

'X-Chem' marks the spot for Bayer in sweetened drug discovery deal

By Marie Powers, News Editor

Bayer AG and privately held X-Chem Inc. expanded their global drug discovery collaboration, initiated in 2012, to encompass the entire bandwidth of therapeutic areas and target classes from Bayer's R&D pipeline. The agreement, which extended Bayer's access to X-Chem's Dex technology platform, comes after the Leverkusen, Germany-based pharma licensed two programs from X-Chem, each encompassing several series of small molecules, to address complex target structures, such as protein-protein interactions.

The enlarged agreement is designed to uncover lead structures for drug targets in undisclosed areas of high unmet medical need. Although Bayer has drawn headlines in recent months for its \$62 billion bid to acquire Monsanto Co., its pharmaceuticals division remains the largest in terms of sales, encompassing assets in oncology, cardiology, hematology, gynecology, neurology, infectious diseases, men's health and ophthalmology.

In 2014, as part of what X-Chem co-founder and CEO Rick Wagner called the "pilot deal" between the companies, Bayer licensed an early stage drug discovery program against an undisclosed epigenetic drug target and a second drug discovery program against a cardiovascular drug target. The new deal significantly expands the boundaries of that arrangement.

Bayer initially provided X-Chem, of Waltham, Mass., with a few of its "most challenging targets, which hadn't worked with any other method used by Bayer," Wagner said. "The success we had with a couple of those programs led to discussions about how we could have a closer relationship where we could work on key pipeline programs at Bayer in a much more collaborative manner."

Bayer gained broader access to X-Chem's technology platform across "each and every one" of its core discovery efforts, said Ed Koval, X-Chem's senior vice president of corporate and business development, including the right to examine real-time data emerging from the collaboration. In return, X-Chem is set to receive an undisclosed up-front payment and research funding and is in line for potential preclinical, clinical and regulatory milestone payments, up to a total of \$528 million.

Bayer also secured an exclusive option to license programs generated over the course of the four-year collaboration, with X-Chem due royalties and sales milestones for each commercial

product emerging from the deal.

Bayer officials could not be reached for comment.

X-Chem's Dex drug discovery platform is based on a library – currently numbering more than 120 billion compounds – generated by iteratively combining and synthesizing small molecules tethered to DNA tags that record the synthetic history of each. The library is screened as a mixture, using affinity-based binding to a target of interest. Molecules that bind to the target can be fished out, while the rest are washed away. X-Chem then uses DNA sequencing methods to detect molecules that are enriched when bound to the target.

The nature of the library produces multiple families, or clusters, of related molecules that bind to the target, forming a basis for structure-activity relationships that can be used by medicinal chemists to guide the chemical maturation of a molecule into a drug. Based on the synthetic history encoded in the DNA sequence information, molecules are then fabricated without the DNA tag and tested for activity in conventional assays.

VISION TO BE 'ONE OF CENTRAL PILLARS OF DISCOVERY'

X-Chem, which has disclosed partnerships with an array of biopharmas – among them, Alexion Pharmaceuticals Inc., Astrazeneca plc, Johnson & Johnson unit Janssen Biotech Inc., Navitor Pharmaceuticals Inc., Pfizer Inc., Roche Holding AG and Sanofi SA – has remained true to the partnering model that served as the foundation for the company's formation in 2009. (See *BioWorld Today*, Sept. 25, 2013.)

"Initially, the vision was that our platform is going to become one of the central pillars of discovery across the industry," Wagner told *BioWorld Today*. "We're committed to work across the industry – not just with pharma companies but also with biotech companies and academic centers of excellence – to go as broad and deep as possible. We see this platform as making a fundamental advancement toward the discovery of novel molecules."

To date, X-Chem has established collaborations across more than six dozen therapeutic programs and licensed 20 of those – about one-fourth of them against challenging protein-

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protein interaction targets.

"We haven't been successful just once," Wagner said. "We've successively delivered against that class of targets."

And X-Chem – whose platform strategy has emulated companies such as Adimab LLC and Nimbus Therapeutics Inc. – is beginning to tweak its business plan. In 2010, X-Chem formed a strategic partnership with Pharmaceutical Product Development LLC (PPD) that included an investment by the drug research firm. In September 2014, PPD exercised its option to acquire the remaining interests in X-Chem while retaining the company's management, scientific staff and business model.

In January, X-Chem was spun out of PPD as an independent company owned by key shareholders of PPD's parent company: private equity firms The Carlyle Group and Hellman and Friedman. The new business structure gives X-Chem more autonomy to launch additional startups following the example of X-Rx Inc., formed in 2012 by X-Chem and PPD to advance X-Chem-discovered or partnered programs in oncology, autoimmunity, inflammation and fibrosis. Last year, X-Rx inked its first exclusive agreement, with Gilead Sciences Inc., to develop small-molecule autotaxin inhibitors targeting multiple

indications, including idiopathic pulmonary fibrosis.

"You'll be hearing about other startup companies in the near future," Wagner promised.

In the meantime, the sweetened Bayer deal offers additional evidence that X-Chem's platform is working, Koval said, citing the expanded collaboration as the first major pharmaceutical agreement for the German company since its \$335 million alliance with Crispr Therapeutics AG, of Basel, Switzerland. (See *BioWorld Today*, Dec. 22, 2015.)

Bayer has a history of bolstering ties with existing partners. Earlier this year, the company broadened its eye disease alliance with Regeneron Pharmaceuticals Inc. through a \$130 million agreement to test their vascular endothelial growth factor trap, Eylea (aflibercept), in combination with the angiopoietin2 antibody, nesvacumab, in patients with wet age-related macular degeneration or diabetic macular edema. (See *BioWorld Today*, March 25, 2016.)

Similarly, "this is further validation of what X-Chem's platform can do," Koval insisted. "The best sign that you're managing a relationship well is when you do the second and the third deals."