Subcontract Executive Summary

Facilities for Chemical Optimization and Synthesis of Small Molecules for the SMA Project[1]

Albany Molecular Research, Inc. (AMRI)

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AMRI will furnish the SMA Project with a core service facility with capabilities for chemically optimizing lead compounds and global compound management support. These activities are required components of the SMA Project's virtual drug discovery and development enterprise.

Structure-activity-relationship (SAR) plans will be developed for chemical scaffolds identified by SMA Project Lead Development Team. The plans will be designed for obtaining the maximum information from the most efficient route, in the shortest turn-around time possible, with the goal of producing compounds with potency and pharmacological properties appropriate for testing in SMA patients. Based on biological results from other SMA Project facilities and data from other reliable sources, the SAR plans will be refined and modified over time. The first chemical scaffold to be optimized for improved bioactivity, safety, and pharmacokinetic characteristics is indoprofen, a discontinued non-steroidal anti-inflammatory drug found to show activity during library screening and follow-up testing.

AMRI's SAR plans will be efficiently executed through purchase of commercially available compounds and the synthesis of compounds for which no reasonable commercial source can be identified. Both traditional medicinal chemistry and parallel synthesis approaches will be applied for rapid generation of novel compounds. Appropriate analytic methods will be used to confirm the identity and purity of all new compounds.

The compounds that are purchased and synthesized by AMRI for the SMA Project will be stored and maintained according to methods that adhere to high standards of quality assurance to insure compound integrity. AMRI will register, ship, archive, and track inventory of chemical compounds and assure the appropriate linkage of structures, lot numbers, plate numbers, and chemical and biological data for compounds registered in the centralized SMA Project informatics system.

Additional capabilities that AMRI may provide for SMA Project's virtual drug discovery and development enterprise are large-scale synthesis of candidate compounds to support testing in animal models and testing aimed at determining whether specific compounds are suitable for development as a drug product intended for human use.

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[1] *A proposal to support this subcontract was submitted to the SMA Project's JL-19704-3, "Facilities for Chemical Optimization and Synthesis of Small Molecules for the SMA Project." SAIC provides management support for The SMA Project to the NINDS through contract N01-NS-3-2356.*