December 2008

Progress Update for Drug Discovery Program to Identify Novel Agents to Treat Duchenne Muscular Dystrophy (DMD)

2008 turned out to be a great year for Project Catalyst! We have been moving the programs forward through the drug discovery process that includes HTS, Lead identification, and now chemical optimization that will ultimately lead us to a drug candidate(s). The initial lead optimization phase of the drug discovery process involves making changes to the lead chemical structures and then evaluating their activity in cell culture systems. The iterative rounds of chemical synthesis and biological testing continue until we have an understanding of the contributions to activity made by the different parts of the molecule. The next phase of the process incorporates in vitro pharmacological studies of the molecules to understand the contributions of the chemical groups to metabolic stability and pharmaceutical properties of the potential drugs. Following in vitro pharmacology tests, the process moves onto animal testing.

We are at an important step in the drug discovery process in which we are performing animal studies to determine the attributes of the molecules that contribute to the pharmacological and physiological activities of the molecule. We have synthesized and evaluated hundreds of molecules in pharmacological assays and more than 50 compounds in animals. It is also important to be able to deliver a sufficient amount of compound to animals to observe activity and pharmaceutical properties. We demonstrated that a subset of the compounds tested has demonstrated activity by increasing the levels of the target proteins in both cells in animal models. This marks a major milestone for the program.

Our achievements have been significant and we have been able to complete and meet the first-year milestones for the NIH grant, and continue to move a subset of these targets forward toward development candidates and potential treatments for DMD. Significantly, later in the year, we also moved our newest target past the high throughput screening (HTS) stage and into the hit characterization stage of the drug development process. We are looking forward to the coming year, where we will continue to strive to achieve important milestones that bring us closer to treatments for DMD.

About the PTC Project Catalyst Collaboration

PTC Therapeutics, Inc. (PTC) and Parent Project Muscular Dystrophy (PPMD) are collaborating to discover new drugs to treat DMD. In an ongoing effort to identify new treatments for DMD patients, PTC is performing lead optimization and assay development to identify compounds that have the best activity against selected DMD targets. Lead optimization is a complex and iterative process where compounds identified through high throughput screens (HTS) are characterized for their ability to modulate endogenous protein expression. PTC is exploring the chemical space surrounding these lead molecules to establish a structure-activity relationship (SAR). SAR is the relationship between chemical structure and biological activity for a series of compounds which imparts understanding of the structural requirements that impact biological activity.

PTC is actively working on characterizing compounds that selectively modulate expression of target proteins that are medically relevant in the treatment of DMD. The targets of interest include growth factors and proteins involved in muscle membrane stabilization. For each target, the initial sets of molecules were identified using PTC’s novel and proprietary drug screening technology called GEMS™ (Gene Expression Modulation by Small-molecules). The GEMS™ technology has proven to be a very robust technology that can identify compounds active against disease targets across multiple therapeutic areas.

For more information on PTC or the GEMS™ technology please visit www.ptcbio.com
For more information on the drug discovery and development process, please visit www.fda.gov

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