Drug and Untargeted Biomarker Distribution by *Tissue-MALDI-Imaging-MS* for Target Engagement and Investigative Toxicology - A Short Introduction of Sanofi Approach

„Tissue mass spectrometry imaging (tMSI) allows the distribution of non-labeled pharmaceutical drugs and its metabolites, concomitant to the analysis and the in-situ distribution of endogenous biomarkers (e.g. lipids, metabolites, peptides, proteins) Due to its broad versatility, tMSI was successfully applied to diverse applications like 1) drug efficacy, target engagement, PK/PD correlation; 2) toxicity investigations; 3)biomarker discovery on a broad screening platform; 4) disease biomarkers, disease progression; 5) spatial localization of proteins, peptides

Continuous improvement in bioinformatics with an increased public access to databases, and pathway analysis, and the increase in lateral spatial resolution and mass accuracy, allow currently the visualization and determination of biomolecules at a spatial resolution of 5-10 µm and a mass accuracy of below 1ppm.
tMSI is a high content technology and its sensitivity and specificity are highly dependent by the chemical matrix, which makes the technology an attractive tool for untargeted biomarker discovery, allowing the analysis of more than 1,000 biomarker features.
Due to the high content, tMSI allows a deeper insight into the molecular mechanism and adds an additional level to classical histological evaluations by monitoring drug in combination with (un)targeted biomarker colocalized in the tissue.
R&D processes are time and resource intensive and the failure rate is high, in many cases due to late stage adverse effects observed in long-term chronic toxicity studies, or the lack of adequate target engagement, resulting in missing pharmacological efficacy.
tMSI studies in research and in early preclinical development phase allows to overcome these issues by elucidation of drug/active metabolites distribution and identification of biomarkers and their regulation, anticipating the safety risk and therefore reduce of attrition rate in research and the number of animals in the sense of 3R.