



**Contacts:** Tularik Inc. Burns McClellan  
Andrew Perlman, M.D., Ph.D. John Nugent (investors)  
650-825-7000 212-213-0006  
Juling Chao (media)  
415-352-6262

**TULARIK AND UNIVERSITY OF CALIFORNIA, BERKELEY RESEARCHERS  
ELUCIDATE A NEW RNA POLYMERASE PROTEIN STRUCTURE**

*Findings published in Science may speed the development of novel  
antibacterial agents*

**South San Francisco, CA – March 31, 2000** --Tularik Inc. (Nasdaq: TLRK) today announced that its researchers, working in collaboration with scientists from UC Berkeley, have elucidated the three-dimensional structure of a protein that plays a critical role in bacterial DNA replication. The findings, published in the March 31 issue of *Science*, provide an atomic-resolution image of the DnaG primase protein, which performs the essential step of producing RNA primers that are required for initiating DNA replication of the bacterial chromosome. This replication is the initial step in most bacterial infections. Tularik researchers hope to use this new structure to speed the development of novel antibacterial drugs.

The emergence of bacteria resistant to treatment has created an enormous need for new classes of antibacterial drugs. In an effort to combat bacterial resistance, Tularik researchers are working to discover new classes of drugs that interfere with novel bacterial targets.

In today's report, researchers described the active site of the core catalytic domain of the DnaG primase protein as determined by x-ray crystallography. The active site represents a novel three-dimensional fold that has not been observed for any nucleic acid polymerase or primase described to date. Researchers working in the Bacterial Diseases program at Tularik are now hoping to take advantage of such information to discover small molecule agents that specifically target essential components of bacterial

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replication systems, such as DnaG primase. To this end, multiple assays have been designed to identify inhibitors of key protein targets derived from the major “problem pathogens” such as *Staphylococcus aureus* and *Enterococcus faecalis*.

“We feel that the bacterial DNA replication machinery as a whole has been significantly under-explored in terms of its potential in providing novel antibacterial targets. We are excited by the possibility of discovering new small molecule agents that should circumvent the multi-drug resistance mechanisms prevalent in the major problem pathogens of today,” said A. Simon Lynch, Ph.D., project leader of the Bacterial Diseases program at Tularik. He added, “Access to atomic resolution structures of target proteins represents a key step in transforming inhibitors identified from high-throughput screening into drugs. We’re now hoping to utilize the DnaG primase structure to provide a better understanding of the precise mechanisms by which our novel drug candidates bind to the target enzyme.”

James Berger, Ph.D., an Assistant Professor at UC Berkeley, whose laboratory is focused on structural studies of proteins involved in the cellular manipulation of nucleic acids, commented “Primase represents one of the final pieces of the replication puzzle. Working with the researchers at Tularik has provided me with a way of linking my academic interest in this area to the more applied science of modern drug discovery. This project provides an excellent example of how researchers from academia and the pharmaceutical industry can work productively together to the benefit of both research communities.”

Tularik is engaged in the discovery and development of a broad range of novel and superior orally available drugs based on gene regulation. Tularik programs address cancer, CMV, diabetes, obesity, inflammation, allergy/asthma, hypercholesterolemia and bacterial diseases, and a class of targets known as orphan nuclear receptors. Tularik has established strategic partnerships with Japan Tobacco Inc., Roche Bioscience and Knoll AG. For additional information, visit Tularik’s Internet website at [www.tularik.com](http://www.tularik.com).

Statements in this press release that are not strictly historical are “forward-looking” statements as defined in the Private Securities Litigation Reform Act of 1995. There can be no assurance that Tularik will obtain necessary regulatory approvals for its drug candidates or be able to develop a commercially viable pharmaceutical product. These and other risks are more fully discussed in the Company’s SEC reports, including the report on Form 10-K for the year ended December 31, 1999.

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