

## Joint Conference

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### Prodrugs as a Strategy for More Effective Anti-Adenovirus Agents

Human adenoviruses (AdV) cause generally mild infections of the respiratory and GI tracts as well as some other tissues. However, certain serotypes are associated with acute respiratory disease and epidemic keratoconjunctivitis. AdV can cause serious infection in severely immunosuppressed individuals, and pediatric patients undergoing allogeneic hematopoietic stem cell transplantation have mortality rates up to 80% with disseminated disease. Despite this significant challenge to health, there are no drugs approved specifically to treat AdV infections. Cidofovir, an analog of cytidine monophosphate which acts as an AdV DNA chain terminator, is used clinically, but has several drawbacks, including relatively low cellular potency and lack of oral bioavailability. USC-087, a novel N-alkyl tyrosinamide phosphonate ester prodrug of HPMPA, the adenine analogue of cidofovir, is markedly more potent than the parent drug or cidofovir itself against multiple AdV types in cell culture. USC-087 is also effective orally against AdV-C6 in a cyclophosphamide immunosuppressed permissive Syrian hamster model. Injection of AdV-C6 (or AdV-C5) intravenously leads to a disseminated infection that resembles the human disease. USC-087 completely prevented or significantly decreased mortality when administered orally up to 4 days post challenge with the median lethal intravenous dose of AdV-C6. USC-087 also prevented or significantly decreased liver damage caused by AdV-C6 infection, and suppressed virus replication up to 4 days post challenge. The potential and scope of the N alkyl tyrosinamide ester prodrug approach will be discussed.

### Biography

Charles McKenna is Professor of Chemistry, Pharmacology & Pharmaceutical Sciences at the University of Southern California (USC), where he is also Director of the USC Center for Drug Discovery. He received his Ph.D. in Chemistry at UC San Diego and was an NIH postdoctoral Fellow at Harvard University. His research interests are primarily in medicinal and organophosphorus chemistry, focusing on design of novel chemotherapeutic agents, bisphosphonate imaging probes for bone, and nucleotide probes of DNA polymerases. Author of over 225 publications and patents and the recipient of numerous awards for his research and teaching, Dr. McKenna has founded several biotech companies.

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