

## Selected centres (and experts):

- NeurATRIS Translational Neurosciences, Paris (Dr. Hantraye)
- VU University Medical Centre, Amsterdam (Prof. Windhorst, Dr. Vugts)
- Turku PET Centre, Turku (Prof. Knuuti, Prof. Solin)
- San Raffaele Scientific Institute - IMINET, Milan (Dr. Picchio, Dr. Todde)
- University Medical Centre, Groningen (Prof. De Vries, Prof. Elsinga, Prof. Boellaard)
- Klinikum rechts der Isar, Technische Universität München (Prof. Schwaiger)
- Uppsala University and Hospital (Prof. Antoni, Prof. Larhed, Prof. Orlova)
- Radboud University Medical Centre, Nijmegen (Prof. Boerman, Prof. Verzijlbergen)
- Vall d'Hebron Research Institute, Barcelona (Dr. Castell)
- Fondazione IRCCS Fondazione Pascale, Naples (Dr. Aloj)

## Literature

- **Slobbe P et al.** PET imaging with small-molecule tyrosine kinase inhibitors. *Drug Discovery Today* 17, 1175-87 (2012)
- **Slobbe P et al.** A comparative PET imaging study with the reversible and irreversible EGFR tyrosine kinase inhibitors 11C-erlotinib and 18F-afatinib in lung cancer-bearing mice. *EJNMMI Res* 20, 14 (2015)
- **Rinne JO et al.** 11C-PIB PET assessment of change in fibrillar amyloid-beta load in patients with Alzheimer's disease treated with bapineuzumab: a phase 2, double-blind, placebo-controlled, ascending-dose study. *Lancet Neurol.* 9, 363-72 (2010)
- **Varrone A et al.** Positron emission tomography imaging of the 18-kDa translocator protein (TSPO) with 18F-FEMPA in Alzheimer's disease patients and control subjects. *Eur J Nucl Med Mol Imaging* 42, 438-46 (2015)
- **Golla SS et al.** Quantification of [(18)F]DPA-714 binding in the human brain: initial studies in healthy controls and Alzheimer's disease patients. *J Cereb Blood Flow Metab.* 35,766-72 (2015)
- **Hirvonen J et al.** Assessment of MAO-B occupancy in the brain with PET and <sup>11</sup>C-L-deprenyl-D2: a dose-finding study with a novel MAO-B inhibitor, EVT 301. *Clin Pharmacol Ther.* 85, 506-12 (2009)
- **Luoto P et al.** <sup>11</sup>C-ORM-13070, a novel PET ligand for brain  $\alpha_2$ -adrenoceptors: radiometabolism, plasma pharmacokinetics, whole-body distribution and radiation dosimetry in healthy men. *Eur J Nucl Med Mol Imaging.* 41, 1947-56 (2014)

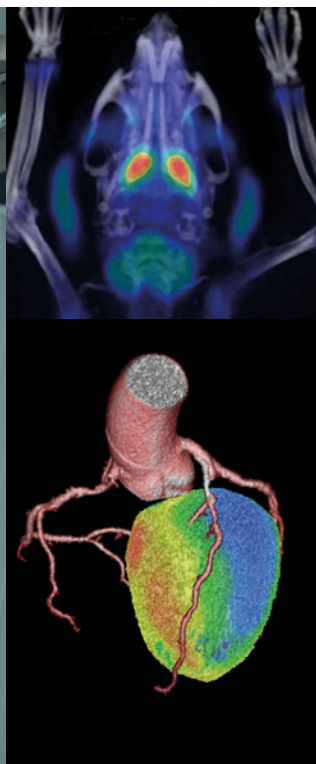
How can  
**small molecule  
tracers** guide  
your drug and  
diagnostics  
development  
programme?

**eatris**

# **SMALL MOLECULE TRACERS:**

**IN VIVO IMAGING OF DISEASE-SPECIFIC MARKERS**

# DECREASE RISK, IMPROVE INSIGHTS, AND INCREASE VALUE



A key challenge in drug and diagnostics development is the adequate and expedite selection of the most promising candidates, while excluding compounds with unfavourable properties to prevent late stage failures. Tracer compounds used in PET or optical molecular imaging are capable of visualising and quantifying in vivo biomarkers at high specificity and sensitivity. EATRIS offers more than 100 validated PET, SPECT and optical tracer compounds with proven safety, high affinity for the target, high (tissue) specificity and (receptor) selectivity. These tracers comprise receptor (ant)agonists, enzyme and transporter substrates to study several biological pathways. The EATRIS consortium offers clients validated methods, high-end infrastructure, the skills sets to visualise and quantify tracers and the expertise to process and interpret images.

**“The development of pharmaceuticals for CNS disorders is complex because it is difficult to provide evidence of pharmacodynamic effects in early human trials. PET imaging is a powerful tool to show target engagement and guide dose selection for Phase II trials in patients.”**

– Juha Rouru, Head of Therapy Area CNS, Orion Pharma

### **How can tracers guide your drug and diagnostics development programme?**

- Accurate delineation and identification of disease to be targeted by the drug
- Picomolar level detection of disease-specific contrast agent, substrate or receptor ligand
- In vivo assessment of (dose-dependent) receptor occupancy in target tissue, also for dose selection in further studies with larger populations
- Target engagement in competitive binding studies with unlabeled candidate drug
- Quantitative assessment of tissue distribution, tissue blood flow
- Metabolic profiling in target tissue (gene expression, enzyme activity)
- Correlation of receptor occupancy with drug plasma kinetics and efficacy
- Accurate detection of drug threshold levels (efficacy vs side effects), optimising dose regimen
- Correlation of non-responders with drug receptor occupancy and tissue distribution

### **Technical and Regulatory (QA/QC) aspects of tracer development and clinical application**

- Production of PET and SPECT radionuclides ( $^{11}\text{C}$ ,  $^{13}\text{N}$ ,  $^{15}\text{O}$ ,  $^{18}\text{F}$ ,  $^{64}\text{Cu}$ ,  $^{68}\text{Ga}$ ,  $^{89}\text{Zr}$ ,  $^{111}\text{In}$ ,  $^{123}\text{I}$ ,  $^{124}\text{I}$ ) and fluorescent dyes
- Various high-end scanners PET/MRI, PET/CT,  $\mu\text{SPECT}$ ,  $\mu\text{PET}$ ,  $\mu\text{MRI}$  (including ultra high field), CT, US and optical
- Custom made design, synthesis, automation and pre-clinical testing of novel tracers (incl. metabolite analysis)
- Smooth transition from rodent and non-human primate studies to approval for human application
- Development and validation of GMP compliant procedures for tracer production “for human use” (incl. generation of SOPs, IMPDs)
- Compliance with regulatory and industry standards (production licenses, audit reports)

### **The EATRIS Imaging & Tracing network**

EATRIS is an expanding network of qualified translational European Imaging & Tracing centres that offers high-end infrastructure for preclinical and clinical molecular imaging to support drug and diagnostics development, in collaboration with the European Association of Nuclear Medicine (EANM).