



# New Class of Immunotherapeutics for Cancer and Other Age-Related Diseases

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COMPANY PRESENTATION

APRIL, 2024

NASDAQ: HCWB

# Forward Looking Statements

Certain information about HCW Biologics Inc. (the “Company”) contained in this presentation and statements made orally during this presentation include forward-looking statements that involve substantial risks and uncertainties. All statements included in this presentation, other than statements of historical facts, are forward-looking statements.

Forward-looking statements contained in this presentation 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 and the initiation of Phase 2 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; 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; that trials may not have satisfactory outcomes; that preclinical studies of product candidates may not be predictive of the results of future preclinical studies or trials; that the Company’s third party manufacturers may encounter difficulties in production of product candidates for clinical trials; the timing and completion of the Company’s new headquarters and manufacturing facility; the timing and ability of the Company to raise additional capital; the risk that costs required to develop or manufacture the Company’s products will be higher than anticipated, including as a result of delays in development and manufacturing resulting from COVID-19 and other factors; the risk that the Company is unable to file INDs to commence additional trials; the risk the Company is unable to obtain access to checkpoint inhibitors to do a combination trial; timing and ability to identify and discover product candidates; the potential advantages of the Company’s current and future product candidates; the Company’s anti-inflammaging clinical development strategy and the Company’s intellectual property strategy; competition and other risks described in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in the Company’s Annual Report on Form 10-K filed with the United States Securities and Exchange Commission (the “SEC”) on April 1, 2024, and in other filings filed from time to time with the SEC. The forward-looking statements in this presentation represent the Company’s view as of the date of this presentation and the Company does not assume any obligation to update any forward-looking statements, except as required by law.

# Our Company

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*HCW Biologics Inc. is a clinical-stage biopharmaceutical company developing proprietary immunotherapies to treat age-related diseases promoted by chronic inflammation created by senescence.*

*Senescence is a cellular response to a variety of stress signals, such as chemotherapy, and is a significant contributing factor to several age-related diseases and conditions. We have created immunotherapeutics that activate the immune system to reduce senescent cells and the proinflammatory factors they secrete.*

*Our immunotherapeutics represent a new class of drug that is expected to fundamentally change the treatment of cancer and many other age-related diseases and conditions, and in doing so, improve healthspan and possibly extend longevity.*



# Experienced Team with Success in Drug Discovery and Development

## Executive Leadership



**Hing C. Wong, PhD**

FOUNDER  
CHIEF EXECUTIVE OFFICER



**Peter Rhode, PhD**

CHIEF SCIENTIFIC OFFICER AND  
VICE PRESIDENT  
CLINICAL OPERATIONS



**Jack Egan, PhD**

VICE PRESIDENT OF  
MANUFACTURING AND  
DEVELOPMENT



**Rebecca Byam, MBA, CPA**

CHIEF FINANCIAL OFFICER



**Lee Flowers**

SENIOR VICE PRESIDENT  
BUSINESS DEVELOPMENT



**Nicole Valdivieso, Esq.**

VICE PRESIDENT  
LEGAL AFFAIRS



**Raquel Diaz, MS, SHRM-SCP**

DIRECTOR  
HUMAN RESOURCES



# Business Highlights and Upcoming Milestones

Phase 1 trial to evaluate HCW9218 in solid tumors completed in February 2024. Ovarian cancer patients showed over 70% (5/7) stable disease.

In February 2024, agreed with University of Pittsburgh Medical Center to sponsor randomized Phase 2 trial that includes one arm to evaluate HCW9218 in ovarian cancer with neoadjuvant chemotherapy.

Phase 1b portion of Phase 1b/2 trial to evaluate HCW9218 in pancreatic cancer completed in February 2024. Over 13% (2/15) subjects showed stable disease.

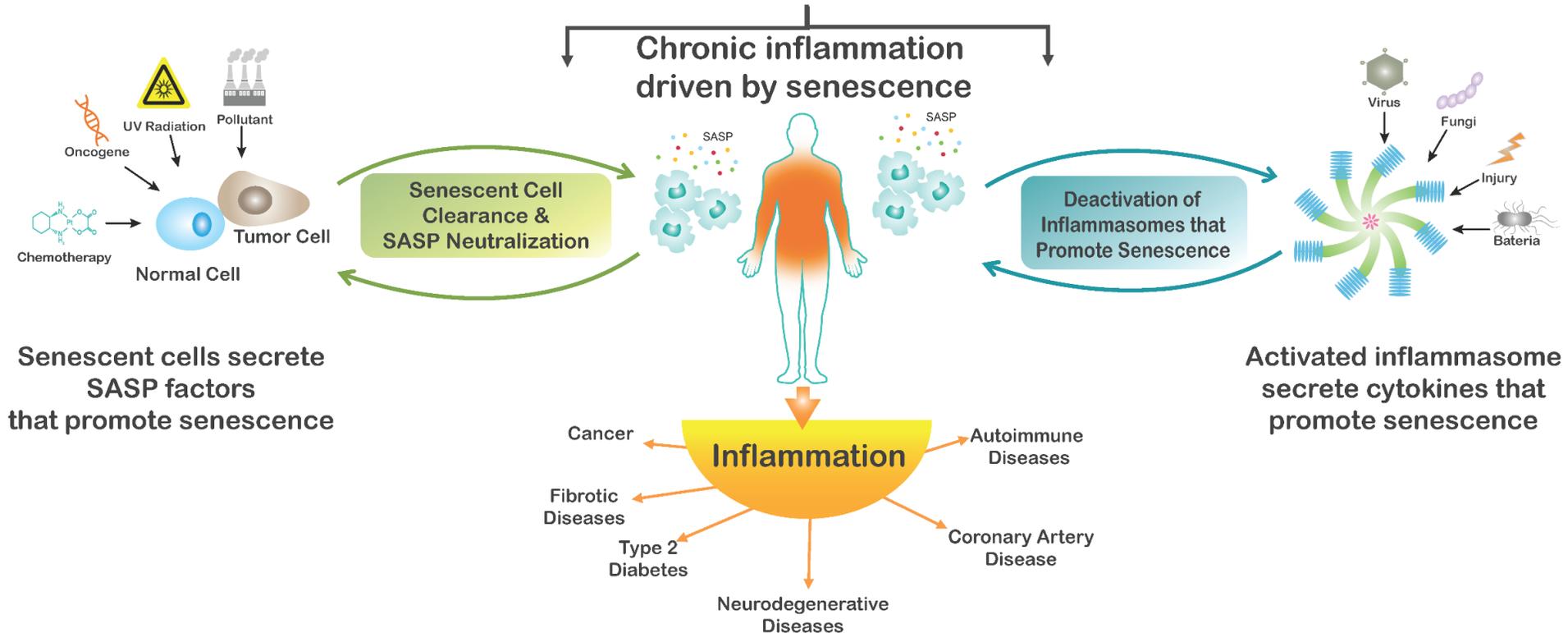
Targeting initiation Phase 2 study to evaluate HCW9218 in pancreatic cancer in combination with chemotherapy as second line treatment in first half of 2024, under the existing CRADA with the National Cancer Institute.

Targeting submission of IND to evaluate HCW9302, lead product candidate for T<sub>reg</sub> expansion and activation, in autoimmune indication in first half of 2024.

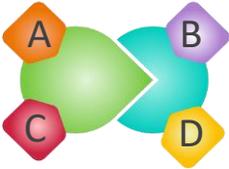
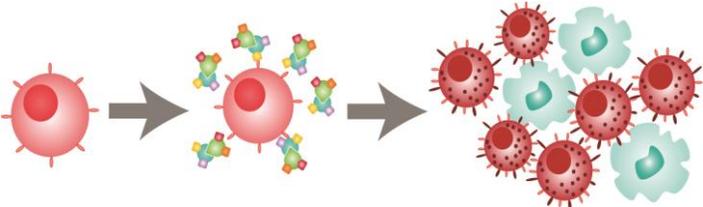
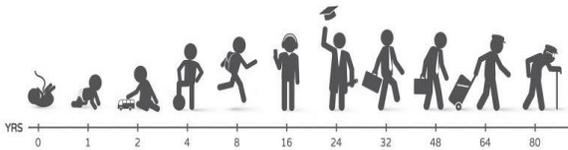
Plan to complete of new manufacturing facility in first half of 2025, gaining control over clinical material supply in highly competitive biologics CMO market.



# HCW Biologics' Immunotherapeutic Approach for Elimination of Chronic Inflammation Targeting Two Primary Pathways for Alleviation of Senescence



# Commitment to Strong Protection of Intellectual Property \*

Single-chain Platform	Multi-chain Platform	Methods of Culturing Immune Cells	Methods of Treating Age Related Disorders
			

- The Company has established a robust intellectual property portfolio evidencing our leadership in immunotherapeutics and senescence. Our aggressive intellectual property strategy has produced, and continues to produce, valuable assets for the Company, its licensees and future business opportunities.
- Several U.S. patents have been granted from the Company’s core patent families:
  - Fundamental patents that cover the technology underlying our TOBI™ discovery platform and our lead molecules, HCW9218, HCW9302, and HCW9206.
  - Method of use patents for the treatment of cancer and elimination of senescence with HCW9218.
  - Method of use patents for activation and expansion of immune cells, including NK and T cells, in adoptive cell therapy using the Company’s molecules.
- Numerous U.S. and national stage applications are pending from several patent families. In addition to the above patent families, other patent families include Treating Age-Related and Inflammatory Disorders, Methods of Activating Regulatory T cells, and Antibodies.

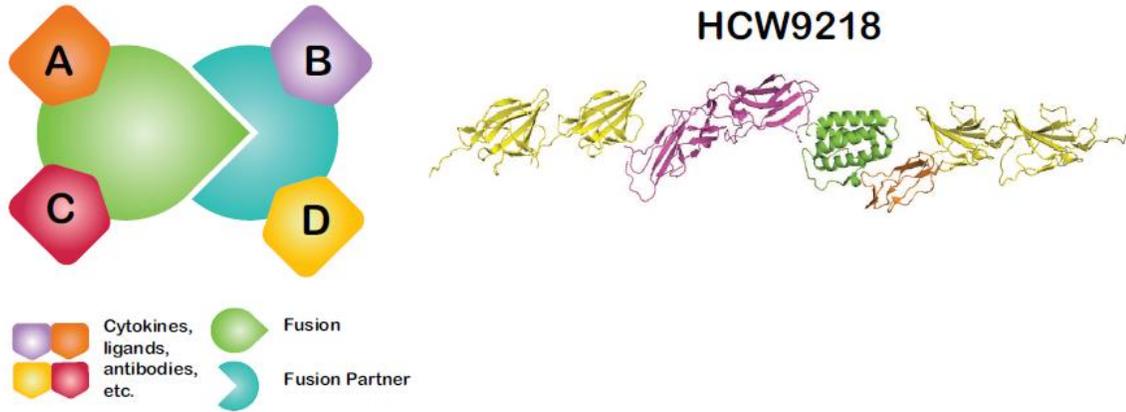
\* Status as of April 1, 2024



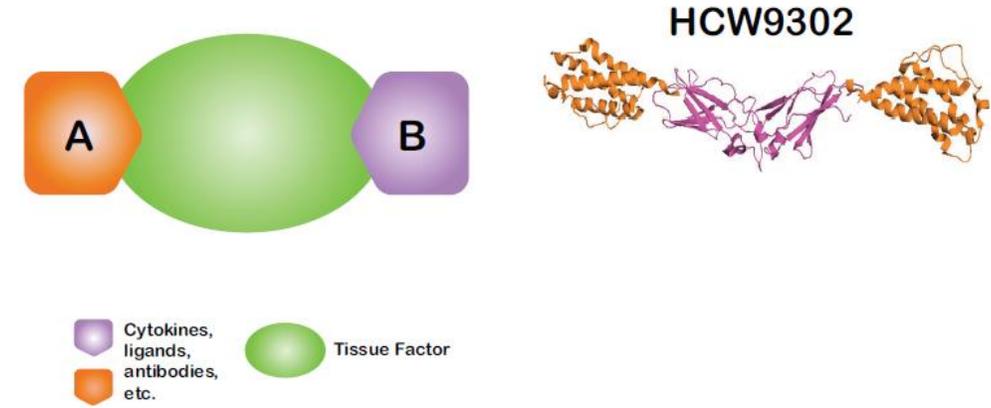
# TOBI™ Platform Technology “Tissue Factor-Based Fusion”

## Patented Novel Scaffold to Generate Proprietary Fusion Molecules

### Multi-Specific Fusion Complex



### Bispecific Fusion



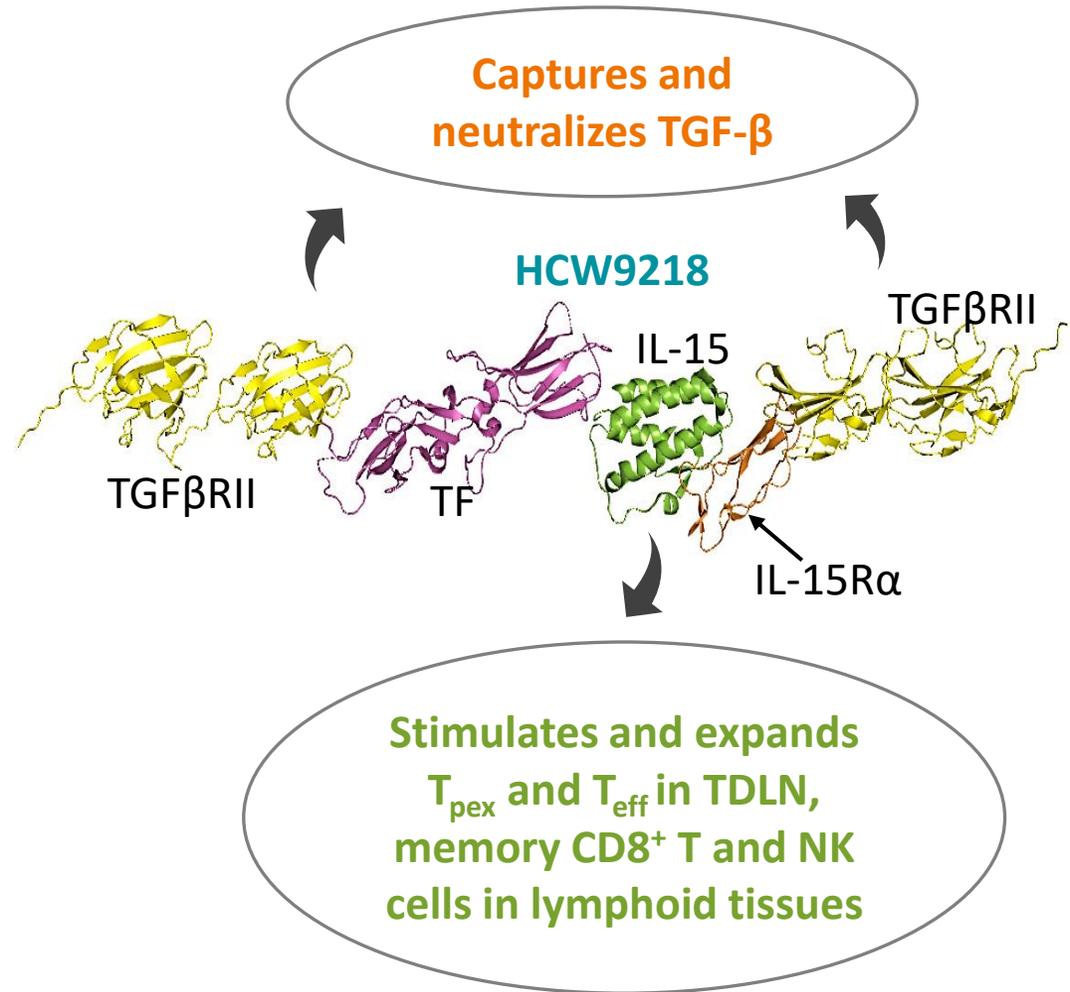
- Internally-developed, versatile scaffold can be utilized to generate designer, novel multi-functional fusion molecules.
- Over 30 molecules created and are proprietary to HCW Biologics, administered by subcutaneous injection or ex vivo in cell-based therapy applications.
- Scalable and reproducible for large-scale cGMP manufacturing. Drug product available to support clinical trials.
- Multiple protein targets (e.g., cytokines, sFvs, ligands, etc.) can be packaged as a single fusion molecule.

Becker-Hapak MK, Shrestha N, et al, A Fusion Protein Complex that Combines IL-12, IL-15, and IL-18 Signaling to Induce Memory-Like NK Cells for Cancer Immunotherapy. *Cancer Immunol Res.* 2021 Sep;9(9):1071-1087

Liu B, et al. Bifunctional TGF- $\beta$  trap/IL-15 Protein Complex Elicits Potent NK Cell and CD8+ T Cell Immunity against Solid Tumors. *Mol Ther.* 2021 Oct 6;29(10):2949-2962. doi: 10.1016/j.ymthe.2021.06.001.

# Lead Bifunctional Immunotherapeutic - HCW9218

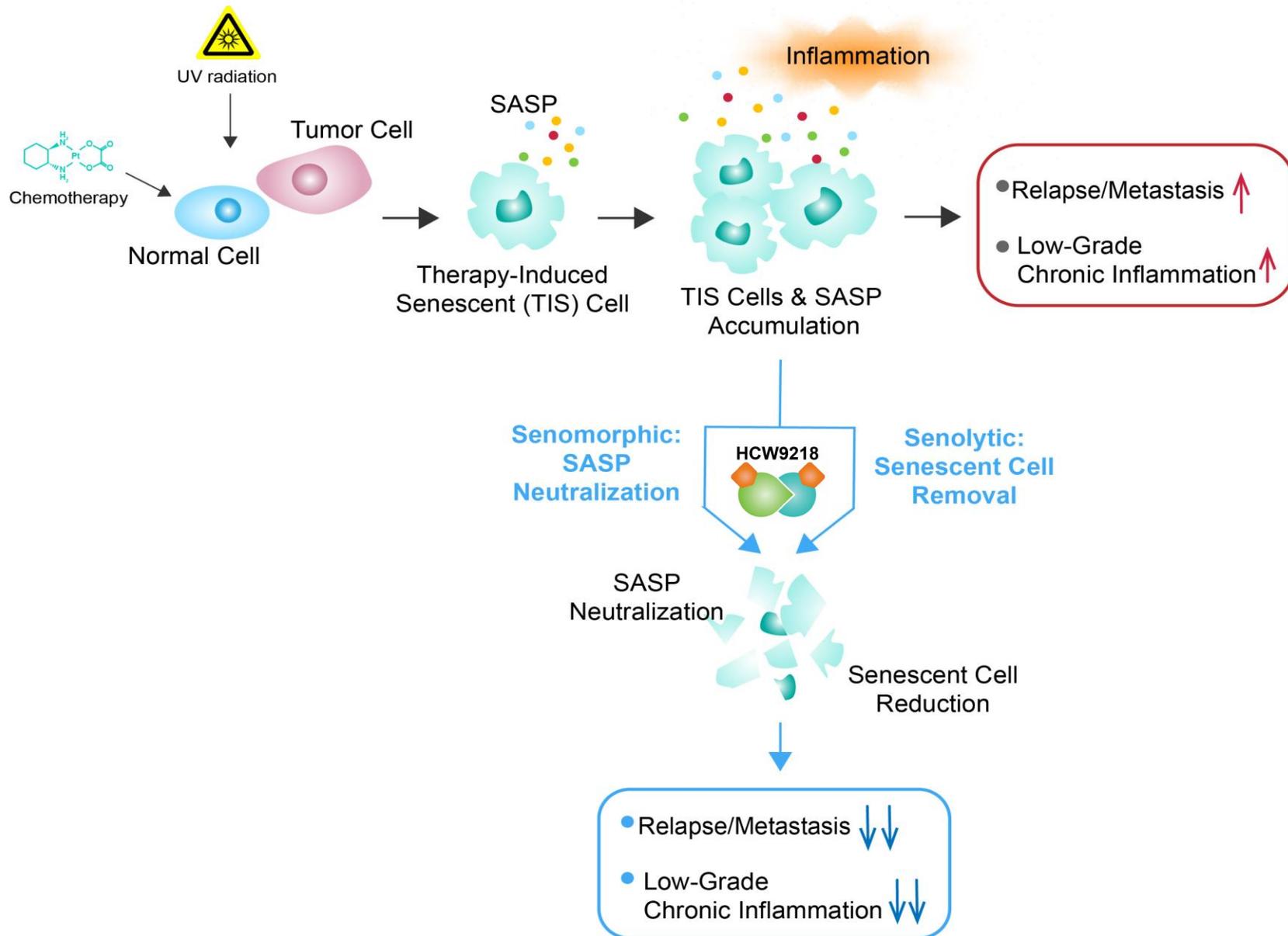
- **Reduces immunosuppression** associated with solid tumors by capturing and neutralizing TGF- $\beta$  in tumor draining lymph nodes and tumor microenvironment.
- **Provides immunostimulation and expansion** of progenitor exhausted stem-like (“T<sub>pex</sub>”) and transitory effector (“T<sub>eff</sub>”) CD8<sup>+</sup> T cells in tumor-draining lymph nodes (TDLN) and memory CD8<sup>+</sup> T cells (“T<sub>cm</sub> & T<sub>vm</sub>”) in lymphoid tissues, and natural killer (“NK”) cells to enhance the cytotoxicity of immune cells against tumor targets.
- **Promotes immune-cell infiltration** to turn “cold” tumors into “hot” tumors.



Liu B, et al. Bifunctional TGF- $\beta$  trap/IL-15 Protein Complex Elicits Potent NK Cell and CD8<sup>+</sup> T Cell Immunity against Solid Tumors. Mol Ther 2021 Oct 6;29(10):2949-2962.

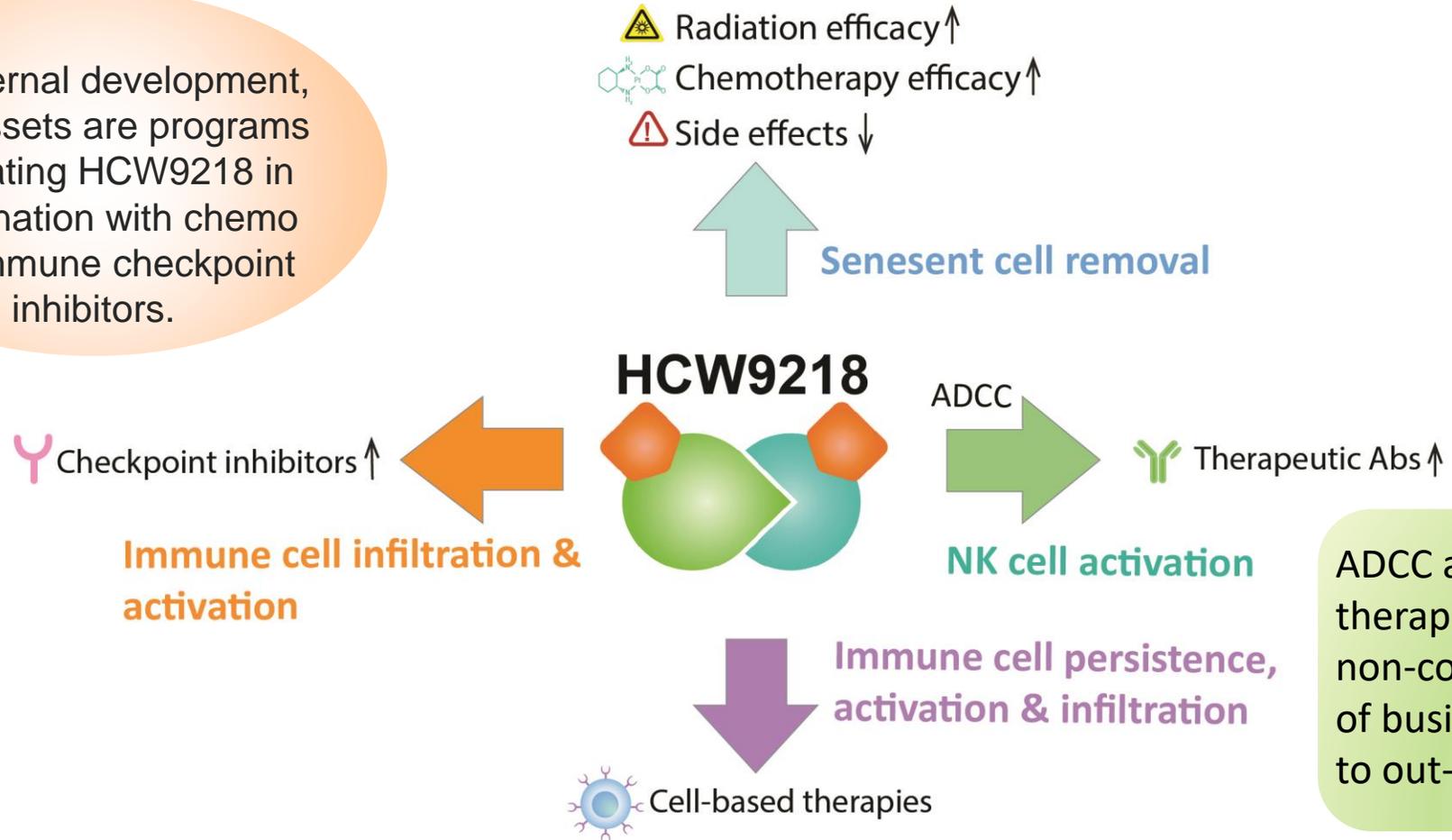
Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. Mol Ther 2022 30:1171-1187.

# Therapy-Induced Cellular Senescence



# HCW9218 Potential Clinical Utilities Against Cancer

For internal development, core assets are programs evaluating HCW9218 in combination with chemo and immune checkpoint inhibitors.



ADCC and cell-based therapies are considered non-core assets and part of business development to out-licensing program.

# HCW9218:

Clinical Study Update:

Phase 1 Solid Tumors Trial and

Phase 1b Advanced Pancreatic Cancer Trial



# Phase 1b Pancreatic Study: Enrollment and Dosing Completed

## Phase 1b/2 Clinical Study Advanced Pancreatic Cancer (NCT05304936)



- In February 2024, Phase 1b study completed.
- Currently defining the safety profile of multidose HCW9218 administration at escalating dose levels and a recommended phase 2 dose (“RP2D”).
- Patients with unresectable, advanced/metastatic pancreatic cancer who have progressed on first line (or later line) therapy.
- 18 subjects participated in the Phase 1b portion of the trial.
- **2 subjects exhibited stable disease.**

# Phase 1 Solid Tumors Trial: Enrollment and Dosing Completed

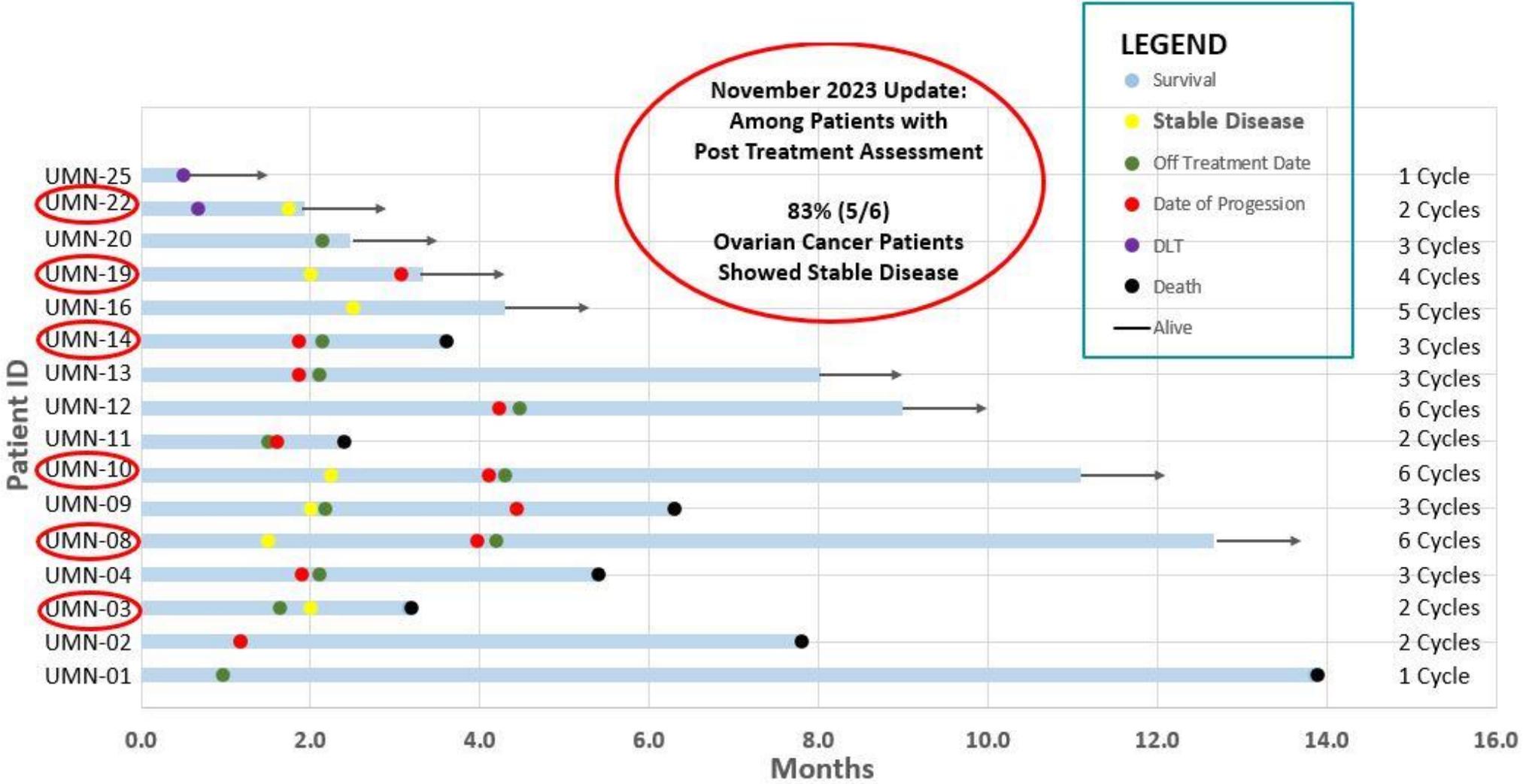
Phase 1 Clinical Study  
Advanced Solid Tumors Cancer  
(NCT05322408)



- In February 2024, final patient dosed and safety-evaluation period cleared. Met objective for RP2D.
- Patients with chemo-resistant/chemo-refractory solid tumors, including ovarian cancer and other difficult-to-treat cancers.
- 15 subjects participated in this trial over 80% failed more than four previous lines of treatment.
- **Over 70% (5/7) of patients with ovarian cancer who underwent post-treatment assessments showed stable disease.**

# Clinical Data for HCW9218

## Disease Response as of November 2023 (Phase 1 Solid Tumors Trial)



# Conclusions:

## Summary of Phase1 Solid Tumors Trial Using HCW9218

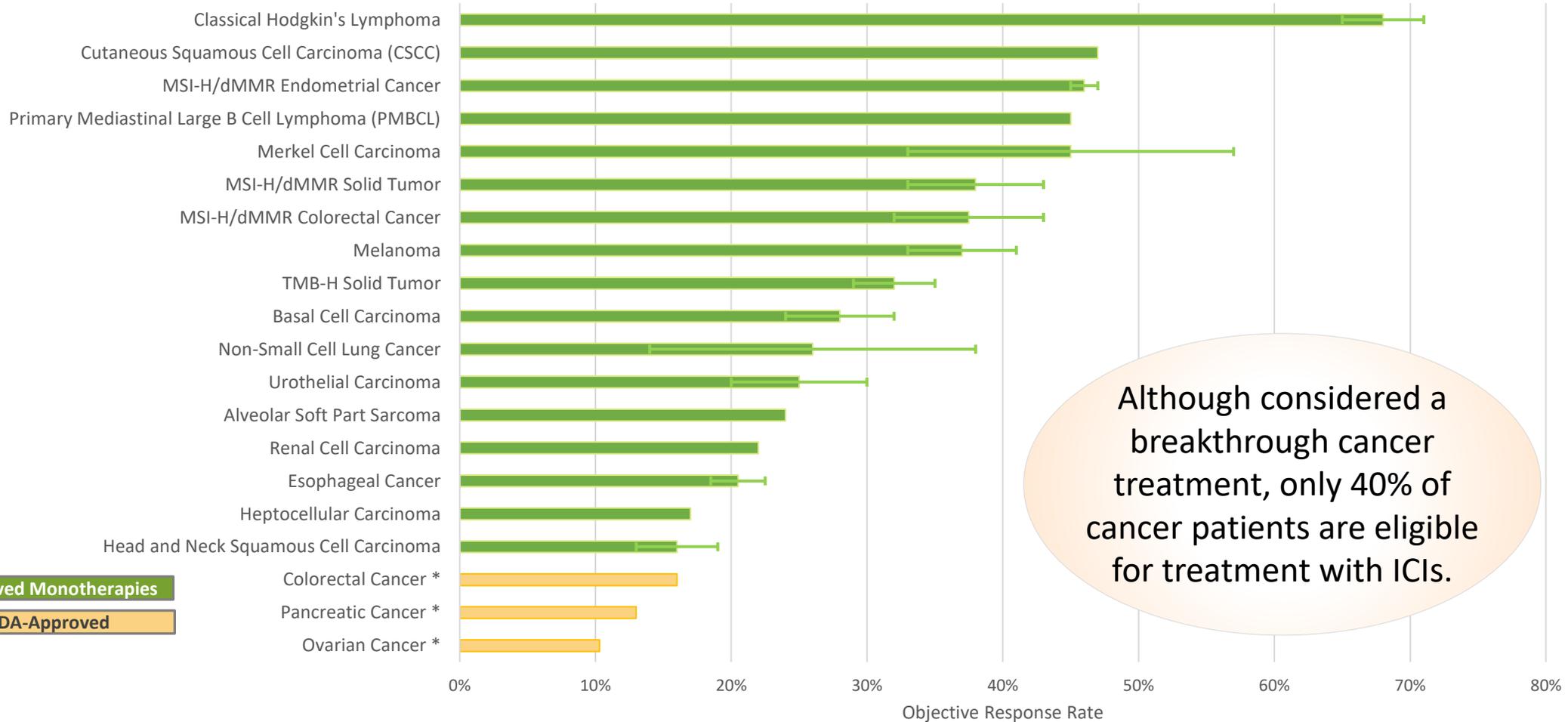
- Robustly promotes NK cell and CD8<sup>+</sup> T-cell expansion and activation in patients with chemotherapy refractory solid tumors.
- Significant increases the CD8<sup>+</sup> T cells infiltration into the tumors: capable of converting “cold tumor” to “hot tumor”.
- Reduces aggressiveness of the tumors and immunosuppressiveness/inflammation of tumor microenvironment.
- Provides clinical benefit to patients with chemo-refractory/chemo-resistant ovarian cancer.

# Immune Checkpoint Inhibitors in Cancer

## Limited Number of Patients are Eligible for Treatment with ICIs

### FDA Approval for Limited Cancer Indications

### Inconsistent Objective Response Rates, with Some Very Low Rates

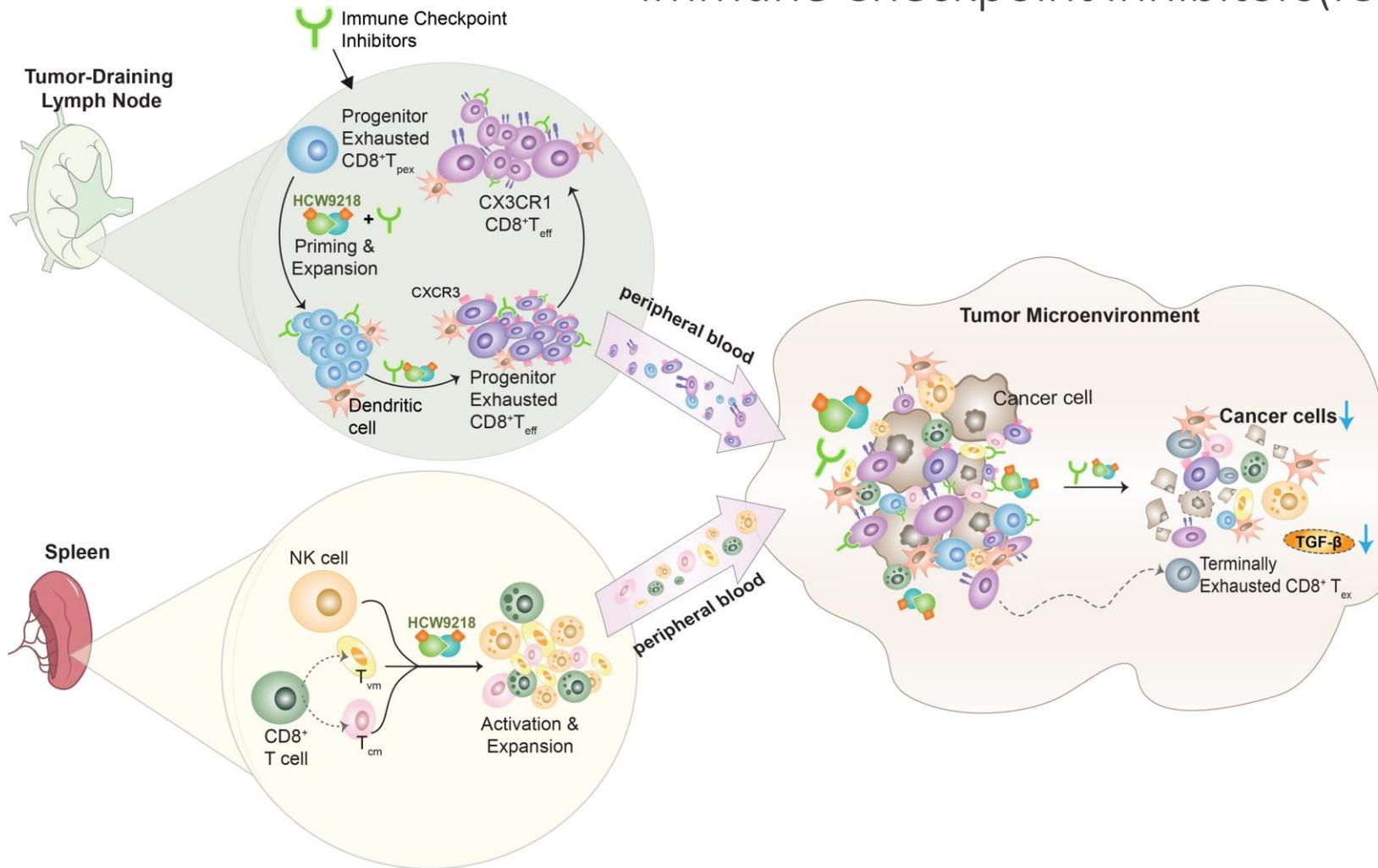


Although considered a breakthrough cancer treatment, only 40% of cancer patients are eligible for treatment with ICIs.

Primary Sources: Review of Indications of FDA-Approved Immune Checkpoint Inhibitors per NCCN Guidelines with the Level of Evidence, *Cancers (Basel)*, 2020 Mar; 12(3): 738. Published online 2020 Mar 20. doi: [10.3390/cancers12030738](https://doi.org/10.3390/cancers12030738) and FDA-approved drug package inserts for immune checkpoint inhibitors



# HCW9218 Studies Show It Boosts Potency of Immune Checkpoint Inhibitors(ICIs)



- HCW9218 activates, expands and induces tumor trafficking of progenitor exhausted stem-like and transitory CD8<sup>+</sup> T cells.
- HCW9218 induces Natural Killer (“NK”) cell and CD8<sup>+</sup> T cell activation, proliferation, and infiltration into the tumor microenvironment which correlates with disease stabilization.
- HCW9218 significantly reduced blood levels of TGF-β in cancer patients in a dose-dependent manner, without causing treatment-emergent skin lesions and bleeding events previously reported with TGF-β antagonists in clinic.

Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. *Mol Ther* 2022 30:1171-1187  
 George, V et al., Bifunctional immunotherapeutic HCW9218 facilitates recruitment of immune cells from tumor draining lymph nodes to promote antitumor activity and enhance checkpoint blockade efficacy in solid tumors. *Cancer Res* (2023) 83 (7\_Supplement): 4441.

# Clinical Development Strategy for HCW9218

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- Plans for Phase 2 clinical trials in cancer indications
  - Initiated randomized Phase 2 clinical trial against ovarian cancer in the neoadjuvant settings with UPMC.
    - HCW9218 + neoadjuvant chemotherapy vs. chemotherapy alone.
  - Initiate Phase 2 studies to evaluate HCW9218 in combination with standard-of-care chemotherapies in 2024.
    - Second-line for pancreatic cancer with chemotherapy.
    - Second-line for chemo-refractory/relapsed advanced ovarian cancer.
- Investigative studies in other areas related to aging – aesthetics
  - Pilot study on senile lentigo and deep wrinkles in 2024, as secondary endpoints in skin cancer trial.



# Clinical Trial Strategy

## Mitigate Execution Risk

- Lower risk of delays for patient recruitment and enrollment at clinical sites by partnering with National Cancer Institute (“NCI”) Designated Comprehensive Cancer Centers, NCI Designated Cancer Center, and NCI itself.
- Work with the strongest principal investigators with passion for the underlying science and search for breakthrough therapeutics.

## Mitigate Financing Risk

- When possible, partner with clinical sites with funding, e.g., NCI and National Institutes of Health.
- Employ strategies to use our compounds with standard-of-care treatments. This provides some insurance reimbursement.
- Join randomized trials as an arm of a larger study.
- Strategically use smaller, shorter trials if they can achieve valid endpoint(s).
- License non-core assets and marketing rights.

## Focus Clinical Trials on HCW9218 in Near Term

- Focus on evaluating HCW9218 in combination with standard-of-care cancer therapies.
- Select indications with P1 stable disease and strong evidence from correlative studies – ovarian and pancreatic cancer.
- Branch out to other indications opportunistically, in cases where trials are funded by strong sponsors and indication is appropriate.
- Pursue the potential of HCW9218+PD1 combination thru collaborative agreement with big pharma or sponsor.



# Clinical Pipeline

Product	Administration Route	Mechanism of Action	Indication	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3
HCW9218	Subcutaneous Injection (In vivo)	Immune-Cell Activation & TGF- $\beta$ Neutralization	Solid Tumors <sup>1</sup>	<i>Enrollment Completed February 2024</i>				
			Ovarian Cancer <sup>2</sup>	<i>Initiation Phase 2 Study 1H 2024</i>				
			Pancreatic Cancer <sup>3</sup>	<i>Enrollment Completed February 2024</i>				
HCW9302		T <sub>reg</sub> Expansion	Autoimmune Disorders	<i>IND: 1H 2024</i>				
HCW9201 + HCW9206 <sup>4</sup>	Cell-based Therapy (Ex vivo)	NK Cell Expansion	AML	 <i>Clinical Readout 2H 2024</i>				

1. Investigator-sponsored Phase 1 clinical trial with University of Minnesota to evaluate HCW9218 in patients with chemo-refractory/chemo-resistant solid tumors, including ovarian, prostate, breast and colorectal cancers.
2. Investigator-sponsored Phase 2 clinical trial with University of Pittsburgh Medical Center with metastatic advanced stage ovarian cancer patients to evaluate HCW9218 in a combination with neoadjuvant chemotherapy.
3. Company-sponsored Phase 1b/2 clinical trial with five clinical sites, including the National Cancer Institute, to evaluate HCW9218 in patients with advanced chemo-refractory/chemo-resistant pancreatic cancer.
4. Wugen's lead clinical program, WU-NK-101, is based on HCWB licensed molecules. Wugen holds an exclusive worldwide license for two of our molecules, HCW9201 and HCW9206. The Wugen License conveys limited rights to develop cell-based therapy treatments for cancer using the licensed molecules. HCW Biologics has retained all other rights to HCW9201 and HCW9206, including, but not limited to, manufacturing rights and injectable rights.



# Thank You!

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CFO

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