated with healthcare costs of \$3.8 trillion per year and projected to double over the next 30 years<sup>21</sup>. Decreases in healthcare expenditures and dependency on caregivers would enable reallocation of resources to other priorities, such as education.

Thus, the benefits of healthy aging accrue not only to older people, their families, and their communities, but also governments, insurers, employers, investors, entrepreneurs — every player in the economic engine of society. These are the stakeholders that the AAPLM has been created to benefit via incentivizing the development and approval of longevity medicines.

<sup>18</sup> https://link.springer.com/referenceworkentry/10.1007/978-3-030-22009-9 397

<sup>&</sup>lt;sup>19</sup> https://doi.org/10.1016%2FS0140-6736(14)61464-1

<sup>&</sup>lt;sup>20</sup> https://www.gov.uk/government/publications/macroeconomic-impact-from-extending-working-lives-wp95

<sup>&</sup>lt;sup>21</sup> https://www.fiercehealthcare.com/hospitals-health-systems/fitch-rain