

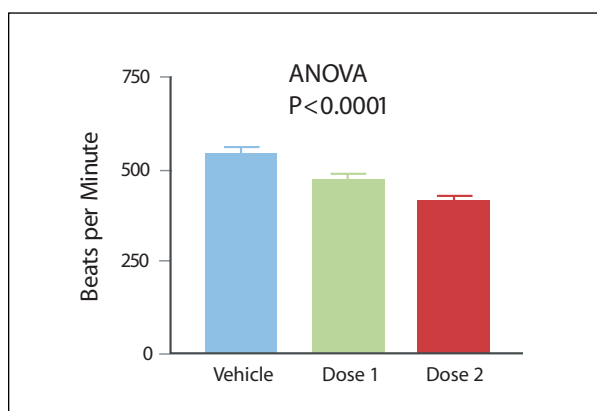
Caliper Discovery Alliances & Services ('CDAS') In Vivo Compound Profiling Program

CDAS will design a compound profiling program tailored to your timeline, budget, and areas of therapeutic interest using existing validated assays and/or developing new assays.

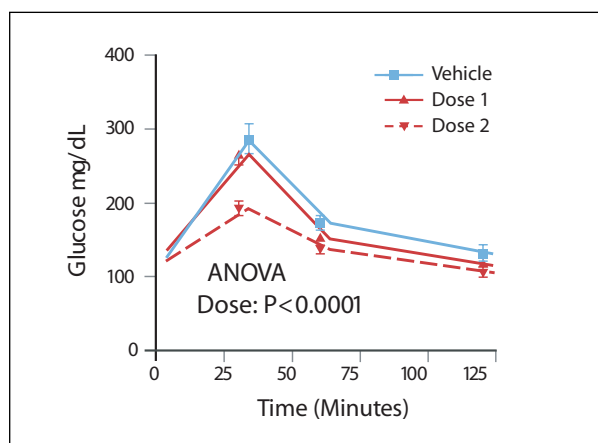
Thoughtfully designed preclinical drug studies are essential to the support of any Investigational New Drug application. In recent years, this has been especially true for most pharmaceutical companies, as the consequences of product candidate failures can be devastating, both scientifically and financially. Accordingly, there is a need to decide, much earlier in the process, if and when a pre-clinical drug development candidate is ready to go into clinical trials, and how to recognize the greatest value while minimizing the escalating development costs for such candidates.

Although the pharmaceutical industry has invested prodigious amounts in novel discovery technologies with hopes of improving R&D productivity, the output has not improved as a result of the gap in productivity.

This productivity problem, coupled with worldwide pressure on drug pricing, mounting challenges from generics and ever-increasing regulatory hurdles, has forced drug development personnel to focus on identifying new uses for existing drugs. The process of finding new uses outside the scope of the approved medical indication for existing drugs is also known as "repositioning" or "reprofiling."



A dose-dependent effect of an anxiolytic drug on the heart rate in C57Bl6/J mice



A dose-dependent effect of an anxiolytic drug on glucose excursion in the Oral Glucose Tolerance Test in C57Bl6/J mice

CDAS has long recognized the value that data obtained from animal models can bring to preclinical research. As such, we are pleased to introduce our new comprehensive In Vivo Compound Profiling program: a customized battery of pharmacological tests (measuring over 450 parameters relevant to 15 therapeutic areas) to (i) assess the therapeutic efficacy of (optimized) lead compounds and/or drug development candidates by analyzing their effects on key physiological functions in animals, and (ii) screen for potential side effects caused by the administration of such compounds, and/or (iii) discover disease indications for such compounds that were not previously known, thus expanding the market potential of those drug candidates. The program also leverages our proprietary optical imaging (i.e., bioluminescent and/or fluorescent) technology to characterize some mechanism of action parameters of test compounds. Moreover, we expect that this program's greatest impact will be to expand the market potential of certain drug or drug candidates through the discovery of critically important the discovery of critically important secondary or additional indications for marketed as well as for preclinical/clinical drug development candidates.

Compound Profiling Platform

The CDAS in vivo compound profiling platform includes over 85 standardized and validated bioassays relevant to the following therapeutic areas:

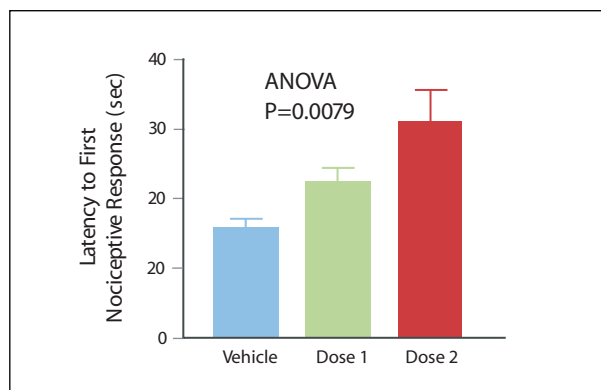
- Allergic diseases
- Arthritis
- Cardiovascular diseases
- Diabetes
- Gastrointestinal disorders
- Immunology and inflammation
- Neurodegenerative disorders
- Oncology
- Obesity
- Osteoporosis
- Pain
- Psychiatric disorders
- Sexual health
- Tissue repair
- Urological disorders

The representative data incorporated within this brochure were generated using a generic anxiolytic compound and validated bioassays from the CDAS in vivo compound profiling platform. These observations suggest that, in addition to the main anxiolytic effect observed in human patients, this drug is likely to have other effects on a number of physiological parameters, such as glucose excursion, heart rate, pain sensitivity, and male sexual performance. These examples illustrate the potential value of early in vivo evaluation of pharmaceutical compounds.

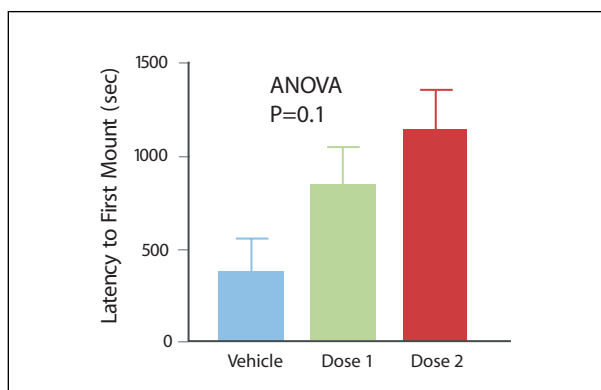
Efficacy Data in Rodents

Our In Vivo Compound Profiling platform offers direct disease-related physiological and behavioral endpoints for in vivo assessment. Over the years, many approved drugs for use in humans were first shown to demonstrate efficacy in rodent models: Enbrel, Singulair, Zolof, Lipitor, Capoten, Evista, and Fosomax, just to name a few. Further this platform:

- Allows for multiple routes of administration for test compounds (i.e., oral gavage, oral with diet, i.p., i.v., i.m., sub-Q, topical)
- Allows for acute or chronic dosing paradigms
- Provides MOA insights by leveraging physiological challenge bioassays with the capabilities of our proprietary in vivo bioluminescent/fluorescent imaging platform
- Allows for access to a cost effective program for the comprehensive profiling of any drug development candidate

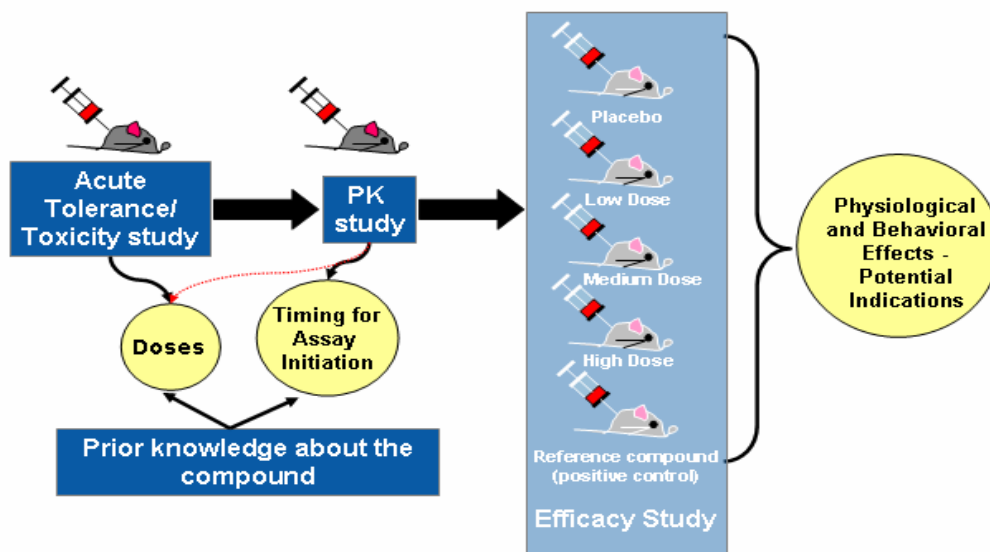


A dose-dependent effect of an anxiolytic drug on nociceptive behavior in the Hot Plate test in C57Bl6/J mice



A dose-dependent tendency to delayed initiation of sexual behavior in the anxiolytic-treated C57Bl6/J male mice

Comprehensive Compound Evaluation in Rodents



The diagram above portrays a typical workflow for an In Vivo Compound Profiling study – designed to test three different dose groups, a vehicle group and a reference compound group in a mutually selected battery of bioassays.

- Specific doses used in functional assays are chosen based on the results of a limited toxicity and pharmacokinetic (PK) study – this may be by-passed if customer already has this data
- Study Deliverables include:
 - All data from toxicity, PK and efficacy studies
 - Summary of observed physiological and behavioral effects of test compound
 - Conclusions/interpretations regarding potential indication(s) and/or side effect(s) of test compound



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