ACADIA Applies Chemical Genomics to Discover Small Molecule Leads for Numerous GPCRs and Nuclear Rececptors

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Proprietary platform has identified novel chemistries for over 60 targets including the first agonists for HNF4α and PAR2

SAN DIEGO, CA, June 13, 2002 – ACADIA Pharmaceuticals announced the successful application of its proprietary chemical-genomics approach to more than 100 G-protein coupled receptor ("GPCR") and nuclear receptor targets. The presentation was made by Mark R. Brann, Ph.D., ACADIA's President and Chief Scientific Officer, at the Chemical Genomics Session of the 28th National Medicinal Chemistry Symposium in San Diego, California. ACADIA reported that its discovery efforts to date have resulted in the identification of novel small molecule ligands for over 60 of these targets, including agonists for several targets previously believed to be non-druggable.

Chemical genomics is an emerging, highly productive approach to drug discovery where novel chemistries are systematically sought for a diversity of targets in large gene families. Identified specific chemistries are used as critical tools to help elucidate the therapeutic potential of these targets. Equally important, once functionally relevant and drug-like chemistries are discovered for a given target, efficient lead optimization efforts may be rapidly initiated.

ACADIA's chemical genomics efforts have focused on two gene families that are particularly rich in drug targets, the GPCRs and nuclear receptors. Together, these two important gene families are believed to be the targets of more than half of the known drugs. ACADIA has established functional assays for more than 250 targets out of the approximately 500 GPCRs and nuclear receptors within its chemical-genomics platform. To date, ACADIA has applied its chemical-genomics approach to over 100 of these targets, and has successfully identified novel small molecule chemistries for more than 60 targets.

"It is very exciting to compare the chemistries for such a diversity of targets," said Mark R. Brann, Ph.D., ACADIA's President and Chief Scientific Officer. "This approach has provided ACADIA with a wealth of opportunities for drug discovery programs and has already led to several drug candidates rapidly approaching the clinic. In addition, we have identified the first ligands for several unexploited targets that provide us with new and exciting program opportunities. Two particularly interesting examples are small molecule agonists for HNF4α is an orphan nuclear receptor that when mutated causes MODY, a form of diabetes mellitus. While HNF4α is an exquisitely well-validated target, the pharmaceutical industry has not reported suitable small molecule chemistries for this target. PAR2 is a GPCR that is activated by the protease trypsin. Many lines of evidence point to a role of this receptor in inflammatory disease and neuropathic pain. These exciting discoveries position ACADIA to launch the first small molecule drug discovery efforts aiming at innovative therapies that exploit HNF4α and PAR2 modulation."

ACADIA has used its chemical-genomics platform to generate a broad drug discovery pipeline that addresses large unmet medical needs and major commercial markets, including psychosis. "Our inverse agonist for the $5HT_{2A}$ receptor, ACP-103, is scheduled to enter clinical trials later this year," said Robert E. Davis, Ph.D., ACADIA's Executive Vice President of Drug Discovery and Development. "In this program, we used our chemical-genomics platform to rapidly identify compounds with the desired combination of potency, specificity and efficacy for use as antipsychotics. In our muscarinic m1 psychosis program, our platform enabled the discovery of highly specific chemistries that interact with a unique 'ectopic' binding site on the m1 receptor. This discovery led to a program now in late-stage preclinical testing, which positions ACADIA to exploit the therapeutic opportunities afforded by the first truly selective m1 agonist."

ACADIA is a drug discovery and development company that efficiently discovers small molecule drug candidates using its proprietary chemical-genomics platform. ACADIA's uniquely productive platform integrates genomics, chemistry and biology to rapidly identify and validate drug targets while simultaneously discovering chemistries specific to those targets. ACADIA has successfully applied its chemical-genomics platform to generate a broad discovery pipeline that includes advanced programs directed at major diseases, including psychosis, chronic pain, and glaucoma. ACADIA's corporate headquarters as well as its genomics and biological research facilities are located in San Diego, California and its chemistry research facilities are located in Copenhagen, Denmark.

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