NEW SYNTHETIC METHODS FOR NATURAL PRODUCT-INSPIRED DRUG DISCOVERY STRATEGIES

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Abstract: REVOLUTION Medicines is developing new anti-cancer therapies through an innovative approach that harnesses the complex chemicals of life by reconfiguring natural products into best-in-class medicines. The company is based on Prof. Marty Burke's novel technology that enables simple connection of diverse bi-functionalised chemical building blocks (containing halogenated MIDA-boronate moieties) using robust and sequential chemo-selective Pd catalysed cross-coupling reactions to construct medicinally important natural products or "natural product inspired compounds" with potentially enhanced pharmaceutical properties.

Our novel drug discovery platform utilizes a rapid, standardized and powerful process for conducting advanced medicinal chemistry by assembling these simple chemical building blocks into optimized natural product inspired structures as potential drug candidates (REVBLOCKS™). As our product engine and drug discovery programs evolve, we are continuing to investigate the development of additional lead discovery strategies for tackling frontier oncology targets. We believe that fragment based drug discovery (FBDD) is a productive and information rich lead discovery paradigm that has successfully delivered hits, leads and candidate drugs against a diverse range of challenging industry targets. As such, we are investigating the feasibility of developing a unique natural product inspired fragment library for drug discovery purposes, based on our proprietary knowledge-driven informatics system (REVEAL™), which is designed to recognize advantageous structural and functional properties of scaffolds that differentiate them from the many other chemicals found in nature. The modular synthesis platform we have developed will then enable rapid iteration of these small, relatively complex 3D fragments, allowing our medicinal chemists to routinely access novel Sp3 rich molecules for a range of potential drug targets.

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