

PRESS RELEASE FINAL

# X-Chem Licenses Epigenetic Drug Discovery Program to Bayer Pharma

-- Discovery of Novel and Selective Small Molecules for Epigenetic Target Enabled by X-Chem's DNA-Encoded Library of 100 Billion Compounds --

WALTHAM, Mass. – February 13, 2014 - X-Chem, Inc., a privately held biotechnology company focused on applying its innovative drug discovery capabilities to the generation of novel small molecule therapeutics, today announced it has achieved a success milestone with Bayer Pharma AG in the multi-target collaboration the companies established in July 2012. Bayer is licensing an early-stage drug discovery program directed against an epigenetic drug target. Inhibiting epigenetic targets is widely recognized as a promising emerging therapeutic option for cancer and other diseases; however, identifying small molecule inhibitors for these targets is technologically challenging. Fueled by a proprietary library comprised of 100 billion small molecules. X-Chem's product engine has proven highly effective for discovering novel and selective inhibitors to multiple classes of targets, including those that have historically been difficult to address.

Under the terms of the existing agreement, Bayer provided an upfront payment and ongoing research funding. X-Chem is applying its DNA-encoded small molecule library and discovery engine to the identification of novel leads to several Bayer targets from different classes and therapeutic areas. Bayer has an exclusive option to license programs generated in the course of the collaboration. Each X-Chem program licensed by Bayer will receive an upfront exercise fee in addition to payments based on the achievement of defined pre-clinical, clinical and sales milestones, as well as royalties. The financial terms of the licenses are not disclosed and are commensurate with terms X-Chem has established in its collaborations with other large pharmaceutical companies.

"We recognize the innovative potential of X-Chem's team and technology platform," said Prof. Dr. Hanno Wild, Senior Vice President and Head of Candidate Generation & Exploration at Bayer HealthCare Global Drug Discovery. "We look forward to continuing to work with X-Chem."

"We share Bayer's mission to bring innovative treatments to patients by addressing disease areas with a high unmet medical need. Epigenetic targets are of increasing interest for treating cancer and other life-threatening disorders, yet are particularly challenging from a drug discovery perspective," said Rick Wagner, Ph.D., Chief Executive Officer of X-Chem. "X-Chem has built its library and discovery platform to meet the challenges of tackling these highly difficult targets and enabling the discovery of multiple chemical series directly out of our primary screens."



"In the short period of time since our founding, X-Chem has established a track record of success for our partners by delivering novel small molecule modulators for several challenging drug targets, including epigenetic proteins, protein:protein interactions, ubiquitin ligases and antibacterial enzymes," said Diala Ezzeddine, Ph.D., Chief Business Officer of X-Chem. "X -Chem is emerging as the drug discovery collaborator of choice in the area of novel lead generation with our DNA-encoded technology."

### **About Epigenetics**

Epigenetics refers to the study of alterations in gene expression in cells that are not caused by changes in DNA. Examples are modifications of DNA by a process called methylation, or of the histones themselves. Such changes can cause chromatin remodeling, resulting in changes in gene expression. Various enzymes, known as "readers", "writers" and "erasers," cause these dramatic changes.

## About the X-Chem Drug Discovery Platform

Due to the size and diversity of the library, X-Chem can discover multiple series of novel, potent and selective lead compounds at an unprecedented rate of success against a wide range of targets, including some that previously failed using conventional screening methods. A number of proprietary innovations in library design, screening methodology and bioinformatics underlie the exceptional performance of the platform. A key advancement was a library synthesis process that enables addition of the DNA tag using chemical methods, as exemplified in the following publication by X-Chem scientists: Litovchick A, Clark MA, Keefe AD. Universal strategies for the DNA-encoding of libraries of small molecules using the chemical ligation of oligonucleotide tags. Artificial DNA: PNA & XNA 2014; 5 (1). X-Chem's superior approach to library design allows for additional chemical reactions to become useable in DNA-encoded library synthesis. Together, these developments result in a much greater repertory of diversity for small molecules, which cover a range of categories, including fragment molecules, small molecular weight heterocyclic compounds, and macrocyclic structures. This diverse library, combined with a heightened ability to detect active molecules, has yielded a robust process that has been highly successful against targets categorized as difficult or intractable.

#### **About DNA Encoding**

The X-Chem drug discovery engine is based on a library generated by iterative combinatorial synthesis of small molecules tethered to DNA tags which record the synthetic history of the small molecule. Every small molecule in the library has a unique DNA barcode attached to it. The library is screened as a mixture using affinity-based binding to a target of interest. Certain rare molecules in the library that bind to the target can be "fished out," while the rest of the molecules wash away. DNA sequencing methods are then used to detect molecules that are enriched when bound to the target. The diverse nature of the library produces multiple families or clusters of related molecules that bind to the target, forming a basis for emergent structure-activity relationships. Structure-activity relationships are typically used by medicinal chemists to



guide iterative chemical maturation of a molecule into a drug. Based on the synthetic history encoded in the DNA sequence information, molecules are then made without the DNA tag attached, and tested for activity in conventional assays.

**About X-Chem.** X-Chem, Inc. is a biotechnology company based in Waltham, MA. The company's mission is to apply its powerful product engine to the discovery of small molecule compounds against high-value therapeutic targets. X-Chem has established partnerships with Roche, AstraZeneca and several other leading pharmaceutical companies, biotechnology organizations, and academic centers.

In 2010, X-Chem and Pharmaceutical Product Development, LLC (PPD) formed a strategic partnership, including an investment from PPD. For further information on X-Chem. please visit: http://www.x-chemrx.com/.

#### **About PPD**

PPD is a leading global contract research organization providing drug discovery. development, lifecycle management and laboratory services. Our clients and partners include pharmaceutical, biotechnology, medical device, academic and government organizations. With offices in 46 countries and more than 12,500 professionals worldwide, PPD applies innovative technologies, therapeutic expertise and a commitment to quality to help clients and partners accelerate the delivery of safe and effective therapeutics, and maximize the returns on their R&D investments. For more information, visit www.ppdi.com.

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## Forward-looking Disclaimer

Except for historical information, all of the statements, expectations and assumptions, including statements, expectations and assumptions about X-Chem's small molecule drug discovery technology and its collaboration with Bayer, contained in this news release are forward-looking statements that involve a number of risks and uncertainties. Although X-Chem attempts to be accurate in making these forward-looking statements, it is possible that future circumstances might differ from the assumptions on which such statements are based and could cause actual results to differ materially from the forward-looking statements. Other important factors that could cause future results to differ materially include the following: rapid technological advances that make our services less competitive; risks associated with and dependence on strategic relationships; the ability to attract, integrate and retain key personnel; competition in the outsourcing industry; X-Chem's ability to win new business; the rate of conversion of backlog into revenue and earnings; actual operating performance; overall global economic conditions; economic conditions, research and development spending, and outsourcing trends in the



pharmaceutical, biotechnology and government-sponsored research sectors; consolidation in the pharmaceutical and biotechnology industries; loss, delay or modification of large contracts; compliance with drug development regulations; changes in the regulation of the drug development process; risks associated with acquisitions and investments; and the ability to control SG&A spending. PPD and X-Chem assume no obligation and expressly disclaims any duty to update these forward-looking statements in the future, except as required by applicable law. These forward-looking statements should not be relied upon as representing X-Chem's estimates or views as of any date subsequent to the date hereof.