

CASE STUDIES: AI & Computational Chemistry for BioPharma R&D



<u>De-novo Drug Discovery</u>

- Therapeutic Area: Oncology
- **Context:** Assist in the development of a de-novo molecule in oncology
- **Objective:** Utilize advanced NLP/ML and MD technologies to identify and optimize lead oncology entities targeting a specific regulatory protein, streamlining candidate selection for preclinical development through sophisticated simulations and energy calculations

Flow

UniProt PubChem DRUGBANK ChEMBL BindingDB

standardizat

rincipal Component Analysis (PCA)

Drug-target feature vectors

ining Deep Neural Network (DNN) Model

Drug Design Specificatio drug regulation abilit

multiple-molecule drug for

standardizatio

principal Component Analysis (PCA)

Method

2

4

Utilized advanced NLP/ML modules to build a probe for potential binding site

> **Reparametrized force fields to** overcome limitations in current simulation tools

3

Determined binding free-energy through free-energy calculations

Leveraged on advanced MD

(molecular dynamics) technology to

enhance sampling methods through

biased/un-biased equilibrium & non-

equilibrium solutions

Integrated ADME/Tox safety and Automated docking with Virtual Screening Multi-target selectivity compound databases Multiple structure/ligand efficacy evaluation Al rescoring and prediction based on AI provided by synthesis based on multitask deep Advanced MD with FEP based AI methods for (DTI rank) vendors to rank compounds with nolecule generations and learning approaches highest activity activity prediction Vendor-1 combined into coheisve 1B compounds TH A workflow Vendor-2 WV-DDL Deeke





Results

• Created a library of novel fragments targeting allosteric sites with high specificity and stitched them into molecules

• Identified lead entities exhibiting optimal interaction with the regulatory protein's binding site of interest



• Streamlined selection of viable candidates ready for preclinical development pathways











OED Model		
		Target Affinity diction Tool prediction Tool
	<u>Compounds</u>	FEP Score
	Reference Compound	-15.1 kcal/mol
	De novo Molecule 1	-14.3 kcal/mol
	De novo Molecule 2	-16.5 kcal/mol
	De novo Molecule 3	-16.01 kcal/mol