ACADIA Discovers Novel Small Molecule Leads for the V2 Vasopressin Receptor

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Chemical-Genomics Platform Enables Discovery Of Small Molecule Activators Of Numerous Peptide GPCRs

SAN DIEGO, CA and COPENHAGEN, DK, September 26, 2002 - ACADIA Pharmaceuticals announced today the discovery of small molecule lead chemistries for the V2 Vasopressin receptor. The V2 Vasopressin receptor is the major control mechanism for the production of urine. Activation of this receptor by ACADIA's lead compounds resulted in a sustained decrease in urine production in preclinical animal models.

"While V2 peptides that require injection or nasal application have long been used to treat diabetes insipidus, bleeding disorders, and nocturnal uresis (bed wetting), an orally active drug may address much broader markets, potentially including incontinence," said Bo-Ragnar Tolf, Ph.D., ACADIA's Vice President of Chemistry. "ACADIA's small non-peptide molecules have very attractive drug characteristics and provide us with the potential to develop the first oral medication that targets V2."

ACADIA's proprietary V2 chemistry is a product of its chemical-genomics efforts. ACADIA is using functional assays to broadly screen the members of the nuclear and G-protein coupled receptor ("GPCR") families, searching for novel chemistries that act as agonist, antagonists, and inverse agonists. More than 100 of these targets have been screened, with novel chemistries identified for more than 70 targets. The V2 small molecule chemistry is an example of a non-peptide activator of a peptide hormone receptor.

"V2 is just one of the examples where we have found exciting small molecules that activate peptide GPCRs," said Mark R. Brann, Ph.D., ACADIA's President and CSO. "In the upcoming issue of the Journal of Medicinal Chemistry, we report the structure of our small molecule activator of the Urotensin-II receptor, another peptide hormone receptor. We have also discovered the first small molecule activators of the PAR-2 receptor. Our proven ability to consistently discover the first small molecule activators of peptide receptors runs in the face of the pharmaceutical dogma that holds that peptide receptors require complex chemistries that mimic the structure of the natural hormones. The latter are often referred to as peptoids. Our unique small molecule chemistries have obvious commercial advantages in terms of bioavailability and future synthetic opportunities relative to the peptides and peptoids."

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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