Study Published in the Journal of Medicinal Chemistry Demonstrates the Power of Machine Learning to Unlock New Chemistry and Biology to Treat Disease

-Largest Reported Prospective Study Applying Machine Learning for Small Molecule Discovery-

-Underpins launch of Chemome Initiative to find chemical probes for thousands of proteins-

WALTHAM, Mass. – June 11, 2020 – X-Chem, Inc., the leader in DNA-encoded small molecule library screening, and ZebiAI Therapeutics, a drug discovery company unlocking new disease targets, today announced the publication of a large prospective study to evaluate the power of machine learning (ML) to accelerate and improve the drug discovery process. The study, published in the *Journal of Medicinal Chemistry*, titled "Machine Learning on DNA-encoded Libraries: A New Paradigm for Hit-finding," was conducted in collaboration with Google Accelerated Science (GAS), who developed the highly predictive ML algorithms.

The paper describes an effective machine learning platform to accelerate drug discovery based on DNA-encoded small molecule library (DEL) selection data and demonstrates the efficacy of the platform to predict highly potent small molecule inhibitors within a virtual library of compounds across three diverse protein targets. It details the identification of active compounds outside of the DEL library which are structurally different from the molecules used in training. These results indicate that, at least for certain targets, ML applied to DEL data enables access to unlimited chemical space in a time- and cost-effective manner.

Utilizing this methodology as its foundational technology, ZebiAI and GAS have initiated a program, coined the "Chemome Initiative," to collaborate with academic researchers to utilize the platform to further characterize the function of understudied proteins and validate novel therapeutic targets. Thousands of proteins remain understudied with limited or complete lack of understanding about their function and/or relevance to disease pathophysiology. As a result, there is untapped potential for major scientific advances within the unexplored proteome. ZebiAI and GAS will develop chemical probe molecules for the academic community across thousands of novel targets, driving deeper understanding of the biology of intractable diseases.

"This exciting paper demonstrates that combining X-Chem's industry-leading DEL screening data with machine learning can significantly accelerate the discovery of potent small molecules against a diverse set of targets. With our validation against nearly 2,000 molecules and 3 targets, this is the largest published prospective study of virtual screening," commented Patrick Riley, senior researcher of Google.

“This is a major step forward in the quest to utilize machine learning to accelerate the drug discovery process.”

“The quality of our DEL screening data, driven by expert selection protocols, vast compound libraries developed over 10+ years, and sophisticated informatics and data formatting, enabled these exciting results,” commented Matt Clark, CEO of X-Chem. “We look forward to continuing to provide our industry-leading data to ZebiAI to drive powerful ML models.”

Rick Wagner, Founder and Director of ZebiAI said, “The Chemome Initiative will apply the techniques we have developed to efficiently deliver new chemical probes to the research community for thousands of human proteins of interest. We will ultimately apply the algorithms we develop and results of the research using chemical probes to further our understanding of disease pathways. This breakthrough will enable significant new biological discoveries and ultimately accelerate discovery of new therapeutics to treat intractable diseases.”

Chemical probes are small molecules that selectively inhibit or promote the function of specific protein targets, enabling the study of disease systems and pathways. It is common practice to use chemical probes to study the function of specific protein targets. Currently, there are not enough small molecule probes available, with only an estimated four percent of the human proteome having a usable probe. Most screening methods are limited by the scope of chemical space to which they provide access. However, DNA-encoded libraries (DELs) combined with ML present a new solution.

DELs are libraries with millions or billions of distinct molecules that are generated by iterative combinatorial synthesis of small molecules tethered to DNA tags that record the synthetic history of the small molecule. Every small molecule in the library has a unique DNA barcode attached to it, allowing the molecules to be easily catalogued. The library is used to find which small molecules bind to proteins of interest, by mixing the DEL molecules and proteins and “washing away” what doesn’t stick. DNA sequencing methods are then used to determine the DNA barcode of the molecules that are bound to the protein target, therefore identifying the molecules.

Data on the thousands of molecules that bind to a protein target in a DEL screen provide a chemical imprint of the target. This makes it possible to derive a ML model that can predict active compounds from virtual libraries to the protein of interest, opening up unlimited chemical space. Broader and deeper study of the biology of intractable diseases using this approach will accelerate the discovery of novel therapeutics, ultimately improving human health.

About X-Chem, Inc.

X-Chem, Inc. is a privately-owned biotechnology company based in Waltham, Massachusetts. The company's mission is to apply its powerful product engine to the discovery of small molecule leads against high-value therapeutic targets. X-Chem has established partnerships with AbbVie, Alexion, Almirall, Bristol-Myers Squibb, AstraZeneca, Bayer, Department of Defense/Harvard, Gilead, Janssen, Maruho, MD Anderson Cancer Center, Ono, Otsuka, Pfizer, Roche, Sanofi, Taiho Pharma, Vertex, and several other leading pharmaceutical companies, biotechnology organizations, and academic centers. For further information on X-Chem, please visit: http://www.x-chemrx.com/.

About ZebiAI Therapeutics.

ZebiAI Therapeutics is focused on improving human health by powering machine learning to map the chemistry of the genome and discover new therapeutics. The company's core technology applies ML algorithms to vast amounts of high quality protein-small molecule interaction data. ZebiAI was launched in 2019 and has partnerships with Google and X-Chem, the leader in DNA encoded library (DEL) small molecule discovery. Anterra Capital, a Fidelity-backed venture group led a seed round of financing for the company. For more information, please visit: http://www.zebiai.com.