



## Discovering Small Molecule Compounds through The DNA Encoded Library Technology



**Richard W. Wagner- CEO**

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, Bayer, 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/>.

**Interview conducted by: Lynn Fosse, Senior Editor, CEOCFO Magazine**

**CEOCFO: Dr. Wagner, what is the concept at X-Chem?**

**Dr. Wagner:** Our vision is to try to cause a paradigm shift in the way the small molecules are discovered. The way we look at the discovery of novel small molecule drugs is that it is completely a game of chance. Our strategy is to improve the odds by starting with an extraordinarily large library. Traditional screening methods, while they work, end up being time consuming and expensive. This comes at a time when the pharmaceutical industry is trying to decrease R&D spending and increase productivity. In the end, decisions need to be made for cost reasons on focusing a particular compound series to take to the clinic where it has a low likelihood of success. Our idea is that by starting with a much larger library and being able to

screen it much quicker that we can achieve better odds at finding improved, safer molecules faster and cheaper than traditional methods.

**CEOCFO: How does that work on a daily basis?**

**Dr. Wagner:** We have a technology that is called DNA Encoded Library Technology. This is a technology that I started working on back in 2002, when I was an early inventor on the first generation technology that was developed at Praecis Pharmaceuticals and then later sold to GSK. X-Chem has invented a new generation of the technology. The DNA Encoding Technology is based on a library of small molecules that is generated by what is called combinatorial synthesis and when the library is complete, each small molecule gets tagged with a DNA barcode. The DNA barcode records the synthetic history of how each small molecule is made. By reading the barcode, one knows what molecule is attached to the DNA. The molecules are screened as a mixture against a target and once they are screened, the DNA barcodes are read out by DNA sequencing and then translated back into small molecules that were attached. That way we know what molecules interacted with the target.

**CEOCFO: Do you have over a hundred billion compounds?**

**Dr. Wagner:** We have generated over one hundred billion compounds that can be applied towards screening for new drug leads. The entire mixture can be screened essentially by one person in a day.

**CEOCFO: How does your offering compare with methods that are currently being used?**

**Dr. Wagner:** Current methodologies are, for example, high throughput screening methods that are used throughout the industry. Pharmaceutical companies, contract labs and academia use this platform, and in this method individual compounds are amassed -- sometimes anywhere from a couple hundred thousand molecules up to three or four million compounds. These molecules are kept in individual vials, and there are very complicated storage facilities for these compounds. Each compound is arrayed out into a 384 or 1536 microplate that contains little wells so that each compound can be tested individually against the target of interest. It is a time consuming process and requires great deal of coordination to be able to carry out the process with a high accuracy. There is a great amount of room for error along the way, and in the end -- because one is starting with a relatively low number of compounds by our standards -- the output that one gets are often fairly weak interacting compounds with the target. This is contrasted with our method where the

entire library is screened as a mixture; it is a simple and robust way to screen the library. Since the library is much larger, we often discover molecules that are quite far advanced in terms of the potency, selectivity, and pharmaceutical properties.

**CEOCFO: *Where are you in the commercialization and utilization process?***

**Dr. Wagner:** I started the company in 2009. The history was that I left Praecis Pharmaceuticals in 2007, and I then needed to come up with a completely new invention to apply and utilize the technology. Once this was achieved, we started building the library. We have now established three pharmaceutical partnerships that have been announced with Roche, AstraZeneca, and most recently Bayer, and one additional pharmaceutical company collaboration that has not been announced. In addition, we have a number of collaborations with academic groups as well as nonprofit groups. We have currently over sixty partner programs, and we do this in a risk/share model. So, there is a tremendous potential for the platform, we think, to become a major source of blockbuster drugs in the next three to five years.

**CEOCFO: *Would you explain the risk sharing model?***

**Dr. Wagner:** The risk sharing model is based on making a portion of the value that we receive from partners on our collaborative projects contingent upon successful progression of the project. This means that as a drug development project initiated by X-Chem is successfully progressed by our partner towards clinical development and commercialization, we are eligible for event-based clinical and sales milestones along with royalties, depending on the contract.

**“We have developed a paradigm shift in how drug discovery is going to be performed. We think that we will become a major source of new drugs of blockbuster potential in the next three to five years, and this is evidenced by the fact that we already have over sixty partner programs with different companies including several of the top pharmaceutical companies.”**  
- Richard W. Wagner

**CEOCFO: *Why have you chosen this business model?***

**Dr. Wagner:** When we started the company it was our vision that we really wanted to have the technology to be as broadly applied as possible and to do it on a global scale. To get the company started, myself and our Chief Business Officer, Diala Ezzeddine, did it a nontraditional way by starting with a collaboration with Roche Pharmaceuticals. The head of research at Roche, Lee Babiss, subsequently left and became Chief Scientific Officer at a company called PPD, which is a contract research organization. We kept up contact with him and together developed a business model where PPD made an investment into X-Chem. The idea was that PPD had certain capabilities that could allow our business to expand almost on an industrial scale to the point that it could be applied globally. We came up with a partnership model where we could promote the technology out as far and wide as possible. It was not our original intent to develop therapeutics ourselves. However, to generate the kind of data that we needed in order to sign up the pharmaceutical companies, we worked on some internal targets. In 2012, we decided, together with PPD, that it made a lot of sense to take these internal assets and spin them out into a new company. Thus, the X-Chem founders and PPD co-funded a new company called X-Rx, Inc., where PPD has the majority interest. All in, the strategy that X-Chem took was an innovative model for a biotech company, and it has worked out well. Since the initial financing from PPD, X-Chem has supported itself through its partnerships.

**CEOCFO: *As you have worked with partnerships and people are using this system, have there been many changes and tweaks and what have you learned along the way about the technology to make it more user-friendly or more effective?***

**Dr. Wagner:** I had worked on the first generation of technology at Praecis, and what we decided when we started X-Chem was that we really wanted to pick the technology apart and put it back together again, making as many novel and proprietary improvements as we could think of. The technology continues to evolve and improve. This is in terms of the chemistry, how the libraries are put together, the informatics system that is used to handle all of the data, the protein biochemistry to get targets ready for screening -- so across all areas. It is the summation of all of those tweaks, as you say, that comprises what we call the fourth generation of the technology, and it is all these tweaks that give us our competitive edge.

**CEOCFO: *What is ahead?***

**Dr. Wagner:** Our vision is to continue to build the library, and thus, it continues to grow. We believe that when the library reaches sufficient size, we will be identifying molecules from the library that are very close to clinical stage. If you compare this to traditional screening methods, the time it takes to identify hits and take them to the clinic is in the range of three to five years and can cost anywhere from \$10 to \$30 million to do that. Our vision is to do the process in half the time and about a tenth of the cost, which we think will have a major impact.

**CEO CFO: *What are some of the challenges that you might be on the lookout for?***

**Dr. Wagner:** The overall dynamics that are happening in the pharmaceutical industry. The pharmaceutical industry continues to be in a state of flux and we need to be on the pulse of how companies are changing and make sure we are in a position to partner with them.

**CEO CFO: *Why is X-Chem a company to watch?***

**Dr. Wagner:** We have developed a paradigm shift in how drug discovery is going to be performed. We think that we will become a major source of new drugs of blockbuster potential in the next three to five years, and this is evidenced by the fact that we already have over sixty partner programs with different companies including several of the top pharmaceutical companies.

**CEO CFO: *Final thoughts?***

**Dr. Wagner:** It has been extremely exciting to work with such a talented team that we have assembled here at X-Chem. Everyone is highly committed to changing the drug discovery paradigm that makes it extraordinarily fun to come to work every day.

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**BIO:** Dr. Wagner started X-Chem in 2009, and is the President, CEO, and member of the Board of Directors. He is also President and COO of X-Rx, Inc., a spin-out company of X-Chem focused in the areas of oncology and inflammatory disease. In addition, he is Executive Chairman and Co-Founder of X-BODY, Inc., founded in 2008. Dr. Wagner was President and CEO of SRU Biosystems, Inc. from 2007 until 2012. In 2010, Dr. Wagner led the introduction of the BIND® Scanner, a cell-based label-free instrument developed for profiling compounds involved in stem cell biology. Prior to joining SRU, he was Executive Vice President of Research at Praecis Pharmaceuticals, Inc., where he was an inventor of the DirectSelect small molecule screening technology that led to the creation of a ten billion compound screening library. Praecis was acquired by GlaxoSmithKline in 2007. Prior to joining Praecis, Dr. Wagner started operations at Phylos, Inc. in July 1997 and held the position of Senior Vice President, Research. At Phylos he was an inventor on several technologies, including a class of antibody mimetics being developed by Bristol Myers Squibb, now called Adnectins™. Earlier, Dr. Wagner had been Director of Cell Biology and a member of the management team at Gilead Sciences, Inc.

Dr. Wagner received his B.S. in Biochemistry from Trinity College and his Ph.D. in Chemistry from Brown University.

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