



## A Novel Immunotherapeutic Approach to Treating Aging-Associated Diseases

April 3, 2023

*HCW Biologics Published a Pivotal Scientific Paper in Aging Cell*

*Subcutaneous Administration of HCW9218 Systemically Reduces Senescent Cells and Alleviates Senescence-Associated Secretory Phenotype Factors in Mice*

MIRAMAR, Fla., April 03, 2023 (GLOBE NEWSWIRE) -- [HCW Biologics Inc.](#) (the "Company" or "HCW Biologics") (NASDAQ: HCWB), a clinical-stage biopharmaceutical company focused on discovering and developing novel immunotherapies to lengthen healthspan by disrupting the link between inflammation and age-related diseases, published a pivotal scientific paper in *Aging Cell* entitled, "Immunotherapeutic approach to reduce senescent cells and alleviate senescence-associated secretory phenotype in mice," with Dr. Hing C. Wong, the Company's Founder and CEO, as lead and corresponding author. The Company is currently evaluating one of its lead product candidates, HCW9218, a bifunctional immunotherapeutic compound, in patients with chemo-resistant/chemo-refractory advanced pancreatic cancer and solid tumors. In this publication, the Company demonstrates HCW9218 may have much broader therapeutic potential beyond cancer to other age-related diseases and conditions because of its ability to promote cell-mediated mechanisms to reduce senescent cells and alleviate the proinflammatory factors they secrete, known as senescence-associated secretory phenotype ("SASP") factors, as shown in mice.

Cellular senescence is a form of irreversible growth arrest accompanied by phenotypic and metabolic changes, resistance to apoptosis, and activation of damage-sensing signaling pathways. Senescence is considered a stress response that can be induced by a wide range of intrinsic and extrinsic insults, including oxidative and genotoxic stress, DNA damage, telomere attrition, oncogenic activation, mitochondrial dysfunction, or exposure to chemotherapeutic agents. Senescent cells remain metabolically active, and they can influence tissue homeostasis through their SASP factors.

Senescence is considered a physiologic process that is important in promoting wound healing, regeneration, and many other vital functions. However, stressors cause accumulation of senescent cells which modifies the microenvironment in tissues and organs and creates chronic, sterile inflammation. This drives aging and age-related diseases, such as diabetes, osteoporosis, fibrotic diseases, cardiovascular diseases, dementia, renal failure, sarcopenia, macular degeneration, and neurodegenerative diseases, as well as other conditions such as long-haul COVID-19. Senescent-cell removal improves healthspan and life span in experimental animal models. Thus, senescent-cell reduction and SASP neutralization (senomorphic) therapies are being vigorously pursued for a healthy longevity.

Dr. Wong founded HCW Biologics in 2018 with the vision of discovering novel immunotherapeutics to treat age-related diseases and improve healthspan. The Company is driven by its belief that age-related, chronic, low-grade inflammation, or "inflammaging," is a significant contributing factor to several age-related diseases and conditions. The induction and retention of low-grade inflammation in an aging human body is mainly the result of the accumulation of non-proliferative but metabolically active senescent cells.

Scientists from the Company hypothesized that an immunotherapeutic agent that rejuvenates a dysfunctional immune system and neutralizes transforming growth factor- $\beta$  ("TGF- $\beta$ ") can act as an effective senescent-cell reducing and senomorphic drug. In the *Aging Cell* publication, HCW Biologics' scientists demonstrated that HCW9218 can be safely administered subcutaneously to reduce senescent cells and alleviate SASP in mice because of its capabilities to stimulate immune cells and neutralize TGF- $\beta$ .

Dr. Wong stated, "We believe that HCW9218 has the potential to redefine the approach for treating aging conditions and age-related diseases. Aged immune systems can often breakdown and stop operating the way they were intended, and this opens the door to problems that diminish healthspan and longevity." He continued, "In many ways, this paper presents our seminal work on aging based on our primary premise that rejuvenating the immune system creates a systemic change that reduces senescence and SASP factors. We have seen that HCW9218 can do both, even under conditions where the stressors of cellular senescence are poorly defined or unknown."

HCW9218 is currently being evaluated in two initial-stage clinical trials with the primary objectives to determine safety, maximum tolerated dose, and the recommended Phase 2 dose. The ongoing studies are an investigator-sponsored Phase 1 clinical trial to evaluate HCW9218 in the treatment of advanced solid tumors at the Masonic Cancer Center, University of Minnesota, and a Company-sponsored multicenter Phase 1b clinical trial to evaluate HCW9218 in advanced pancreatic cancer. There have been no dose-limiting toxicities reported in either trial to date. The Company believes the Phase 1/1b studies will be completed in 2023.

In the *Aging Cell* publication, Dr. Wong highlighted the work done in diabetic db/db and naturally-aged mice. In the diabetic db/db mouse models, the authors showed that subcutaneous administration of HCW9218 reduced senescent islet  $\beta$  cells and SASP resulting in improved gene expression related to glucose tolerance, insulin resistance, and aging index. Long-term studies also showed that HCW9218 treatment improved the physical performance without compromising the healthspan of naturally-aged mice. Dr. Wong stated, "The long-term changes we observed in the expression of inflammation and senescence-associated genes in naturally-aged mice appeared to 'turn back the clock'. That is, treatment with HCW9218 appears to reverse the expression pattern of key circadian-rhythm genes, as well as genes associated with metabolism and fibrosis in the liver. These data point toward the possibility that we have created a new class of immunotherapeutics for age-related diseases that will fundamentally change the way these diseases are treated."

**About Aging Cell:**

*Aging Cell* is a monthly peer-reviewed, open access journal that aims to publish the highest quality, innovative research addressing fundamental issues in the biology of aging. You may access the article, "Immunotherapeutic approach to reduce senescent cells and alleviate senescence-associated secretory phenotype in mice," via this link: <http://doi.org/10.1111/accel.13806>

**About HCW Biologics:**

HCW Biologics is a clinical-stage biopharmaceutical company focused on discovering and developing novel immunotherapies to lengthen healthspan by disrupting the link between chronic, low-grade inflammation, and age-related diseases, such as cancer, cardiovascular diseases, diabetes, neurodegenerative diseases, autoimmune diseases, as well as other conditions such as long-haul COVID-19. The Company has combined a deep understanding of disease-related immunology with its expertise in advanced protein engineering to develop the TOBI™ (Tissue factOr-Based fuslon) discovery platform. The Company uses its TOBI™ discovery platform to generate designer, novel multi-functional fusion molecules with immunotherapeutic properties. The invention of HCW Biologics' two lead molecules, HCW9218 and HCW9302, was made via the TOBI™ discovery platform. The Masonic Cancer Center, University of Minnesota, has initiated a Phase 1 clinical trial to evaluate HCW9218 in chemo-refractory/chemo-resistant solid tumors that have progressed after prior chemotherapies (Clinicaltrials.gov: NCT05322408). The Company is also enrolling patients in a Company-sponsored Phase 1b/2 clinical trial to evaluate HCW9218 in chemo-refractory/chemo-resistant advanced pancreatic cancer (Clinicaltrials.gov: NCT05304936). The Company's lead molecule for its regulatory T cell expansion program, HCW9302, is currently undergoing IND-enabling studies for an autoimmune indication.

**Forward Looking Statements:**

Statements in this press release contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this press release may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast" or other similar words, including the expected completion date for Phase 1/1b clinical trials; the ability of HCW9218 to be an effective senescent-cell reducing and senomorphic drug against age-related diseases; the ability of HCW9218 to rejuvenate the immune system and create systemic changes that reduce senescence and SASP factors without compromising the healthspan; and the ability of HCW9218 to affect expression of circadian-rhythm, metabolism and liver fibrosis genes; and statements regarding the potential for HCW9218 to redefine or fundamentally change the approach for treating aging conditions and age-related diseases, or constitute a new class of immunotherapeutics. Forward-looking statements are based on the Company's current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. Factors that could cause actual results to differ include, but are not limited to, the risks and uncertainties that are described in the section titled "Risk Factors" in the Company's Annual Report on Form 10-K filed with the United States Securities and Exchange Commission (the "SEC") on March 28, 2023 and in other filings filed from time to time with the SEC. Forward-looking statements contained in the press release are made as of as of this date, and the Company undertakes no duty to update such information except as required under applicable law.

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