Groundwork for Draft Healthspan Legislation at Metabesity 2022

One of the most often-cited challenges to the translation of advances in aging research into products that prevent chronic diseases and extend healthy longevity is the lack of a clear regulatory pathway. Key stakeholders, including pioneer scientists in the aging research field, regulatory experts and legislators participated in a unique, far-ranging discussion that took place during the "***Achieving Evidence to Support Healthy Longevity Therapeutics & Products***" session on Day 1, October 9, 2022, of the Targeting Metabesity conference.

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Moderated by **David Fox, JD**, Partner, Hogan Lovells, and **Alexander Fleming, MD**, Founder and President of the Kitalys Institute and Executive Chairman of Kinexum, the discussants included:

Steven Austad, PhD, Senior Scientific Director of the American Federation of Aging Research (AFAR)

Tom DiLenge, JD, Senior Partner, Flagship Pioneering, and former President, Advocacy, Law and Policy of BIO

Martin Hahn, JD, Partner, Hogan Lovells

Ellis Unger, MD, Principal Drug Regulatory Expert, Hyman Phelps & McNamara, PC and former Director, Office of Drug Evaluation-I, CDER, FDA

The following questions initiated panel discussions:

- *Do we need a universal system for Healthspan products, or do we need a system that breaks Healthspan products out into different categories (such as foods/supplements, drugs and devices)?*
- *What types of rules and evidentiary standards should govern science to support the marketing of Healthspan products?*

- *How much uncertainty should we be willing to accept in the evidence?*

- *What type of incentives are going to be needed to back the development of Healthspan products?*

- *What is the appropriate role of surrogate markers, molecular biomarkers or clinical endpoints for the assessment of aging?*

The following key points made by the moderator and the discussants were noted:

- Healthspan products can be defined as those "*intended to reduce the risk or delay the onset of age-related disability or the occurrence of multiple chronic age-related conditions*".

- In regulatory science, there are standards of evidence based on statutes about the types of products that can be marketed, the claims that can be made and about how much uncertainty people are willing to accept to allow interventions to be available sooner rather than later.

- A major distinction between Healthspan products from the types of products that FDA approves as therapeutics is that they are upstream in the unfolding of the disease or involve multiple systems that may lead to distinct diseases, while FDA usually approves products that target one specific disease.

- When targeting something as deeply rooted in biology as aging, Healthspan products will face the risk of developing side effects (though the acceptability of such side effects would depend on the countervailing benefits).

- The possibility of millions of healthy people taking a Healthspan product regularly for decades to prevent the development of age-related diseases means drug safety is paramount. Hence, researchers in the aging field are proposing to repurpose existing drugs, whose safety has already been proven, as Healthspan products.

- From the food perspective, there are no incentives to do research or clinical trials on dietary supplements and food products as companies may spend millions of dollars to prove that their interventions decrease the risk of disease development, but no proprietary value can back this claim and, therefore, any company with a similar product can benefit from the same claim. Similar risks may be faced by developers of repurposed drugs that are used as senescence-retarding products in healthy longevity trials.

- In addition to safety, Healthspan products need to be followed for a large number of years to demonstrate efficacy.

- Scientists need to identify molecular biomarkers of aging that can show efficacy of an intervention in shorter timeframes.

- Scientists and VCs, such as, Flagship Pioneering support the use of AI and ML to mine large databases in biobanks for correlations and causal relationships between biomarkers and aging, though the FDA will need to be convinced of their applicability, aided by Congressional encouragement and increased funding from new entities, such as ARPA-H.

- Geroscientists and sponsors should work early and often with the FDA to agree on the validation of AI and ML.

- In a model where a composite endpoint of the first appearance of one or another age-related chronic disease is used, then the event rate would come sooner in effect on average, and one would be able to identify within three to five years a change in the composite.

- If investigators can show improvement across a few domains, that are seemingly unrelated to each other, but related to aging, then a regulatory approval with aging as an indication may be obtained.

- Indicative clinical endpoints that can be utilized to prove Healthspan drug effects on prevention or reversal of aging may include the six-minute walk, the curve of the spine and muscle strength and others.

- If aging is considered as a fatal disease, then the accelerated approval pathway may be appropriate for Healthspan projects.

- If geroscientists can demonstrate to people that there is an 80%-90% risk of developing a chronic disease because of the changes occurring in their body, then people would be willing to accept certain risks to get some type of intervention.

- Private enforcement, instead of relying on the FDA to take action, can help developers of generics preserve their economic incentives for generating new data that support healthy longevity.

- A predictable and coherent system is needed to create a vibrant commercial market that is based on strong clinical evidence and calibrated on the risks and benefits of Healthspan products.

The panelists further discussed the need to develop a **Healthy Resiliency and Healthy Longevity Interventions (HRHLI) Act.** The **HRHLI Act** would establish a framework to oversee and incentivize the development of products regulated by the Food and Drug Administration (FDA) that are intended to lengthen the period of life during which individuals remain in good health, free from the chronic diseases and conditions responsible for most mortality and disability in the general population.

A recording of the session is available here**.**

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