CDD WEBINAR

Artificial Intelligence Drug Discovery — Where are we now?

LIVE

June 22, 2023
8:00AM (PDT), 11:00AM (EDT), 16:00 (BST)

MATTHEW SEGALL, PHD
CEO, Optibrium Ltd

ALPHA LEE, PHD
Co-founder & CSO, PostEra

HANJO KIM, PHD
SVP Strategic Planning, Standigm

CDD VAULT®
Complexity Simplified

Featuring these leading scientists...

Matthew Segall, PhD

CEO · Optibrium Ltd

Matt Segall is the CEO of Optibrium Ltd, which provides integrative, intuitive software for small molecule design, optimisation and data analysis. From advanced artificial intelligence technologies to user-friendly drug design platforms, such as StarDrop™ and Cerella™, all Optibrium products and services are backed up by rigorous scientific research and support scientists in their decision making throughout the drug discovery process. Dr Segall has a Masters of Science in Computation from the University of Oxford and a PhD in Theoretical Physics from the University of Cambridge.

Hanjo Kim, PhD

SVP Strategic Planning · Standigm

Hanjo Kim is a Senior Vice President at Standigm, an AI-driven drug discovery company based in Seoul, Korea. At Standigm, he has held multiple roles, including SVP of Global Strategy, Head of Medicinal Chemistry and Deputy Head of Research. Dr. Kim received a Bachelor of Science in Chemistry, Masters of Science and PhD in Organic Chemistry degrees from Yonsei University in Korea.

Alpha Lee, PhD

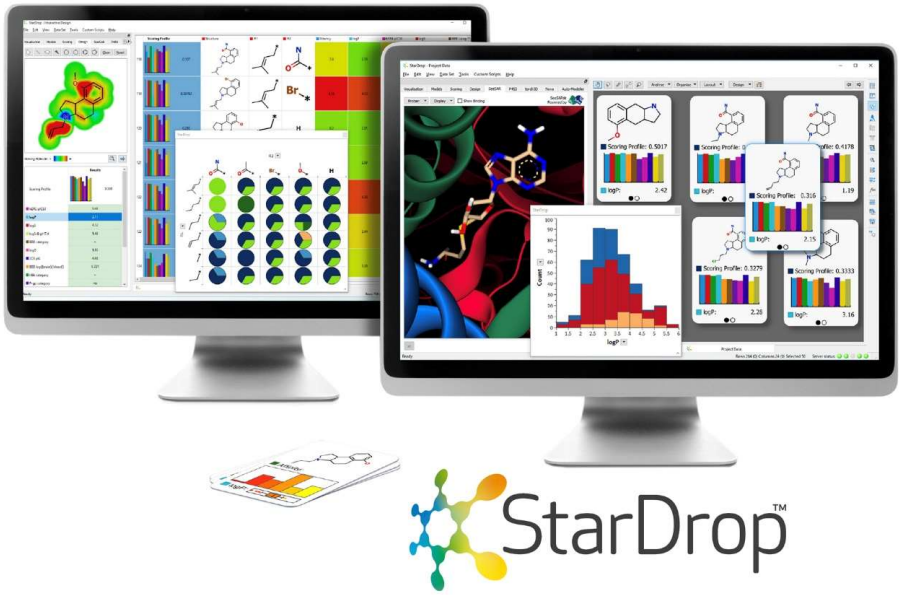
Co-founder & CSO · PostEra

Alpha Lee is the Co-founder and Chief Scientific Officer of PostEra , a biotechnology company specializing in machine learning for preclinical drug discovery. The company focuses on using advances in machine learning to close the Design-Make-Test cycle of Medicinal Chemistry. Dr. Lee has a Bachelor of Science in Chemistry from Imperial College London and Masters of Mathematical Modeling and Scientific Computing and PhD degrees from University of Oxford.

Have a question to ask our panel?
Open the ZOOM Q&A and type in your question at anytime !

Saving your Questions to the end

Introduction to Optibrium



StarDrop™

Augmented Chemistry®

Cerella™
an Augmented Chemistry software product

inspyra™
an Augmented Chemistry software product

A complete package of fully integrated, elegant software for small molecule design, optimisation and data analysis

Enhance your expertise with unique AI solutions to guide more effective drug discovery strategies

To learn more, visit www.optibrium.com or contact us at info@optibrium.com

optibrium™

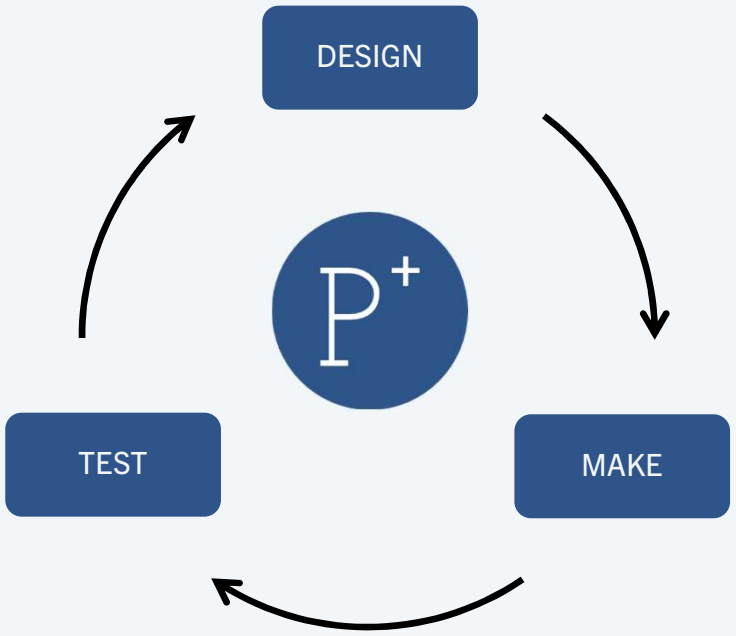
About PostEra

We are building the world's best
***Chemistry AI platform** to get more cures to patients*

- Founders are scientists trained at Oxford, Cambridge, Harvard and Yale who pioneered the latest advances in AI for Medicinal Chemistry
- **$370M** deal value in 2022 from Pfizer and the NIH
- Launched **COVID Moonshot** and achieved zero-to-candidate in 18 months | **$10M grant** to prepare for Phase I trial
- PostEra is developing its own drug pipeline and establishing a limited set of deep pharma partnerships to complement our overall portfolio

PostEra's Proton Platform

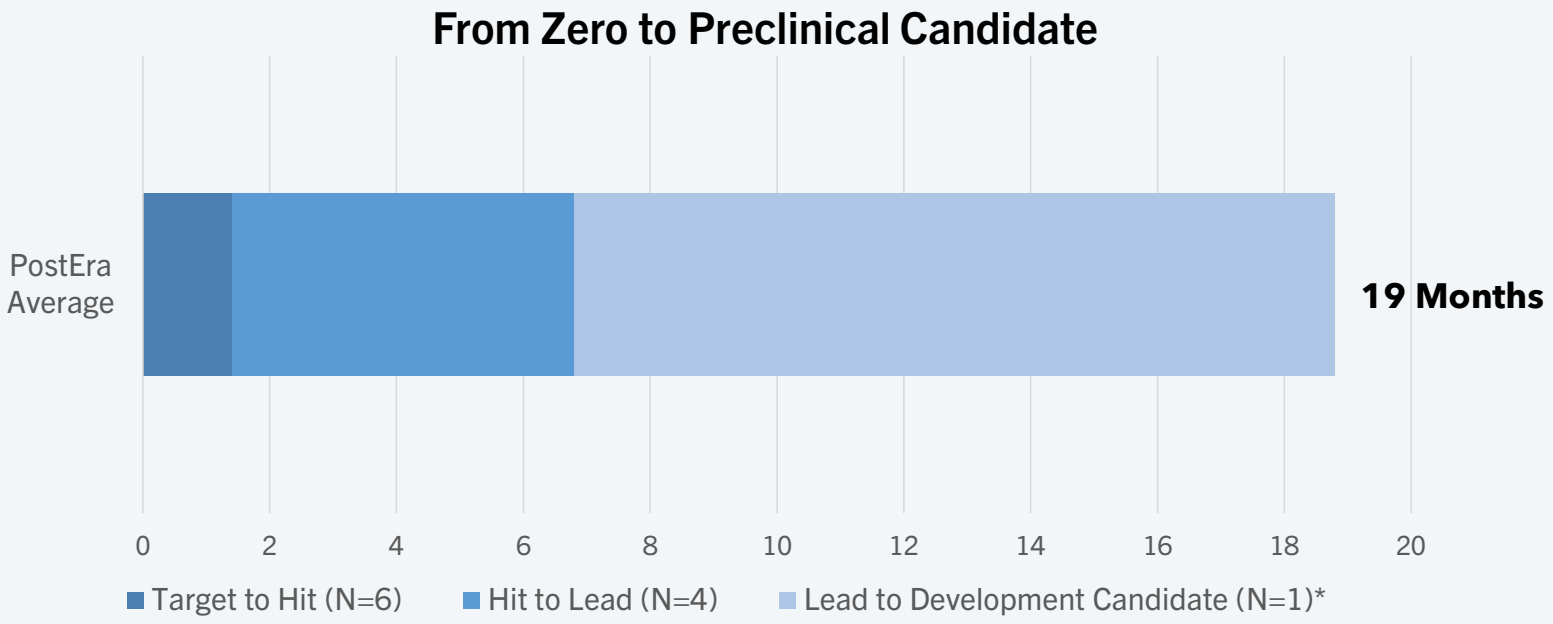
- *Proton* is PostEra's end-to-end machine learning platform for medicinal chemistry
- We use *Proton* to develop small molecule drug candidates from zero to DC
- We address key challenges at each stage of the DMT cycle:
  - **DESIGN**: Low-data models to extract chemical signal from noise
  - **MAKE**: Synthesis-driven design for rapid data generation without combi-chem weaknesses
  - **TEST**: Probabilistic modelling to optimally select molecules for assays



Our platform has accelerated programs across a diversity of challenges

- GPCRs, kinases, proteases, and ion channels
- Disease areas: Viral infections, metabolic diseases, oncology, and CNS.
- Covalent peptidomemetic → Non-covalent, small molecule

- Majority programs worked on novel biology and/or first-in-class therapeutics
- Pure phenotypic assays
- Fragment-based starting points



*3 structurally differentiated candidates

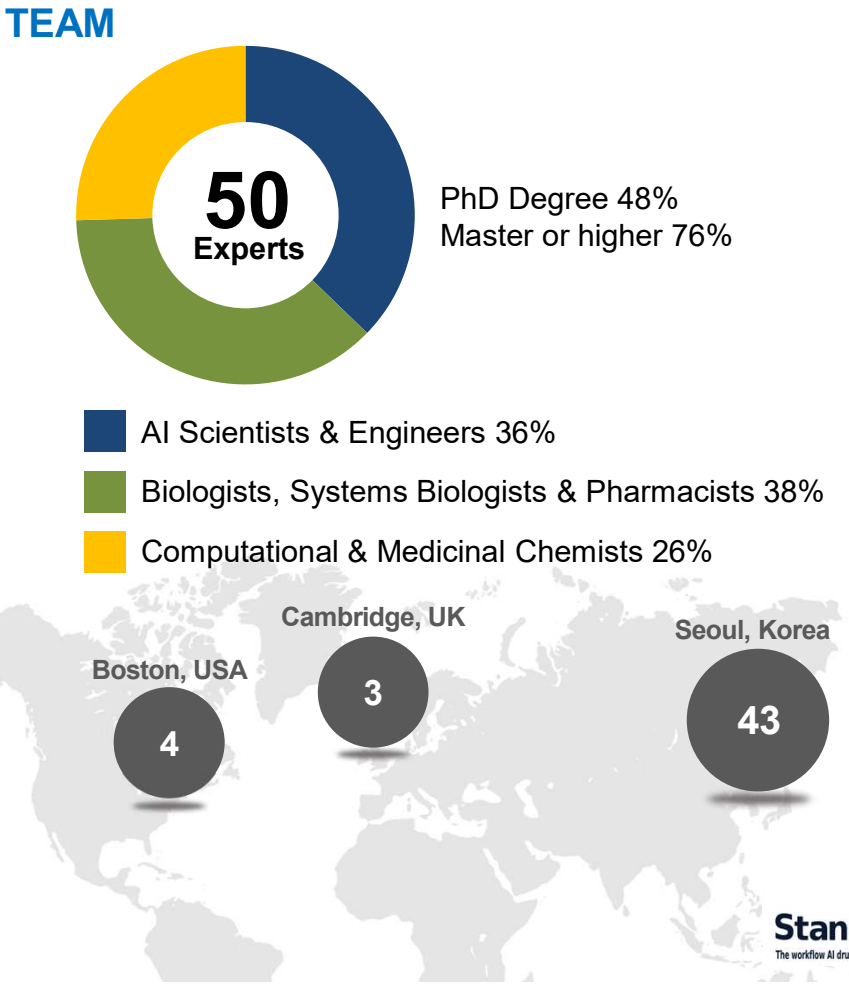
PostEra

About Standigm

Standigm (which came from the 'standard paradigm') was founded in **2015** by three co-founders with different expertise in AI, systems biology, and chemical engineering.

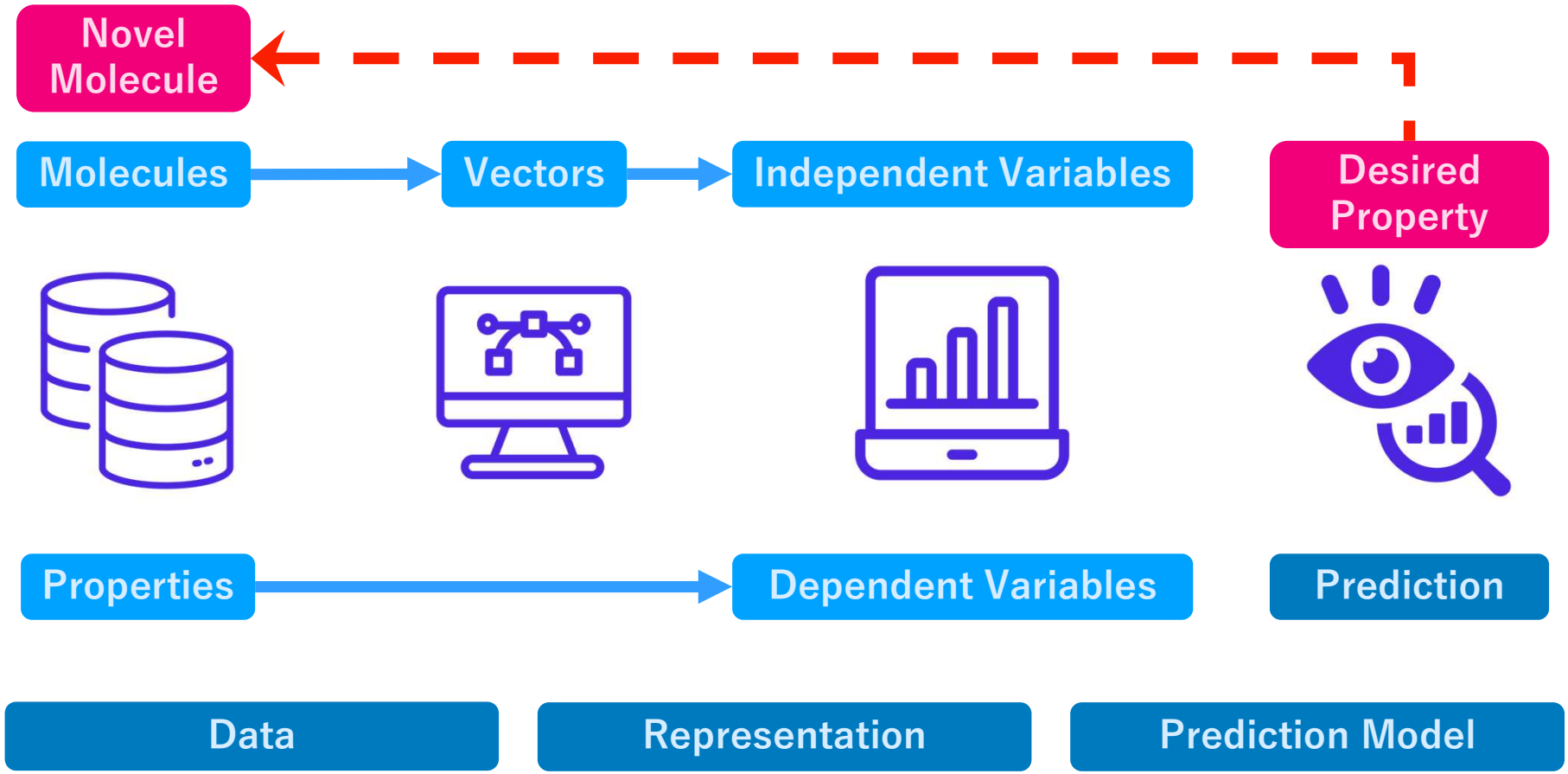
Our leading technology includes **Standigm ASK™** (target ID) and **Standigm BEST™** (novel compound design).

We have conducted collaborative projects with **more than 20** partners.



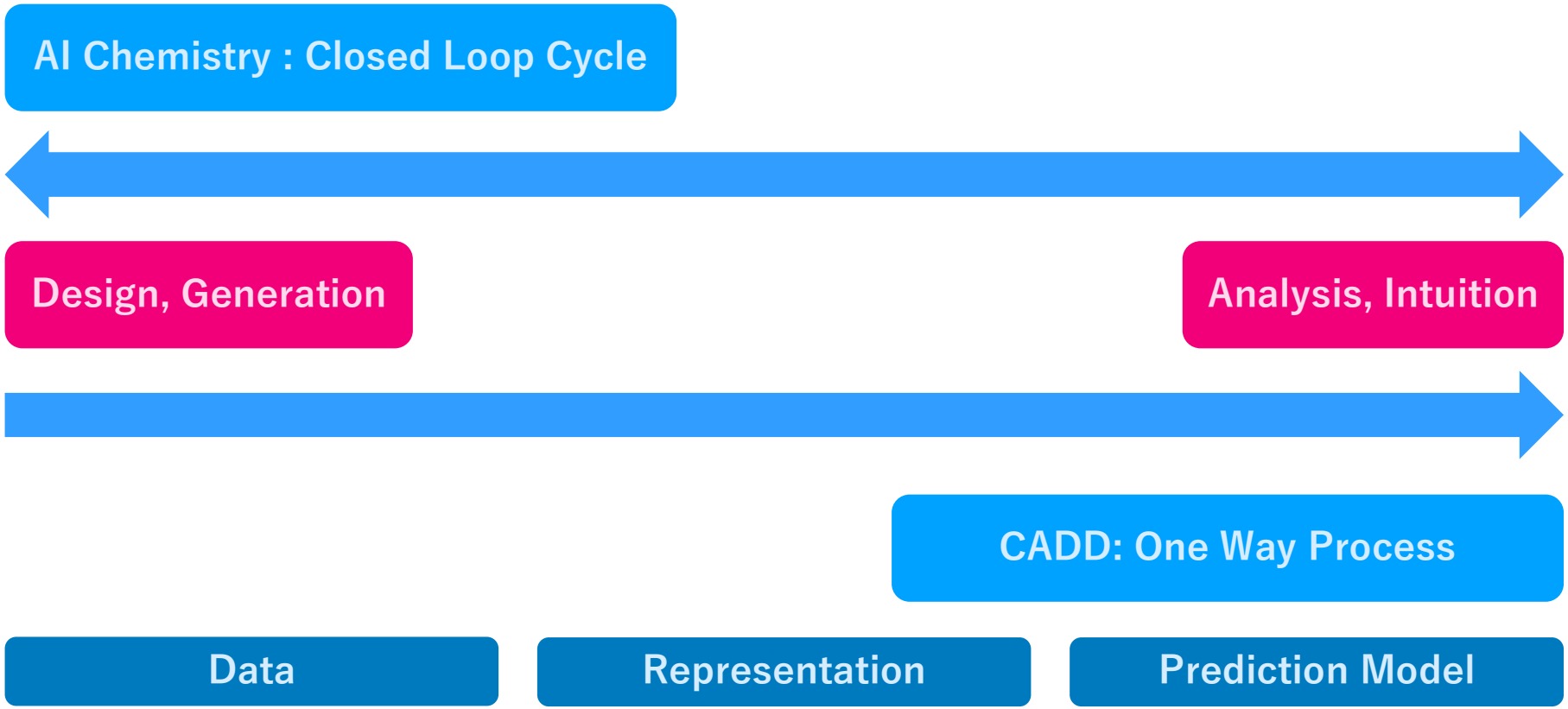
AI is not magic!

Generative Chemistry



Standigm
The workflow AI drug discovery company

AI Chemistry vs CADD



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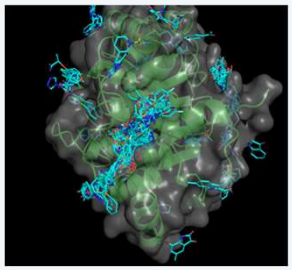
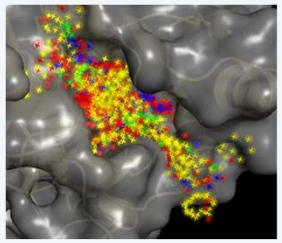
How does PostEra DESIGN molecules?

Hit Identification – Fragments to Hits

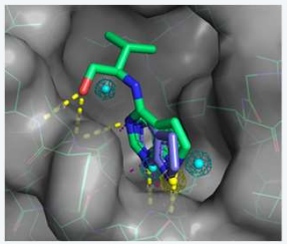
Crystallographic fragment screen



Identify interaction patterns as a pharmacophore field

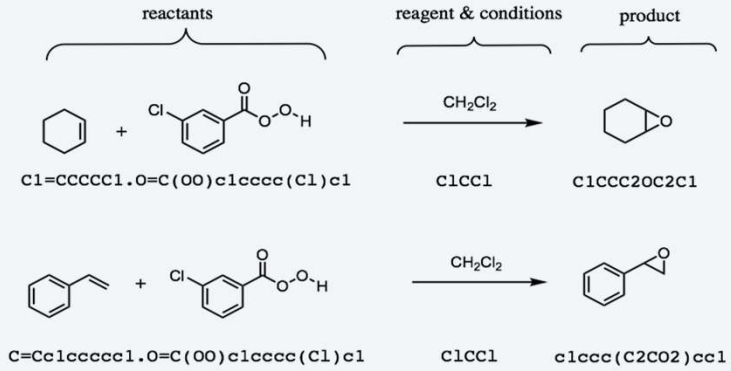


Generate hits that fit persistent pharmacophore patterns



How does PostEra MAKE molecules?

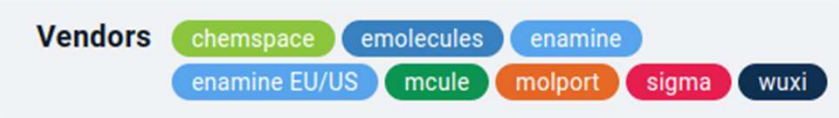
- We learn the rules of chemistry using a **natural language processing** approach.



- Our **Molecular Transformer** model is state-of-the-art.
- Molecular Transformer is competitive with expert chemists.

	Jin et al. (2017)	IBM (2018)	Coley et al. (2019)	**Molecular Transformer**
Test set accuracy	79.6%	80.3%	85.6%	**90.4%**

- We combine MT with the industry's largest collection of **CRO catalogs** enabling efficient retrosynthesis



Schwaller…**AAL**, ACS Central Science (2019)

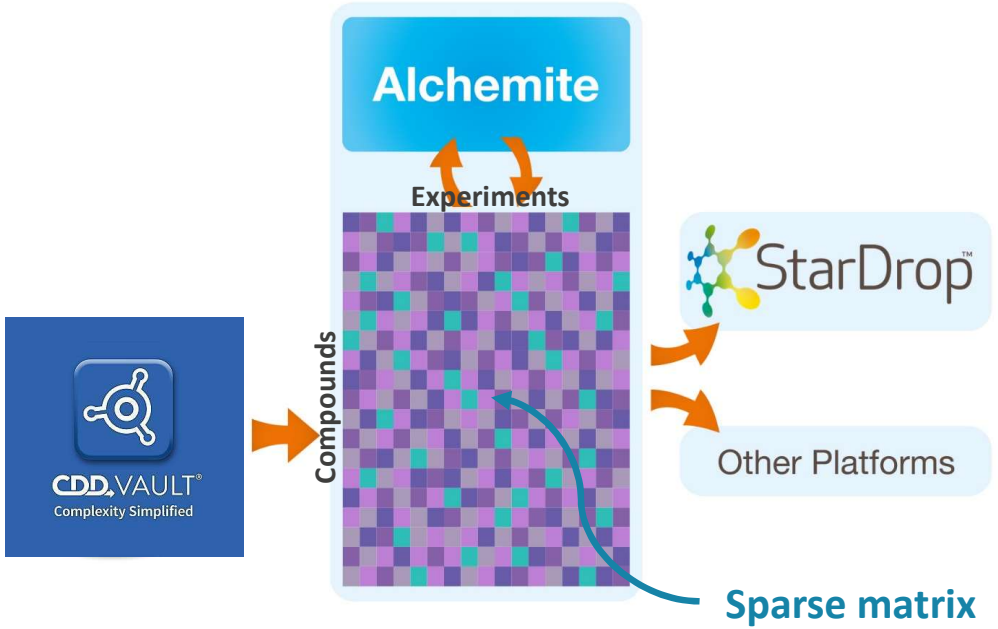
PostEra

Seamless Integration of Data and AI in the Cloud

CDD Vault™ and Cerella™

Cerella™
an Augmented Chemistry™ software product

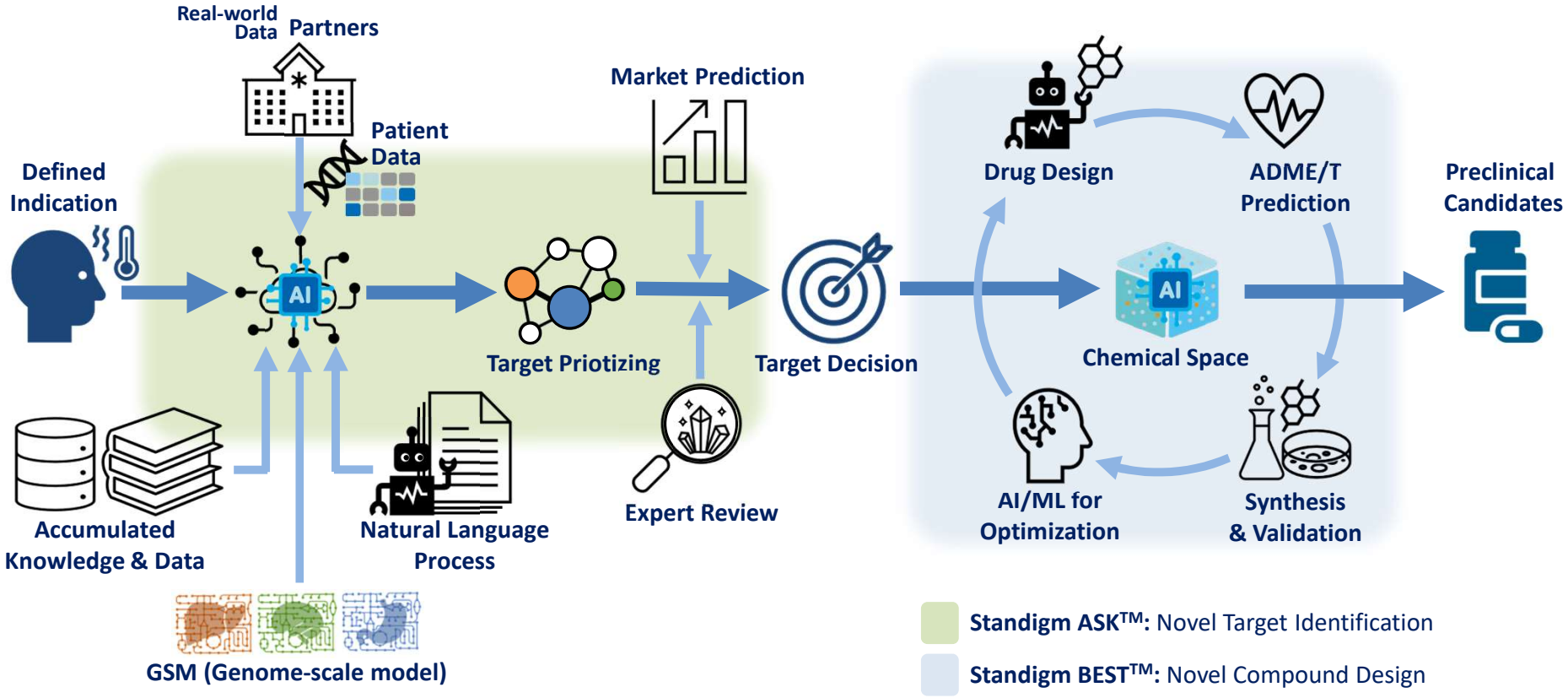
- Deploys the unique Alchemite™ method for deep learning imputation
  - Proven success in diverse drug discovery applications
- Automatically updates and prepares data from CDD Vault for model building
  - Applies cleaning and business rules to data
  - Transforms data for best model performance
- Updates Alchemite models as new data become available
- Manages ‘massive matrix’ of imputed and experimental results for easy access
  - May contain O(10^{10}) data points!
- Provides seamless access to results
  - Using StarDrop or any platform via a RESTful API



Watch our webinar at https://bit.ly/cerella_intro

The Standigm Technology

End-to-End Solution from disease to drug candidates



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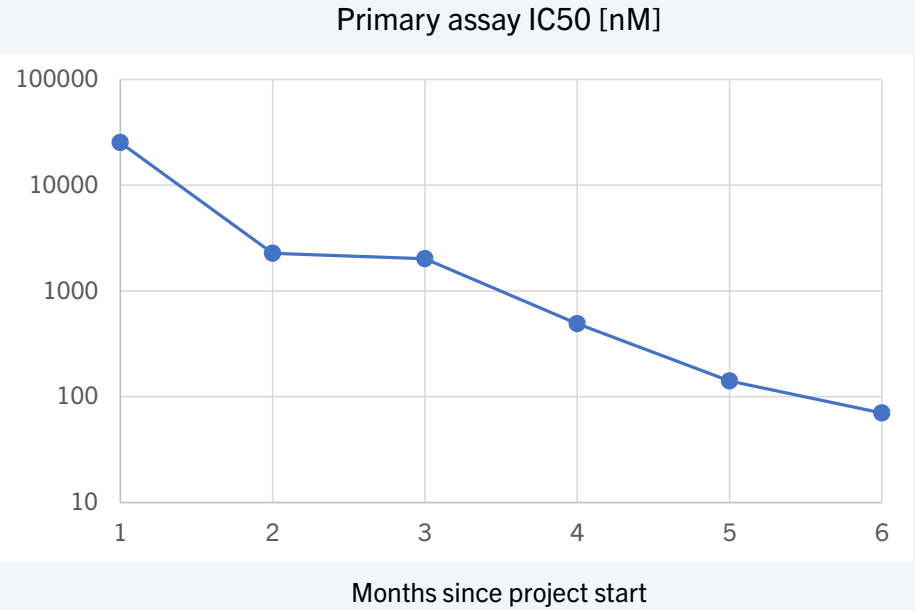
Case Study: Macrodomain

- SARS-CoV-2 nsp3-mac1 is a viral ADP-ribosyl hydrolase, conserved across coronaviruses, hypothesized to counteract host immune response.
- Potential first-in-class therapeutic. MoA of viral-host immune interactions is distinct to current approved treatments.

- 350x potency gains in 6 months
- 5 FTE chemistry team
- 534 compounds made and tested



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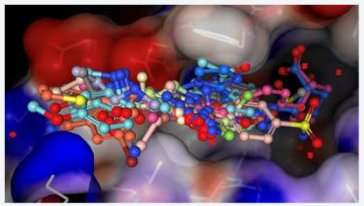
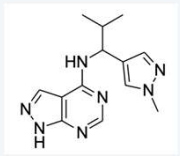
Case Study: Macrodomain

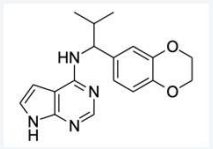
Crystallographic fragment screen





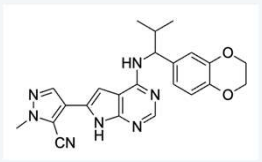
IC_{50} = 43 µM

- **Pharmacophore based hit identification**
- One Design-Make-Test cycle
- Catalogue compound

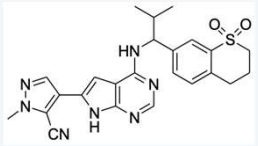


IC_{50} = 2.3 µM

- Library design using ML **activity similarity**
- First tool compound to understand target-phenotype linkage



IC_{50} = 520 nM

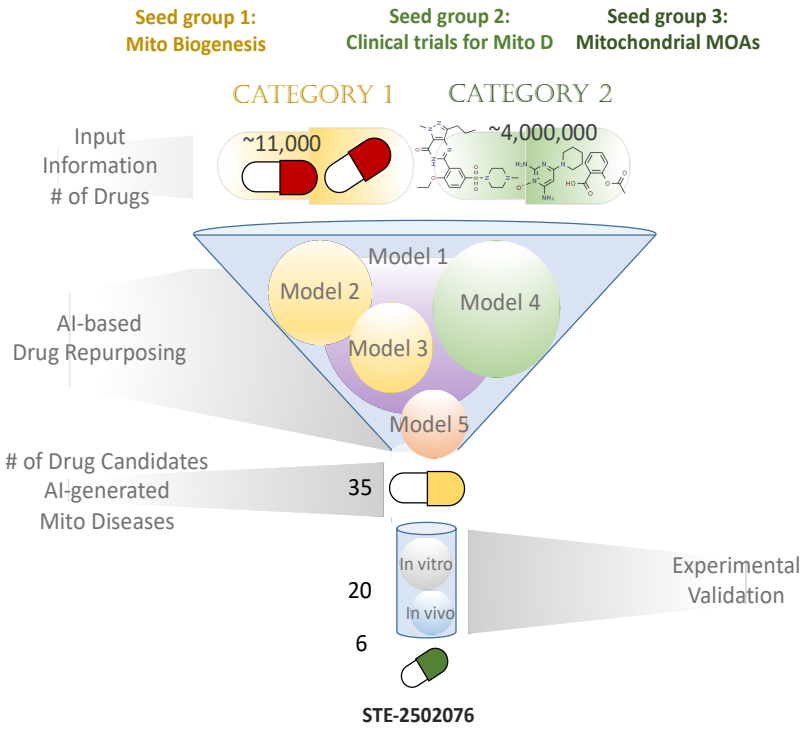


IC_{50} = 25 nM

- Generative **Med Chem Move** to vary benzodioxane motif

Property	Value
LogD	3
Mac1 HTRF IC50/uM	0.5
SARS-CoV-2 HelaACE2 EC50/uM	1.3 (n=2)
MDCK-MDR1 Papp (A->B)/ (10^{-6} cm/s)	4.2
Kinetic solubility/uM	17
Series screened against Eurofins kinase panel to derisk off-target due to “hinge-binder” motif	

Models of Standigm Insight™



Model 1	Graphic knowledge database
Model 2	Drug repurposing model based on the drug-perturbed transcriptional gene expression pattern
Model 3	Clustering model of the pathophysiological property-embodied latent space of Module 2
Model 4	Drug repurposing model based on structural and drug-like similarity
Model 5	Drug-focused information searching model

Efficacy of STE-2502076 for Mitochondrial disease

in vitro MPP$^+$-induced human cell model

Cell viability ↑
Cellular ATP content ↑
Mitochondrial membrane potential ↑
Mitochondrial ROS content ↓
Cellular ROS content ↓

in vivo Mitochondrial disease animal models

***C. elegans gas-1(fc21)* model**

Life span ↑
Body size ↑

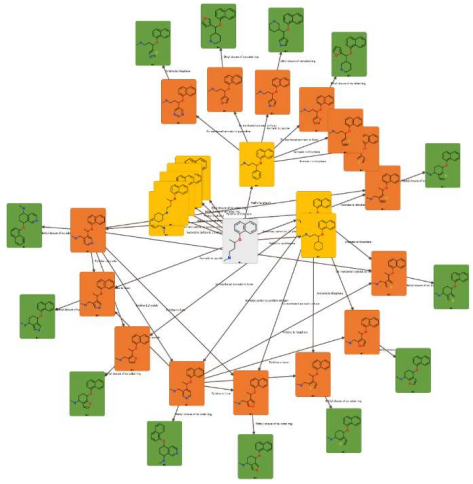
***D. rerio surf1*$^{-/-}$ model**

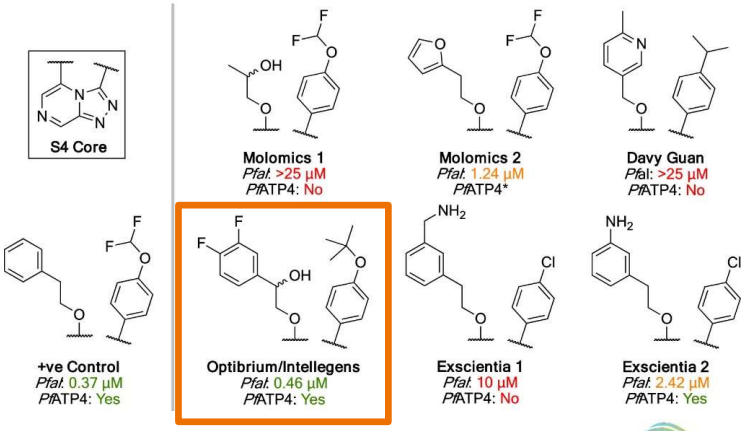
Neural and locomotor activities ↑

Standigm
The workflow AI drug discovery company

Collaboration with Open Source Malaria (OSM)
Combination of deep learning with generative chemistry methods

- Application of Cerella to **sparse antimalarial activity data**
  - Targeting novel MoA – *Pf*ATP4
- New compound ideas were generated using the generative chemistry methods in Inspyra™
  - Prioritised for good activity profile and properties
- A **confidently** predicted compound was synthesised and tested by OSM
  - **Only confirmed active** of those proposed by four organisations
- "The Optibrium/Intellegens suggestion… was thought by the human team to be a certain inactive… yet this compound displayed good potency and is a particularly useful outcome (i.e., the **"Machine Overlords" class**)"





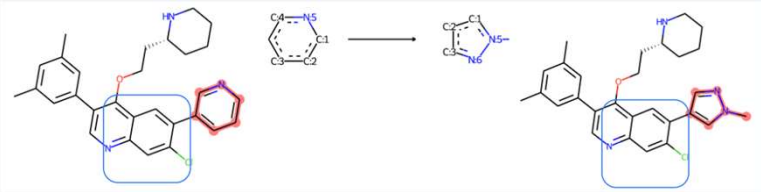
Watch our webinar http://bit.ly/ai_antimalarials

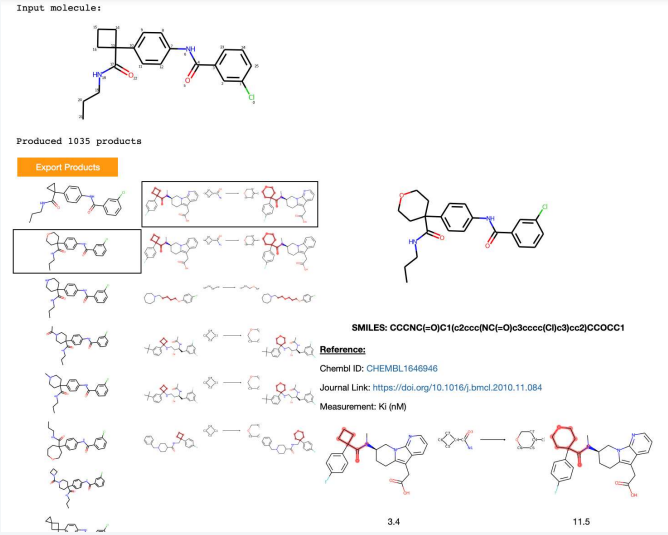
Irwin *et al.* Int. Pharm. Ind. (2020) **12**(2) pp. 28-31, Tse et al. J. Med. Chem. (2021) **64**(22) pp 16450-16463

How does PostEra DESIGN molecules?

Hit to Lead – MedChemMoves

1. Extract 10M chemical ‘moves’ from historical assays
2. Form ontologies of move ‘types’ for interpretable references
3. Score generated molecules





PostEra

How to Maximise the Impact of AI in Drug Discovery

Algorithm

Proof of concept

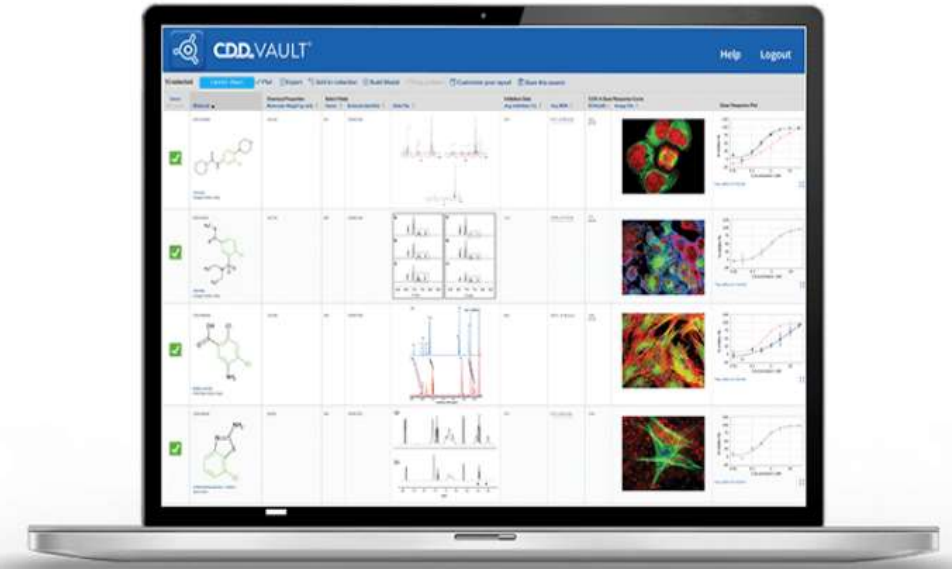
Deployment and accessibility

Organisational change

Questions?

Activity & Registration
Store and organize your data

Inventory
Keep Track of Compounds



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Visualization
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