

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

SEPTEMBER 2023

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 check point 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 March 28, 2023, the latest Quarterly Report on Form 10-Q filed with the SEC on August 11, 2023, 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.

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

HCW Biologics: A Leader in the Emerging Field of Inflammaging

Human data readout for two Phase 1/1b clinical trials in cancer indications expected in next 3 - 6 months.

Human data readout for Phase 1 study in solid tumors anticipated at major industry event in the fall 2023. Phase 1b pancreatic cancer readout expected 1H 2024.

Gaining control over supply chain and improve lab space in new headquarters.

Project financing obtained for buildout. Planned to come online in 2H 2024.

HCW9218 anti-cancer mechanism of action studies show utility in boosting efficacy of standard-of-care cancer treatments.

Ability to stimulate and expand precursor exhausted T cells that are the engine that drive immune checkpoint inhibitors (ICIs). Also can eliminate therapy-induced senescence in chemo.

Initiation of first Phase 2 clinical study for HCW9218 expected in next 6 months.

First Phase 2 study in neoadjuvant setting. Later in 2024, plans for studies in combination with ICIs and chemotherapy.

Financing planned 1H 2024 with momentum from achieving clinical milestones.

Debt or equity offering. Also pursuing non-dilutive forms of financing: grants and licenses for rights to non-core assets and non-core marketing rights.

Established thought leadership through pivotal scientific papers.

Numerous publications in peer-reviewed, high-impact journals, such as *Aging Cell, Frontiers in Immunology, and Molecular Therapy.*



Commitment to Strong Protection of Intellectual Property *



- 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 two lead molecules, HCW9218 and HCW9302.
 - Method of use patents that protect 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 August 24, 2023

TOBITM Platform Technology "<u>T</u>issue Fact<u>O</u>r-<u>B</u>ased Fus<u>l</u>on" Patented Novel Scaffold to Generate Proprietary Fusion Molecules



- 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-β 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

- <u>Reduces immunosuppression</u> associated with solid tumors by capturing and neutralizing TGF-β in tumor draining lymph nodes and tumor microenvironment.
- **Provides immunostimulation and expansion** of progenitor exhausted stem-like (" T_{pex} ") and transitory effector (" T_{eff} ") CD8⁺ T cells in tumor-draining lymph nodes (TDLN) and memory CD8⁺ T cells (" $T_{cm} \& T_{vm}$ ") 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-β 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.

HCW9218 Potential Clinical Utilities Against Cancer



HCW9218: Senescent Cell Removal: Utility in combination with Chemotherapy and Therapy Induced Senescence ("TIS")

Therapy-Induced Cellular Senescence



Clearance of TIS Cancer Cells by HCW9218



Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. Mol Ther. January 17, 2022. https://doi.org/10.1016/j.ymthe.2022.01.025

HCW9218 Enhances the Anti-Tumor Activity of Chemotherapy



Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. Molecular Therapy. January 17, 2022. https://doi.org/10.1016/j.ymthe.2022.01.025

HCW BIOLOGICS

13

HCW9218 Alleviates Off-Target Effects of Chemotherapy in Normal Tissue



HCW BIOLOGICS

14

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:

Immune Cell Infiltration and Activation: Utility in Combination with Immune Checkpoint Inhibitors

Future Commercial Potential: Utilizing HCW9218 + ICIs for Cancer Treatment

HCW9218 is a promising immunotherapeutic to enhance the response rate of immune checkpoint inhibitors for solid tumors.



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.

Immune Checkpoint Inhibitors Objective Response Rates Vary Across Indications



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 and FDA-approved drug package inserts for immune checkpoint inhibitors

Immune Checkpoint Inhibitors: Market Research

The global PD-1 and PD-L1 inhibitors market size is driven by the increased demand for more effective cancer treatment solutions and an aging population.

- Market is dominated by three players:
 - Merck's Keytruda (over 50%)
 - o BMS' Opdivo
 - o Roche's Tecentriq
- Patent expiration for market leaders:
 - Keytruda: Patent expires in US in 2028 and in EU 2031.
 - Opdivo: Patent expires in US in 2027 and in EU in 2026.
- Per patient average treatment cost can exceed <u>\$150,000</u>, while combination therapies can exceed <u>\$300,000</u> for some treatment options.

Rationale of Combining HCW9218 and Immune Checkpoint Inhibitors for Cancer Treatment

HCW9218 studies show it boosts potency of immune checkpoint inhibitors:

- Stimulates and activates immune cells
- Promotes immune cell infiltration
- Reduces
 - immunosuppression of TGF-β

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.

HCW BIOLOGICS

20

HCW9218 Enhances the Efficacy of Immune Checkpoint Therapy

Chaturvedi, P et al., Immunotherapeutic HCW9218 Augments Anti-tumor Activity of Chemotherapy via NK Cell Mediated Reduction of Therapy Induced Senescent Cells. Molecular Therapy. January 17, 2022. https://doi.org/10.1016/j.ymthe.2022.01.025

HCW BIOLOGICS

21

HCW9218: Clinical Study Update: Phase 1 Solid Tumor Trial and Phase 1b Advanced Pancreatic Cancer Trial

US Clinical Sites: Internationally Recognized National Cancer Institute Designated Comprehensive Cancer Centers

Ancillary Studies to Clinical Trials Gathering Human Data and Expected to Support HCW9218 Anti-Cancer Utility

- Robustly promotes NK cell and CD8⁺ T-cell expansion and activation in patients with chemotherapy refractory solid tumors.
- Significant increases the CD8⁺ 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.
- Activates and expands progenitor exhausted stem-like and transitory CD8⁺ T cells: enhancing anti-cancer and anti-aging activities of immune checkpoint inhibitors.
- Activates and expands T_{cm} and T_{vm} CD8⁺ T cells and NK cells to provide anti-cancer and anti-aging activities.

Clinical Development: Upcoming Milestones

Product 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-β Neutralization	Solid Tumor Cancer	Clinical				
			Pancreatic Cancer	Clinical	Readout: Q1 2	024		
HCW9302		T _{reg} Expansion	Autoimmune Diseases	IND: Q4 2023				
HCW9201 + HCW9206	Cell-based Therapy (Ex vivo)	NK Cell Expansion	AML	Wug	gen Clinical Read	out: Q2 2024		

(As of September, 2023)

Future Drug Development Strategy for HCW9218

• Plans for Phase 2 clinical trials in cancer indications:

- Initiate randomized Phase 2 clinical trial against ovarian cancer in the neoadjuvant settings in 2023.
 - HCW9218 + chemotherapy vs. chemotherapy alone. The Phase 2 IND has been submitted in August 2023.
- Combine HCW9218 with chemotherapies for Phase 2 clinical trials in early 2024.
 - Second-line for chemo-refractory/relapsed advanced ovarian cancer.
 - Second-line for pancreatic cancer with G+A.
- Combine HCW9218 with immune checkpoint inhibitors for Phase 2 clinical trials in 1H 2024.
- Plans for other age-related diseases:
 - Pilot study on senile lentigo and deep wrinkles in 2024.

HCW9218: Upcoming Financing in 2024

Financing Event - 2024

- Current cash runway expected to last at least into Q4 2024, without additional funding.
- Timing for 2024 investment 1H 2024, with momentum from the following milestones we expect to achieve prior to that time:
 - Human data readout from Phase 1 solid tumor trial at SITC conference 2023.
 - Completion of Phase 1 solid tumor trial.
 - Announcement of first Phase 2 solid tumor trial.
 - Human data readout of Phase 1b pancreatic cancer trial.
 - Announcement(s) of funding from private research organizations and NIH.
- Amount of investment \$30 million to \$50 million.

Thank You!

Rebecca Byam CFO HCW Biologics Inc. (NASDAQ: HCWB) 2929 North Commerce Parkway Miramar, FL 33025 Email: RebeccaByam@hcwbiologics.com Website: https://hcwbiologics.com/

