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Xencor Designs Novel TNF Alpha Inhibitors To Treat Inflammatory Disease

Xencor's Protein Design Automation Technology Creates New Modality for Blocking TNF Alpha and Related Proteins

Monrovia, CA – September 26, 2003 – Xencor, a drug discovery company, today reported the creation of a new class of inhibitors of TNF alpha, a critical protein involved in inflammatory disease. Scientists from Xencor used Protein Design Automation (PDA) technology, Xencor's proprietary structure-based engineering platform, to design variants of TNF alpha that neither bind to nor stimulate signaling through TNF receptors, but retain the capacity to rapidly bind to native, disease-causing TNF, thereby rendering it biologically inactive. These new molecules, called Dominant Negative TNFs (DN-TNF), block the signaling of native TNF by sequestering it from its disease-mediating receptors. Testing of DN-TNFs in vitro and in rodent models of rheumatoid arthritis show potent inhibition of TNF alpha. This report was published in today's issue of Science.

"Creating a completely new mechanism for inhibition of TNF alpha is a significant achievement for Xencor, and we are currently advancing DN-TNFs into pre-clinical development," said Bassil Dahiyat, Ph.D., President and CEO of Xencor. The Dominant Negative approach offers many potential advantages for therapeutics, including ease of production in *E. coli*, targeting of specific receptors of TNF alpha (R1 versus R2) and tunable pharmacokinetics. We have long and short acting versions of DN-TNFs that we created by rationally engineering, with PDA technology, PEGylation sites into the molecule. The initial disease indications that we are exploring are rheumatoid arthritis and multiple sclerosis."

"This approach establishes a new intellectual property position in a crowded space by creating novel compositions of matter and mechanism of action," Dr. Dahiyat said. "In addition, the Dominant Negative strategy can be applied to a number of other important targets that are structurally related to TNF alpha, such as BAFF for lupus and other autoimmune diseases and RANKL for osteoporosis."

About Protein Design Automation (PDA) technology

PDA technology combines high performance computing with sensitive biochemical assays to create broader protein diversity with far greater control than other optimization technologies, such as directed evolution and phage display. 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 Xencor's patent portfolio by generating sets of novel protein sequences which are distinct from naturally occurring proteins.

About Xencor

Xencor discovers and develops protein therapeutics using its proprietary rational protein design platform. Xencor's platform applies high performance computing and advanced molecular 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.