



pivotpark
screeningcentre



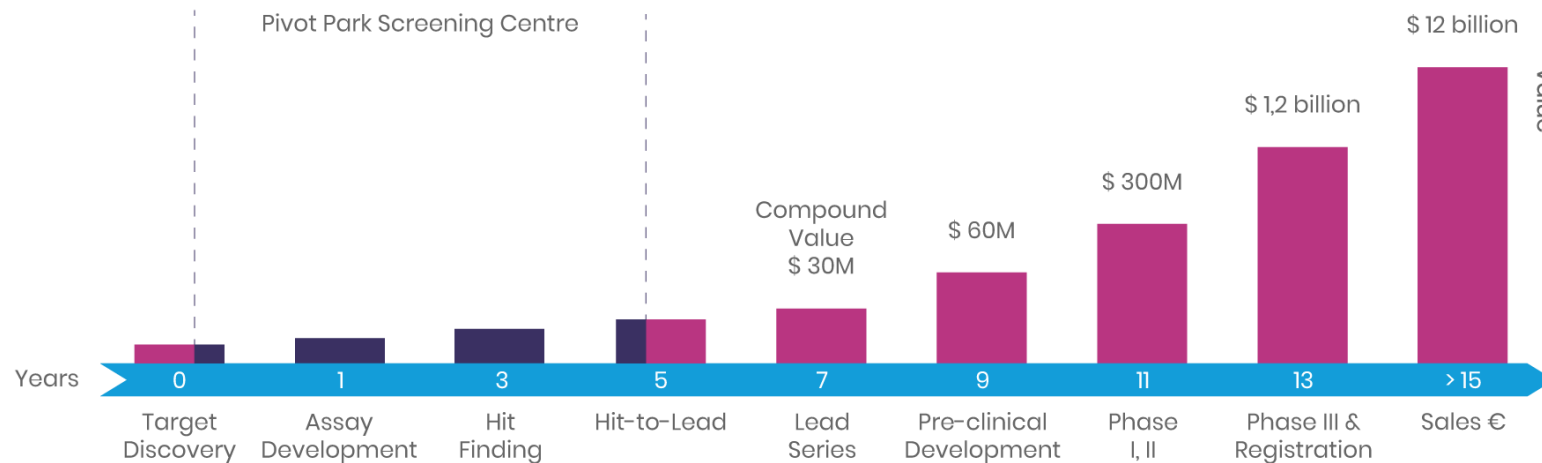
Integration of MALDI-MS into a fully automated ultra-High-Throughput Screening Platform

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Oss, The Netherlands

Drug Discovery 2022:
driving the next life science revolution

Pivot Park Screening Centre (PPSC)

- Contract Research Organization (CRO) based in Oss, the Netherlands
- Early drug discovery services
 - **Biochemical and cellular assay development**
 - **Medium to ultra-High-Throughput Screening**
 - **Hit-to-lead biological profiling**

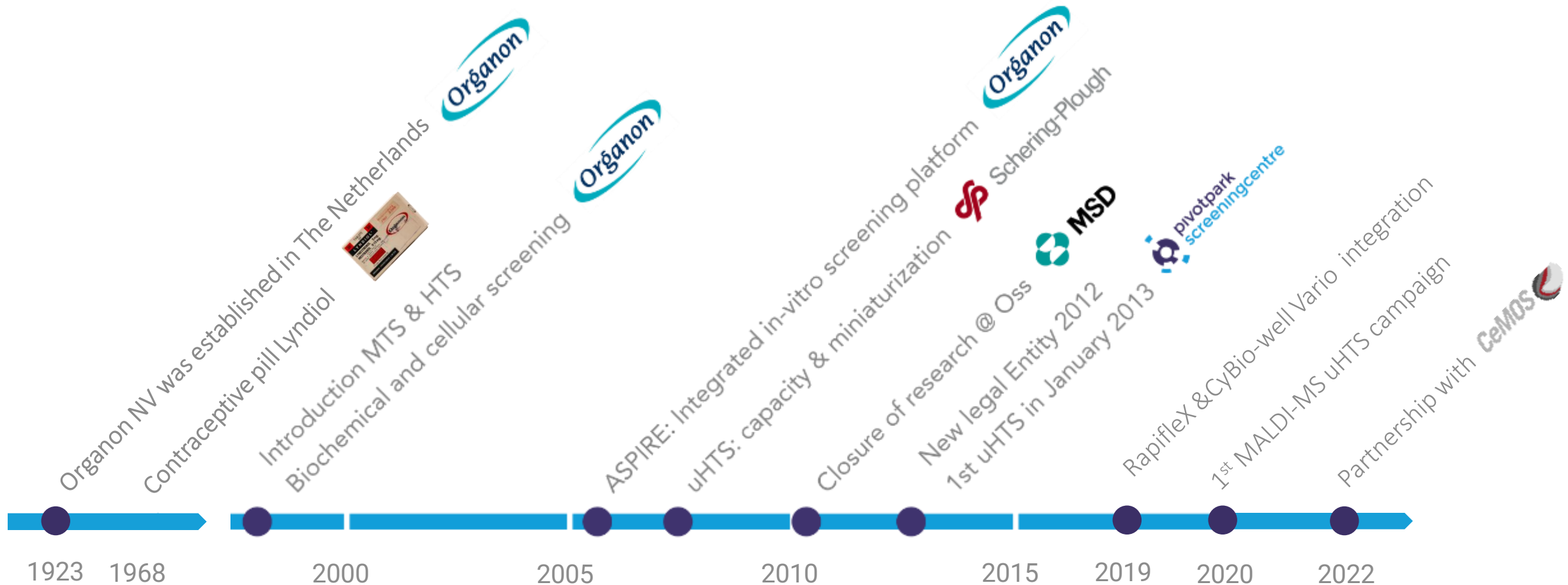


Our mission
The discovery of new medicines
for a healthier society



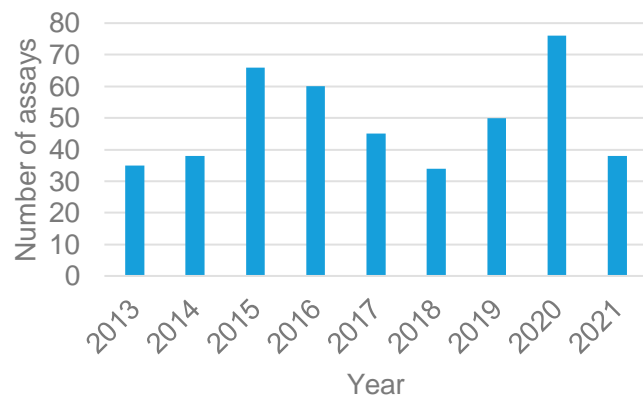
Pivot Park screening history

a strong pharma heritage

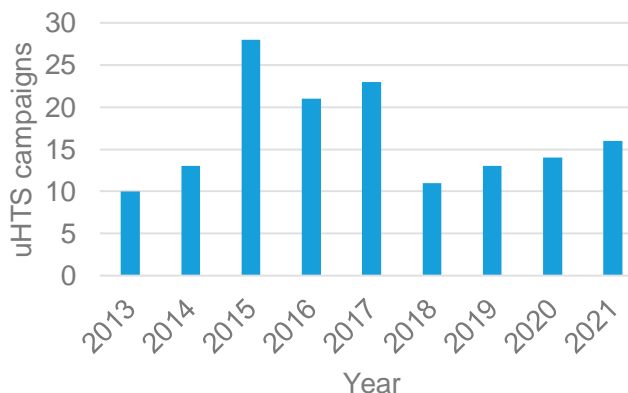


Track record from 2013 to 2021

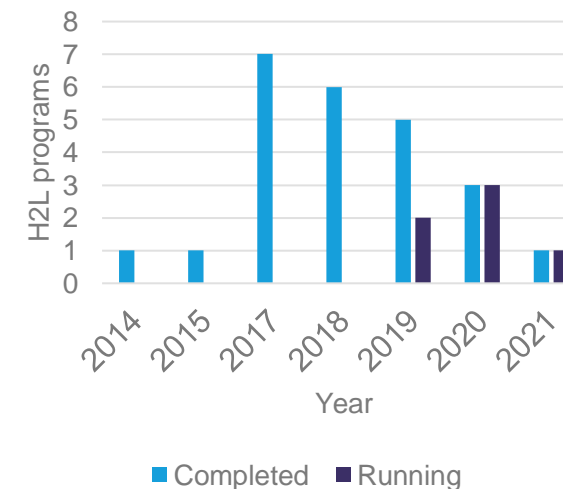
Assays developed annually



Annual uHTS campaigns



Annual H2L programs



- **~450** assays developed including
 - Primary (239)
 - Deselection (131)
 - Orthogonal (56)
 - Selectivity (23)

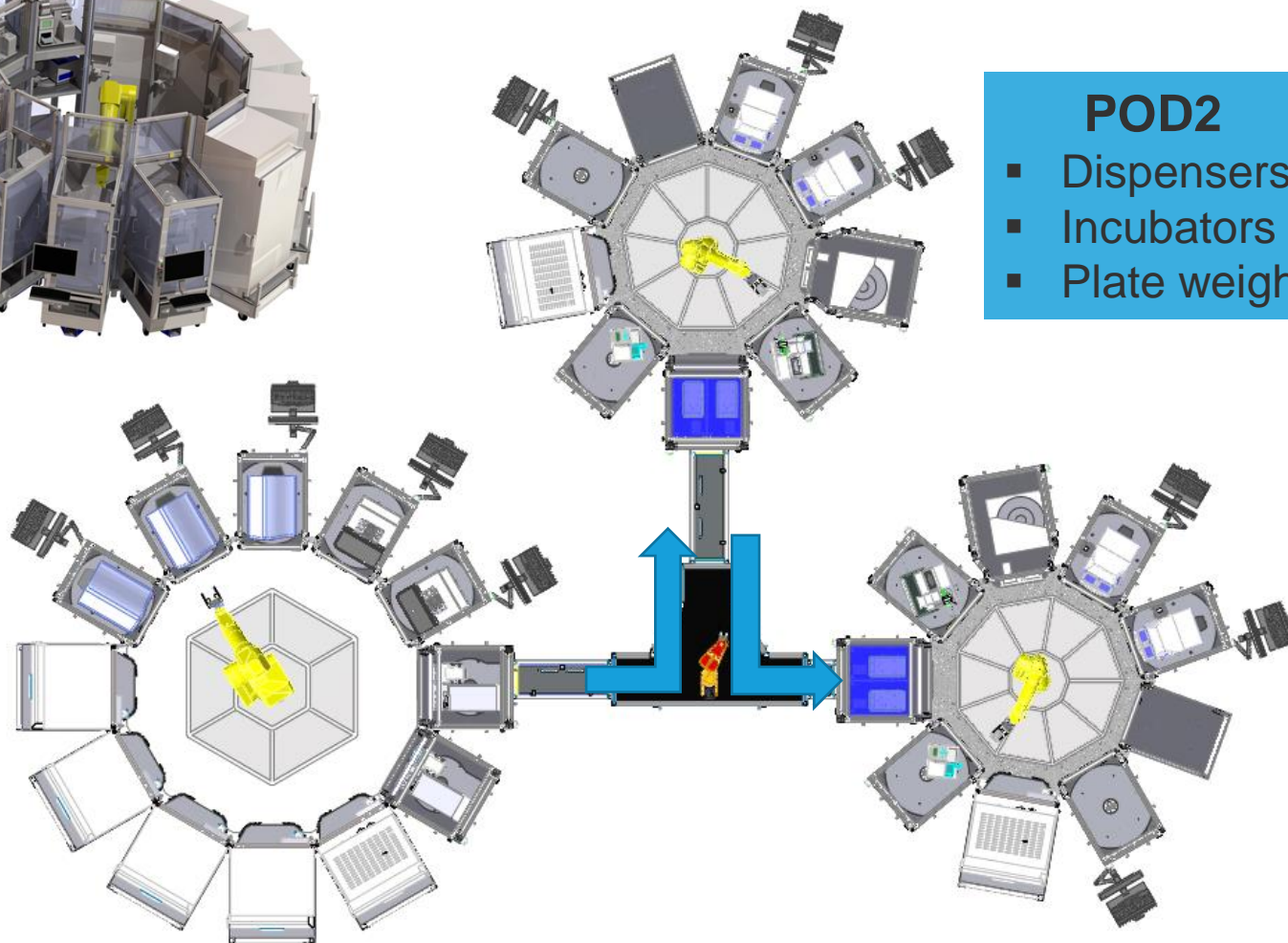
- **~150** full-deck HTS campaigns
- **> 50 million** datapoints generated

- **25** programs completed
- **5** programs ongoing

Automation system from HighRes at PPSC



- POD1**
- Compound store
 - Compound transfer; Echo



- POD2**
- Dispensers
 - Incubators
 - Plate weigh

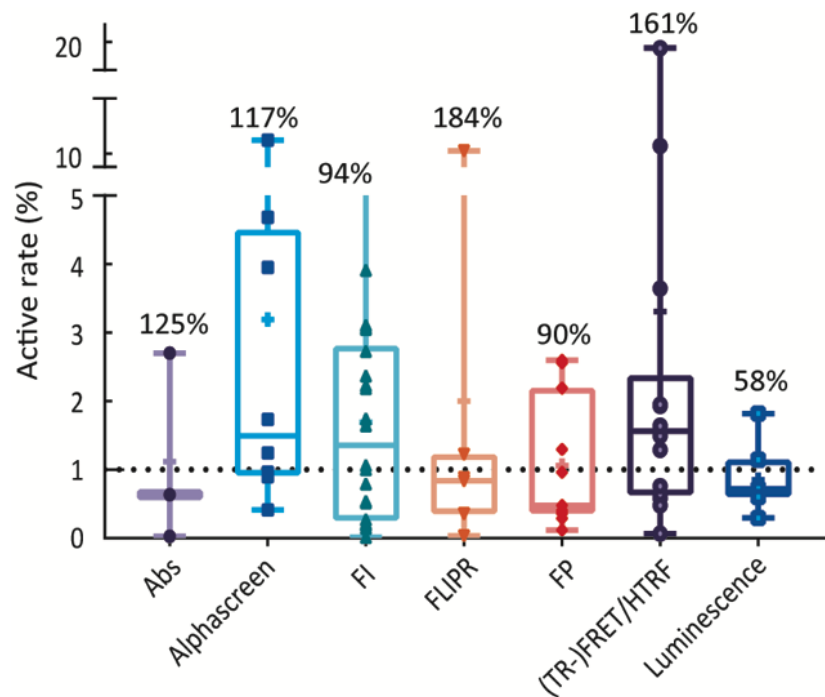
- POD3**
- Readers; CyBio-well Vario and rapifleX

Keeping uHTS platform at PPSC up-to-date

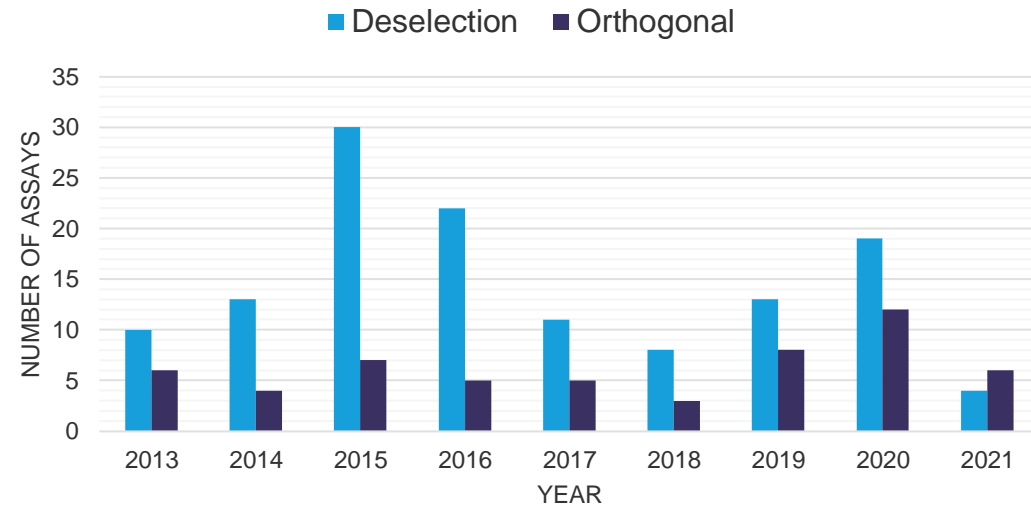


Primary active-rate is independent of target class/readout.

Conventional primary HTS readouts



Number of assays developed



Mass Spectrometry uHTS at PPSC since 2020

RapifleX MALDI PharmaPulse® Bruker








CyBio-Well vario 1536 Analytik Jena



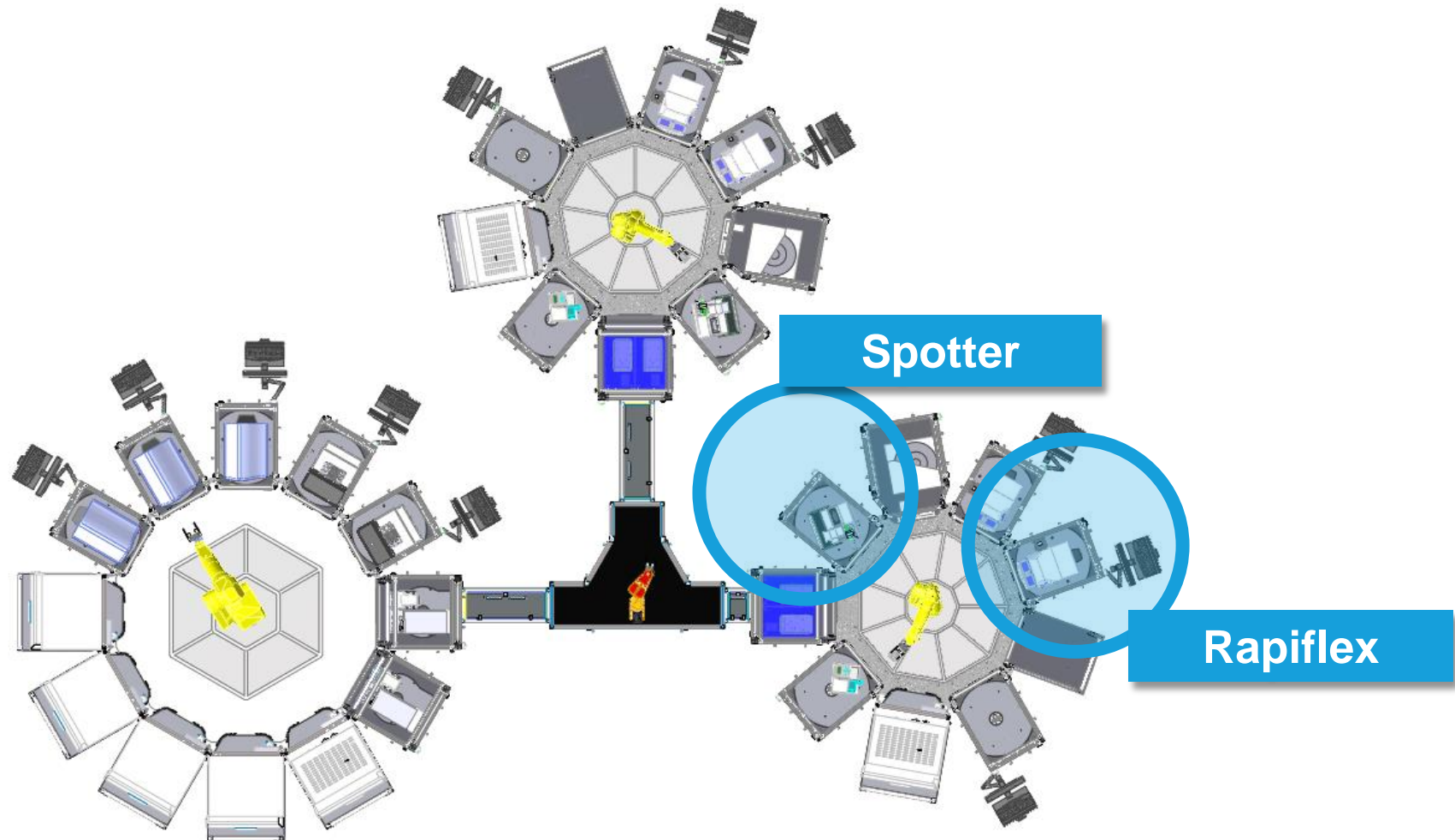
From ideation to implementation timelines



Mass Spec Requirements at PPSC

-  Off-the-shelf products
 -  Compatible with uHTS
 - 1536 format
 - ~100+ plates per day
 -  Integration in HighRes system
 -  Technical and scientific support
 -  Training and knowledge building
- Extend workforce – mass spec experience
 - Setup experienced project team
 - Follow literature
 - Visit conferences
 - Learn from industry peers
 - Setup collaborations
 - Bruker & Analytik Jena
 - UMC Maastricht
 - CeMOS

Mass Spec implementation in uHTS



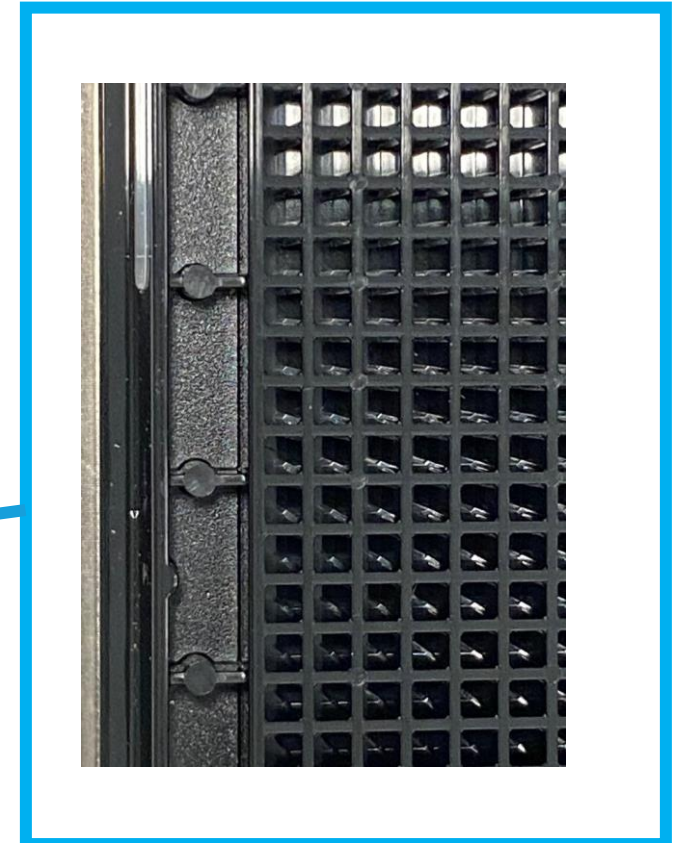
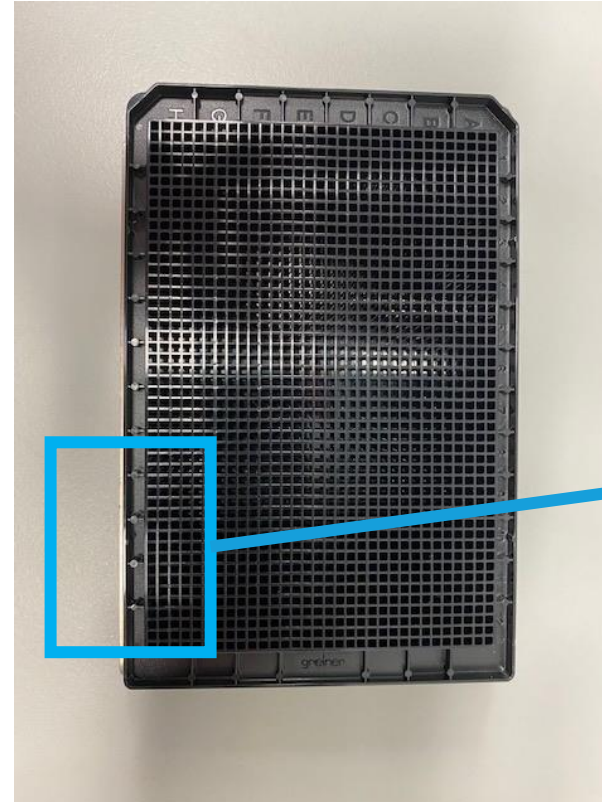
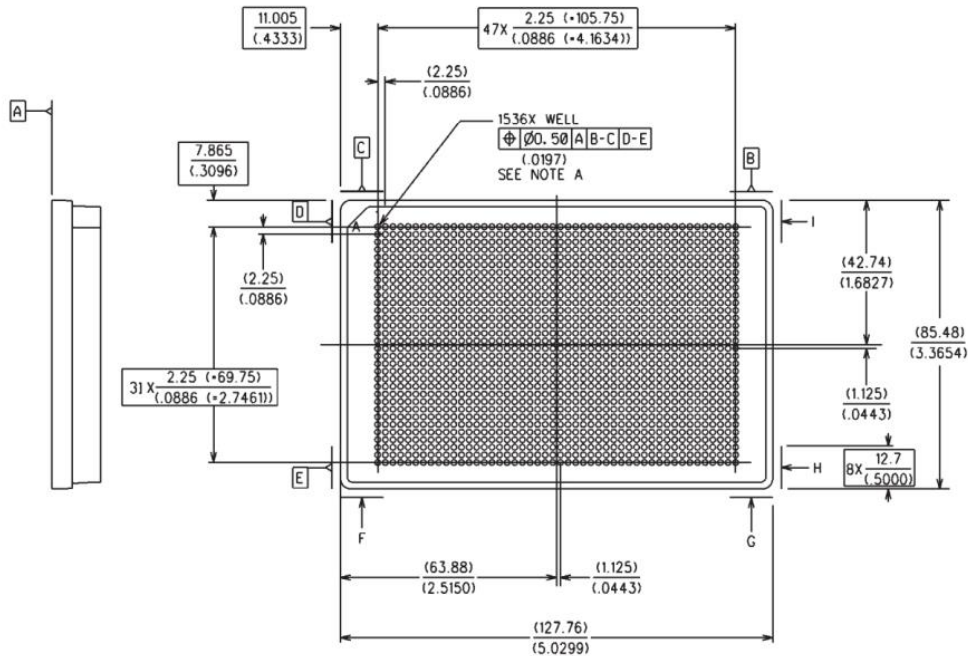
Cart design was not possible



Spotter enclosure design



Microplate Standards: MALDI plate SBS format?



The American National Standards Institute (ANSI) and the Society of Biomolecular Screening (SBS) now named the Society For Laboratory Automation And Screening (SLAS) approved a standard for microplates in 2004. In 1995, as early as the first meeting of the SBS, a need for clearly defined dimensional standards of a microplate were identified.

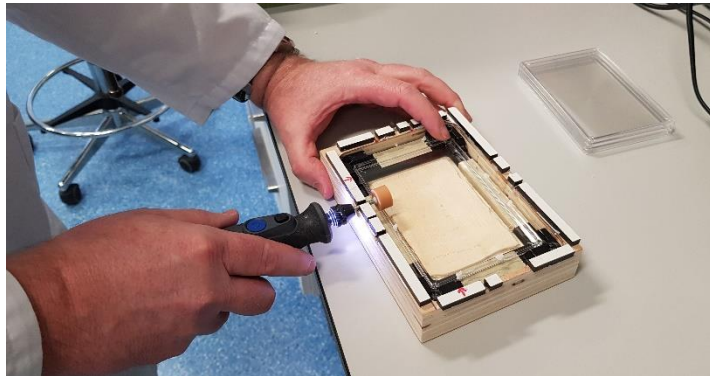
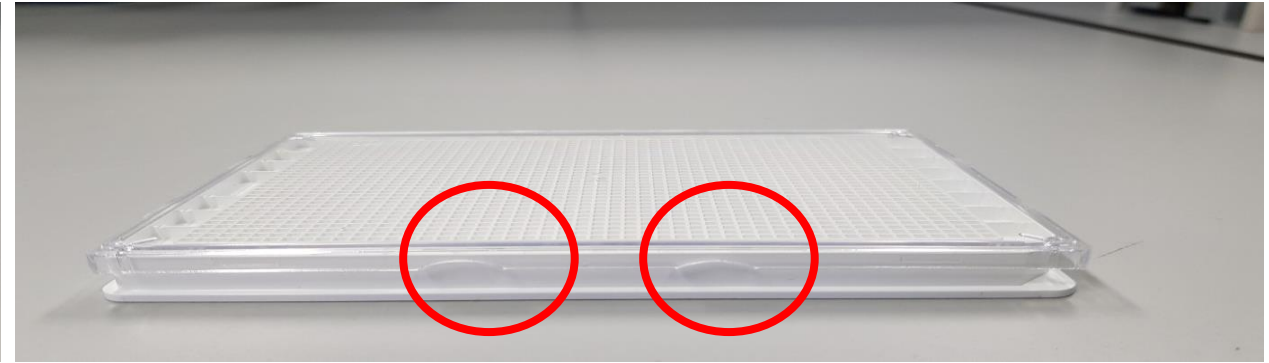
Modified plate orient (regrip station)



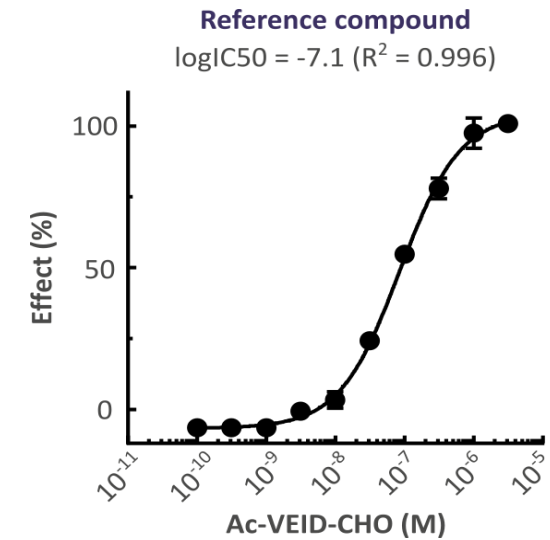
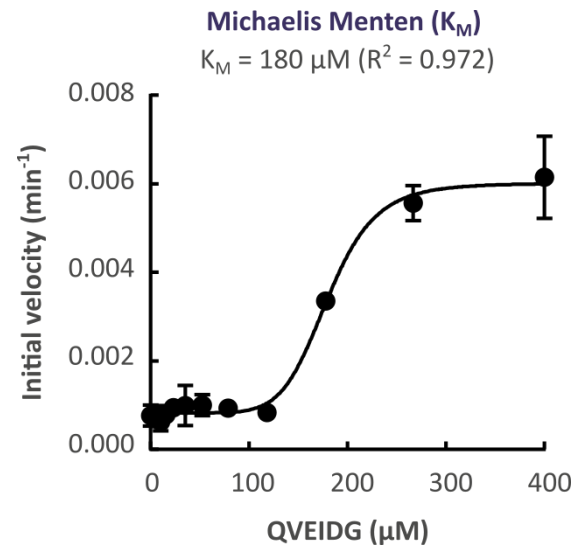
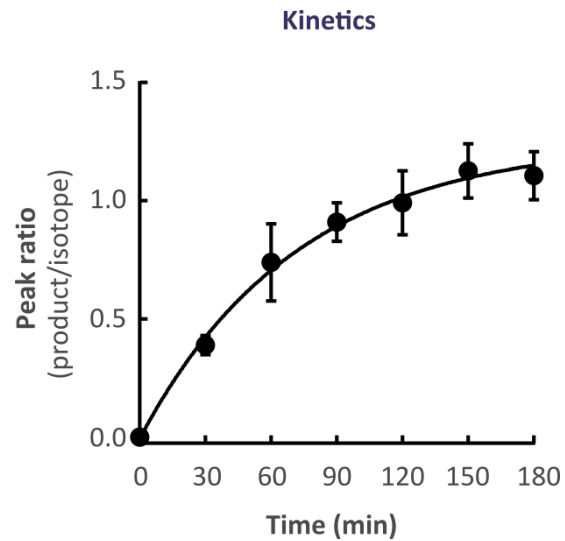
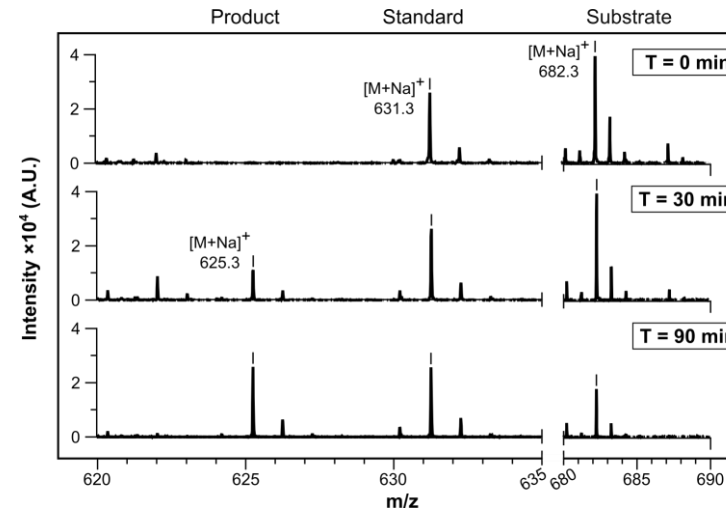
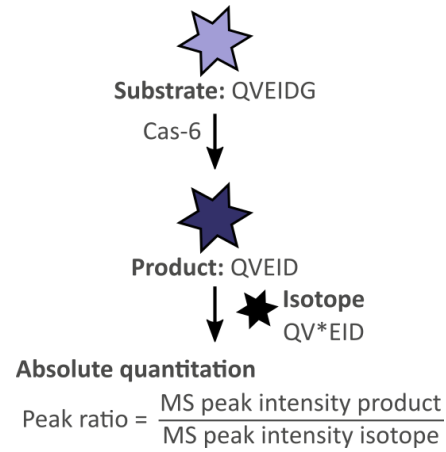
New gripper finger



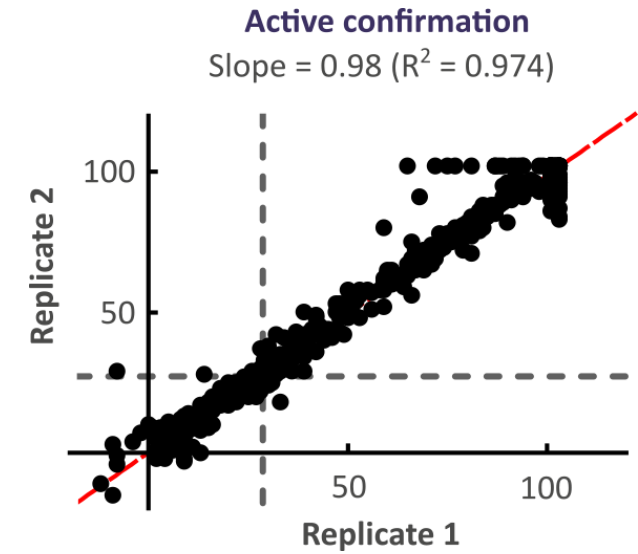
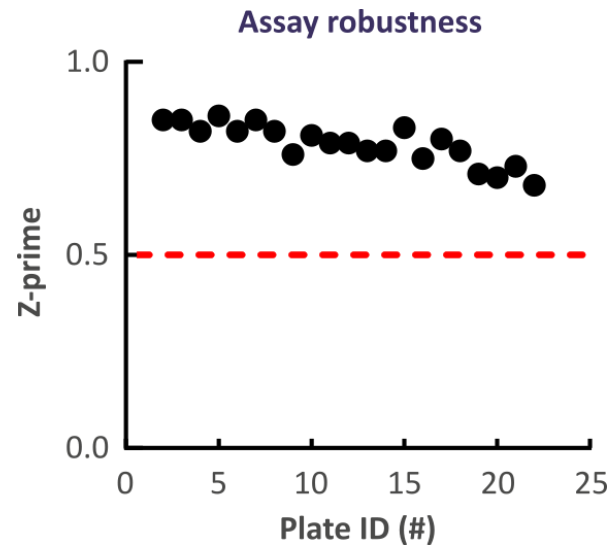
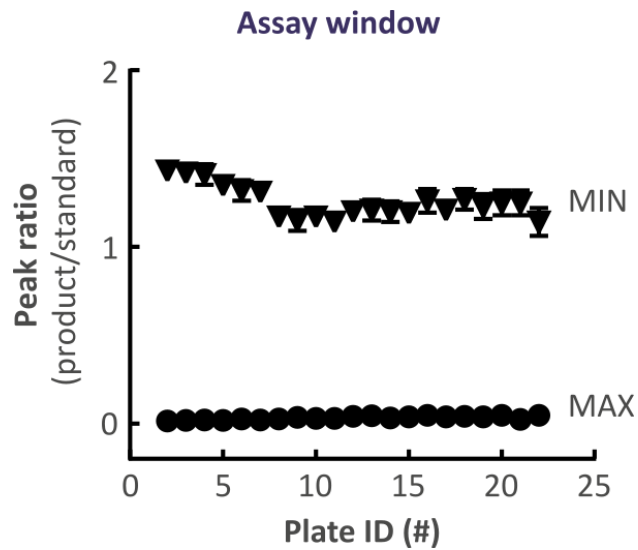
Handmade lid design and milling workshop



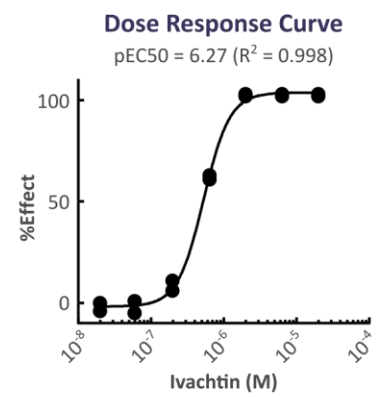
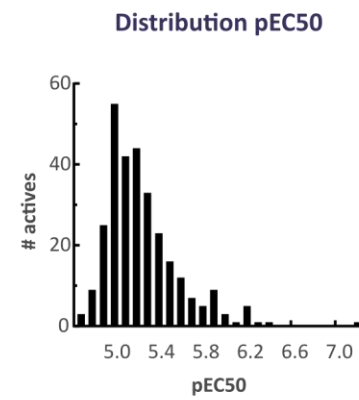
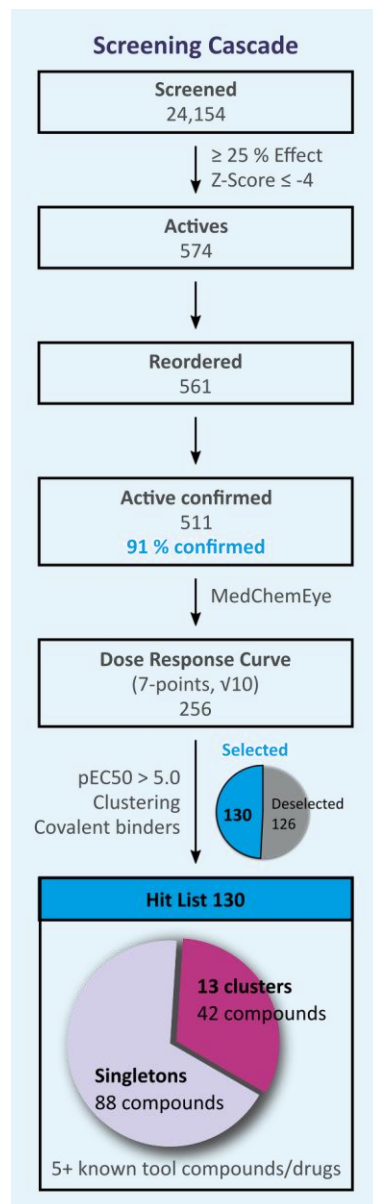
Biochemical MALDI-MS assay for caspase-6



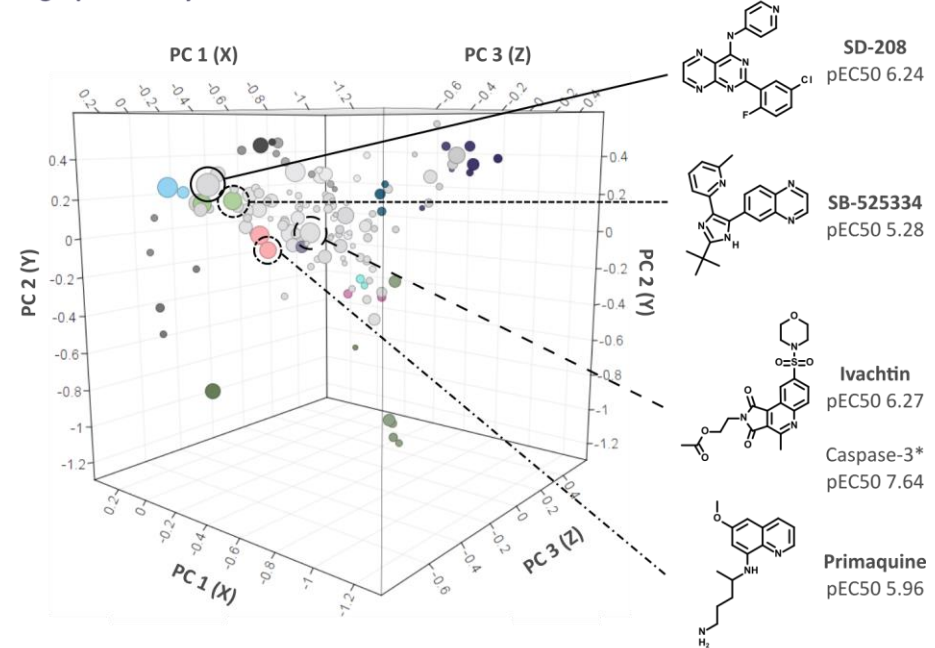
Quality of the output from fully automated MALDI-MS uHTS



Discovery of known and novel inhibitors of Cas-6.



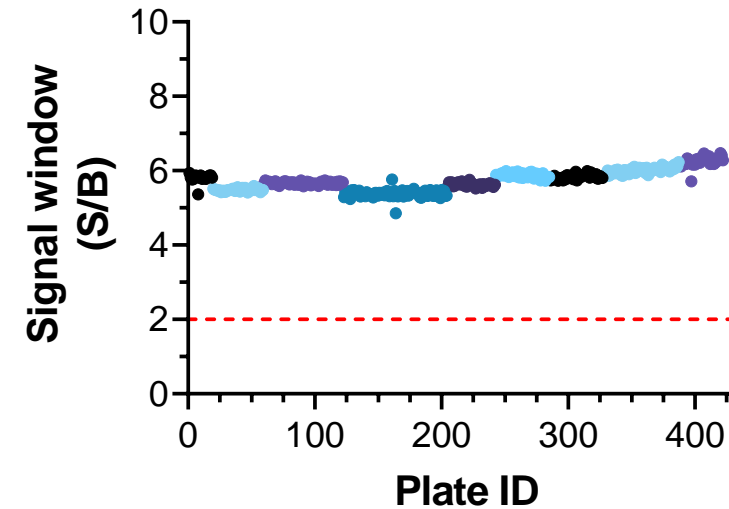
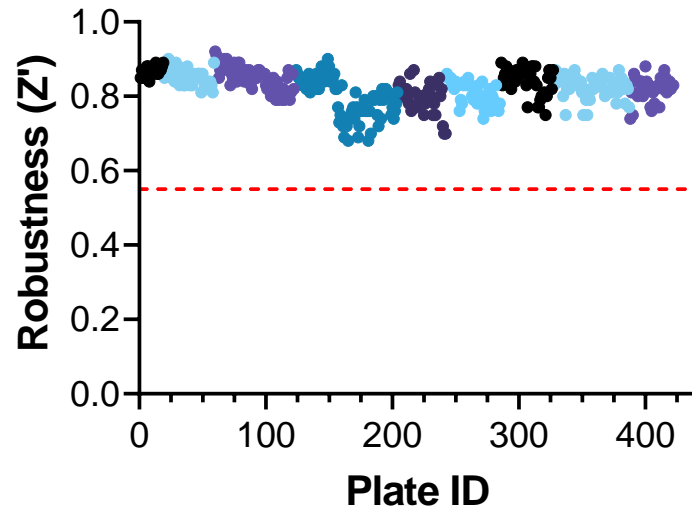
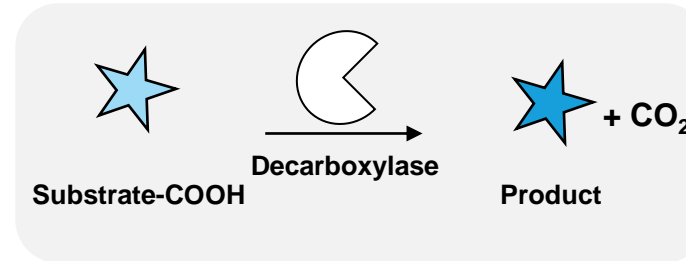
Fingerprint analysis of 130 hits



*Reported by Kravchenko, D.V. et al. 2005 J. Med. Chem. 48, 3680

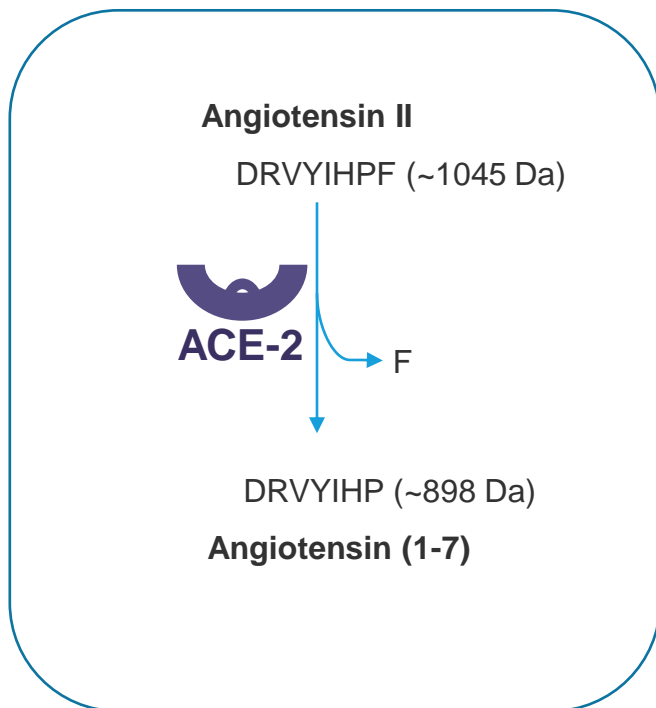
Example of MS-uHTS in > 0.5 million compounds

- Natural substrate assay of a decarboxylase

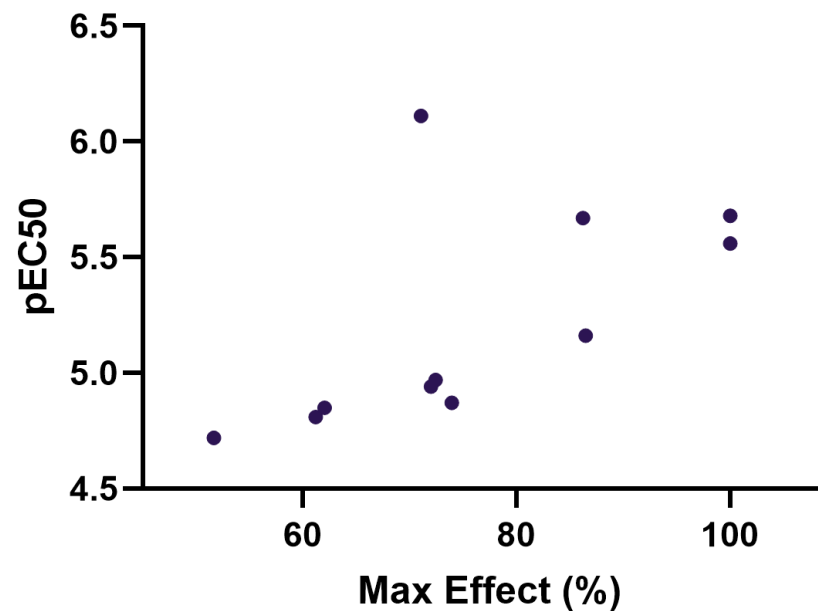


Using label-free MALDI MS for hit triage

Functional ACE-2 MALDI-TOF MS deselection assay

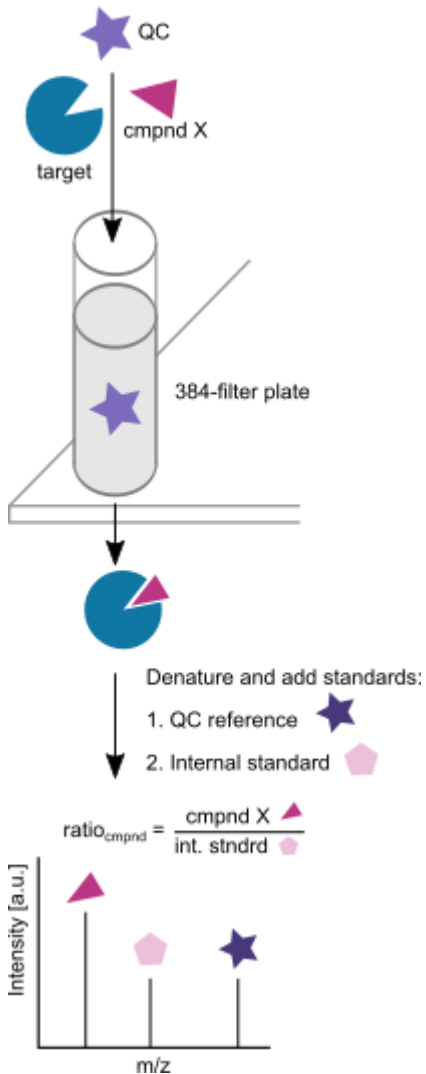


DRC analysis in ACE-2 MS assay

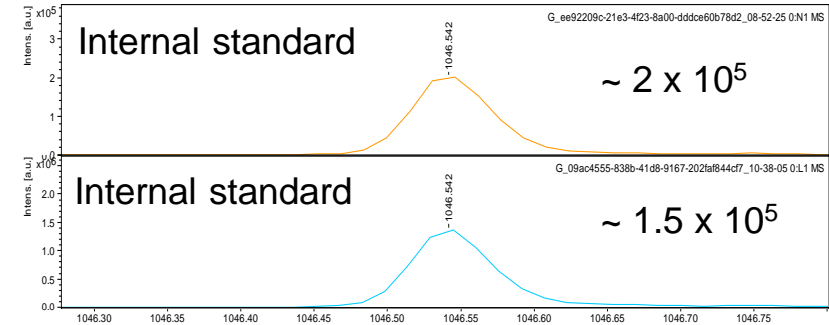
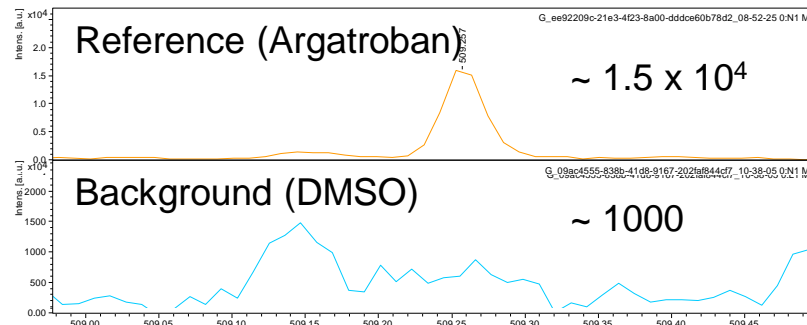


Affinity Selection Mass Spectrometry for target engagement

Active/Binding



Case study: Thrombin



$$\text{Fold Change Argatroban} \sim 11 \left(\frac{\text{ratio}_{\text{compound}} 0.075}{\text{ratio}_{\text{background}} 0.007} \right)$$

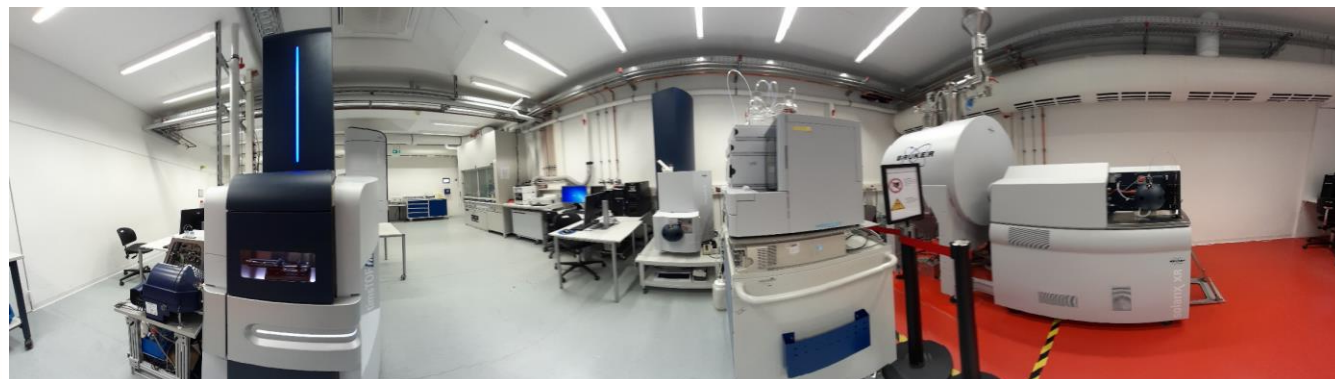
PPSC and CeMOS form a strategic partnership for joint label-free cellular lead discovery screening services



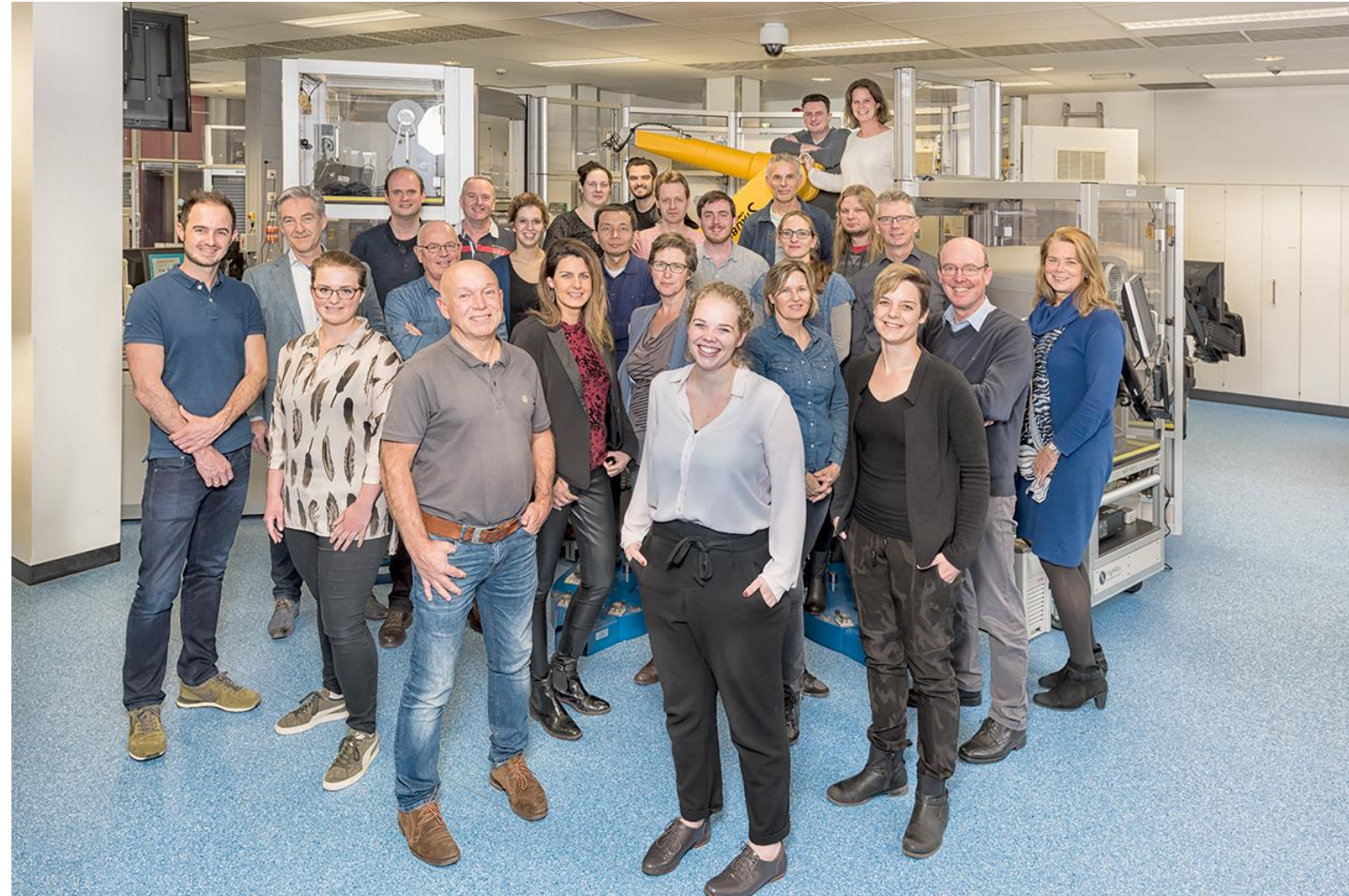
PPSC - Oss, NL



CeMOS - Mannheim, DE



Acknowledgements





Thank you!

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