Clinical Research Services Turku CRST – partnering with Turku PET Centre

- Private CRO that conducts clinical studies for the pharmaceutical industry and for other customers
- Experienced in demanding phase 0-2 clinical trials and proof-of-concept studies
- Employing Positron Emission Tomography (PET) to assess efficacy and pharmacokinetics

CRST

- Scientific and regulatory consultancy
- Medical writing, regulatory submissions
- Subject recruitment
- Investigators, study nurses and clinical wards with 24/7 safety monitoring
- In-house bioanalytical laboratory for analysis of PK and biomarker samples
- Clinical study monitoring
- Project management

Turku PET Centre

- State-of-the-art PET imaging facilities
- MRI, CT and ultrasound imaging
- PET radiochemistry expertise with cyclotrons and GMP radiopharmaceutical laboratories
- Extensive track record in pharma trials from preclinical to clinical

www.pet.fi
Valuable information for the advancement of CNS drug development programs

Unique benefits
- Detection of early signs of efficacy
- Confirmation of mode-of-action
- Dose guidance for Phase II/III studies
- Improved patient selection and stratification
- Monitoring of the time extent and course of drug binding

Useful applications
- Visualization and quantitation of CNS disease-specific biological targets and events
- Receptor/transporter occupancy after single or multiple doses of a test drug
- A broad range of disease and target-specific tracers in Turku PET Centre
Applications for the clinical testing of Alzheimer’s disease drugs

Several PET tracers are available for visualization and quantitation of:
- beta-amyloid deposits
- glial inflammation markers in the brain
- cholinergic neurotransmission

Imaging approaches for treatments with other primary mechanisms of action:
- Imaging of brain glucose consumption is possible with $^{18}$F-FDG
- Changes in many neurotransmitter and receptor systems may be investigated with the broad range of PET tracers available in Turku
Commonly used tracers for neurotransmitter receptors, transporters and enzymes

<table>
<thead>
<tr>
<th>Target system</th>
<th>Tracer</th>
<th>Mechanism and target</th>
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<tbody>
<tr>
<td>Opioid system</td>
<td>^11^C-Carfentanil</td>
<td>μ-opioid receptor agonant</td>
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<tr>
<td>Neurokinin system</td>
<td>^1^8^F-SPA-RQ</td>
<td>Neurokinin 1 (NK₁) receptor antagonist</td>
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<td>Monoamine oxidase B (MAO-B)</td>
<td>^11^C-Deprenyl</td>
<td>MAO-B ligand</td>
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<tr>
<td>GABAergic system</td>
<td>^11^C-Flumazenil</td>
<td>GABA&lt;sub&gt;A&lt;/sub&gt;-receptor antagonist</td>
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<tr>
<td>Cholinergic system</td>
<td>^11^C-Nicotine</td>
<td>Nicotinic receptor agonant</td>
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<tr>
<td></td>
<td>^11^C-MP4A</td>
<td>Acetylcholinesterase (AChE) analog (for AChE activity studies)</td>
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<tr>
<td></td>
<td>^11^C-MP4B</td>
<td>Butyrylcholinesterase (BChE) analog (for BChE activity studies)</td>
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<tr>
<td>Serotonergic system</td>
<td>^11^C-MADAM</td>
<td>Serotonin transporter (SERT) ligand</td>
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<td></td>
<td>^11^C-WAY100635</td>
<td>5-HT₁&lt;sub&gt;A&lt;/sub&gt; receptor antagonist</td>
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<tr>
<td>Adenosine system</td>
<td>^11^C-TMSX</td>
<td>Adenosine A&lt;sub&gt;2A&lt;/sub&gt; receptor antagonist</td>
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<tr>
<td>Dopaminergic system</td>
<td>^1^8^F-DOPA</td>
<td>Dopamine precursor (dopamine synthesis and storage)</td>
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<td>^11^C-Raclopride</td>
<td>D&lt;sub&gt;2&lt;/sub&gt;/D&lt;sub&gt;3&lt;/sub&gt; receptor antagonist (for striatal receptors)</td>
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<tr>
<td></td>
<td>^11^C-FLB457</td>
<td>D&lt;sub&gt;2&lt;/sub&gt;/D&lt;sub&gt;3&lt;/sub&gt; receptor antagonist (for extrastriatal/cortical receptors)</td>
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<td></td>
<td>^11^C-SCH22390</td>
<td>D&lt;sub&gt;1&lt;/sub&gt;/D&lt;sub&gt;5&lt;/sub&gt; receptor antagonist (striatal and extrastriatal receptors)</td>
</tr>
<tr>
<td></td>
<td>^11^C-PE2I</td>
<td>Dopamine transporter (DAT) ligand</td>
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Success stories of the utilization of PET imaging in CNS drug development

- Occupancy study of antidepressant target in the brain of healthy volunteers – provided important guidance for dose level selection in Phase II trials and helped to reach a no-go decision before Phase III
  Bergström M et al., Biol Psychiatry 2004, 55:1007-12
  Link to MEDLINE: http://www.ncbi.nlm.nih.gov/pubmed/15121485

- Occupancy study of therapeutic target in the brain of Alzheimer’s patients and healthy control subjects – provided important information for Phase II dose selection
  Hirvonen J et al., Clin Pharmacol Ther 2009, 85:506-12
  Link to MEDLINE: http://www.ncbi.nlm.nih.gov/pubmed/19129751

- Amyloid imaging study to assess efficacy of anti-amyloid therapy in Alzheimer’s disease – suggested that the treatment has anti-amyloid efficacy and that $^{11}$C-PiB PET imaging is useful in assessing the effects of potential anti-amyloid treatments in Alzheimer’s disease
  Rinne JO et al., Lancet Neurol 2010, 9:363-72