Media Contact:

John Cashman, Ph.D.
Human BioMolecular Research Institute
San Diego, California 92121
JCashman@hbri.org
(858) 458-9305

"A novel small molecule inhibits tumor growth and synergizes effects of enzalutamide on prostate cancer".

Potent Inhibitor of prostate cancer, **PAWI-2**, featured in *Journal of Pharmacology and Experimental Therapeutics.*

San Diego, Calif., October 3, 2019 - Researchers at the Human BioMolecular Research Institute and ChemRegen, Inc., reported that a small molecule potently inhibited prostate cancer. Publishing October 3, 2019, in the *Journal of Pharmacology and Experimental Therapeutics*, the team describes how they tested **PAWI-2**, a man-made, drug-like chemical that can be used to inhibit prostate cancer and other cancers.

"Prostate cancer is the second leading cause of cancer-related death for men in the United States and resulted in an estimated 29,430 deaths in 2018. About 35% of prostate cancer recurs and is often transformed to castrate-resistant prostate cancer, the most deadly and aggressive form of prostate cancer. However, the standard-of-care treatment for castrate-resistant prostate cancer (i.e., enzalutamide with abiraterone) usually has limited efficacy. We need to develop effective new medications for prostate cancer," said John Cashman, Ph.D., President of Human BioMolecular Research Institute and co-author of the study. "Using a non-toxic small molecule to stop prostate cancer either by itself or in combination with standard of care chemotherapy is very appealing."

Dynamic medicinal chemistry affords anti-cancer drug

A team of medicinal chemists at the Human BioMolecular Research Institute, led by John Cashman, Ph.D., using dynamic medicinal chemistry, developed the compound **PAWI-2**. When added to prostate cancer cells, **PAWI-2** potently stimulated inhibition of prostate cancer cell proliferation.

"At this point, this molecule appears to have all the properties for a new therapeutic drug candidate for prostate cancer," explained Jiongjia Cheng, Ph.D., a researcher in Cashman's lab and lead author of the paper.

Cashman and Cheng in collaboration with other scientists are now working with San Diego biotech company ChemRegen, Inc. to further develop **PAWI-2** into a therapeutic drug candidate.

How PAWI-2 works

Developing new medications for castrate-resistant prostate cancer and other cancers is important. Currently, prostate cancer is the second most common cause of cancer in men in the United States. For prostate cancer, the difficult part is: 1) figuring out the cellular signals that direct cancer growth and 2) understanding the basis for resistance to current cancer therapies.

PAWI-2 works as a non-toxic DNA damage pathway inhibitor and activates mitochondrial-controlled p53-dependent apoptotic signaling. Apoptosis is a process that tells the cell when to stop dividing and it influences other cell behaviors, such as proliferation and differentiation. With apoptosis signaling potently turned on, cancer cells are set on a course toward destruction and removal. **PAWI-2** activated an apoptosis protein in mitochondria and chokes cell proliferation, ultimately altering cellular behavior - in this case decreasing prostate cancer cell growth.

In this report, it was shown that anti-cancer **PAWI-2** is an anti-prostate cancer compound that works against androgen-sensitive prostate cancer and androgen-insensitive castrate-resistant prostate cancer and also patient-derived bone niche prostate cancer. **PAWI-2** synergized currently clinically used enzalutamide in in vitro inhibition of prostate cancer and also enhanced inhibition of tumor growth in a PC-3 xenograft model. **PAWI-2** may afford more efficacious treatment with decreased side effects and also afford a molecule for both androgen-dependent and androgen-resistant prostate cancer treatment.

###

Media contacts: To arrange on-site, phone, or Skype interviews with the researchers involved in this study, please contact John Cashman at (858) 458-9305 / JCashman@hbri.org.

This research was funded by the Human BioMolecular Research Institute and the National Institute of Health.

The study was co-authored by Jiongjia Cheng, Human BioMolecular Research Institute; Stephanie Moore, Human BioMolecular Research Institute; Jorge Gomez-Galeno, ChemRegen Inc; Dong-Hoon Lee, Human BioMolecular Research Institute; Karl Okolotowicz, Human BioMolecular Research Institute and ChemRegen Inc and John Cashman, Human BioMolecular Research Institute. The paper can be found at: https://doi.org/10.1124/jpet.119.261040 (doi: 10.1124/jpet.119.261040).

About Human BioMolecular Research Institute

The Human BioMolecular Research Institute is a non-profitresearch institute conducting basic research focused on unlocking biological and chemical principles related to diseases of the human brain, cardiovascular disease and cancer. The Institute conducts fundamental studies of central nervous system disorders, heart disease and cancer including stem cell approaches and

translates findings into new drug development to address human illness. In addition, the Institute promotes scientific learning through community service and public access by disseminating information and sharing research with collaborators, colleagues and the public. For more information, visit us at www.HBRI.org.

About ChemRegen Inc.
ChemRegen is a for-profit company doing research directed at identifying small molecules of use for addressing human diseases. The approach is to develop regenerative medicines to work in conjunction with human stem cells to cure major human diseases including heart disease, cancer and other diseases. For more information, visit www.ChemRegen.com.