We can produce and scale-up mammalian phase I and II metabolites using microbial catalysts, mammalian tissue fractions and recombinant enzymes:

- For DMPK / ADME / TOX
- For Met ID
- As standards for quantitation

**Proven Reactions**

Methyl hydroxylation
Methylene hydroxylation
Methine hydroxylation
Aromatic hydroxylation
*N*-oxidation
*N*-methylation
*N*-dealkylation
*N*-acetylation
*O*-dealkylation
Carbonyl reduction
Heterocycle oxidation via aldehyde oxidase
Aromatic *O*-glucuronidation
Aromatic *N*-glucuronidation
Non-aromatic *O*-glucuronidation
Non-aromatic *N*-glucuronidation
Acyl-glucuronidation
Other glycosidations (AgChem)
*N*-sulfation
*O*-sulfation
Thiol conjugation (GSH/NAC)
Transamination
Amino acid conjugations
Sequential reactions e.g. hydroxylation & glucuronidation

*For more information contact us at*
mail@hyphadiscovery.com

# Scale-up of human metabolites from mixed metabolism of epacadostat

## Supply of a glucuronide, gut metabolite and secondary CYP metabolite to support clinical development

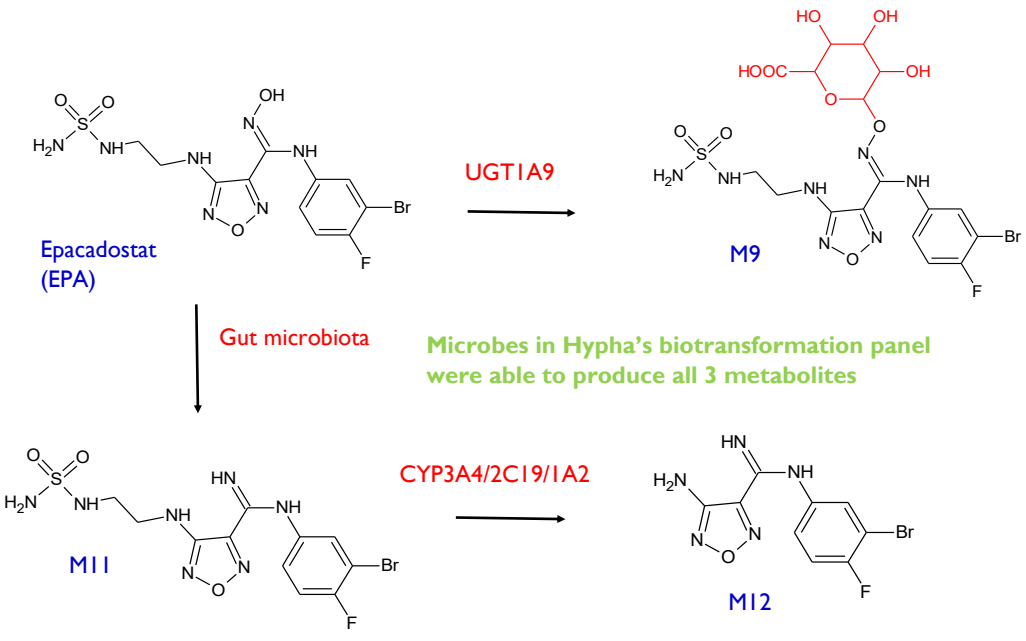
Formation and scale-up of human metabolites formed through **mixed metabolic pathways** is possible using Hypha's microbial biocatalysis system.

*In vivo* human metabolism of Incyte's IND epacadostat (EPA) forms 3 major circulating metabolites, from both primary and secondary pathways. Glucuronidation of EPA forms M9, the dominant metabolic pathway, in conjunction with formation of an amidine M11 and an *N*-dealkylated metabolite, M12. Boer *et al.* showed reductive metabolism by gut microbiota results in M11, which is absorbed and further modified by CYP enzymes to form the secondary metabolite M12.

Hypha's microbial panels provided a route to achieve formation of **all three human metabolites**, with several strains shown able to effectively biotransform EPA. Different strains and dosing regimes were found to be optimal for production of each metabolite. Although M12 was produced by the microbes, it was more easily synthesised.

Scale-up of the most productive biotransforming strains for M9 and M11 enabled the supply of 112mg of the glucuronide and 69mg of the gut metabolite at 95% purity to Incyte Corporation.

Ref: Roles of UGT, P450 and Gut Microbiota in the Metabolism of Epacadostat in Humans. Boer *et al.*, 2016. DMD 44(10), 1668-1674.




### About Hypha Discovery

Hypha Discovery Ltd is a UK-based microbial biotechnology company providing solutions to pharmaceutical and agrochemical R&D partners through the production of mammalian and microbial metabolites, as well as specialising in microbially-derived chemicals. As part of our extensive client base, we work with 8 out of 10 of the top pharma companies and 4 out of 6 of the top agrochemical companies worldwide.