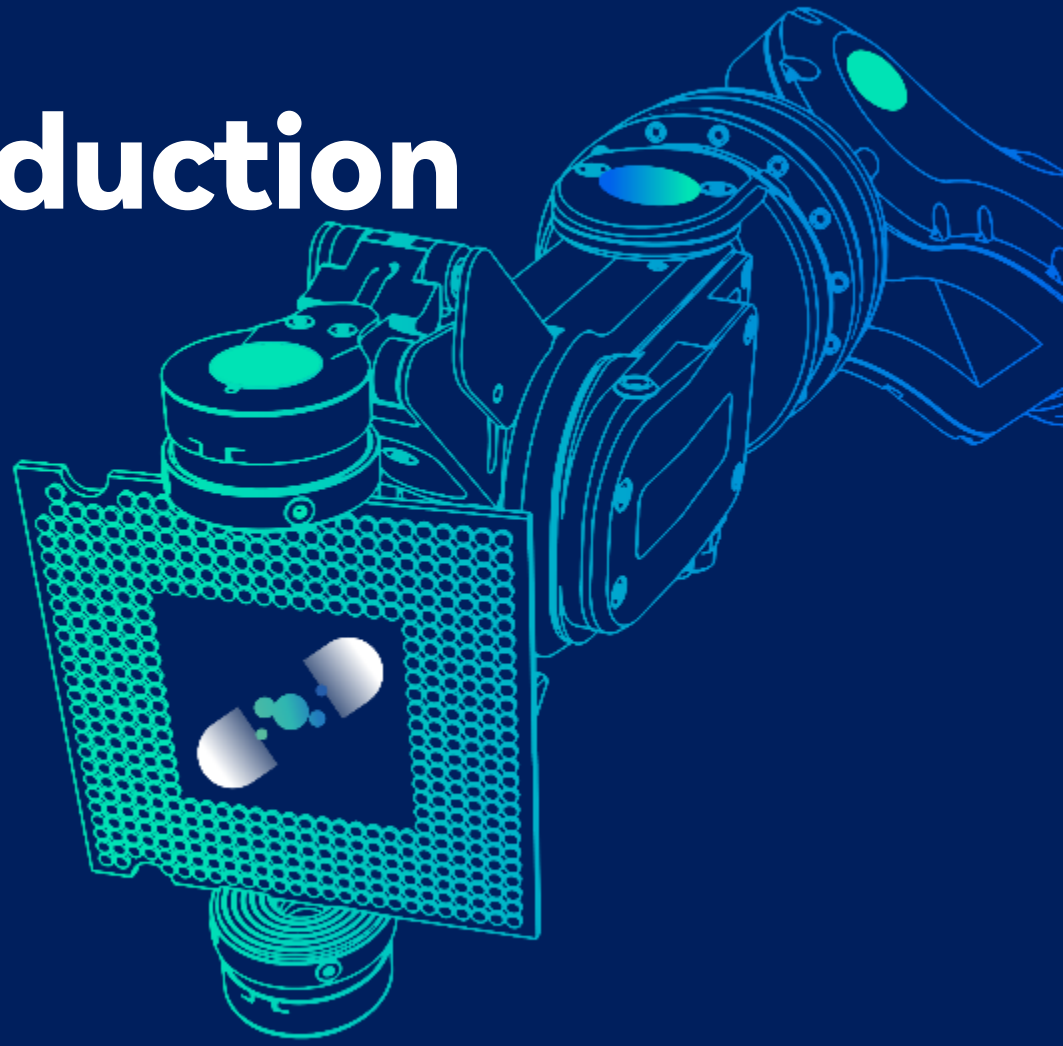
XtalPi

XtalPi Corporate Introduction

Accelerating Discovery with AI and Next-Generation Automation

Q1 2024

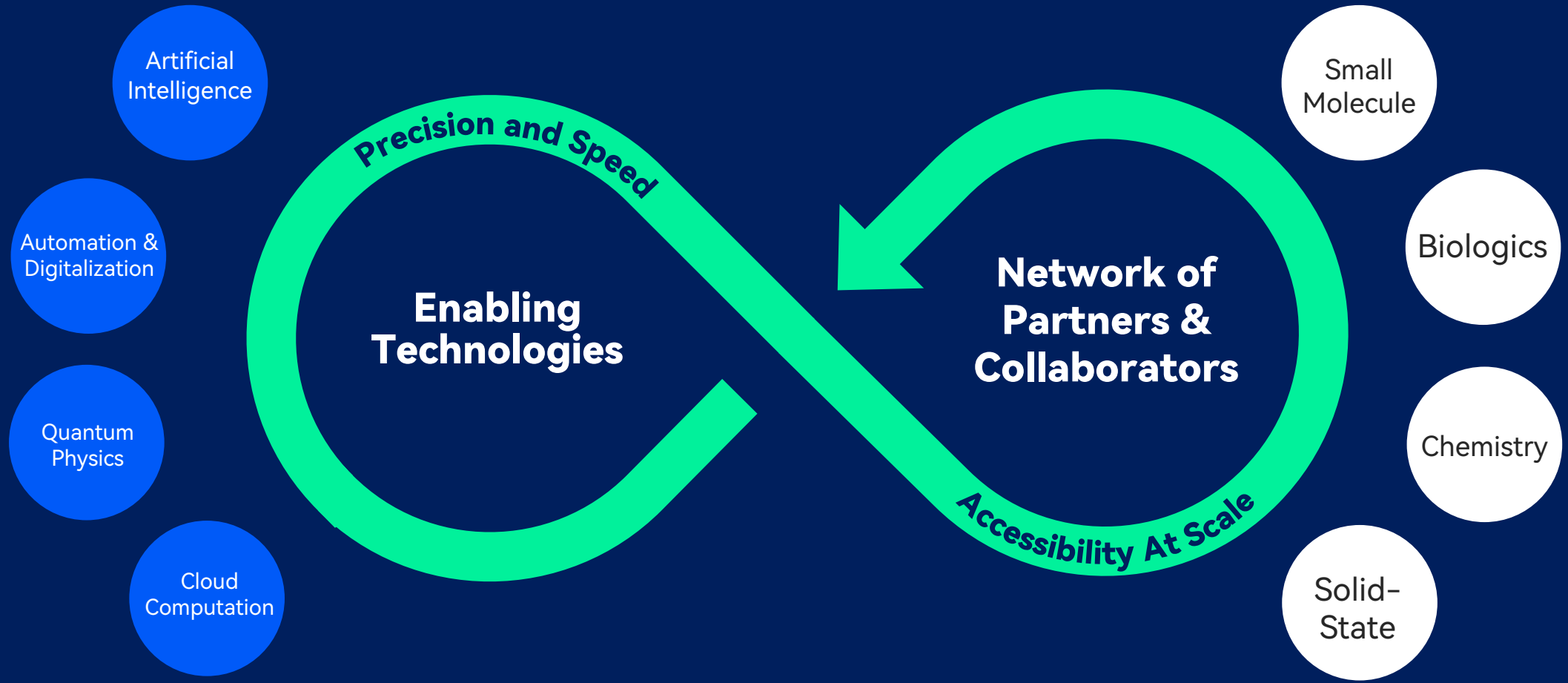


CONTENT

Part 1 About XtalPi

XtalPi is a technology ecosystem company

At XtalPi, we focus on creating accessible, enabling technologies at scale. We provide partners of all sizes in drug R&D with the foundational tools to accelerate the discovery of impactful, life-changing therapeutics and products.



Robust R&D infrastructure with strong global presence

XtalPi

Our technical and management teams operate closely together across 4 different sites

989
Employees

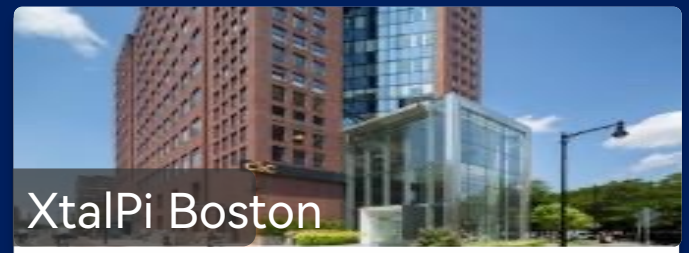
700+
Scientists & Technologists

120+
Granted Patents

10000+m²
Lab Space

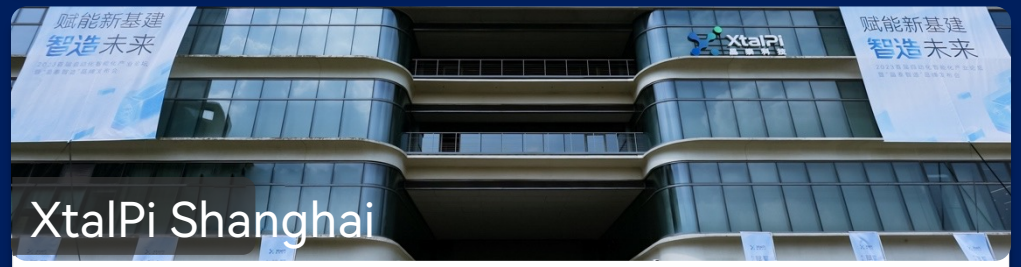
Shenzhen Futian International Biopharma Industrial Park

XtalPi Global Headquarter, R&D Center for XtalPi Core Technology & AI-driven Drug Discovery



CIC Cambridge, MA

Business and Innovation Center for XtalPi Global Partners



Shanghai Zhangjiang Science Park

Drug Discovery and Development Center, Greater China Business and Marketing Center

Beijing Zhongguancun

AI Research and Algorithm Center for XtalPi Technology Development

Access our innovative technology ecosystem through various collaboration methods

XtalPi

Services & Solutions

- Traditional FTE or FFS model for discovery and development projects
- Access to our products and digital/computational platforms with a fee

Partnership

- Leverage expertise and technological capabilities from both parties to co-develop or discover different assets

Industry-leading, empowering drug discovery and development platforms

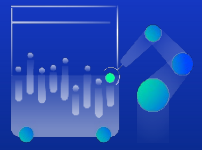
XtalPi

Small-Molecule Drug Discovery Platform and Solutions

- Integrated Drug Discovery Services
- ID4Idea™ AI-based Platform
- ID4GibbsTM High-accuracy Computational Chemistry Platform
- ChemArtTM: Automation-aided Discovery Chemistry & Library Synthesis
- Special Chemistry ADC/PROTAC/DEL/Peptides

Solid-State R&D Platform Driven by Automation + Computing

- Rapid, High-Precision Solid Form Screening and Selection Platform
- XtalCSP™ Crystal Structure Prediction Platform
- MicroED Structural Analysis Polymorph/Salt/Cocrystal Screening
- AI-driven, Automation-aided Crystallization and Execution



Intelligent, AI-Empowered Automation Technology Platform

- Flexible, Integrated Automation for Chemical and Analytical Processes
- Complete Digitalization Software Suite Empowered by AI

AI-empowered Antibody Discovery and Engineering Platform

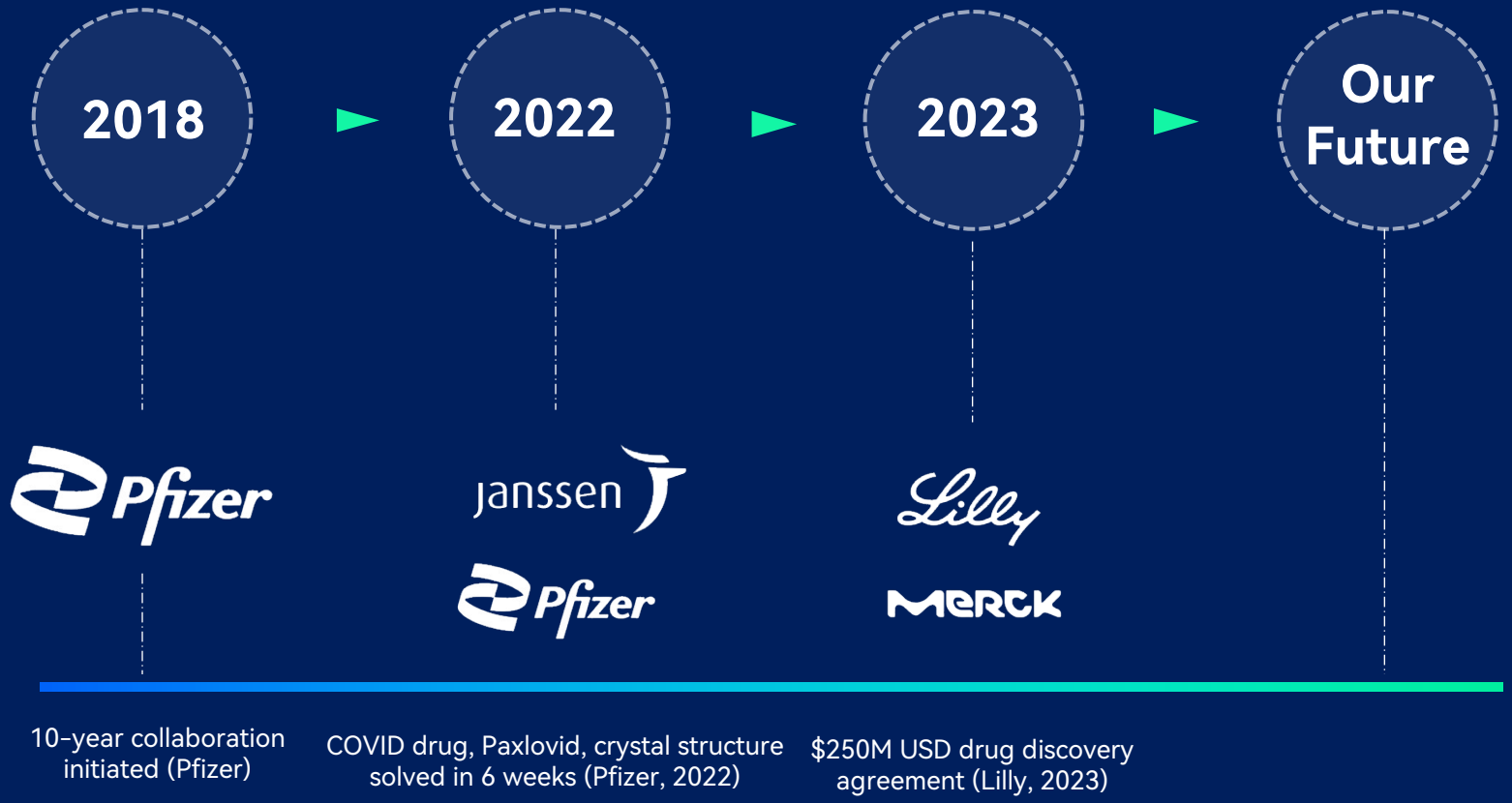
- XmartFluidics™ Single B Cell Screening
- XpeedPlay™ Phage Display Platform
- XtalFold™ Structure Prediction
- XcelDev™ Developability Evaluation
- XploreSeq™ NGS Discovery Platform
- XrossXeven™ GPCR mAb Discovery Platform
- Xffinity™ Affinity Modulation
- XuperHuman™ Immunogenicity Engineering

Examples of our recent partners and collaborators

XtalPi

Strong track record in partnering with major global pharma

XtalPi



Partner Testimonials

The collaboration with XtalPi is already changing the way Pfizer performs its screening work and has the **potential to disrupt the industry as a whole.**
—— Geoff Wood,
Principal Scientist, Pfizer

Our collaboration with **XtalPi is transforming pharmaceutical development**. By seamlessly incorporating computer simulations with our experimental formulation expertise in a **"digital-first" approach**, we are boosting drug development processes and positively impacting patients' lives.
—— Dr. Jan Gerit Brandenburg,
Head of Digital Chemistry, Merck KGaA

XtalPi

Part 2 Small Molecule Drug Discovery

XtalPi drug discovery platform increases precision and speed

XtalPi

Design Smarter, Make Faster

63+

Active projects with growing numbers and a proven track record of success in challenging projects

10X

Increased hit/lead rate driven by superior success rates from a more **diverse chemical space** with **precise molecular design**

AIDD

CADD

50%+

Enhancing **speed by leveraging automation and efficient evaluation through** industry-leading chemistry computational software and cloud infrastructures

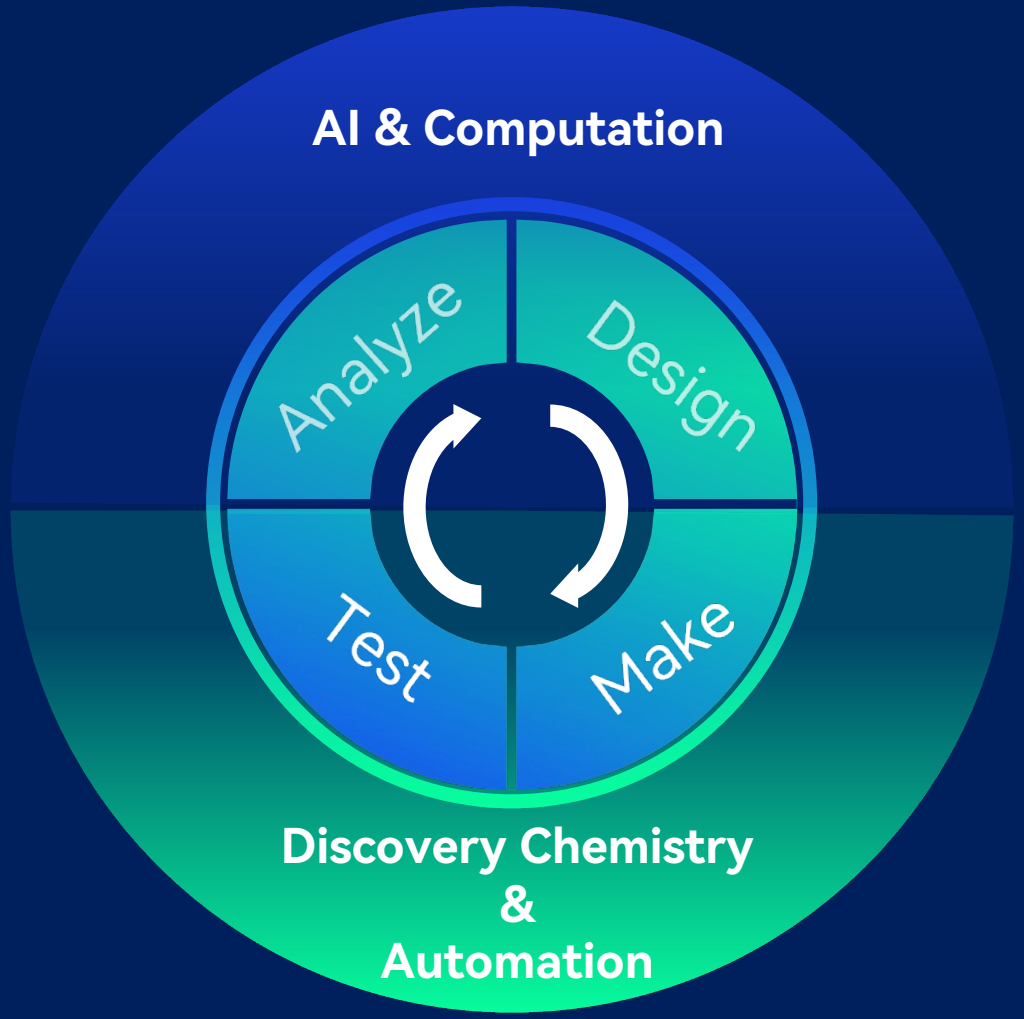
Chemistry Automation

Cloud Computing

Accelerate the DMTA Cycle via integrated drug discovery solutions

XtalPi

Tailored solutions empowered by the synergy of AI, computational chemistry, and automation platform



ID4Inno™

Generative AI- and quantum physics-based computation for exploring diverse chemical space and precise property prediction

ChemArt™

Removing discovery chemistry bottlenecks with automation platforms that offer swift deliveries with quality results

ID4Inno™ Synergize AI brilliance with physics precision

XtalPi

Integrating AI creativity with physics insight for superior capabilities in R&D

AI / Machine Learning

Pros

- Computationally fast
- Handles large datasets
- Effective at interpolation
- Generate novel ideas

Cons

- Requires training set
- Cannot extrapolate
- Interpretability

ID4Ideo™

ID4Inno™

ML dataset crafted through physics-guided data generation

- ✓ Accurate
- ✓ Fast and capable of handling large datasets
- ✓ Can extrapolate to new chemical space
- ✓ Generate novel ideas
- ✓ Provide structural insights

AI

ID4Gibbs™

Physics-based Methods

Pros

- First principle, no training required
- Extrapolate to new chemical space
- Accurate
- Structural insights

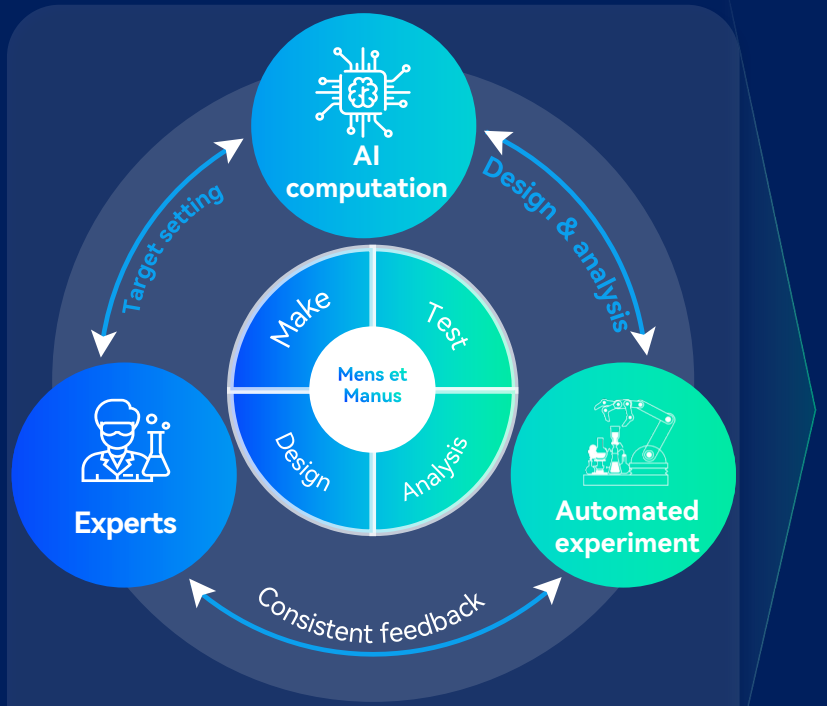
Cons

- Computationally intensive

ID4Inno™ Drives a full R&D DMTA cycle

XtalPi

Access broader chemical spaces with superior screening precision



Iterative DMTA cycles drive drug discovery across modalities, creating and screening molecules to identify biologically relevant candidates

ID4Ide™

ID4Inno™

ID4Ide™

ID4Globus™

Structure-/ligand-based drug design & AI generative design

Active learning virtual screening

XFEP
High-precision affinity prediction

Automation-aid chemistry

Assay data

Compounds
10^6
10^2

XtalPi builds a unique platform that **combines AI, physics-based methods, and automation** to augment human expertise and accelerate DMTA cycles

ID4Ideo™ Elevating drug discovery with cutting-edge AI XtalPi

A comprehensive solution harnessing generative AI and active learning for innovative and efficient drug discovery

AI generative design

Crafting novel solutions with customizable models tailored for diverse scenarios

First-in-Class

- Structure-/Ligand-based idea generation
- De Novo compound design

Best-in-Class

- Scaffold hopping
- Molecule hybridization
- Library design
- Fragment replacement

Property optimization

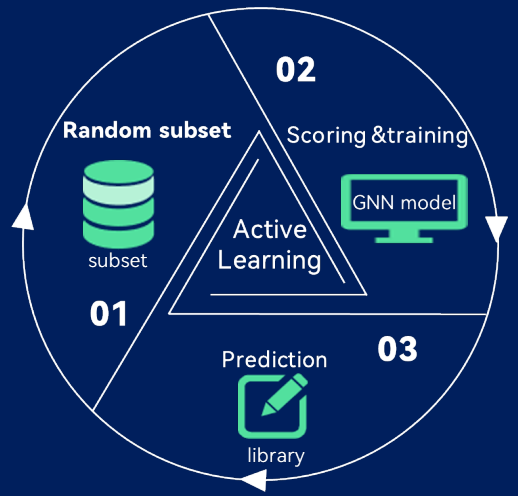
- Physicochemical property prediction
- ADMET optimization

Active learning virtual screening

Adapting to evolving data for continuous model performance improvement

High-throughput virtual screening

- 10% computational cost
- High enrichment powered by active learning



Tailored library design

- Project-specific models
- 5X enrichment factor

Diversity exploration

- Chemical space enhancement
- Novelty > 0.5 after 10^{10} ideas

High precision and throughput via cloud-native physics-based computation

XFF

- Enhanced accuracy in distinguishing bioactive conformations
- Tailored parameter training for client-specified projects

Xpose

- Incorporating protein motion for induced-fit in small molecules
- Excels in precise and detailed binding poses

XFEP

Novel algorithms for precise & efficient prediction

- Physics-based models offer **robust structure-based drug design (FEP+Pose+FF)** backed by 150+ internal & public dataset validations
- Demonstrates industry-leading precision, especially in **high-accuracy predictions**, through analysis of 30+ public datasets
- Delivers **cost-effective, high-throughput solutions** for a competitive edge when integrating AI and predictive models

RBFE

✓ Lead-opt

✓ Hit-to-lead

ABFE

✓ Hit screening

✓ Fragments

Structural Diversity

✓ Scaffold hopping

✓ PROTAC

Irreversible Binding

✓ Covalent inhibitor

Protein Mutation

✓ Selectivity ✓ Antibody

✓ Resistance ✓ Mini-protein

Oligomers

✓ Peptides

✓ Macrocyclic

Case study: AI-driven novel scaffolds discovery uncovering promising leads with double-digit nanomolar range bio-activity

Goal: Discover and develop novel small-molecule inhibitors targeting autoimmune and inflammatory diseases

Virtual screening

Of the initial 30 compounds purchased, 8 demonstrated μM activity in the first round

General & customized library

↓

Ligand-receptor docking

Selecting based on **IFP & docking score**

↓

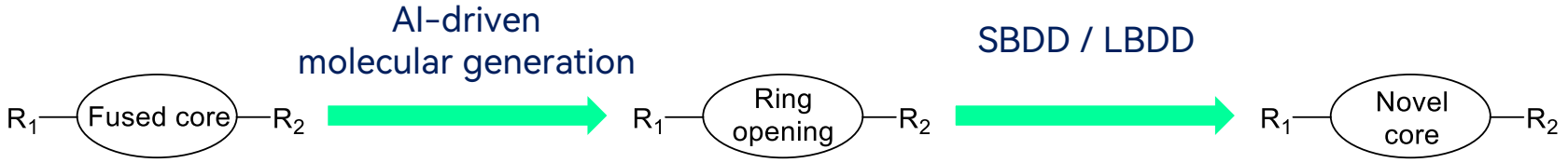
Ligand-receptor docking

Selecting based on **MMGBSA & ABFE Prediction**

↓

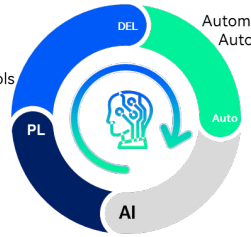
Selected compounds

Integration of AI-driven, structure-based, and ligand-based design models for identifying promising leads with novel scaffolds



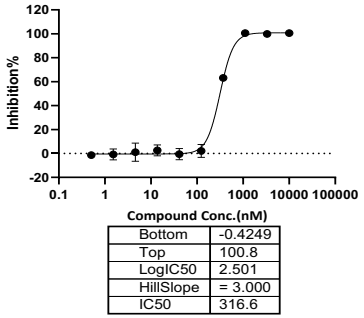
DEL
Novel library
Legacy BBs
Focused library
Hit expansion
Novel screening protocols
Novel data analysis

Pipeline
High quality hits
With SAR
Bonus valuable info
Multiple series
Target validation
Bucket approach



Automation
Automated DEL Synthesis
Automated Off-DNA Hits Follow up
Automated on-DNA focused DEL
Mini scale Automation

AI
Library Design
BB picking
Signal calling
Prediction outside DEL chemical space
XtalPi's proprietary FEP calculations



Bottom	-0.4249
Top	100.8
LogIC50	2.501
HillSlope	= 3.000
IC50	316.6

Key results:

- Strong correlation between XFEP prediction and biochemical activity **expedites lead optimization**.
- Identification of **two novel scaffolds** with sub-micromolar activity **within two months** via virtual screening.
- Integrating AI-based, structure-based, and ligand-based molecular generation produces promising leads with **novel scaffolds** in the **double-digit nM range.**
- Successful identification of **two novel scaffolds with nM activity** achieved through the synergy of AI, automation, and DNA-encoded library (DEL) screening.

XtalPi

Part 3 Discovery Chemistry and Automated Synthesis

ChemArt™ Rapid discovery chemistry & library synthesis services

XtalPi

Break free from chemistry bottleneck with innovative, large-scale chemistry automation

50,000 ft²

Automated lab space

200+

Workstations

80%

Common medicinal chemistry toolbox covered

Rapid Library Synthesis

On-spec purity and amount

Enabling discovery chemistry with flexible business models

XtalPi

Full-Time Equivalent (FTE)

- Flexible team sizes
- Agility to targets or project reprioritization

Fee for Service (FFS)

- Premium compound synthesis available from mg to kg scale
- Pay for successfully delivered compounds

Chemical Synthesis

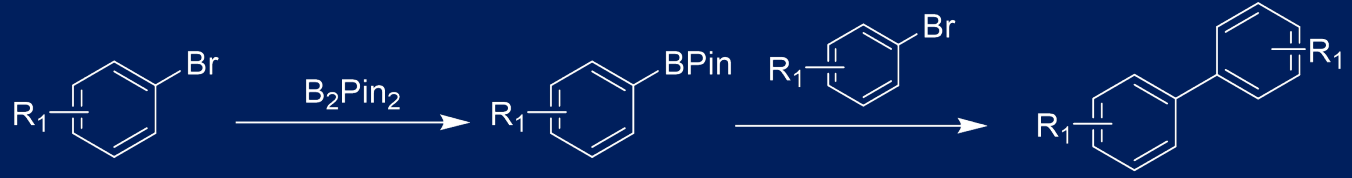
- Final compound synthesis
- Building block synthesis
- Library synthesis
- Intermediate/scaffold synthesis
- Reference standard synthesis
- Synthetic routes design and scouting
- Reaction condition optimization
- Catalyst screening
- Custom synthesis
- Chiral SFC separation

Customized Synthesis

- Peptides
- PROTAC
- ADC
- Macrocyclic compounds
- Stable-isotope labeling chemistry
- PhotoRedox Catalysis

Case study 1: reaction conditions screening

XtalPi systems expedite reaction condition optimization through the streamlined execution of parallel reactions



Literature Conditions:

- **34%** yield over 2 steps
- Required **20 mol%** catalyst loading

1st Round
Catalyst & Solvent Screening

$Pd(dppf)Cl_2$·DCM (5 mol%),
B_2Pin_2 (50 mol%) in DCE
62% Yield

65 parallel reactions
1 day

2nd Round
Base Screening

The [Pd] catalytic environment with
K_2CO_3 (300 mol%)
60% Yield

6 parallel reactions
0.5 day

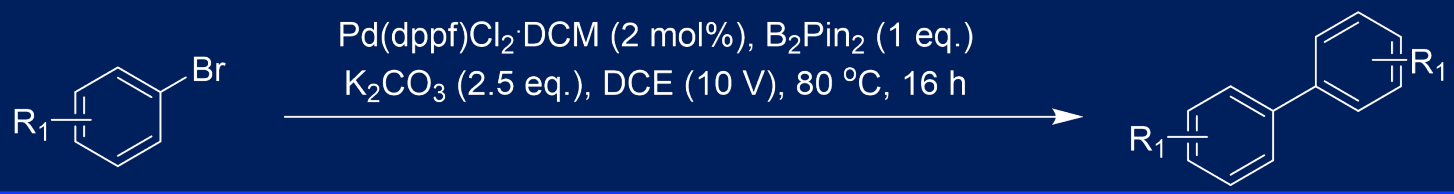
3rd Round
Other parameters Screening

Reagents ratio, solvent volume, and temperatures
66% Yield

12 parallel reactions
0.5 day

Optimized Conditions:

- Single step with **66%** yield
- Catalyst loading down to **2 mol%**
- Gram-scale up to **20 g**



Case study 2: rapid, parallel compound library synthesis

XtalPi

Goal

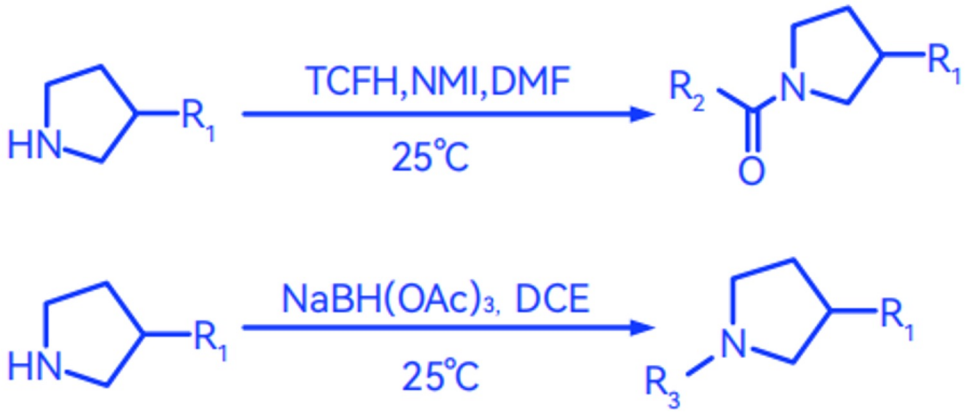
Synthesize 400 library compounds within 4 weeks with one chemist

XtalPi Approach

1 Chemist and 1 automation operator utilizing the automated synthetic platform

Deliverables

- **600** reactions ran by a human-robot combination workflow within **5** days
- **392** compounds, at a specified scale, were purified over **9** days



XtalPi

Part 4 Solid-State Platform for Drug Formulation Development

A superior track record in solid-state research

XtalPi

Our Team

50+ Solid-state researchers

20+ AI algorithm experts

70% Masters & PhD

10+ Years of experience in solid form R&D

20+ Published Papers

47 Patents

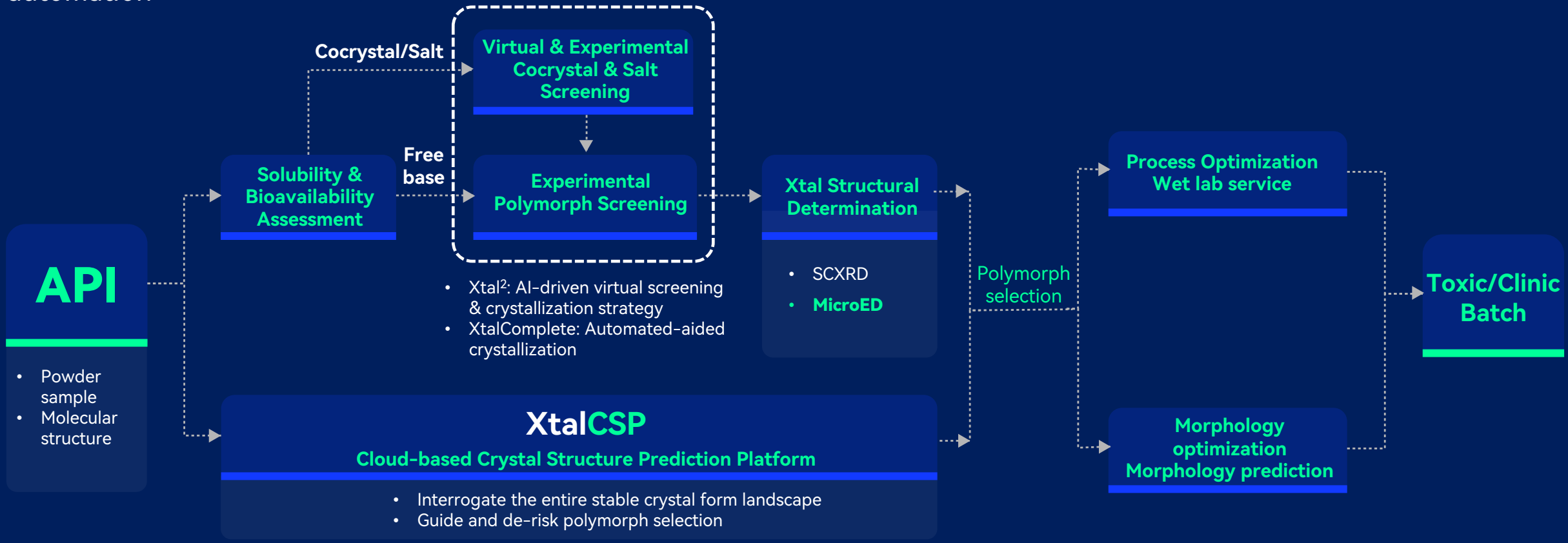
100+
Small molecule pipelines at IND stage

1000+
Completed solid-state research projects

50+
Longstanding collaborations

Rapid discovery of the desired form for formulation development

Multi-pronged, risk-mitigated approach that harnesses the power of proprietary AI algorithm, quantum physics, and automation



- Survey the **complete stable crystal landscape**
- Design experiments smarter
- Screen polymorphs **faster**
- Make decision under unparallel timelines

Advantages of XtalPi solid-state platform

XtalPi

Speedy Delivery

25% - 50%
Increase in speed

Risk Mitigation

Eliminate risk for disappearing polymorph

Accessibility to All

Break free from computational resource limitations

IP Advantages

Proactively look for the best polymorphs to protect or break patents

Comprehensive, flexible solid-state solutions

XtalPi

Intelligent

Experimental Solid-State and Formulation Services

- Polymorph/salts/cocrystal screening and selection (**empowered by AI-guided condition strategy**)
- Crystallization process development
- Solid dispersion formulation development
- Analytical method development
- Pre-formulation development

Industry-leading

Computational Structural Prediction Services and Platform

- Crystal structure prediction
- Virtual salt/cocrystal screening
- Solvate/solid dispersion propensity prediction
- Morphology prediction
- **Access to our XtalCSP computational platform (coming)**

Rapid

Crystal Structure Determination

- Single crystal preparation and structure determination
- Rapid crystal structure determination using in-house MicroED analysis

XtalCSP Fast, versatile, cloud-native CSP platform

XtalPi

Advanced solid-state computational services

Computation Platforms

CSP

XtalCSP™

Crystal structure prediction to fully de-risk the system

CSP-Lite

CSP-Lite

Fast crystal structure prediction

Other Applications

Coformer Screening

Virtual Co-former screening

Perform virtual screening between API and co-former (counter ions)

MP

Morphology prediction

Predict the morphology of target polymorph in solvents

Computation and Data Infrastructure

Cloud Computing Platform

Data Center

Quantum Physics

AI + Machine Learning

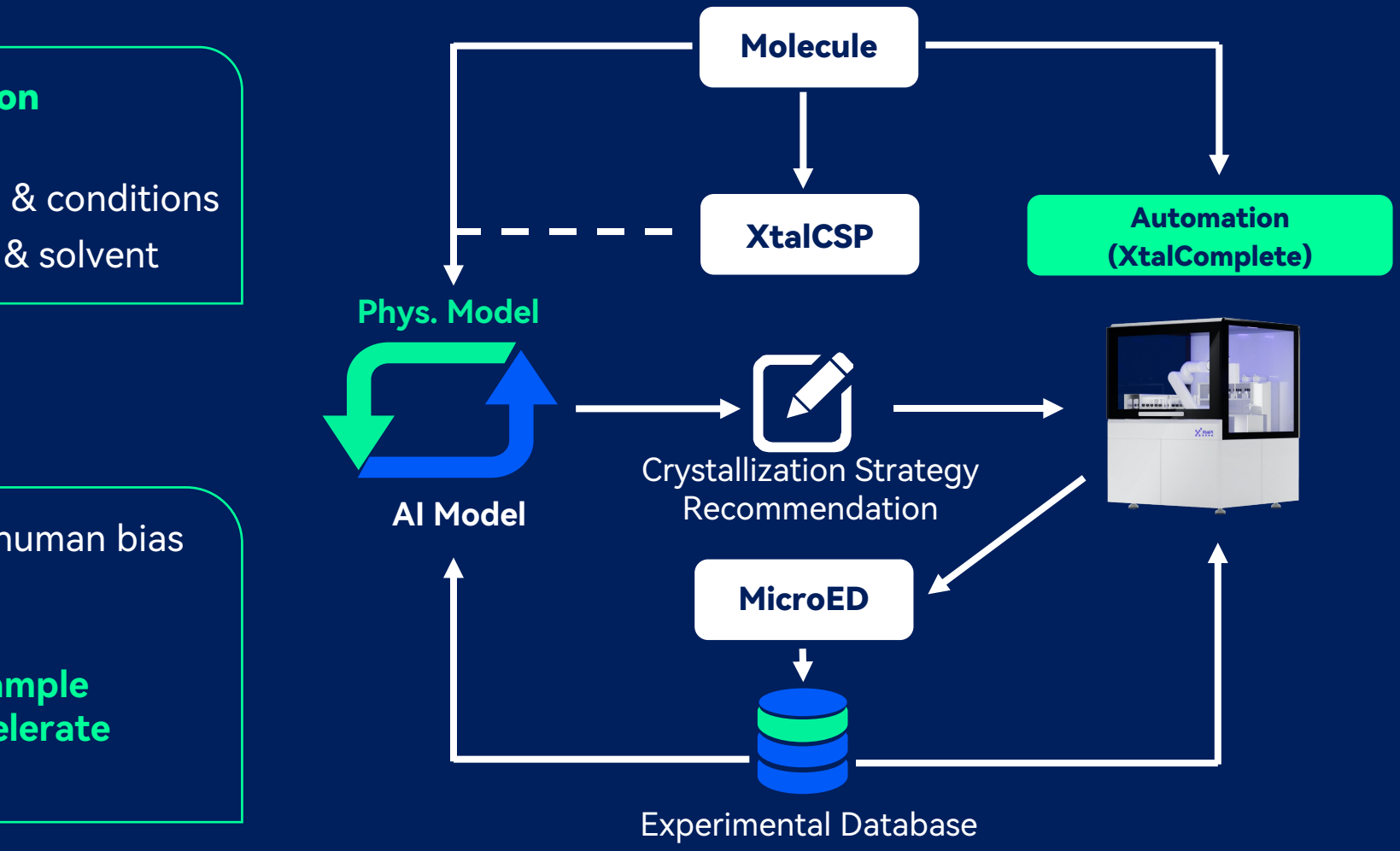
Xtal² Proprietary AI-driven polymorph strategy

Xtal² combines physics-based (virtual) data and real-world crystallization results to perform virtual screening. significantly increasing the screening efficiency of polymorphs including salt and co-crystal

Crystallization condition recommendations

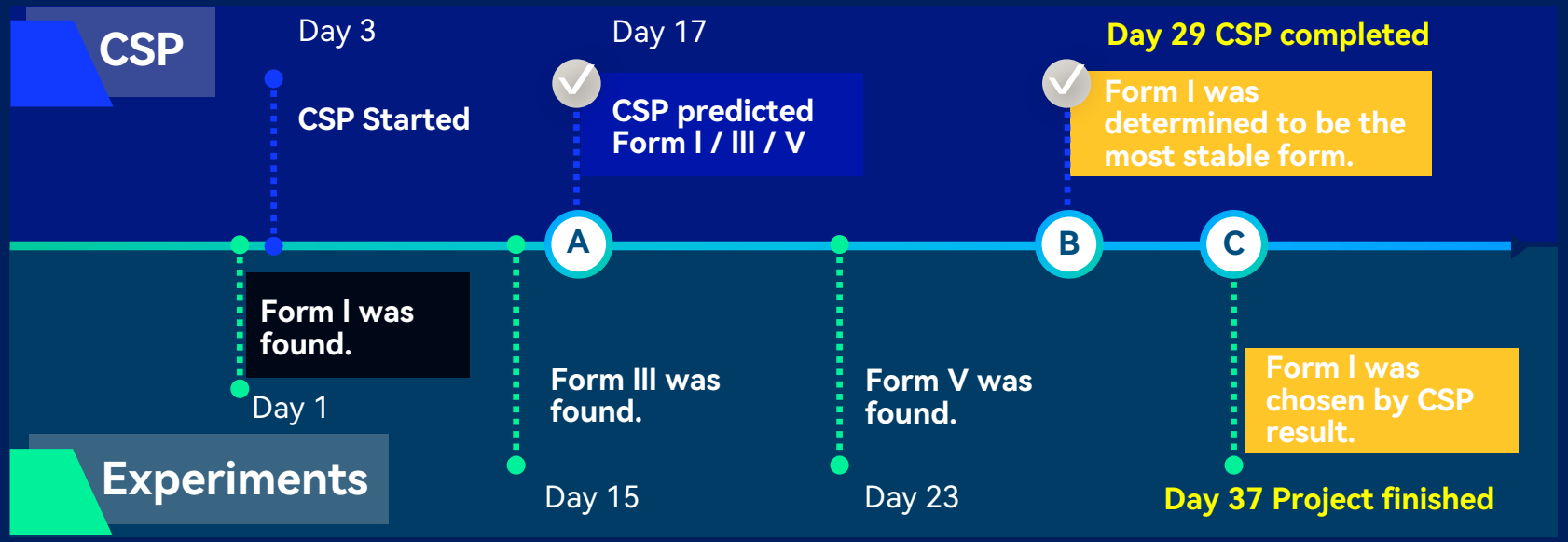
- Crystallization methods & conditions
- Coformer & counterion & solvent

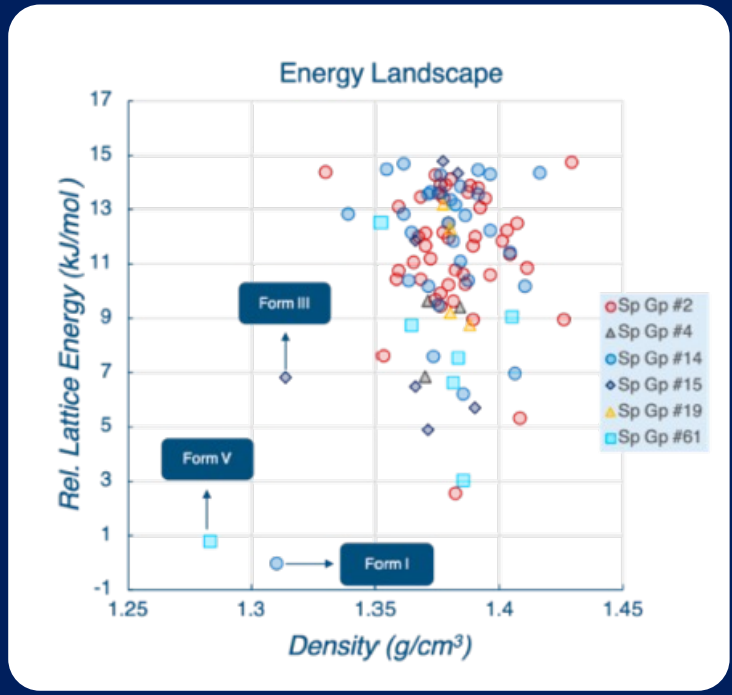
- Breaking limitation of human bias in experimental design
- 80%+ powder yield
- Significantly **reduce sample consumption** and **accelerate experimental cycles**



Case study 1: accelerate solid form selection

Determining a solid form needed for a clinical study in two months by leveraging a combination of XtalPi's CSP platform and experiment methodologies





- **A** Found potential polymorphs other than Form I; results guided further experimental screening
- **B** Thermodynamic stability calculation lowered decision-making risk
- **C** Time needed for decision-making was shortened given confirmative CSP results

Case study 2: polymorph screening guided by AI and accelerated by automated crystallization platform

Achieving quality-results under an accelerated timeline using XtalPi intelligent approach

1 × 

200 manual experiments designed by experts
3.5 weeks, 4.0 g sample

# of exp.	# of solids obtained	Hit Rate	# of discovered forms
200	174	87%	3

VS

0.4 ×  1 × 

70 automated experiments guided by intelligent crystallization strategy
2 weeks, 1.5 g sample

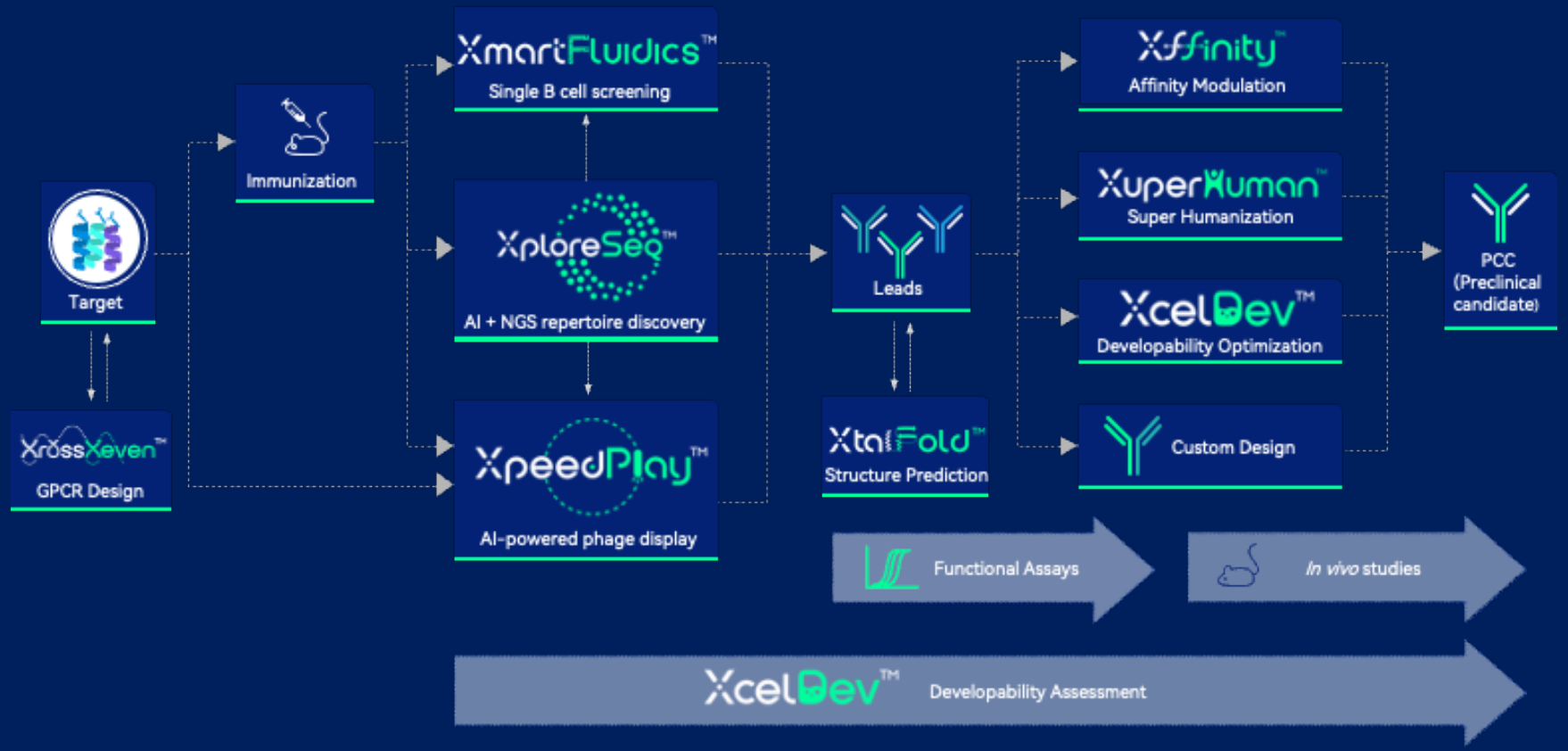
# of exp.	# of solids obtained	Hit Rate	# of discovered forms
70	64	92%	3

Part 5 **Antibody Discovery**

XupremAb™

XtalPi

AI-powered next-gen antibody discovery and engineering platform



INTEGRATE DRY & WET LAB

EXPAND SEARCH SPACE

EXCEL IN ALL DIMENSIONS

BEND RULES OF NATURE

1

XrossXeven™

AI-powered one-stop solution for GPCR antibody discovery

XtalPi

AI-Guided GPCR Antigen Design with Large-Scale Mutations

GPCRs

are hard to express in their native forms, making GPCR antigen preparation a challenge.

Mutations

are usually required to thermostabilize GPCRs for expression. Reported cases usually contain <10 point mutations.

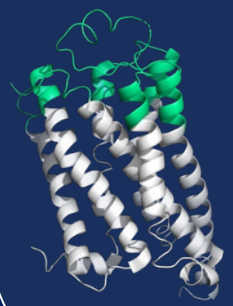
Human

judgment & trial-and-error are needed to identify mutations, which is tedious and time-consuming.

Goal

- Rapid identification of mutations
- Maintain conformation of ECL
- Enhance stability and expression level

WT GPCR



Generative AI

Proprietary LLM AI generated "fit" mutants

160K

Predictive AI

Narrowed down by stability and ECL conformation

10K

MD Modeling

Fine-grained assessment of stability

100

Expression

Expression of top mutants

15

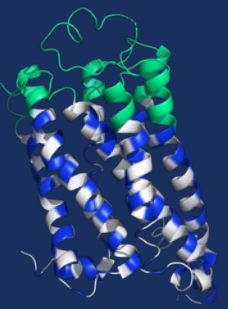
Validation

Bound to BMK antibody & cleared stability test

11

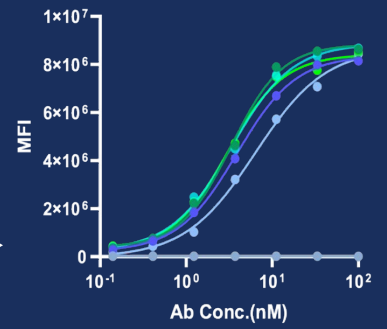
AI-designed Mutants

- 120-160 pt. mutations in TM & ICL
- ECL conformation maintained



Immunization & Screening

13 hits identified that bind both protein & cell

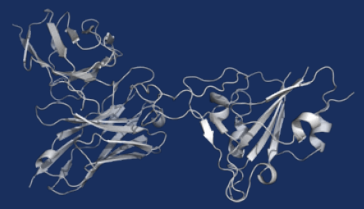
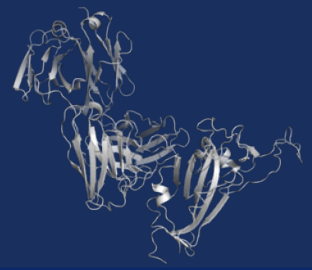
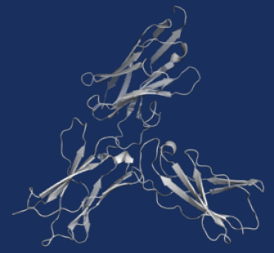
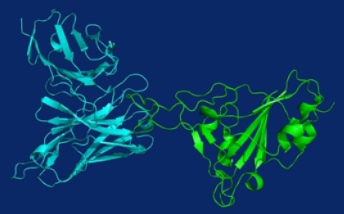
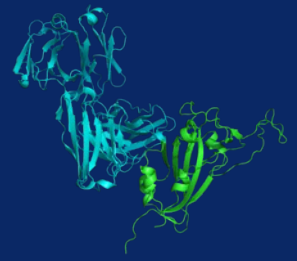
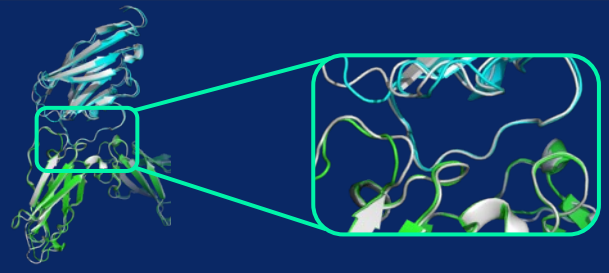
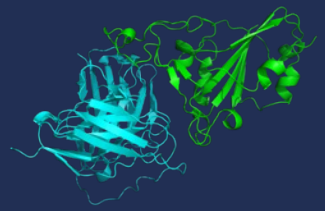
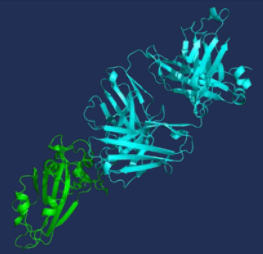
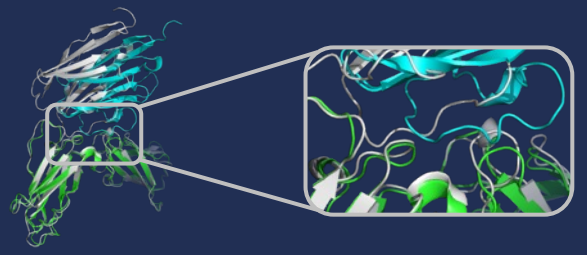


ECL: Extracellular Loop; TM: Trans-membrane; ICL: Intracellular Loop
LLM: Large Language Model

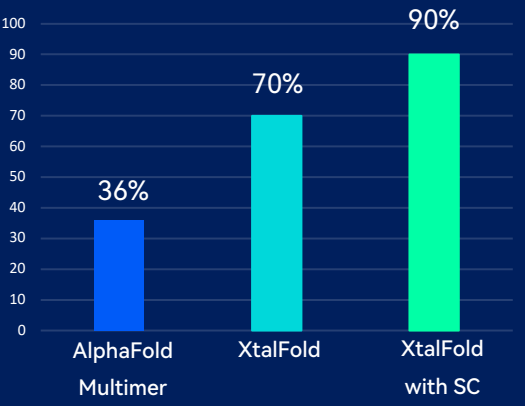
2 XtalFold™ Protein complex structure prediction

XtalPi

- High-confidence antibody-antigen complex structure prediction, only primary sequences needed
- Significantly outperforms AlphaFold-Multimer (AFM), especially in the Ab-Ag interface region

	Ab-Ag Complex 1 PDB ID: 7F12	Ab-Ag Complex 2 PDB ID: 7VZT	Ab-Ag Complex 3 PDB ID: 7S2R
PDB Structure			
XtalFold™	 DockQ: 0.90 iRMSD(Å): 1.44	 DockQ: 0.75 iRMSD(Å): 1.67	 DockQ: 0.86 iRMSD(Å): 1.02
AlphaFold-Multimer	 DockQ: 0.05 iRMSD(Å): 8.89	 DockQ: 0.02 iRMSD(Å): 16.15	 DockQ: 0.35 iRMSD(Å): 9.79

Success Rate*



XtalFold™ significantly outperforms AlphaFold-Multimer (AFM) in terms of success rate & quality.

* N=39. DockQ ≥ 0.23 is considered success.

3 Xffinity™ AI-guided affinity modulation

XtalPi

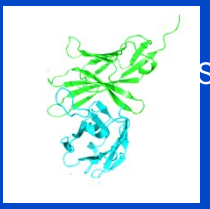
Case study:
Rapid affinity maturation of a VHH

2 rounds of optimization

73 variants expressed

3.5 weeks

100x increase in affinity



XtalFold™
Structure Modeling
Ab-Ag complex structure from primary sequences

Parental
1.53E^{-7} (M)

20^{25}
"Interface" mutants
25 residues identified at the Ab-Ag interface from XtalFold™ structure

Generative AI
LLM trained on proteins

50,000
"Fit" mutants
Recommended mutants that are developable

Affinity AI
Rank all mutants by predicted K_D

In silico workflow

In vitro workflow

23
Expressed & Tested
Cell-free expression & BLI

AI Fine-tuning
Wet lab data feeds back & optimizes AI model

2^{11}
Single-mutation combinations
11 single point mutations predicted to increase affinity

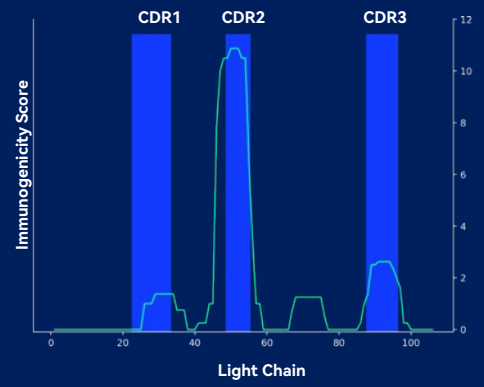
Affinity AI
Rank all mutants by predicted K_D

50
Expressed & Tested
CHO expression & BLI/SPR

Top clone
1.53E^{-9} (M)
100x

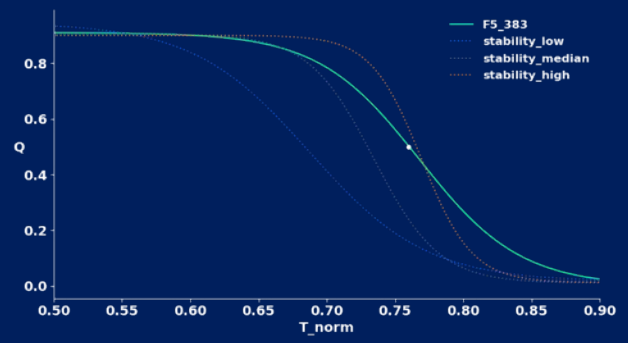
4 XcelDev™ AI-powered developability assessment and optimization

XtalPi



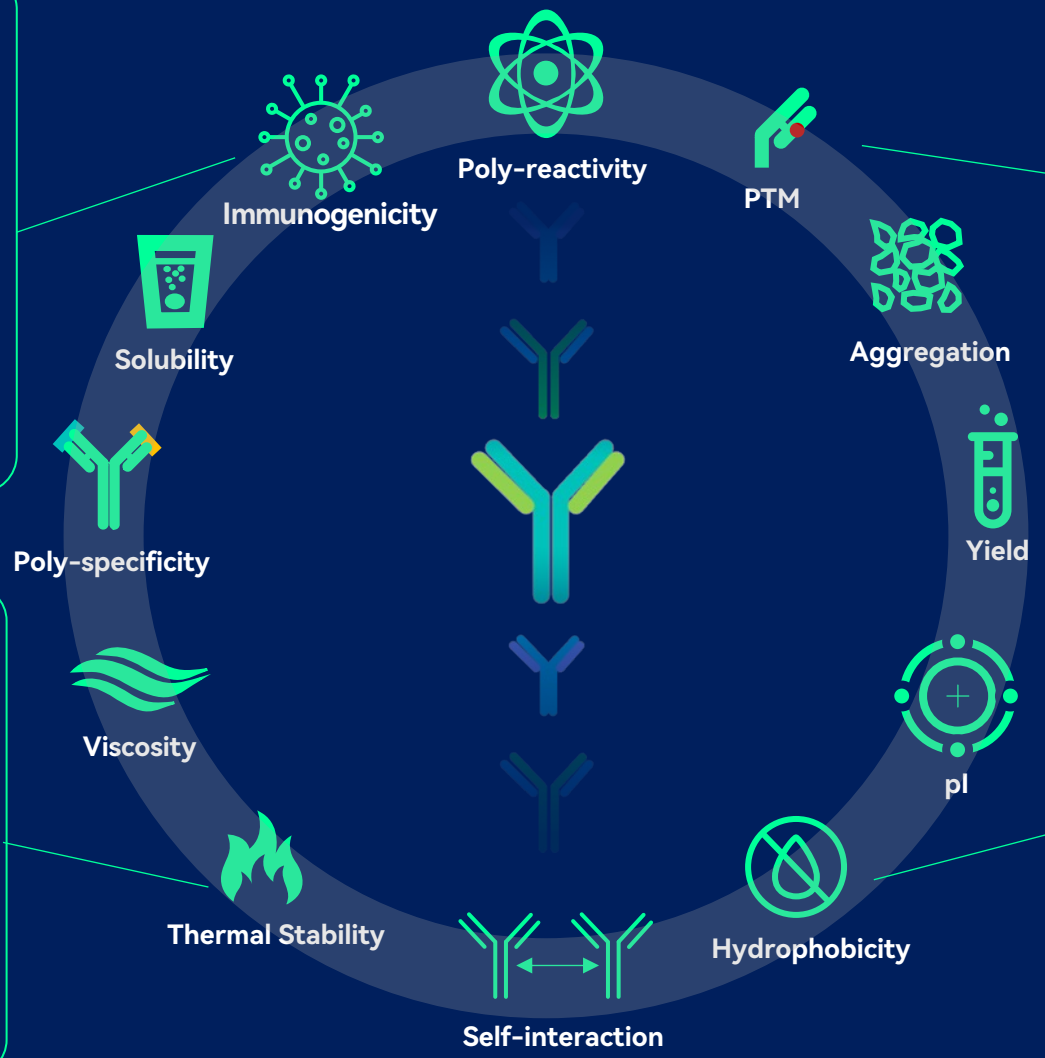
Immunogenicity hotspot detected in LCDR2.

Risk: High



Thermal stability in optimal range.

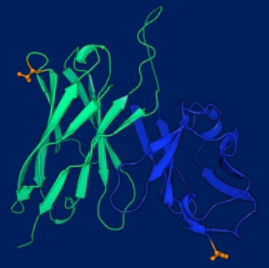
Risk: None



VH:
QVQLVQSGAEVKKPGSSVKVSCKASGYSFTDYHIHWVRQAPGQGLEWMGVINPNGGTTDYNQR
FKGRVTITADESTSTAYMELSSLRSEDTAVYYCARYDYFTGTGVYWGQGTLVTVSS
VL:
DIVMTQTPLSLSVTPGQPASISCRSSRSLVHSRGNTYLHWYLQKPGQSPQLLIYKVSNRFIGVPDRF
SGSGSGTDFTLKISRVEAEDVGVYYCSQSTHLPFTFGQGTKLEIK

Deamidation motif detected.

Risk: Medium



HC V75 and LC L107 in hydrophobicity patch, prone to aggregation.

Risk: Medium

XtalPi

Part 5 Automation & Digitalization Platform

XtalPi's AI-driven automation for revolutionary chemistry

XtalPi

Crafting the future of chemistry through intelligent software design, data structuring, and automated workstations

Software

Core System for experiment operations

- Intelligent scheduling
- Automation executing
- In-house design ELN

Intelligent Algorithm

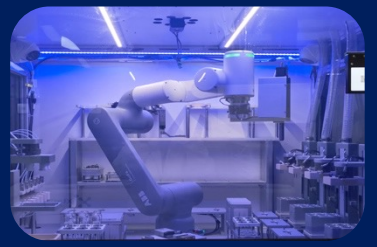
Data structuring and AI training

- Rxn. conditions recommendation
- Synthetic process planning
- Substances handling

Modular Workstations

Automation platform for chemistry execution

Precise chemical handler



Hands-free technologies

Seamless Rxn QC/analysis

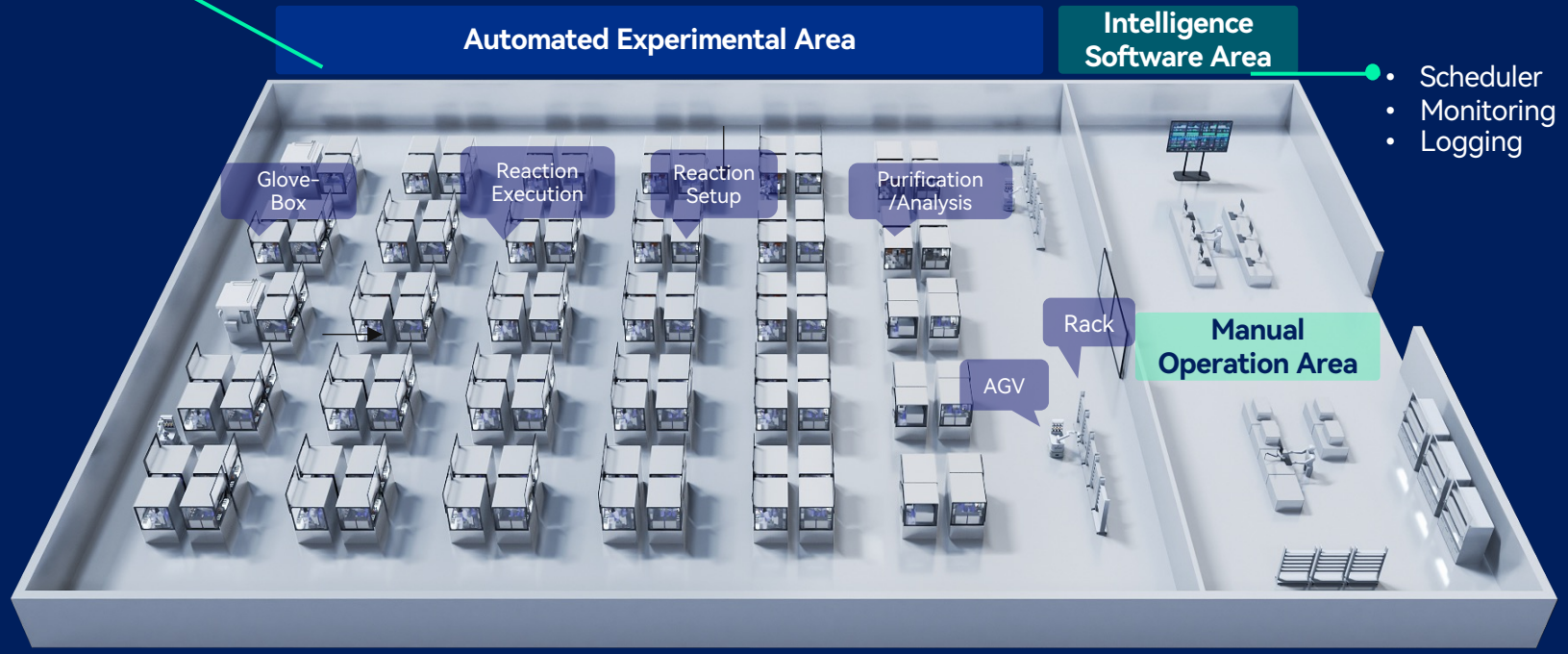
XtalPi's cloud-native automation cluster

XtalPi

Integrating precision chemistry execution and intelligent software management for cutting-edge research

- Automated workstations
- Unit control system
- Data collection system

Cloud Lab platform



- Scheduler
- Monitoring
- Logging

Standard chemistry modules and automated workflows

XtalPi

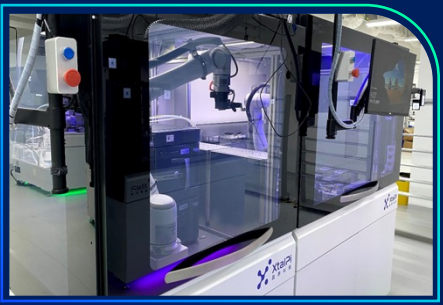
XtalPi's automation platform covers a range of applications in chemistry

Dispensing Workstation

- Solid/liquid dispensing
- Caps opening and closing
- Nitrogen blow

Reaction Workstation

- High-throughput
- Temperature controlled stirring
- Quick sample preparation



Analytical Testing Workstation

- Sample preparation
- LC-MS Analysis
- Online report review in ELN

Purification Workstation

- Nitrogen evaporator
- SPE Celite columns
- SPE silica gel columns

Glove-box Workstation

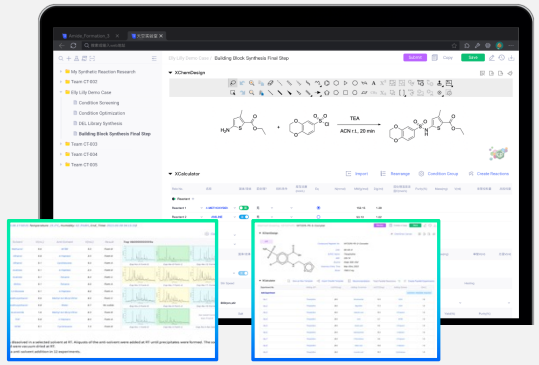
- Reaction operation
- Sample preparation
- High-throughput for moisture and air sensitive reactions

Full digitalization solutions to accelerate discovery

XtalPi

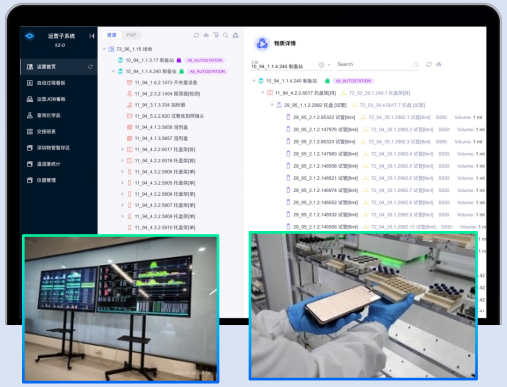
Chemist-Centric ELN

A streamlined ELN and data management for chemistry applications



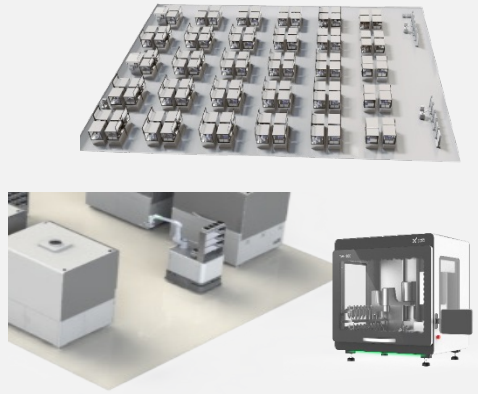
LIMS

Resource and quality management with a focus on automation cluster



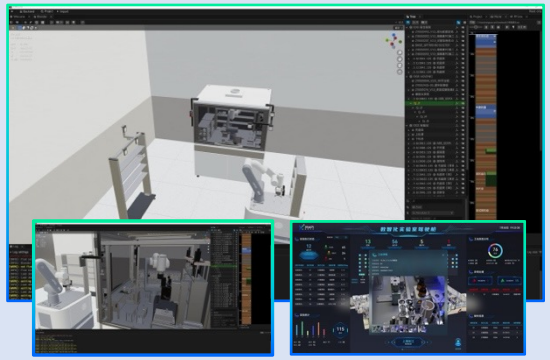
Scheduling and Controlling System

AI-empowered process control for human-machine interaction (HMI)



Digital Twins System

Planning tools for process optimization and lab/experiment design validation



Flexible system and process integration for automation infrastructures of any scale

XtalPi

Scan the QR code to learn more about our offerings

Get in touch with us at bd@xtalpi.com

XtalPi

THANK YOU !