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Xencor Optimizes Key Pharmaceutical Proteins

(BW Healthwire)–May 29, 2002—Xencor's Protein Design Technology Provides Superior Control and Flexibility in Biotherapeutic Creation

Monrovia, CA – May 29, 2002 – Xencor, a drug discovery company, today reported results from two protein optimization programs on key pharmaceutical proteins, recombinant human growth hormone (hGH) and granulocyte-colony stimulating factor (G-CSF). Using its proprietary Protein Design AutomationTM (PDATM) technology, Xencor computationally redesigned hGH and G-CSF, obtaining highly stabilized variants of each with improved pharmacokinetics. Improving the stability and physicochemical properties of biotherapeutics can enhance their shelf life, reduce production costs and make them more amenable to alternate delivery systems and formulations, thus providing added convenience and improved patient compliance. The data was published in the May and June issues of Protein Science.

"The results of these studies are examples of the utility of our PDATM technology, which allows for the creation of a new generation of biotechnology products. We can create proteins tuned for specific commercial needs, such as increased potency, specificity and novel therapeutic modalities. Also, we can lower manufacturing costs by improving solubility and stability," said Bassil Dahiyat, Ph.D., President and Chief Executive Officer of Xencor. "We are currently working with partners to bring these attributes to drugs in development."

Xencor uses its protein optimization and chemical genomics technologies for drug discovery and development. Earlier this year, it announced the signing of a three-year agreement with Syngenta's Torrey Mesa Research Institute for the design and discovery of novel proteins that will enable new products in the food, pharmaceutical and personal care industries. Xencor also signed licensing agreements with the California Institute of Technology and Pennsylvania State University to further expand its proprietary PDATM platform and strengthen its dominant patent position in the field of protein optimization.

"Our PDATM technology combines high performance computing with sensitive biochemical assays to create broader protein diversity with far greater control than current optimization technologies, such as directed evolution and phage display," Dr. Dahiyat added. "It uses the information embedded in protein structure to optimize protein activity, binding affinity and specificity, stability, expression level, and potency. This process also creates new intellectual property, continually broadening our patent portfolio by generating sets of novel protein sequences which are distinct from naturally occurring proteins."

Granulocyte-colony Stimulating Factor (G-CSF) Protein Optimization Results

G-CSF is used worldwide to prevent neutropenia caused by high-dose chemotherapy. It has strict formulation and storage requirements and because of poor oral absorption must be administered by injection (typically daily). Thus, there is significant interest in developing analogs with improved pharmacological properties.

Xencor used its ultrahigh throughput computational screening methods to create novel G-CSF variants with improved physicochemical characteristics1. Over 1028 variants were rapidly screened, exceeding the capacity of directed evolution by approximately 20 orders of magnitude, to design proteins with 10-fold improvements in shelf life, excellent activity in mouse and primate models, and improved pharmacokinetics. These results demonstrate the power of Xencor's combination of computational and experimental screening for developing improved pharmaceuticals.

Recombinant Human Growth Hormone (hGH) Protein Optimization Results HGH is used world wide for the treatment of pediatric hypopituitary dwarfism and in children suffering from low levels of hGH. Increased hGH stability could greatly facilitate development of sustained-release formulations and alternatives to injectable delivery that would increase bioavailability and make it easier for patients to use. Xencor computationally redesigned hGH by screening over 1040 sequences2. Novel variants were created with dramatically increased stability and full biological activity in cell proliferation studies.

Xencor discovers and develops protein and small molecule therapeutics using its proprietary rational protein design and chemical biology platforms. Xencor's platforms apply high performance computing and advanced cell biology to rapidly discover drugs with novel mechanisms and improved safety and efficacy. Xencor is a privately held biopharmaceutical company located in Monrovia, CA. Additional information is available at www.xencor.com.

1 Luo, P.; Hayes, R.; Chan, C.; Stark, D.; Hwang, M.; Jacinto, J.; Juvvadi, P.; Chung, H.; Kundu, A.; Ary, M.; Dahiyat, B., "Development of a cytokine analog with enhanced stability using computational ultrahigh throughput screening," Protein

Science (2002), 11:1218-1226.

2 Filikov, A.; Hayes, R.; Peizhi, L.; Stark, D.; Chan, C.; Kundu, A.; Dahiyat, B., “Computational stabilization of human growth hormone,“ Protein Science (2002), 11:000-000.