



SRI

**7th International Conference:
Neurodegeneration in Alzheimer's Disease;
Parkinson's Disease & Related Disorders**

April 18 - 19, 2005

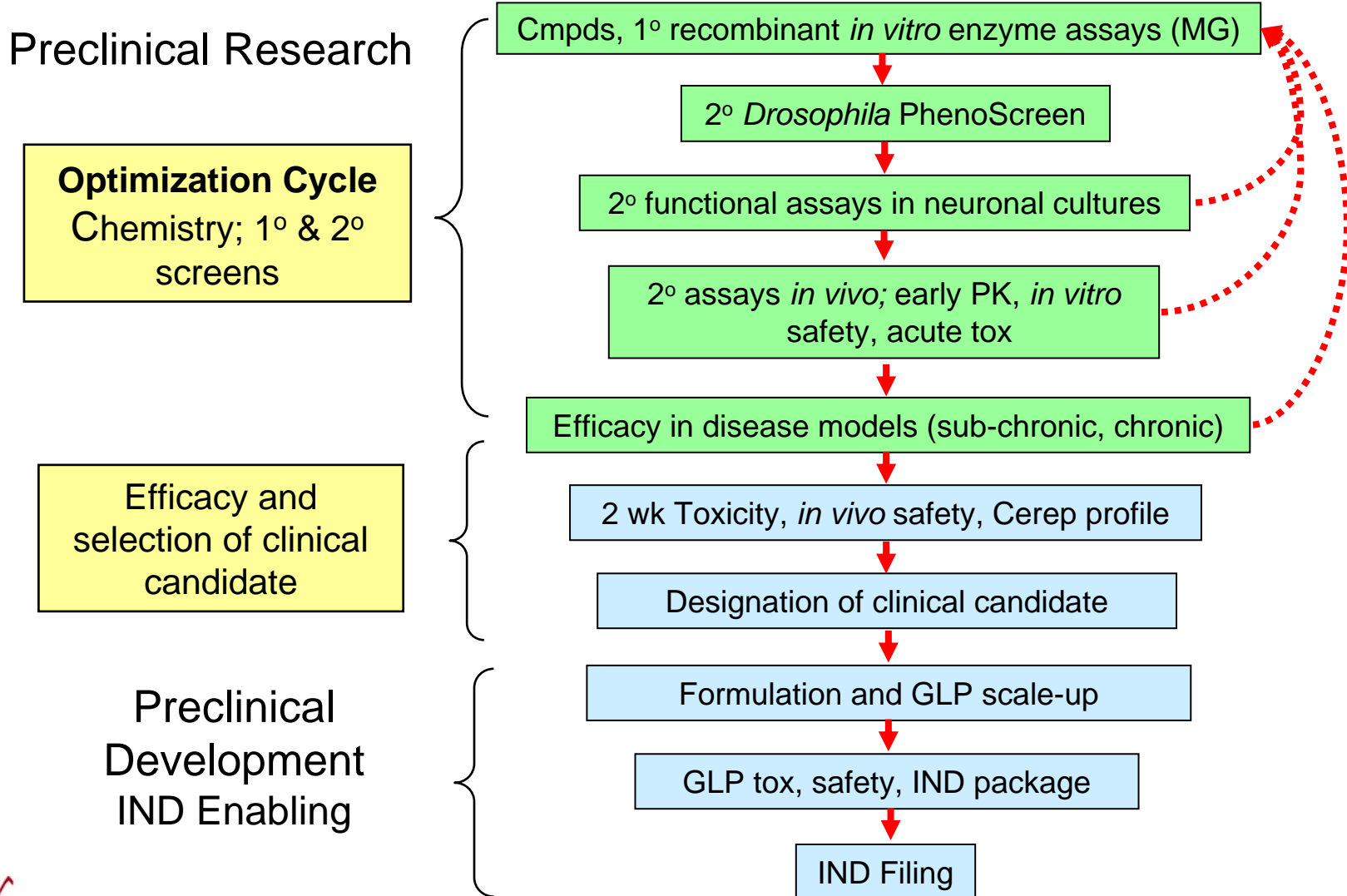
Hyatt Regency Princeton - Princeton, NJ

Title

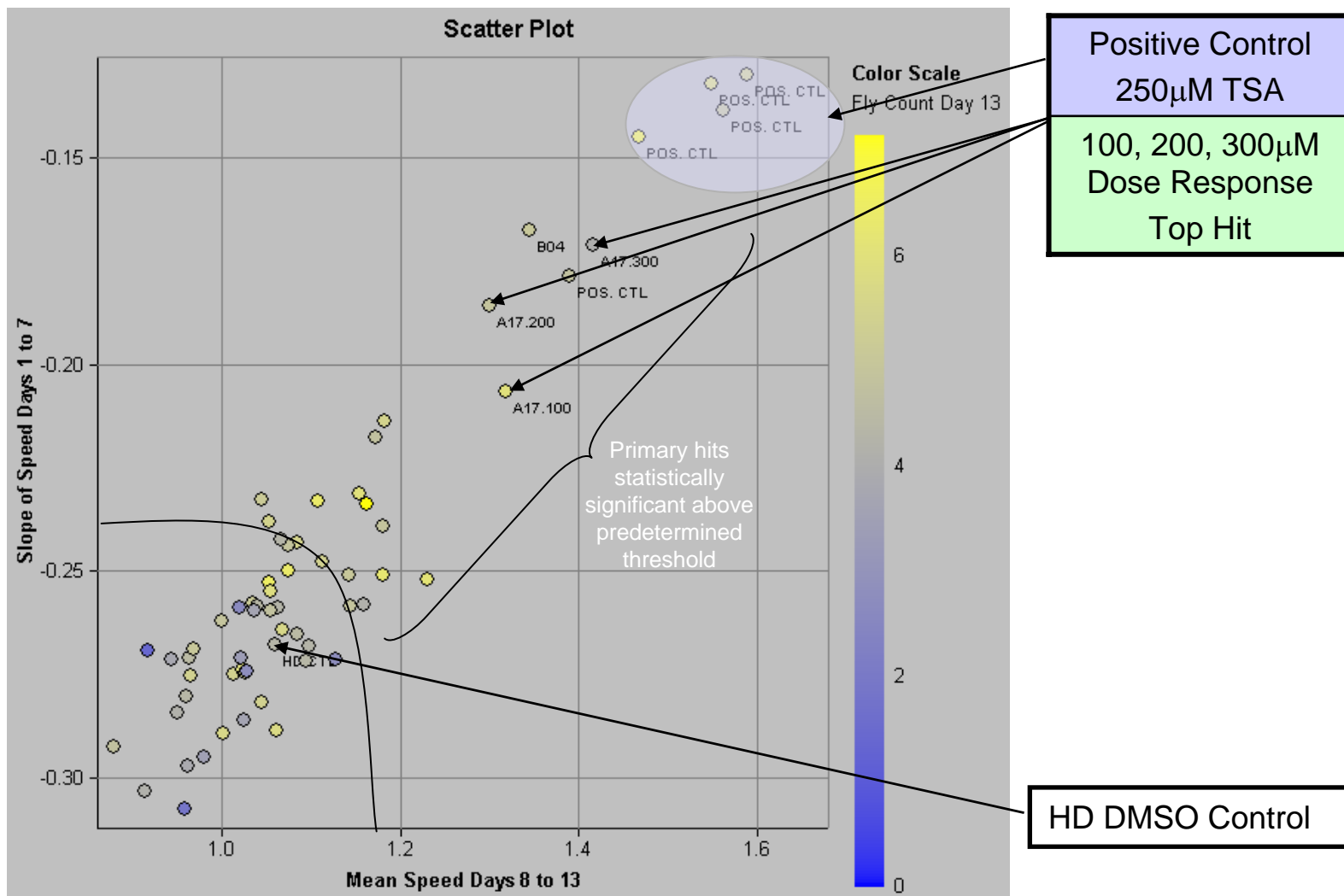
Automated Screening of Drosophila Neurodegenerative Disease Models Facilitates CNS Drug Discovery

*Gerhard Koenig
Envivo Pharmaceuticals
Watertown, MA 02472*

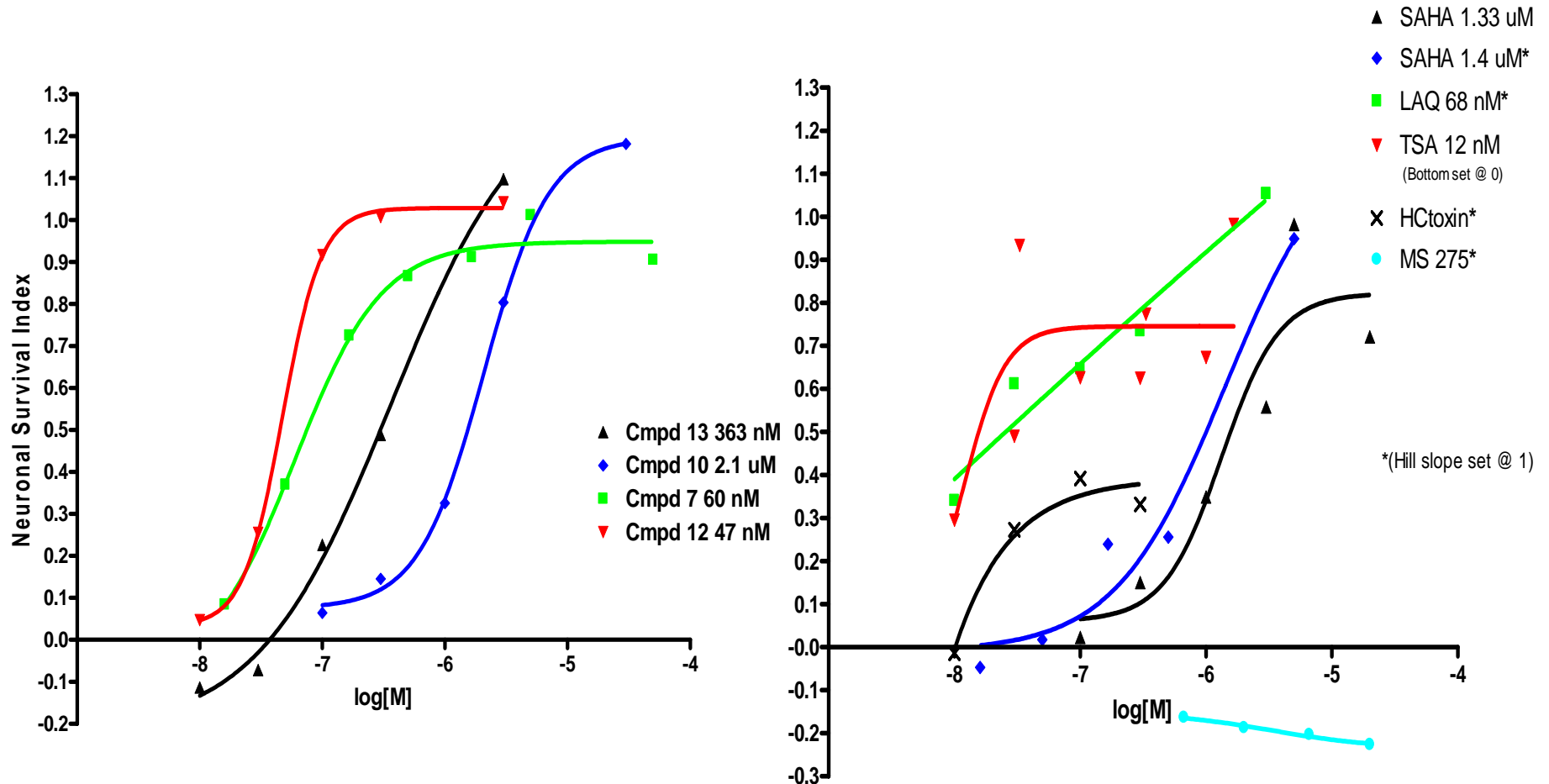
HDAC Project Screening Cascade



Proprietary Screening Platform is Instructive for Chemistry Optimization

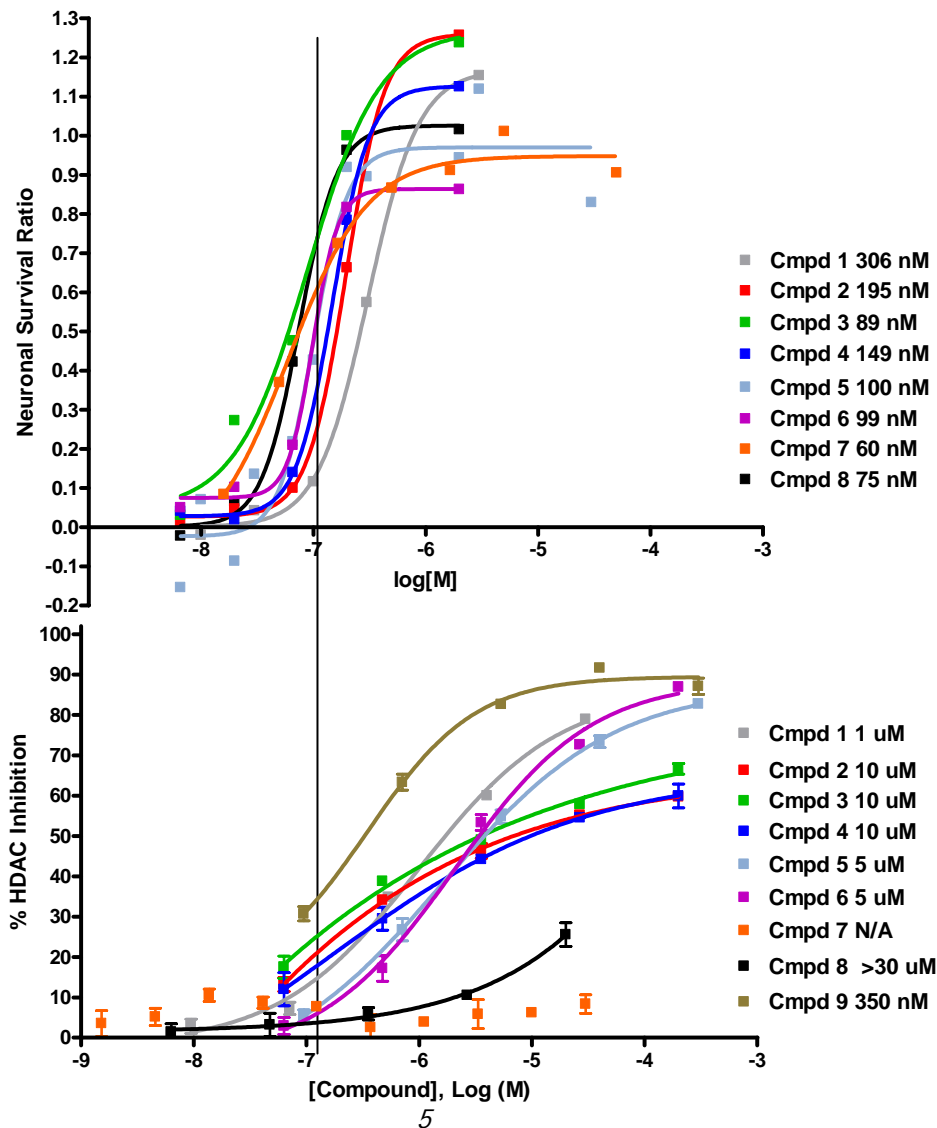


Neuroprotection from Oxidative Stress-Induced Death

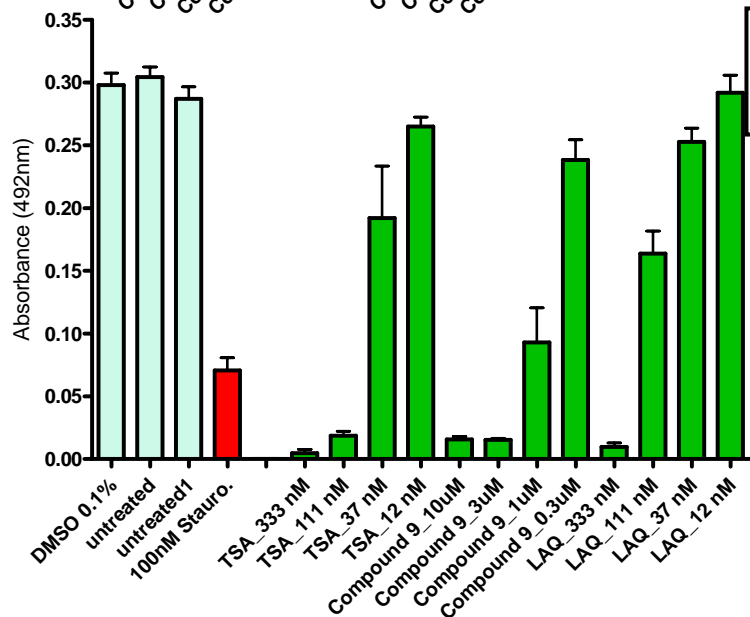
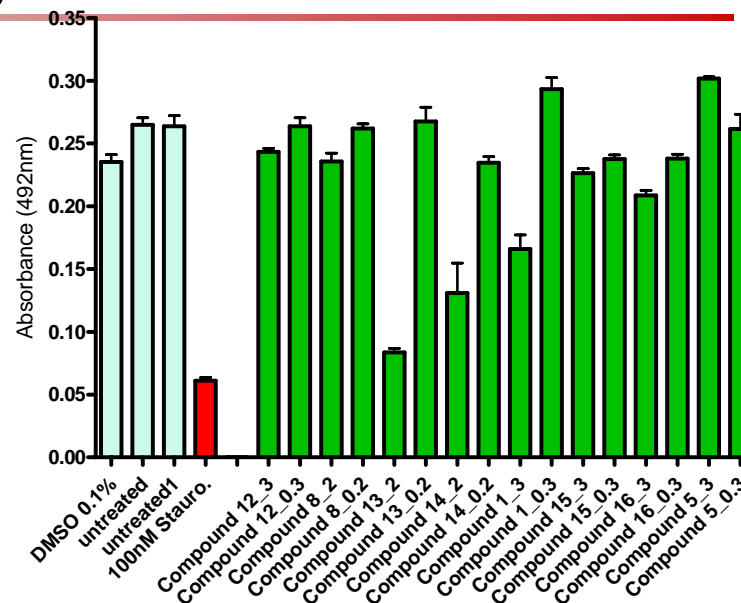
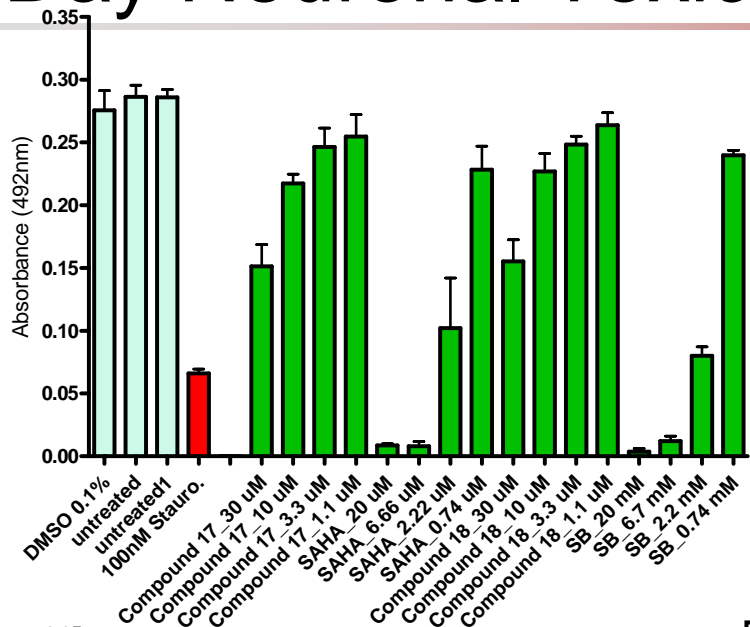


Neuroprotection Potency vs. Whole Cell HDAC Activity

Potent neuroprotective hits showed mostly small effects on whole cell HDAC activity



5 Day Neuronal Toxicity of HDAC Inhibitors

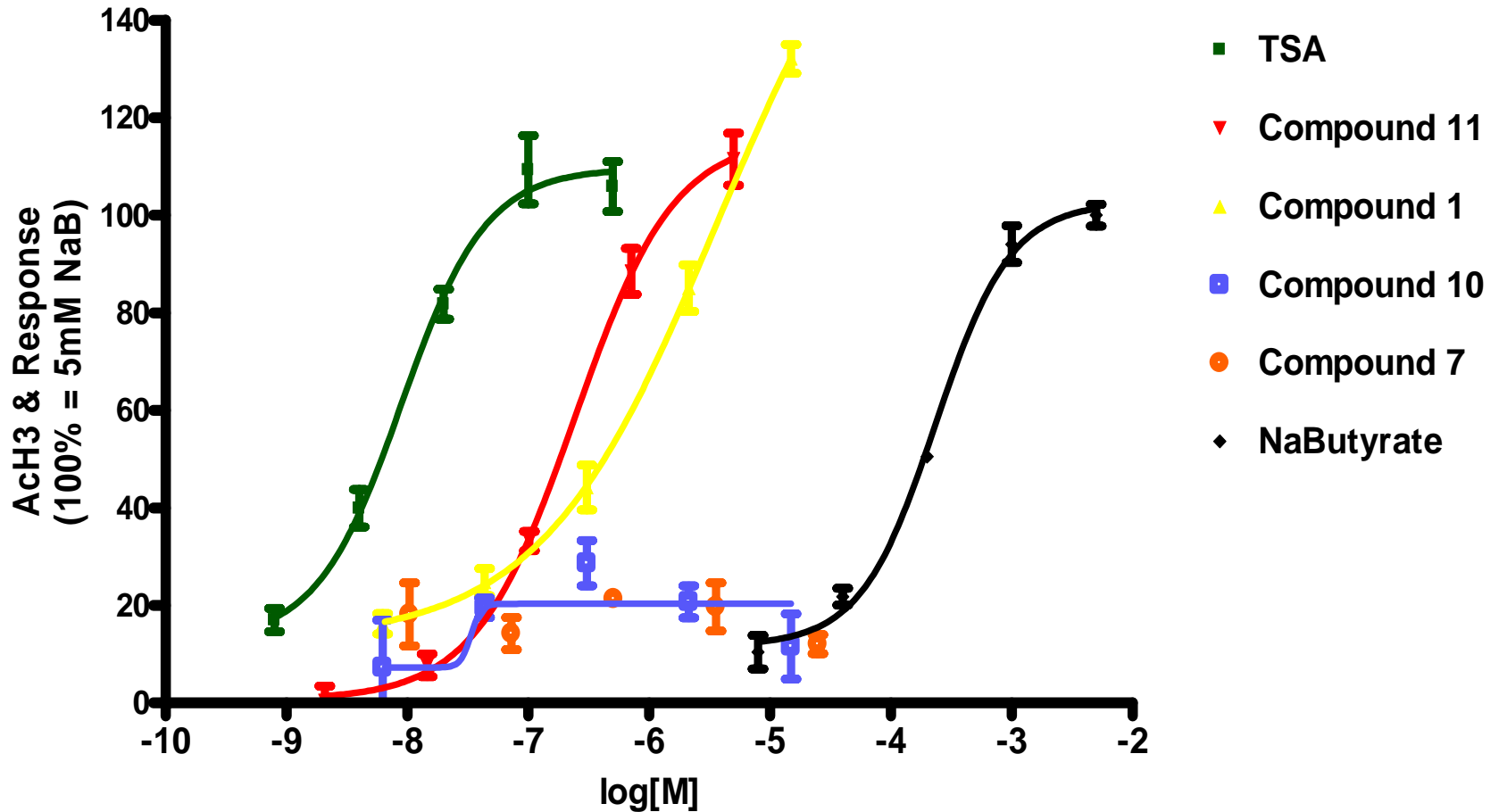


**Treatment of cortical neurons: DIV2 - DIV7
No medium change or cmpd replenishment**

~ EC₅₀

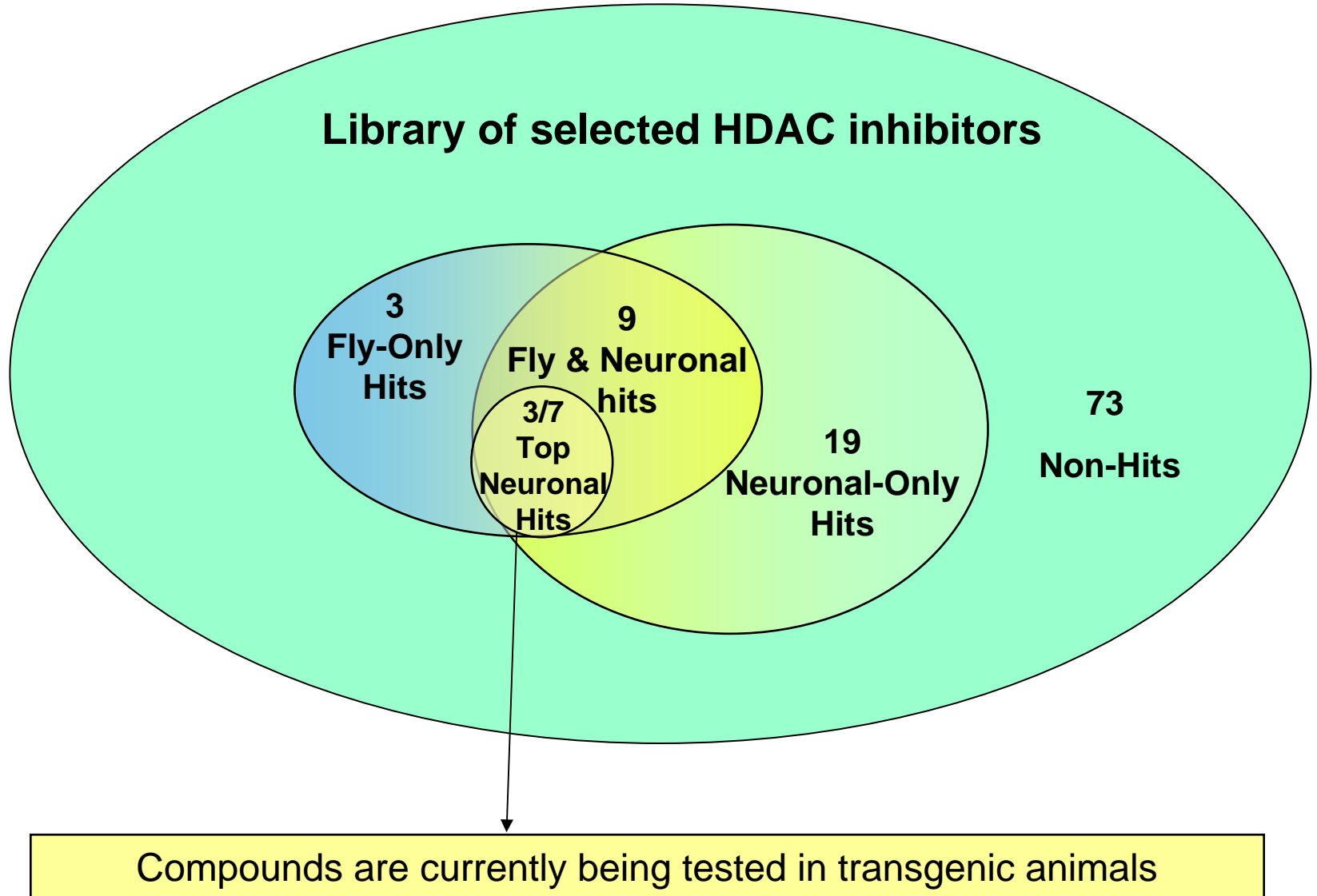
	Protect	Tox 5d	Tox 1-2d
TSA	(12 nM)	70 nM	None
SAHA	1.4 μM	2 μM	None
LAQ	70 nM	100 nM	None
SB	No test	2 mM	None

FLISA Assay



H3 acetylation determined by FLISA corresponds to whole cell HDAC activity assay

Selection of Compounds for Testing in R6/2



Compounds are currently being tested in transgenic animals