

Automated Screening of *Drosophila* Neurodegenerative Disease Models Facilitates CNS Drug Development

C.J. Cummings*, F. Albayya, M. Boeckeler, E. Faelt, L.A. Hrdlicka, M.M. Huang, F. Huet, M.B. Mahoney, D.M. Perrino, N. Sankrithi, C.M. Singh, J. Schulte, H-P. Shih, C.Y. Tschibelu, J. Hotchkiss, G. Koenig

EnVivo Pharmaceuticals, Inc. 480 Arsenal Street, Suite 1, Watertown, MA 02472

Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and the trinucleotide repeat disorders together affect tens of millions of people worldwide. However, the development of drugs that stop or slow the progression of these CNS diseases has been challenging and requires new drug screening approaches. EnVivo Pharmaceuticals has developed an *in vivo*, high throughput screening platform using whole animal models. By expressing human disease genes in *Drosophila*, we generated models that demonstrate progressive, age-dependent neurodegeneration as well as other human disease hallmarks, such as protein aggregation and locomotor dysfunction. Integral to our proprietary platform is the mass industrialization of *Drosophila* production and their handling, compound dosing, and automated phenotypic assays. One exemplary assay uses robotics and proprietary video based motion tracking software to sensitively and rapidly measure multiple metrics of locomotor behavior and toxicity. From these metrics, a Phenoprofile is generated, which reveals phenotypic impairment and improvements with drug treatment. As proof of concept, treatment of our *Drosophila* model of Alzheimer's disease with an FDA approved compound significantly improves their behavior. EnVivo is actively screening compound libraries through these various CNS models and has started to move hits from these screens forward in the drug discovery process (see poster by J.K.T. Wang *et al.*) The output of such a discovery platform has the potential to generate information on the efficacy and toxicity of a compound in an intact nervous system, allowing hits to quickly advance into preclinical development.