



Pan-PIM Kinase Program

Highly potent Pim 1,2,3 inhibitors for
partnering or development

Substantial Market Potential

Hematologic and select solid tumor indications

Targeted Cancer Agents

- Exploit validated Pim kinase targets
- Pan-Pim inhibitors (Pim-1,2 and 3)
- Ability to dial out FLT3

Development Stage

- Late discovery and optimization
- Activity in multiple animal models
- Small molecules with ease of synthesis

Attractive Clinical Qualities

Cylene Owns All IP Rights

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Cylene's Pim Kinase Inhibitor Program

Cylene has created four unique chemical scaffolds (Series A-D) as pan-Pim inhibitors, and molecules from these scaffolds inhibit Pim-1, Pim-2 and Pim-3 in the low nanomolar to picomolar range while exhibiting no inhibitory activity of the FLT3 protein kinase at the high test concentration of 1,000 nM (Figure 2). These highly selective Pan-Pim inhibitors also decrease phosphorylation of the Pim substrate S112 residue of the protein BAD (Figure 3A), demonstrating effective inhibition of the Pim kinases in cells. Pim inhibition also translates to potent (low nanomolar) antiproliferative activity against relevant leukemia cell lines (Figure 3B).

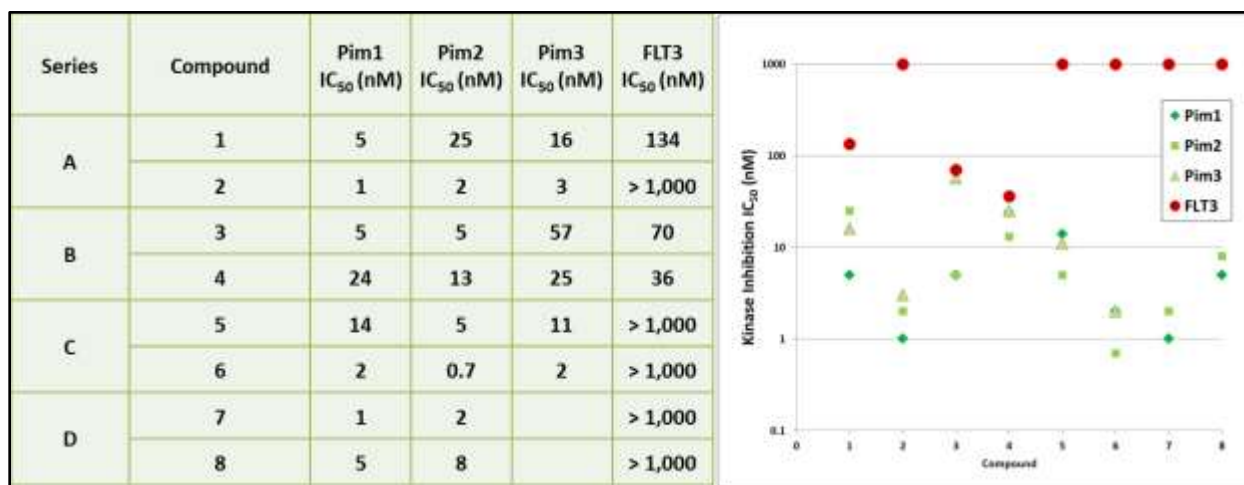


Figure 2. *In vitro* kinase inhibition IC₅₀ values (in nM) for each compound against Pim-1,2,3 (in green) and FLT3 (in red) are shown in the table and graph (log scale). The compounds are potent against all three Pim isoforms and selective versus FLT3.

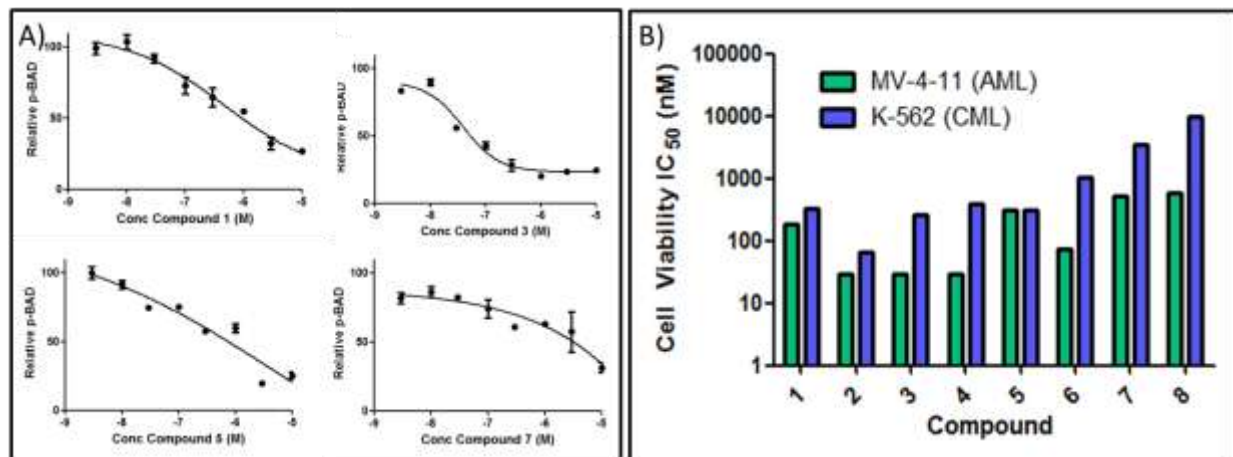


Figure 3.A) Compounds from each structural class inhibit phosphorylation of BAD S112 in a dose dependent manner. B) Pim inhibitory compounds kill leukemia cell lines in the low nanomolar range.

The *in vivo* and *in vitro* profiles of these chemically diverse series are indicative of an effective and potent anticancer mechanism mediated through the selective inhibition of Pim kinases. **Cylene's unique chemistry and experience in the development of serine/threonine kinase inhibitors has driven the development of multiple proprietary chemical series of Pan-Pim inhibitors exhibiting picomolar potency and discerning selectivity.**