

# PRESS RELEASE

# X-Chem First Biotech to Exceed 100 Billion Compounds with its Unique and Proprietary Small Molecule DNA-Encoded Library

-- Company publishes breakthrough DNA-encoding strategy in peer-reviewed chemistry journal --

WALTHAM, MA, USA – February 4, 2014 - X-Chem, Inc., a privately held biotechnology company focused on applying its powerful product engine to the generation of novel small molecule therapeutics, today announced that the company has created the first biotech-owned screening library of DNA-encoded small molecules to ever surpass 100 billion compounds. Its size now far exceeds that of even the largest conventional small molecule screening libraries by 10,000-fold, and its diversity is unprecedented. The library was created using the company's cutting-edge and proprietary DNA-encoded platform. As described in a recent publication authored by X-Chem scientists ((Litovchick A, Clark MA, Keefe AD. Universal strategies for the DNAencoding of libraries of small molecules using the chemical ligation of oligonucleotide tags. Artificial DNA: PNA & XNA 2014; vol.5, number 1)) a key advancement is a library synthesis process that enables the addition of a DNA tag using chemical methods.

X-Chem's vision is to continuously increase the size and diversity of the library to enable identification of small molecules with the safety and efficacy profile of drug candidates directly out of the primary screen. To interrogate a library of such magnitude, the company has built a state-of-the-art screening platform designed to optimize detection and a suite of advanced bioinformatics tools capable of maximizing the signal-to-noise ratio when processing the massive quantities of data generated in the course of each screen.

"DNA-encoded library technology has achieved significant momentum in the drug discovery world. At X-Chem, we have pushed this technology to a new level, uniquely enabling the virtually unlimited expansion of our library and the ability to productively screen such a large number of compounds," said Richard W. Wagner, Ph.D., Chief Executive Officer of X-Chem. "Size and diversity of the library can radically improve the rate of lead discovery and also drive expansion of the universe of 'druggable' targets. This has the potential to dramatically increase the proportion of lead compounds that will result in safe, effective, and innovative medicines not conceivable previously and to accelerate the drug development process while also reducing its overall cost."



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 X-Chem, Inc.
 100 Beaver Street, Waltham, MA 02453
 781.419.6900
 781.419.6903
 fax



"We have licensed to our partners multiple novel, potent and selective compounds that target notoriously difficult-to-drug targets including, among others, protein:protein interaction (PPI) targets, ubiquitin ligases, antibacterial enzymes, and proteins involved in epigenetic processes", said Diala Ezzeddine, Ph.D., Chief Business Officer of X-Chem. "Access to our game-changing drug discovery capabilities continues to enable breakthroughs for X-Chem's partners on targets of high therapeutic value for which no 'progressable' small molecule had previously been identified."

#### 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. In particular, X-Chem's superior approach to library construction allows for additional chemical reactions to become useable in DNA-encoded library synthesis. Together, these developments result in a much greater repertoire 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 that record the synthetic history of the small molecule. Every small molecule in the library has a unique DNA barcode attached 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. Structureactivity 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.

# For additional information contact:

Diala Ezzeddine, Ph.D. Chief Business Officer X-Chem, Inc. 781-419-6927

Maureen L. Suda (Media) Suda Communications LLC 585-387-9248

# *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, 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.

