



# Novel Immunotherapeutics for Cancer and Other Age-Related Diseases

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H.C. WAINWRIGHT ANNUAL GLOBAL LIFE SCIENCES CONFERENCE

MAY 25, 2022

# Forward Looking Statements

Certain information 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 include, without limitation, statements about the product candidates of HCW Biologics Inc. (the “Company”) and the utility of the TOBI platform in identifying and discovering 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.

Actual results or events could differ materially from the plans, intentions, expectations and projections disclosed in the forward-looking statements. Various important factors could cause actual results or events to differ materially, including, but not limited to, the risk that trials and studies may be delayed or terminated as a result of COVID-19 and other factors, that the Company or its collaborators may be unable to successfully develop and commercialize its product candidates, that the Company may not be able to identify licensees to develop the Company’s internally-developed modules into lead product candidates, that the Company’s novel immunotherapy platform may not result in approvable or marketable products, that the Company is unable to complete the clinical development of or successfully commercialize HCW9218, 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, that the Company will need to raise additional capital, which may not be available on favorable terms, if at all, 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, 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 Quarterly Report on Form 10-Q filed with the United States Securities and Exchange Commission (the “SEC”) on May 13, 2022, and the Company’s Annual Report on Form 10-K filed with the SEC on March 29, 2022, and in other filings filed from time to time with the SEC. Forward-looking statements contained in this press release are made as of this date, and the Company undertakes no duty to update such information except as required under applicable law.

# Investment Highlights



**HCW Biologics is a clinical stage immunotherapy company in the emerging field of inflammaging**  
-- Our goal is to fundamentally change the treatment of age-related diseases

**Our approach is to treat primary underlying causes of chronic inflammation**  
-- Eliminate senescence, deactivate inflammasomes, and reduce proinflammatory factors

**Clinical development strategy: Use cancer as the gateway indication**  
-- Expand indications beyond cancer once safety and dosage established

**Key 2022 milestones: Expect to initiate two Phase 1/1b clinical trials for solid tumors**  
-- Phase 1 solid tumor basket trial has initiated, and Phase 1b pancreatic trial expected to initiate mid-2022

**Cash runway will fund operations to the end of 2023**  
-- Company is actively seeking out-licenses as source of nondilutive financing

# Experienced Team with Success in Drug Discovery and Development

## Senior Management



**Hing C. Wong, PhD**

FOUNDER  
CHIEF EXECUTIVE OFFICER



**Peter Rhode, PhD**

CHIEF SCIENTIFIC OFFICER AND  
VICE PRESIDENT  
CLINICAL OPERATIONS



**Jin-an Jiao, PhD**

VICE PRESIDENT  
DEVELOPMENT



**Jack Egan, PhD**

VICE PRESIDENT  
MANUFACTURING AND  
QUALITY CONTROL



**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**

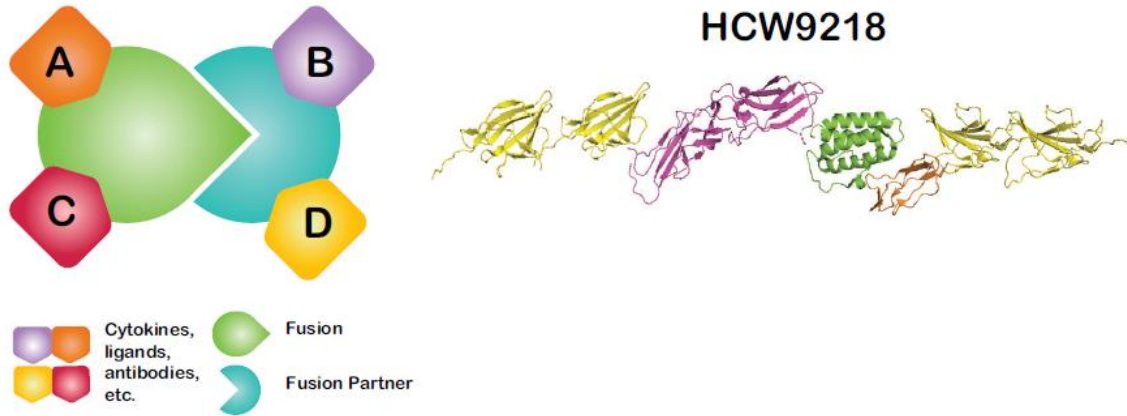
DIRECTOR  
HUMAN RESOURCES



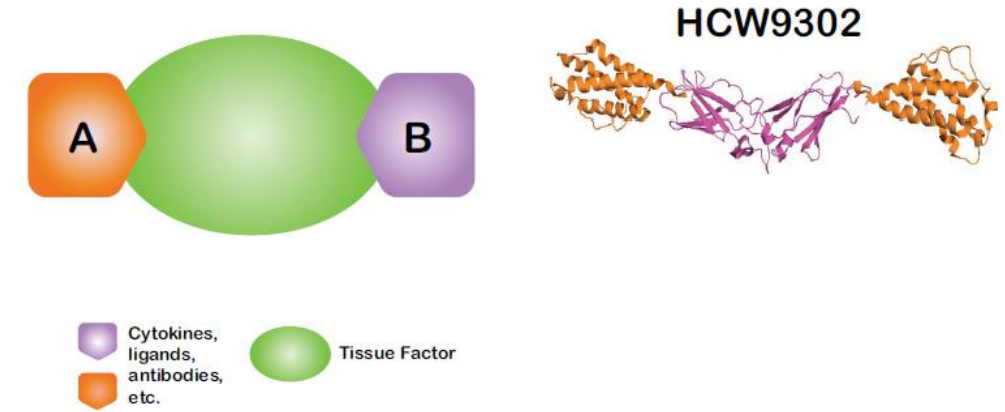
# TOBI™ Platform Technology “Tissue Factor-Based Fusion”

## Novel Scaffold to Generate Proprietary Fusion Molecules

### Multi-Specific Fusion Complex



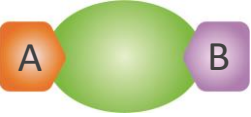
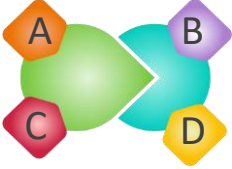
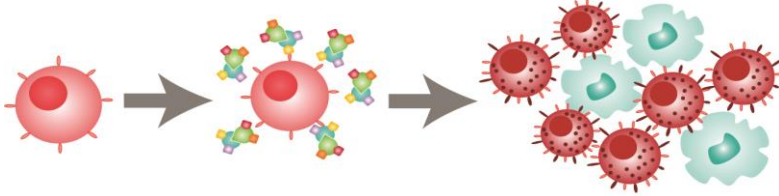
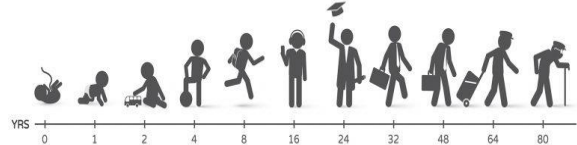
### Bispecific Fusion



- 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.
- 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.

# Commitment to Strong Protection for Intellection Property \*

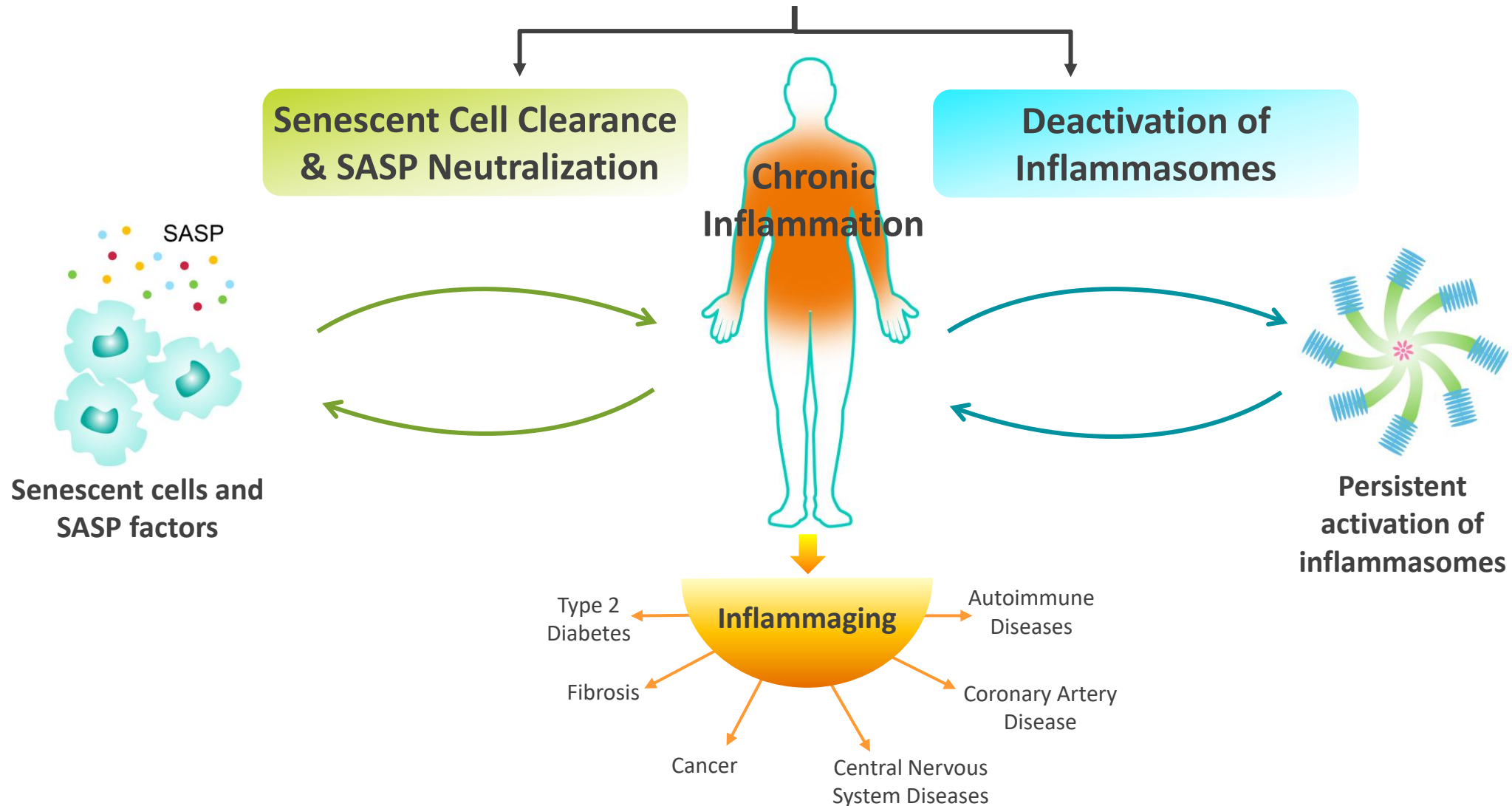
Single-chain Platform	Multi-chain Platform	Methods of Culturing Immune Cells	Methods of Treating Age Related Disorders
			
<ul style="list-style-type: none"> <li>• 61 pending patent applications, worldwide, including 11 pending U.S. utility patent applications, 1 pending provisional U.S. patent application, 6 pending PCT applications, 4 Hong Kong applications, and 39 pending non-U.S. national phase patent applications.</li> <li>• 5 U.S. trademark applications for our corporate name, corporate logo, and the TOBI™ platform.</li> <li>• 20 specific constructs included in the filed U.S. patent applications.</li> <li>• Recently filed U.S. applications include methods for treating age-related and inflammatory diseases.</li> <li>• Advised by preeminent Intellectual Property firm, Fish &amp; Richardson P.C.</li> <li>• Robust IP strategy to aggressively protect company proprietary developments.</li> </ul>			

\* Status as of December 31, 2021



# HCW Biologics' Immunotherapeutic Approach

## Targets Two Primary Pathways for Inflammaging



# Lead Molecules for Anti-Inflammaging Treatments

## HCW9218

### Bifunctional Fusion Molecule

Designed as a senolytic for senescent cell clearance and senomorphic for neutralization of proinflammatory SASP factors, especially TGF- $\beta$ .

### Clinical Stage

Phase 1 trial initiated in solid tumors.

HCW9218



## HCW9302

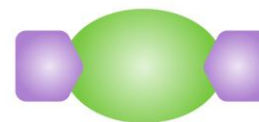
### IL-2-based Fusion Molecule

Designed to activate and expand T<sub>reg</sub> cells to suppress activity of inflammasome-bearing cells and inflammatory factors they secrete.

### IND-Enabling Stage

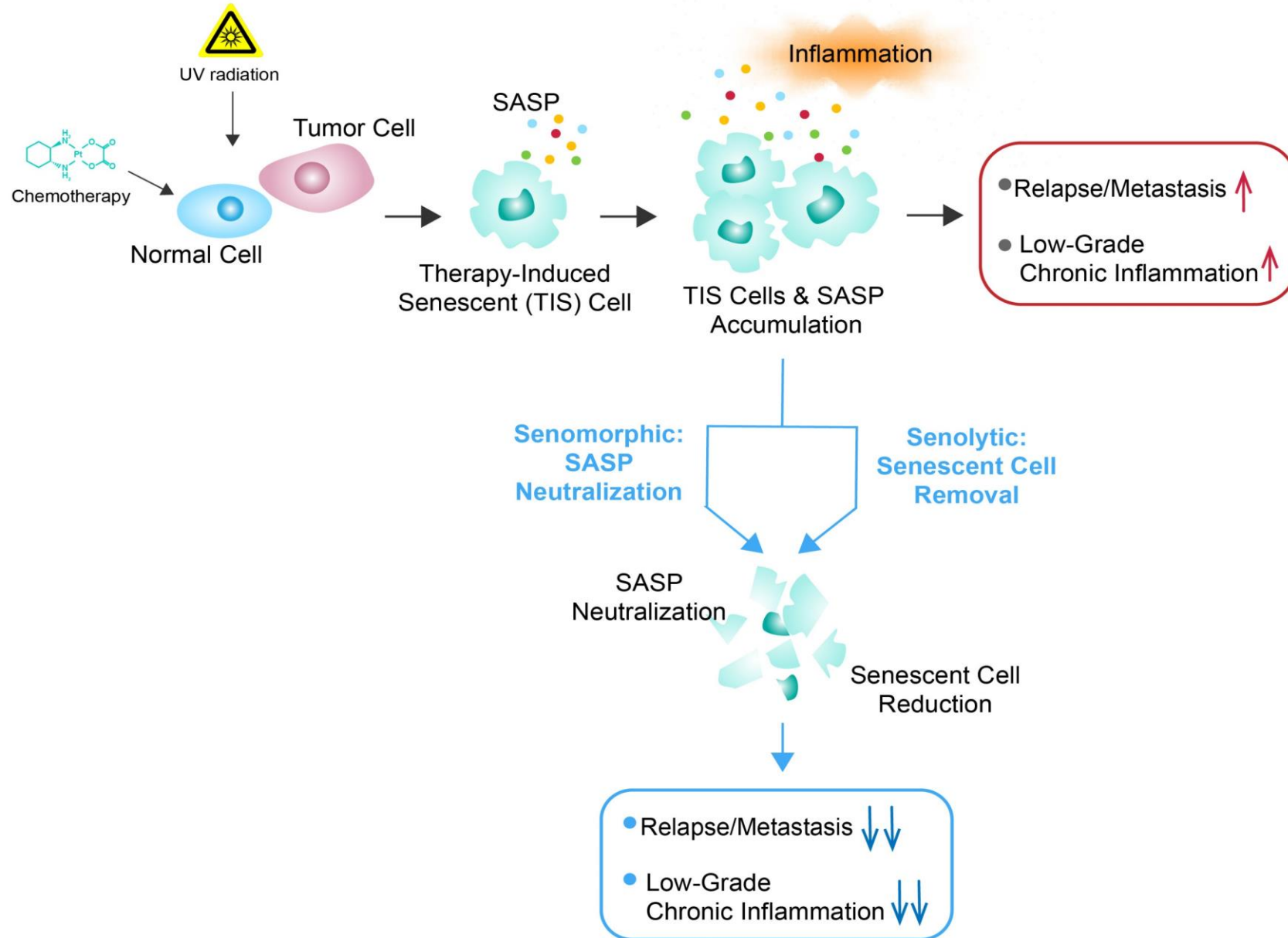
Expect to complete IND-enabling activities in 2H 2022 and file IND in 1Q 2023.

HCW9302





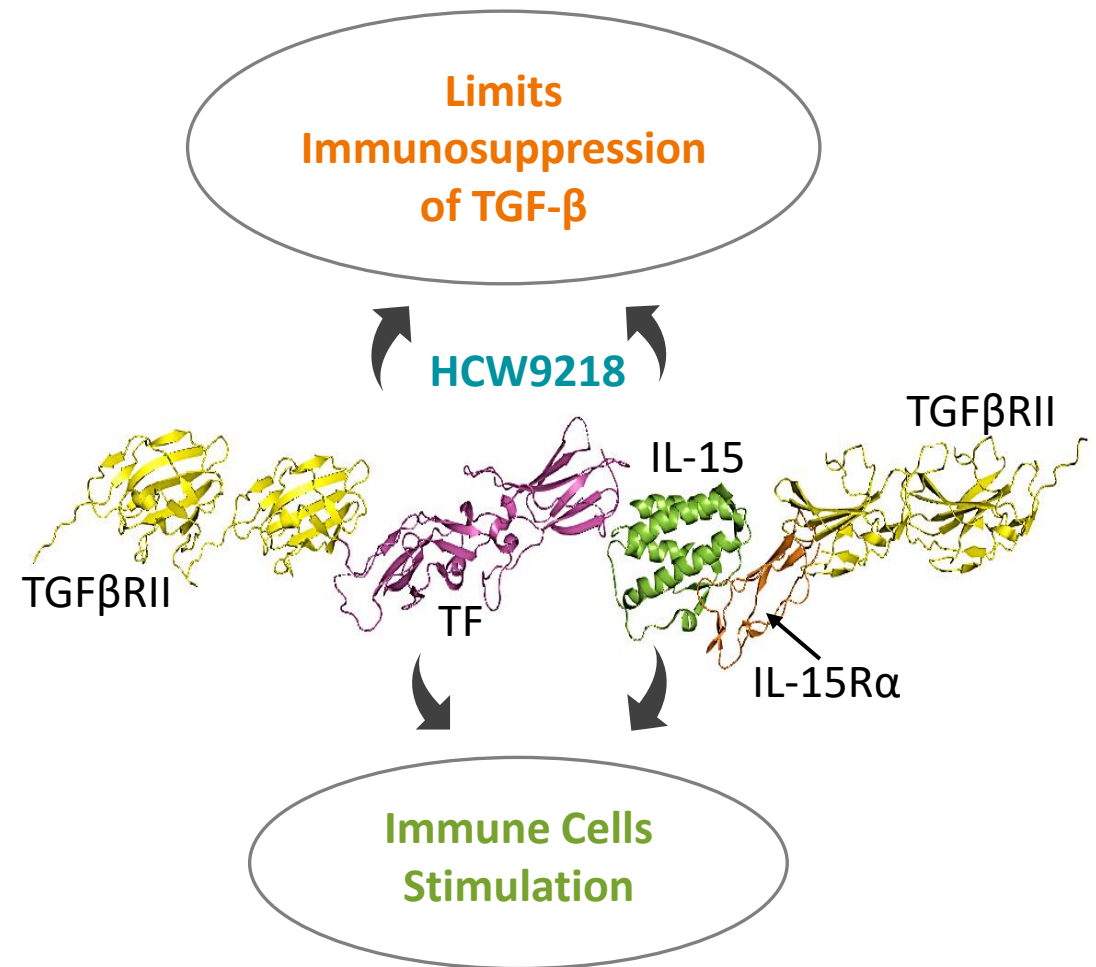
# Therapy-Induced Cellular Senescence in Cancer Therapies



# HCW9218 as Potential Treatment for Cancer and Therapy-Induced Senescence (TIS)

We believe the bifunctionality of HCW9218 will allow it to be effective against solid tumor cancer:

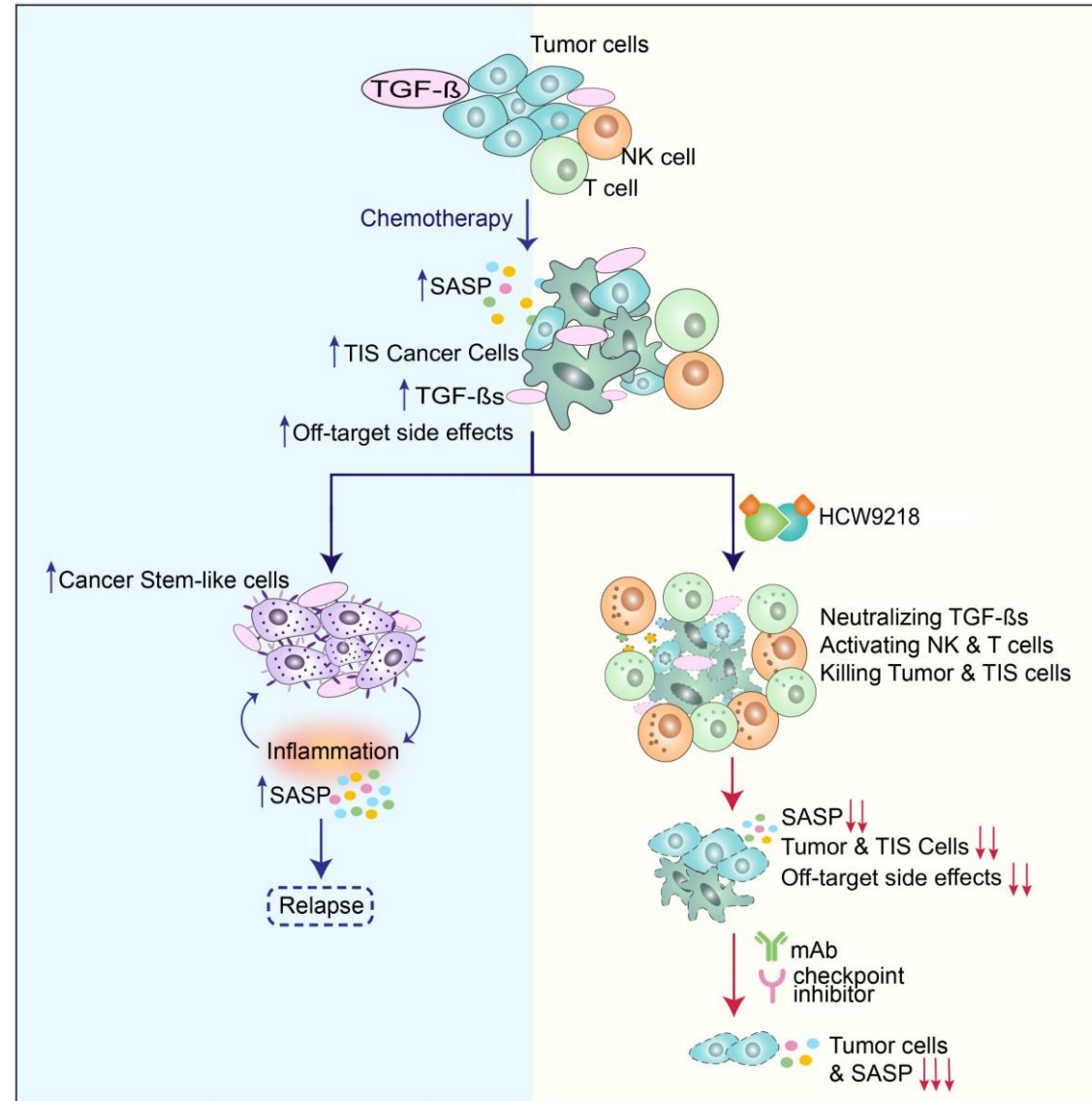
- Reduces immunosuppression associated with solid tumors by capturing and neutralizing TGF- $\beta$ .
- Provides immunostimulation of natural killer (“NK”) cells and effector T cells to enhance the cytotoxicity of immune cells against tumor targets.



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.

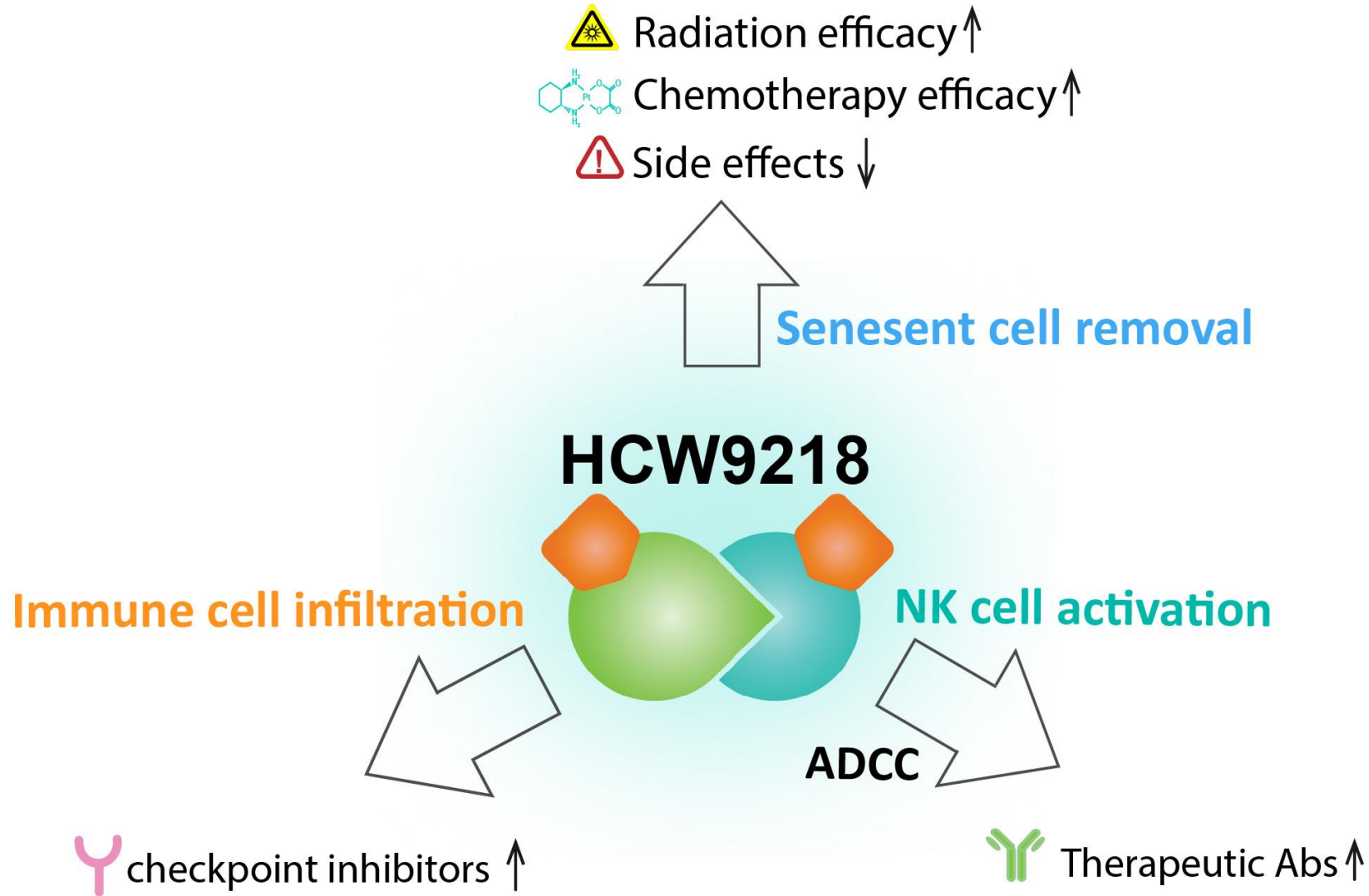
Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. Mol Ther 2022 30:1171-1187.

# Mechanism of Action of HCW9218 for Anti-Cancer Therapy



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.

# HCW9218 Potential Clinical Utilities Against Cancer



# HCW9218: Reduction of Therapy-Induced Senescence to Improve Anticancer Therapy

## ➤ Expert opinions

- “Senescent tumor cells: an overlooked adversary in the battle against cancer”  
*Park S.S. et al., Experimental & Molecular Medicine (2021) 53:1834-1841.*
- “Therapy-Induced Senescence: Opportunities to Improve Anticancer Therapy”  
*Prasanna P.G. et al., Natl Cancer Inst (2021) 113:1285-1298.*

## ➤ HCW Biologics’ publication: HCW9218 removes therapy-induced senescent cells to augment anti-cancer therapy and alleviate side effects of chemotherapies:

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

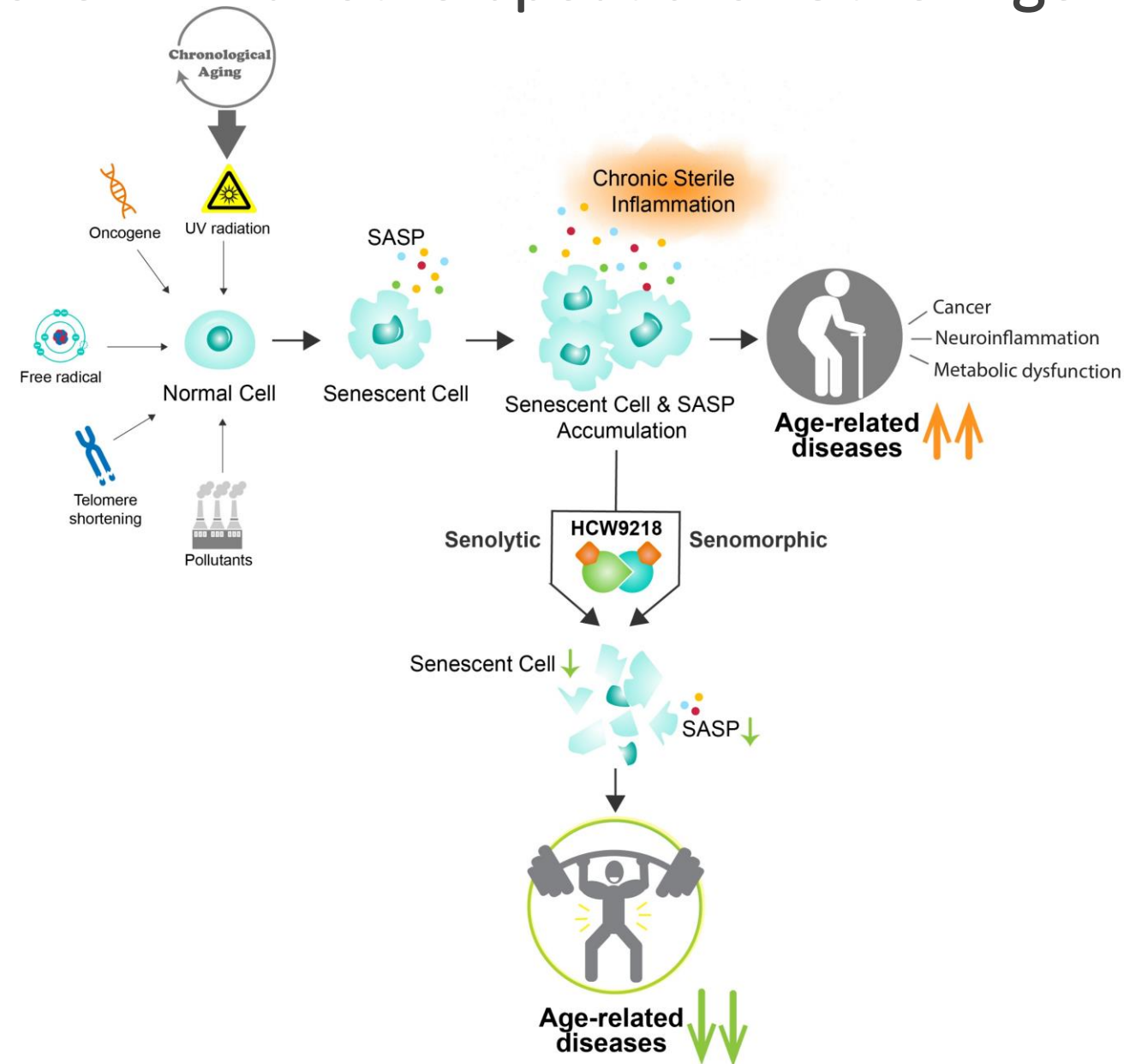


# Clinical Development Strategy of HCW9218: From Cancer to Inflammaging

- **We have selected difficult-to-treat, advanced solid tumor cancers that have progressed after standard-of-care treatments as our initial indications:**
  - Chemotherapy treatments cause TIS which drives tumor cells to senescence, resulting in increased drug resistance, immune evasion, disease relapse, and tumor metastasis.
  - HCW9218 is a potential adjuvant therapy of chemotherapy and immune-checkpoint therapy that may eliminate TIS cancer cells to achieve better anti-tumor responses and alleviate chemotherapy-induced side effects.
- **The identified safe dose and remedies in cancer trials will be used to expand indications to other age-related diseases.**

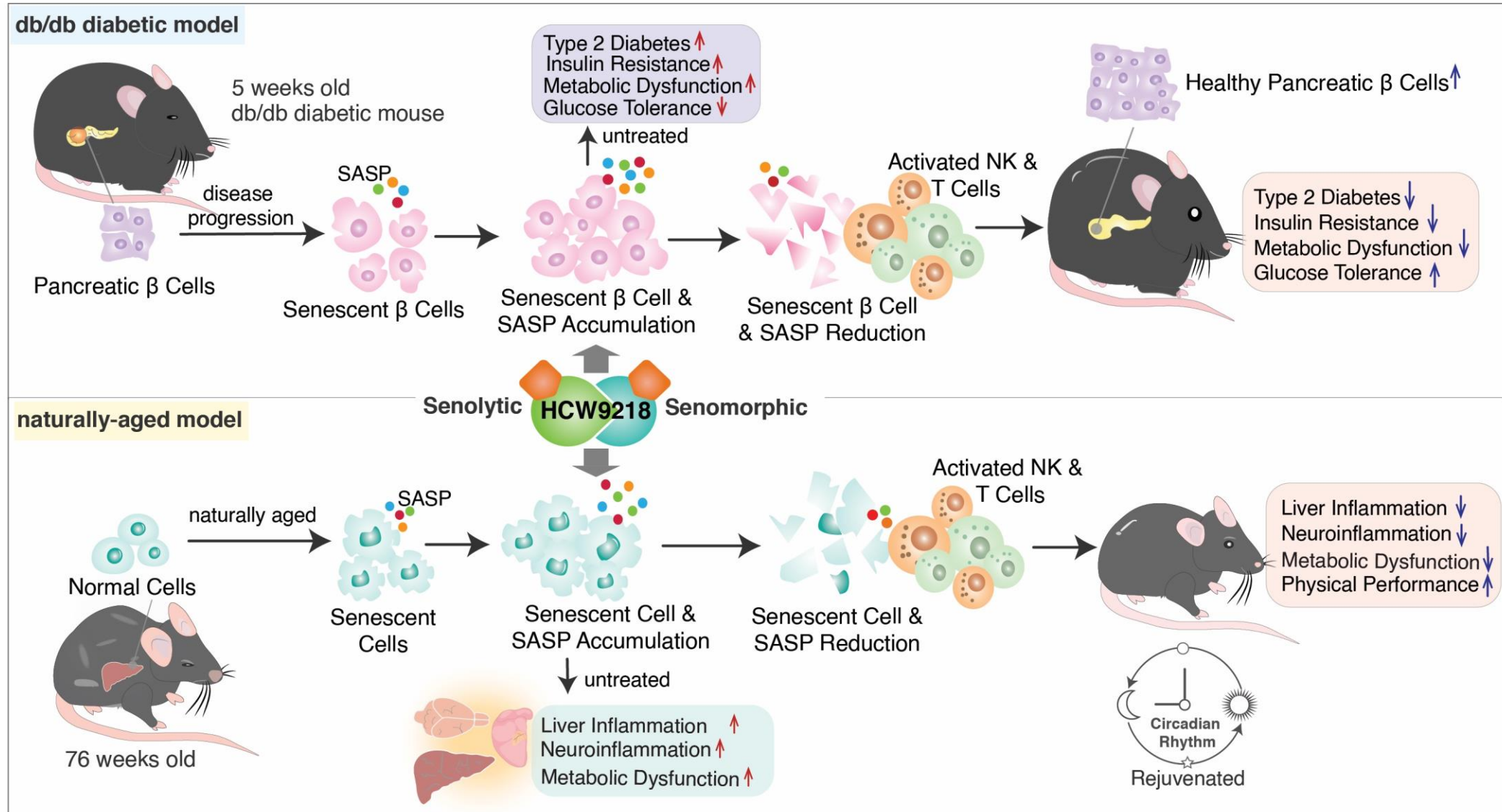


# HCW9218: Novel Immunotherapeutic for Other Age-Related Diseases





# HCW9218: Novel Senolytic and Senomorphic Immunotherapeutic in Mice



# HCW9218: Preclinical Data for Age-Related Pathologies

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## ➤ **HCW9218 shows potential for treatment of Type 2 Diabetes**

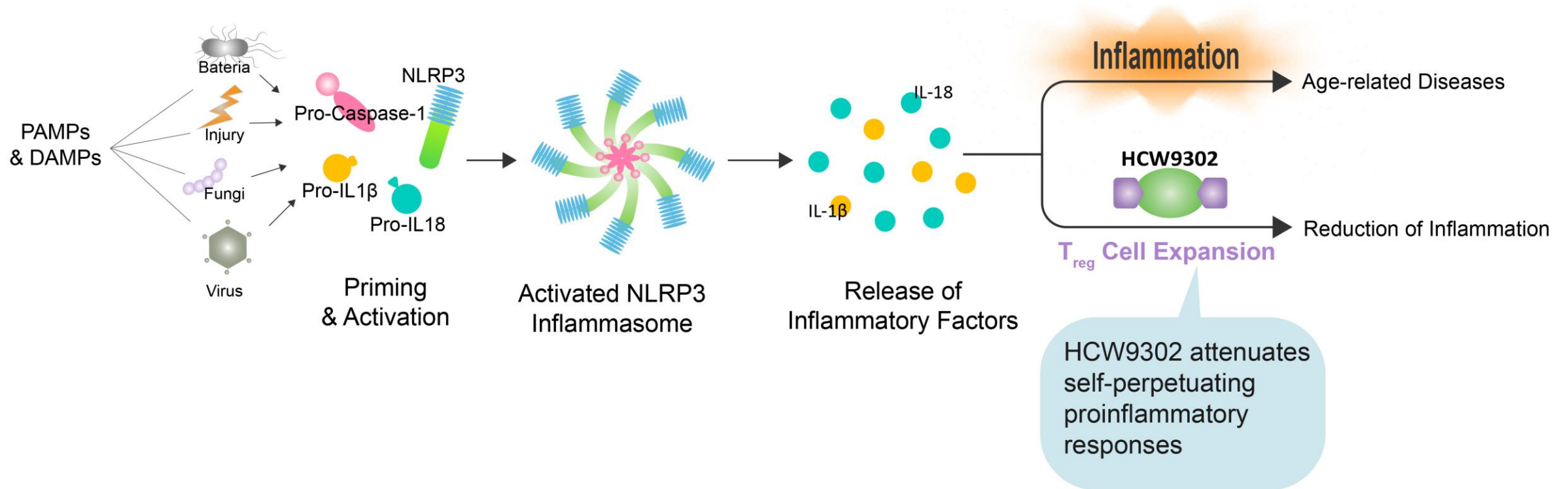
- Studies in db/db diabetic mouse model
- Significantly reduces senescent islet- $\beta$  cells
- Significantly lowers glucose and insulin resistance
- Well tolerated

## ➤ **HCW9218 shows potential for treatment of age-related indications**

- Studies based on naturally-aged mouse model
- Lowers chronic inflammation in peripheral organs and central nervous system
- Improves the health span of naturally-aged mice
- Well tolerated



# HCW9302: Novel Immunotherapeutic T<sub>reg</sub> Expansion











# HCW9302: Potential Treatment of Autoimmune Diseases and Metabolic Disorders \*

Characteristics	Supporting Preclinical Data
<b>50-fold expansion of T<sub>reg</sub> cells</b>	<ul style="list-style-type: none"><li>➤ In studies with human T<sub>reg</sub> cells (<i>ex vivo</i>), HCW9302 showed increased binding activity for IL-2 receptor <math>\alpha</math>.</li><li>➤ HCW9302 increased suppressive activity against responder T cells.</li></ul>
<b>Prolonged half-life compared to IL-2</b>	<ul style="list-style-type: none"><li>➤ In mice models (<i>in vivo</i>) with HCW9302, dose-dependent expansion of T<sub>reg</sub> cells following subcutaneous dosing.</li><li>➤ Repeated subcutaneous dosing was well tolerated (NHP studies ongoing).</li></ul>
<b>Abated inflammation and reduced symptoms of metabolic dysfunction</b>	<ul style="list-style-type: none"><li>➤ In atherosclerosis using ApoE<sup>-/-</sup> mice fed with high fat diet &amp; Ldlr<sup>-/-</sup> mice, HCW9302 treatment:<ul style="list-style-type: none"><li>• Expanded T<sub>reg</sub> cells and repolarized macrophage with anti-inflammatory properties.</li><li>• Decreased plaque area in aortas.</li><li>• Reduced levels of fasting glucose and insulin resistance.</li></ul></li></ul>

\* HCW Biologics evaluating out-licensing opportunities to support adoptive T<sub>reg</sub> cell therapy. The Company's focus is administration using subcutaneous injection.

# Product Pipeline

Product	Administration Route	Mechanism of Action	Indication	Discovery	IND-Enabling	Phase I	Phase II	Phase III
HCW9218	<b>Subcutaneous Injection (In vivo)</b>	Immune-Cell Activation & TGF- $\beta$ Neutralization	Pancreatic Cancer					
			Solid Tumor Cancer <sup>(1)</sup>					
			Liver Cancer					
			NAFLD					
HCW9302	<b>Cell-based Therapy (Ex vivo)</b>	T <sub>reg</sub> Expansion	Alopecia Areata					
HCW9302 <sup>(2)</sup>		T <sub>reg</sub> Expansion	Autoimmune/Inflammatory Diseases					
HCW9201 <sup>(3)</sup>		CIML NK Cell Expansion	AML	 				

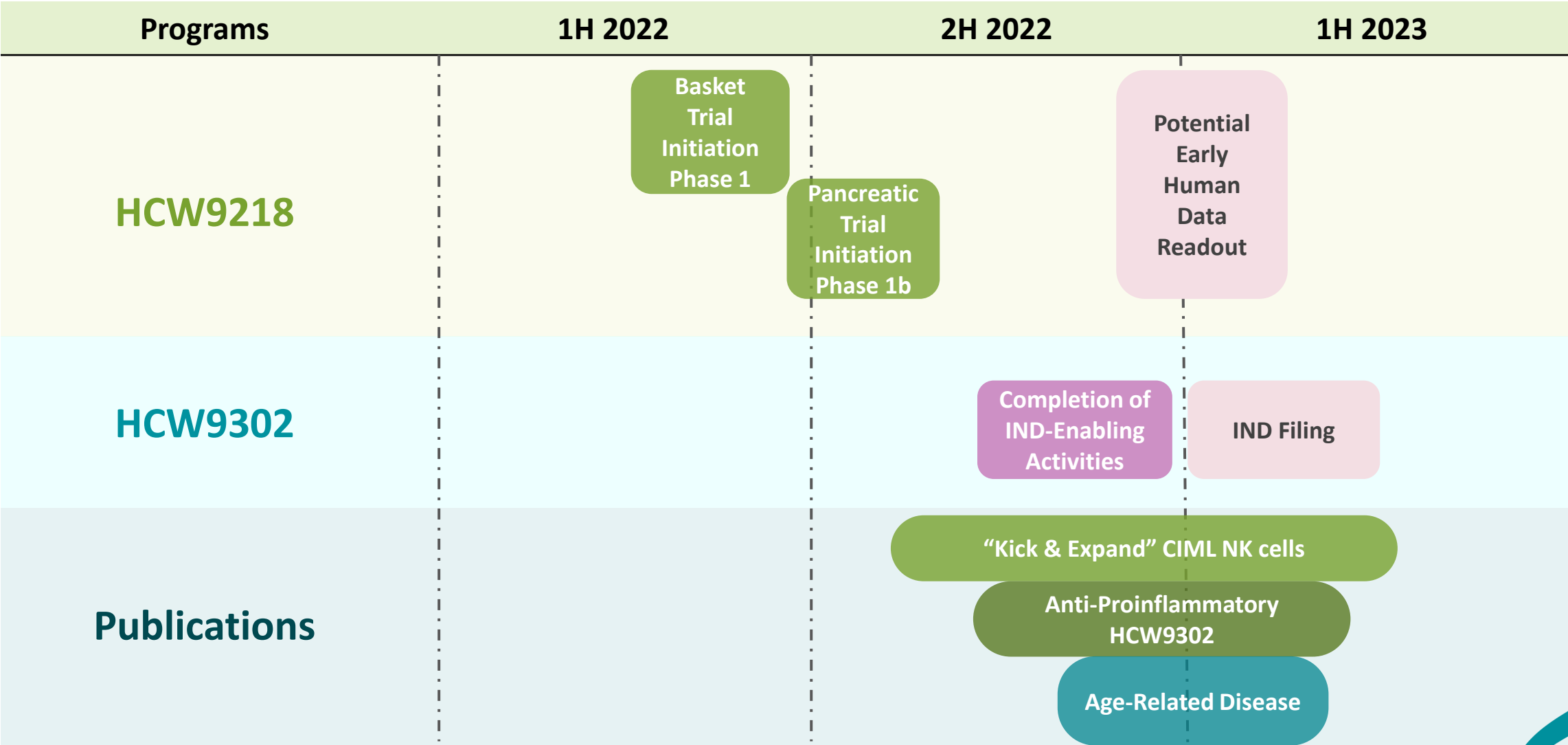
(1) The solid tumor clinical trial is a basket trial that includes patients with breast, ovarian, prostate, and colorectal cancers.

(2) Available for license from HCW Biologics for ex vivo T<sub>reg</sub> cells expansion.

(3) Wugen licensed HCW9201, a clinical-stage molecule, from HCW Biologics for limited rights to develop cell-based therapy treatments. HCW Biologics has retained all other rights to HCW9201.



# Anticipated Events For Potential Value Creation Over Next 12 Months



# Thank You!

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