## PHARMACEUTICAL RESEARCH AND DEVELOPMENT

## INSIGHTS THAT DELIVER CONFIDENCE AND SUCCESS

METABOLOMICS EMPOWERS DECISION-MAKING FROM PROGRAM INCEPTION THROUGH CLINICAL TRIALS

R&D decisions can frequently be based on abstract information. Some technologies, such as transcript profiling, provide an overwhelming amount of data that does not produce clear signals without substantial investment. On the other hand, measuring only a limited number of markers may omit key insights.

There is a need for data that provides a comprehensive, physiologically meaningful assessment of a living system (cells, animal models, human) and links it to how a target/molecule combination is affecting the system. This type of data will enrich decision making from discovery through the clinic—this is what metabolomics does.

Metabolomics is a technology for comprehensively measuring all the small molecules (metabolites or biochemicals) in a living system. As the products of biological networks, the microbiome, or exposure (diet, drugs, etc.), metabolites serve as a proxy to the physiological changes accompanying disease and drug response. This data makes metabolomics a key ally for driving decisions in pharmaceutical R&D.



METABOLON'S UNIQUE PRECISION METABOLOMICS<sup>™</sup> TECHNOLOGY PROVIDES ACTIONABLE INSIGHTS TO IMPROVE THE LINE OF SIGHT FROM DISCOVERY THROUGH CLINICAL DEVELOPMENT.

> TARGET BIOLOGY ↓ MOLECULE PROFILE ↓ CLINICAL DEVELOPMENT

Precision Metabolomics<sup>™</sup> can build pharmaceutical R&D program confidence and reduce attrition by helping you select high-quality targets, molecules and translatable biomarkers across all major therapeutic areas.

## YOUR ALLY IN PHARMA R&D

TARGET BIOLOGY	<ul> <li>Expand understanding of target biology and disease pathophysiology</li> <li>Facilitate target identification and validation through the functional reduction of genomic data</li> <li>Determine concordance level of models with translational metabolomics</li> </ul>	Discovery-Target Selection ↓
MOLECULE PROFILE	<ul> <li>Assess the full landscape of molecule effects: <ul> <li>Safety, Efficacy, MoA</li> <li>Polypharmacology a liability or asset?</li> <li>In the context of competitor drugs</li> </ul> </li> <li>Define a suite of biomarkers for model-based drug development (pharmacometric modeling)</li> </ul>	Lead-Candidate Selection ↓ Preclinical
CLINICAL DEVELOPMENT	<ul> <li>Assess target engagement, dose effects and safety</li> <li>Identify responders and non-responders</li> <li>Delineate baseline characteristics</li> <li>Assess trial quality: site issues, compliance, metabolic outliers</li> <li>Differentiate drug profiles (competitor analysis; post-market support)</li> </ul>	Clinical

Project teams are increasingly using metabolomics to enrich their drug discovery and development programs, because metabolites reflect the physiological changes accompanying disease and drug response. Importantly, these changes are agnostic to the target class (e.g. GPCR, enzyme, nuclear receptor).

Metabolomics is a key technology for understanding target biology, the translational potential of models, and a molecule's mechanism of action and its effects (pharmacodynamics, efficacy and safety). In addition, it is used in clinical development to stratify and evaluate patients and the overall quality of the study and better understand drug effects.

The value of metabolomics is ultimately best realized when used across program milestones. Insights and biomarker assets can be leveraged from discovery through the clinic and build infrastructure across programs.

Metabolon has conducted thousands of studies and works extensively with leading pharmaceutical and biotechnology companies. We offer a continuum of metabolomics services for every stage of R&D.

## Relevant Publications Using Metabolon's Precision Metabolomics<sup>™</sup> Technology

Our technology provides unparalleled breadth of quality metabolomics data, which has led to hundreds of highimpact publications including:

Long, Tao, et al., Nature Genetics 49.4 (2017): 568-578.

B. Yu et al., *Sci Adv* (2016) 2:e1600800.

Yee, Sook Wah, et al., *Clinical Pharmacology & Therapeutics* 100.5 (2016).

Y. Zhang et al., J Clin Invest 124, 2750 (Jun, 2014).

Yin, Wu, et al., Journal of lipid research 53.1 (2012): 51-65.

Ventura, R. et al., *EBioMedicine* 2, 806-822 (2015).

M. Watson et al., *Mol Cell Biol* 29, 5872 (Nov, 2009).

Jenkins, Y. et al., *BMC Res Notes* 7, 674 (2014).; Jenkins, Y. et al., PLoS One 8 (2013).

Zgoda-Pols, J.R. et al., *Toxicol Appl Pharmacol* 255, 48-56 (2011).

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