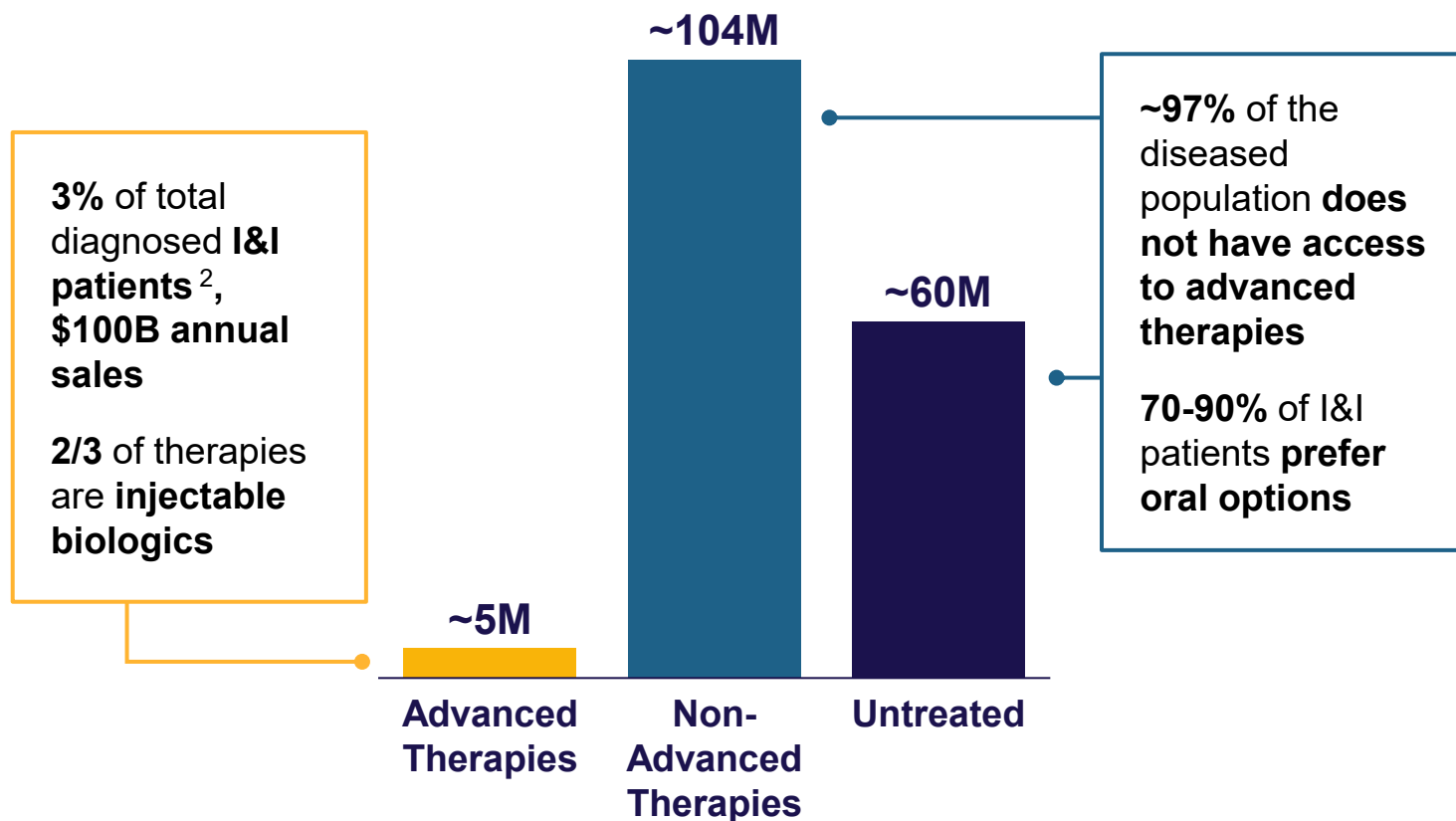


The CONECTA® Platform: Integrating Multimodal Foundation Models with Nature's Chemical Intelligence to Find Solutions for Hard-To-Drug Targets

Hok Hei Tam, Co-founder and CTO

I&I Market: Huge Underserved Market for Once Daily Orals

~169M Total Patients Across Core Immunologic Diseases¹



**Efficacious, Safer
Once Daily Orals Can
Transform the Market**

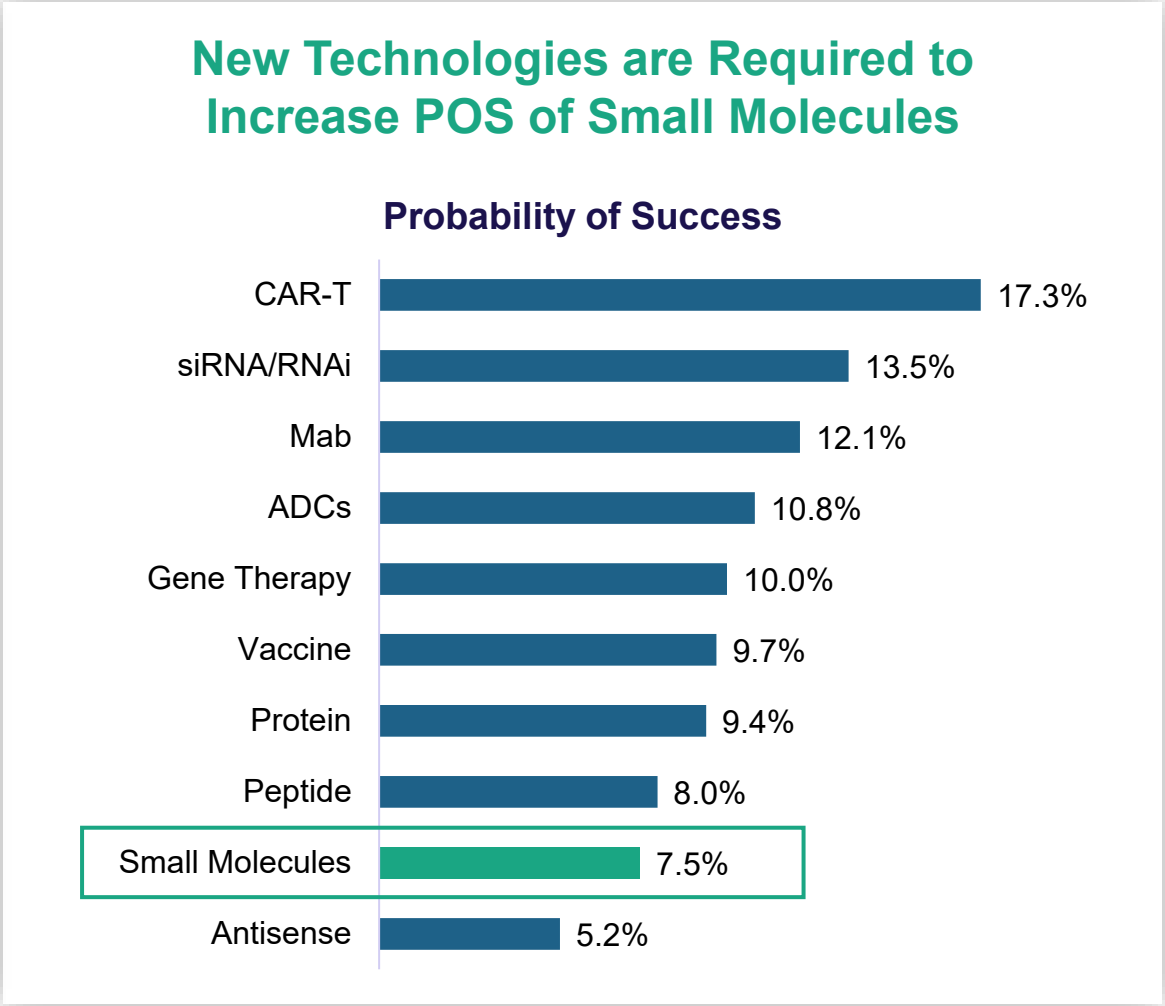


- Replace biologics
- Enable combination therapies
- Provide accessible therapies for 97% unserved and underserved patients

¹ Diagnosed prevalent patient population for US/EU5/JP (Global Data; 2023; key immunologic diseases includes AD, Asthma, COPD, HS, MS, PsO, PsA, RA, SLI, UC, CD; ² Market Forecasts for US/EU5/JP (Global Data'2023)

Montai is Focused on Unlocking Validated Disease Pathways Once the Domain of Only Biologics

Top I&I Blockbuster Biologics Have No Oral Small Molecule Equivalent		
Top 10 Drugs	Peak Sales	Small Molecule Equivalents
Humira® / Remicade® / Enbrel®	\$21 / \$7B / \$6B	In development
Dupixent®	\$12B	No
Stelara®	\$11B	No
Skyrizi®	\$8B	No
Entyvio®	\$5B	In development
Cosentyx®	\$5B	In development
Actemra®	\$3B	No
Nucala®	\$2B	No



¹Top I&I biologics includes top monoclonals targeting indications in autoimmune/immunology, allergy, respiratory, dermatology, GI, infectious disease; target group batches related targets, e.g. Stelara targets IL-12 and IL-23 while Skyrizi only targets IL-23; ²Biologics peak sales from BioMedTracker/Citeline (Sep 2024); ³Likelihood of approval from BIO Clinical Development Success Rates and Contributing Factors 2011–2020 (2021)

THREE CHALLENGES

Hold Back
Development of
Small Molecules
Against These Hard-
to-Drug Targets

- 1 Existing chemistry is biased toward classic small molecule binding pockets
- 2 Hard-to-drug targets are structurally complex and difficult to model
- 3 Optimization of diverse scaffolds to deliver a TCP is often challenging

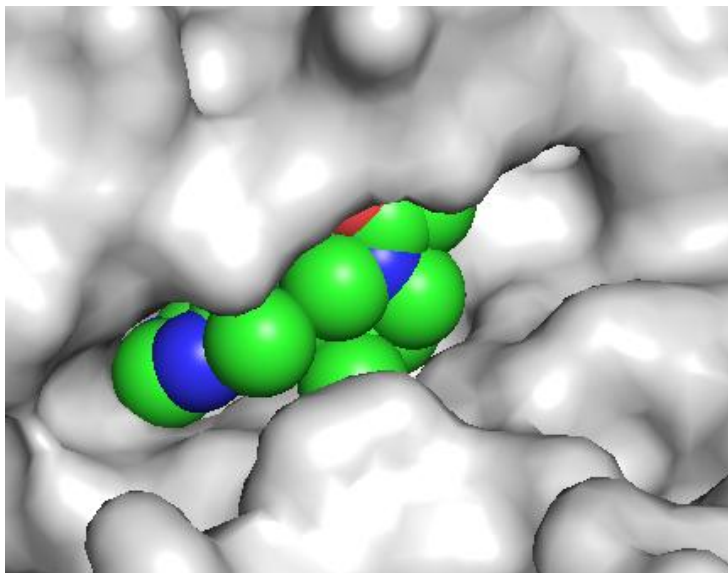


**We've built CONECTA[®]
to address all three**

1. We Unlock Nature's Diverse Chemical Intelligence to Solve Hard-to-Drug Targets

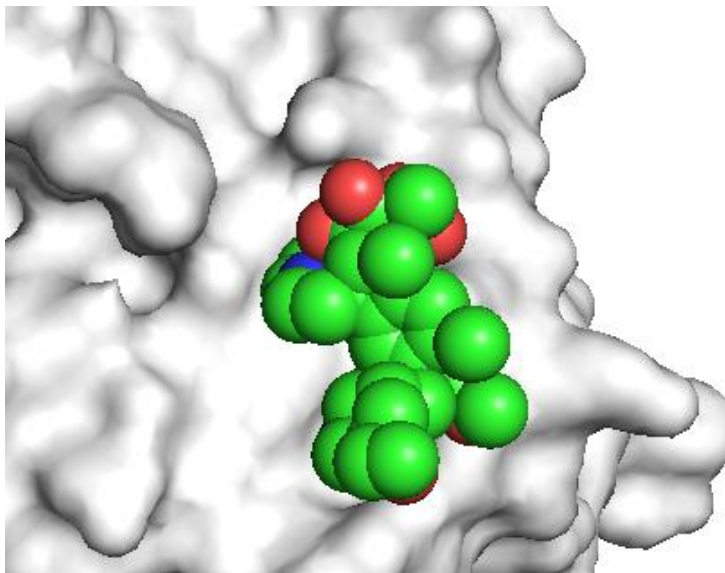
TRADITIONAL Discovery

Limited to known target with
deep, druggable pockets



NATURE'S DIVERSE Chemical Intelligence

Ability to go after target with
limited to no binding pockets

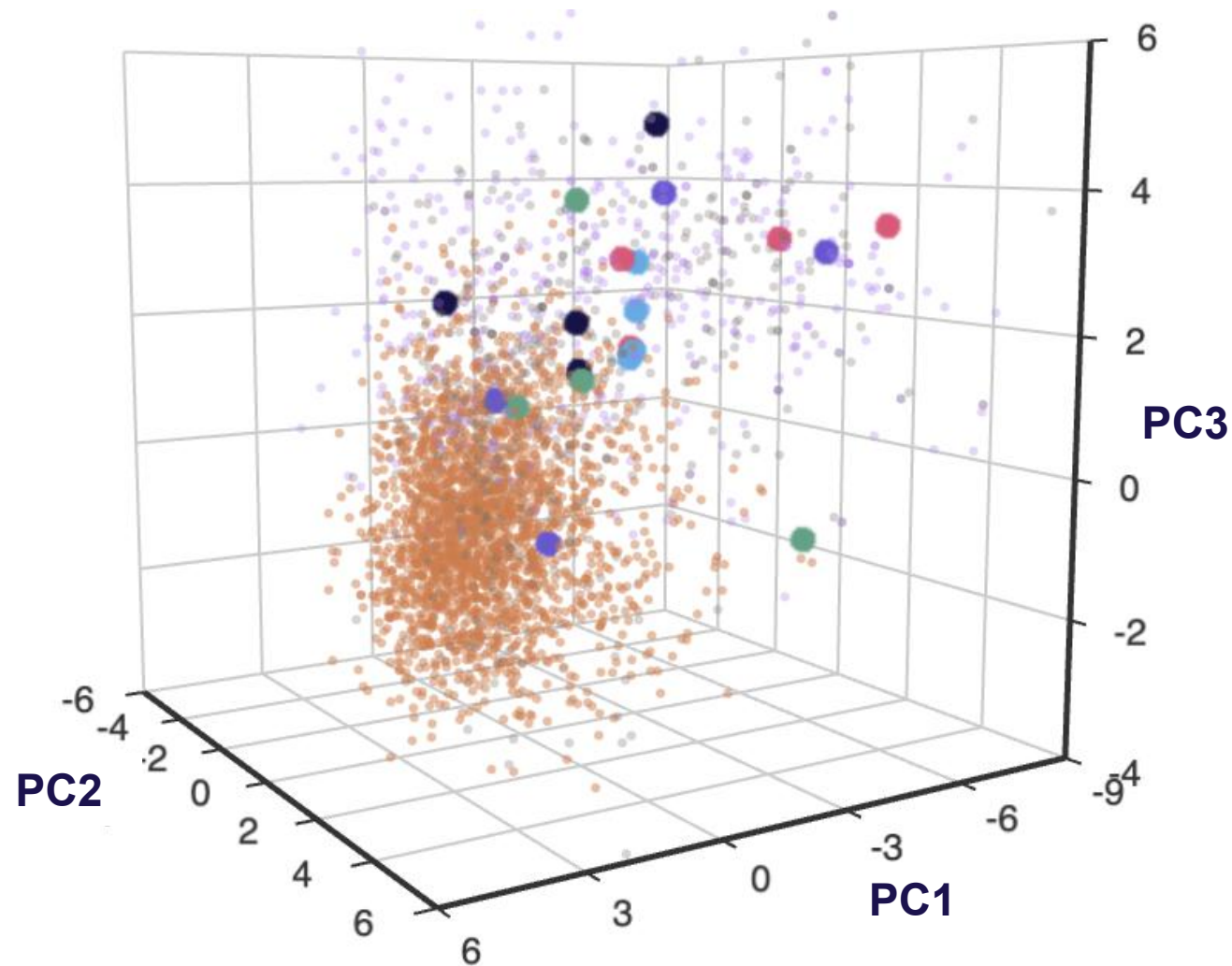


CONECTA® OFFERS 1B+ CURATED DIVERSE STARTING POINTS FOR DRUG DISCOVERY

- **Topologically rich** structures
- **Wider array of vectors** available to engage targets with **precision/selectivity**
- Broadest range of proven mechanisms

1. Our Curated, Diverse Chemical Space Reveals Untapped Solutions for Hard to Drug Targets

DIVERSITY



Transcription Factor Example

Ordered waters in key interfaces

Source: <https://ars.els-cdn.com/content/image/3-s2.0-B9780121486600500147-f13-03-9780121486600.jpg>

Gene Expression

Diverse Chemistry

Cell Morphology Data

ADMET Data

Bioassay Data

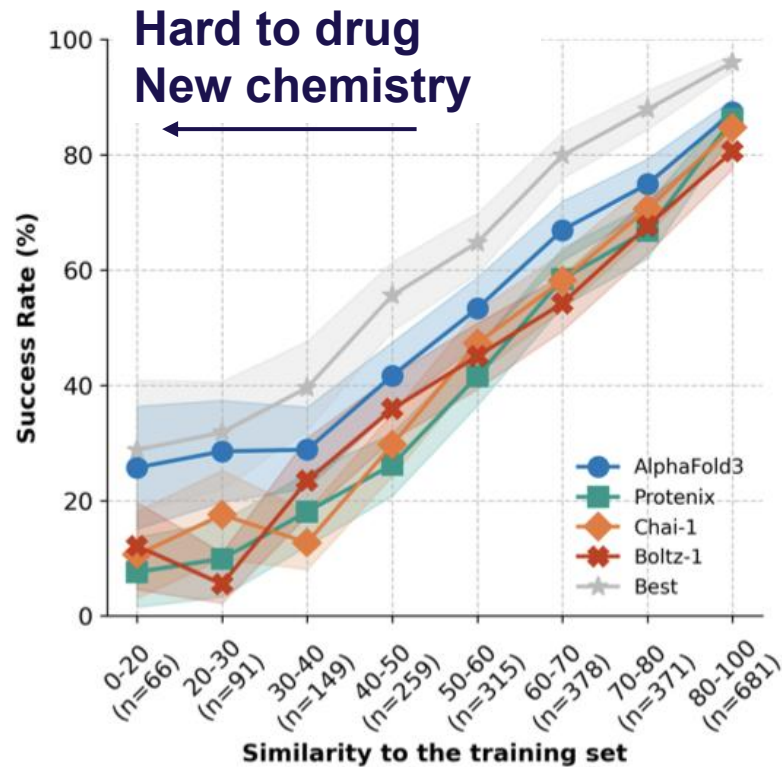
Structural Data

1 B+ high quality, curated proprietary data network
Proprietary generalizable transfer learning methods

~Patent pending

2. CONECTA[®]'s Target Specific and MoA Directed Bioactivity Approach Overcomes Structural Modeling Difficulties

Structure-only AI Methods Perform Best on Problems Similar to What's Known and are Hard to Differentiate

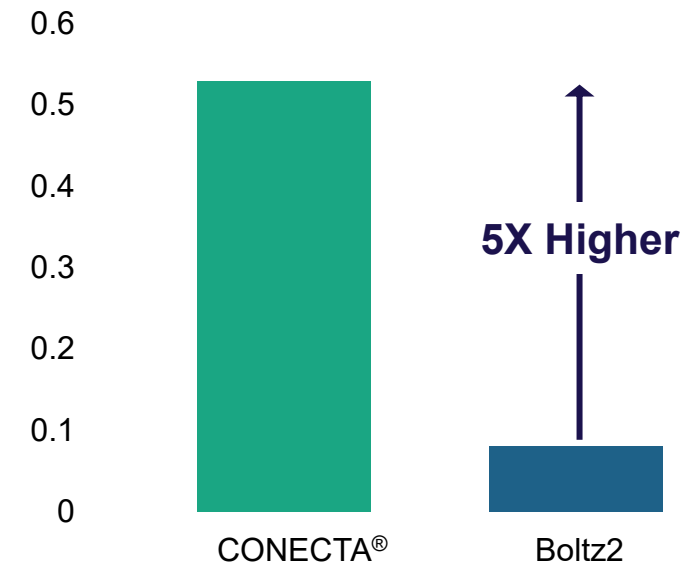


Skrinjar et al, bioArxiv, 2025

CONECTA[®] Outperforms Leading Structure-First Models

Transcription Factor Performance Comparison

Spearman Correlation with Experimental Transcription Factor Potency



3. Optimizing Diverse Chemistry Is Often Challenging, Integrated Decisioning Against TCP Increases Efficiency

Chemical Diversity Often Creates Optimization Challenges

Synthetic complexity

Limited SAR tractability

Supply and scalability issues

ADME challenges

Potential for polypharmacology

Industry timeframe of 3-6 years from hit to optimized candidate

CONNECTA® Ranks Top 1% of Predicted Hits *in silico* Against TCP to Start with the Most Advanceable Leads

	202	215	2267	1856	skyclarys
Bioactivity					
ADME					
Safety					
Accessibility/ Medchem Profile					

Ranked on bioactivity and 60+ drug like properties to deliver a Target Candidate Profile (TCP)

Equivalent to running 1,000 years of wet-lab experiments in < 2 days

3. Precision *In Silico* Hit Ranking to TCP Enables Predictable Path Across Target Types

Targets	Category	Mechanisms
NRF2	Transcription Factor	Covalent
Undisclosed	Transcription Factor	Allosteric, Covalent
Undisclosed	Transcription Factor	Allosteric
Undisclosed	Cytokine receptor	PPI
Undisclosed	Cytokine receptor	Noncovalent, Covalent, PPI

CONNECTA[®] Advantages

- **1 B+** Starting Points Optimized for Drug-like Properties
- **Unparalleled Access** to Diverse Chemotypes and Mechanisms
- **Efficient Path** From Hits to DCs <24 months
- **Higher Probability** of Success and Clinical Optionality

CONNECTA[®] Platform

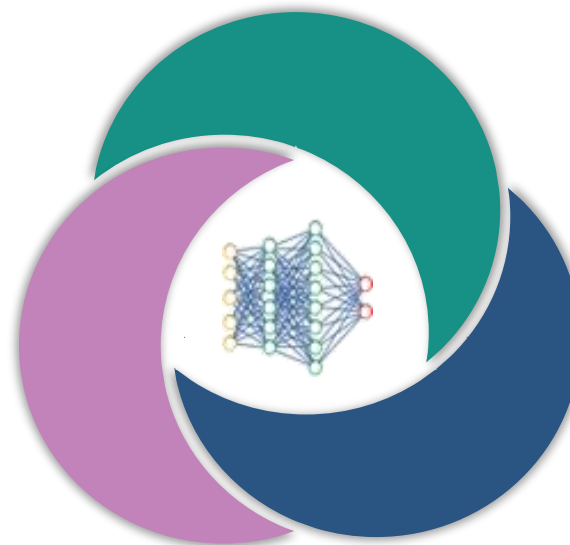
Decoding the language
of nature's diverse
chemical intelligence to
**predictably develop
breakthrough small
molecule medicines**

3 Transformational Pillars

DIVERSE, UNTAPPED

Bioactive Chemical Space

INTEGRATED
Decisioning



PRECISION
Pathway
Connections

First in Class (FIC) Pipeline –

Biologic Replacements and Transcription Factors in
Inflammation and Immunology (I&I)

Montai's High Value I&I Pipeline of FIC Once Daily Orals

Target (Lead Indication)	Discovery	Lead Optimization	IND Enabling	Phase 1	Mechanisms
NRF2 (Ulcerative Colitis)				 FIH 2026	Covalent
Transcription Factor					Allosteric, Covalent
Transcription Factor					Allosteric
Biologic Replacement					PPI, Covalent
Oncology 					Undisclosed

Additional programs in discovery or available for partnering

Learnings on Making AI/ML Work in Drug Discovery

Define the right objective function end-to-end

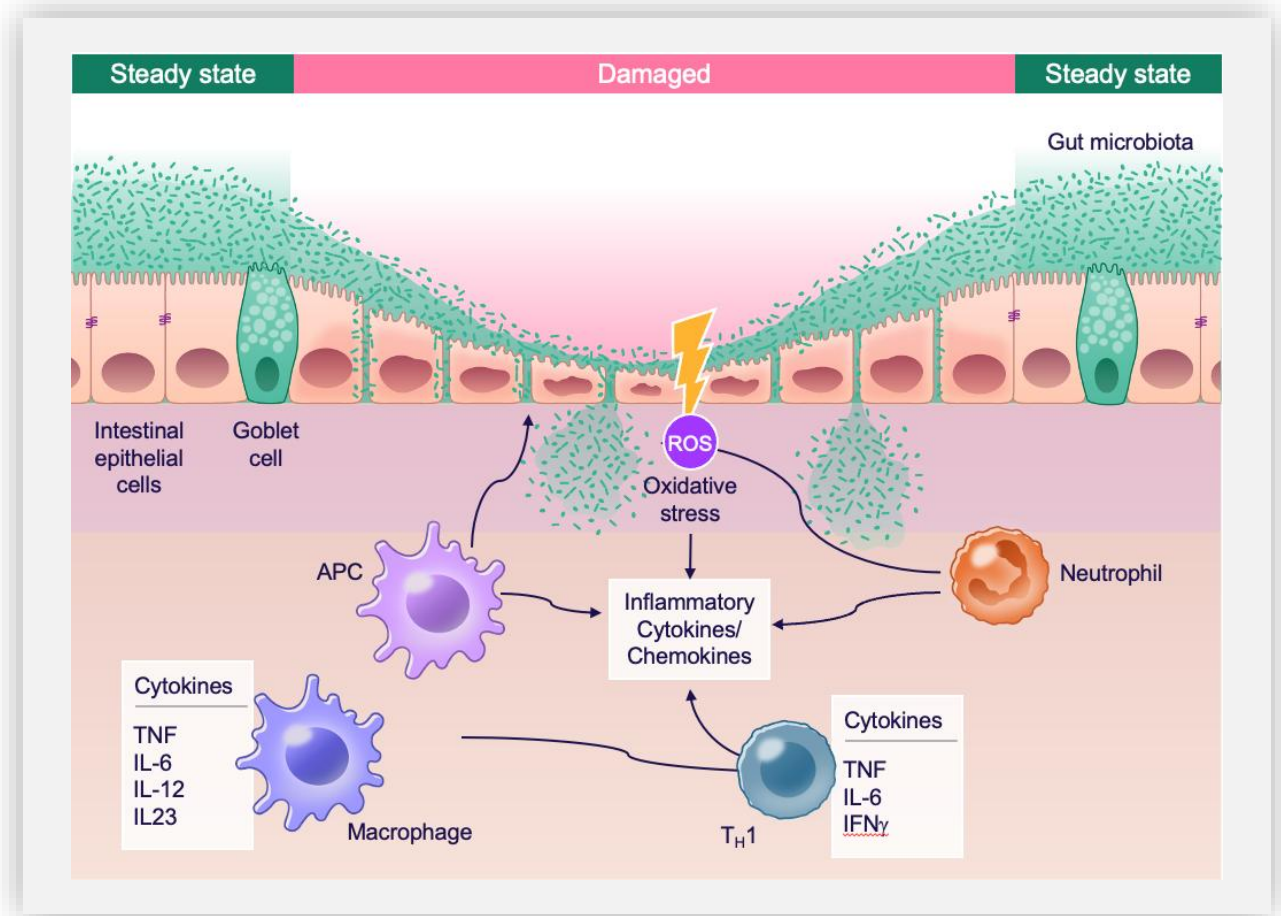
Focus on decisions vs. information or models

Team and culture are critical

NRF2 | Unique Opportunity to Address the 3 Drivers of UC in One Therapy

Primary Disease Drivers

- 1 Epithelial Barrier Disruption
- 2 Immune-mediated Oxidative Tissue Damage
- 3 Acute and Chronic Inflammation



Extensive Body of Preclinical Evidence Demonstrates NRF2 Agonists Are Validated in Multiple Preclinical Models of IBD

Kobayashi, T., et al. (2020). Nat Rev Dis Primers.; Piotrowska, M., et al. (2021). Pharmacological Research.; Kim, M. J. and J. H. Jeon (2022). Int J Mol Sci.; Sahoo, D. K., et al. (2023). Front Endocrinol (Lausanne)

Piotrowska, M., et al. (2021). Pharmacological Research 163; Kim, M. J. and J. H. Jeon (2022). Int J Mol Sci 23(5); Gross, C. C., et al. (2016). Neurol Neuroimmunol Neuroinflamm 3(1): e183; Sahoo, D. K., et al. (2023). Front Endocrinol (Lausanne) 14: 1217165.

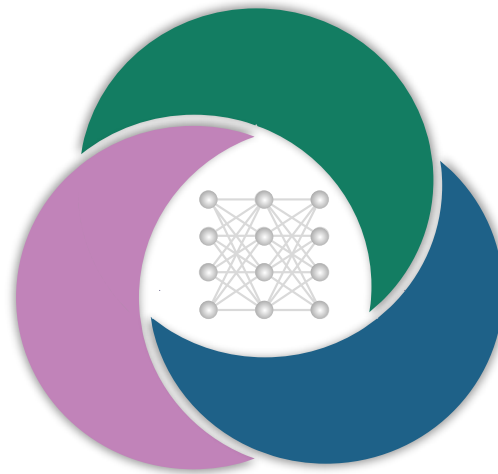
NRF2

CONNECTA® AI Unlocked Precision Targeting of NRF2 Biology

CHALLENGES

NRF2's potential in large chronic diseases like UC has been **limited by potency, bioavailability, and off target safety and tolerability issues**

CONNECTA®



OUTCOME

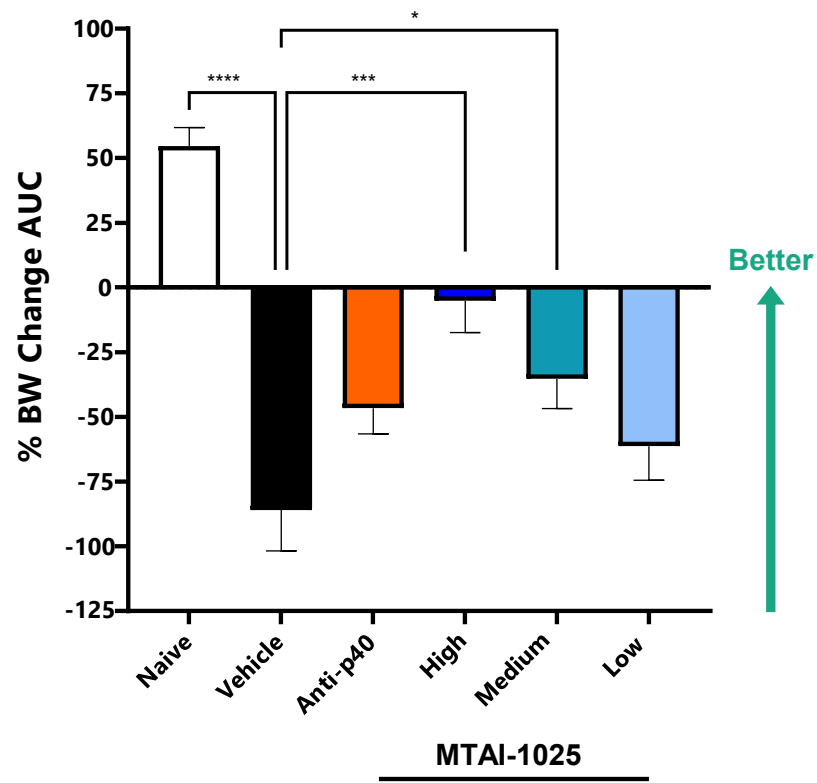
Precision ranked potent KEAP-1 engagers with superior selectivity to known off target liabilities

- **Structurally differentiated chemistry**
- Avoids **niacin receptor** activation like Tecfidera®
- Improved safety panel **selectivity** vs. Skyclarys®

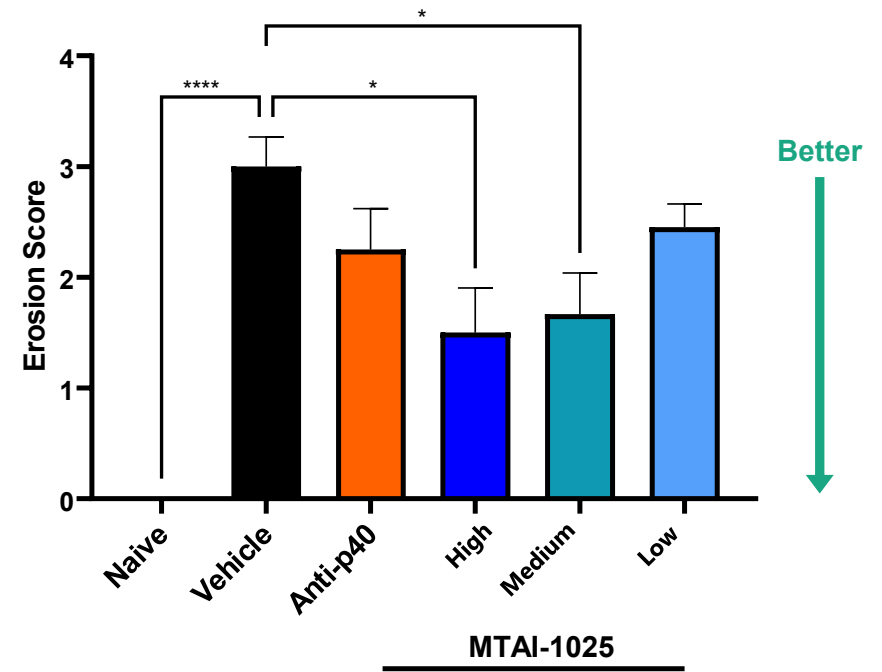
NRF2 | MTAI-1025 Showed Significant Dose Responsive Efficacy Superior to Biologic Control in 14 Day Murine DSS Colitis Model

Oral Once Daily Treatment Improves Weight Loss and Histopathology Score

AUC of Body Weight



Colon Histology Erosion Score



Anti-p40 positive control is mouse equivalent of anti-IL12/IL23 biologic Ustekinumab (Stelara®)
14 day oral once daily treatment, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001

NRF2 | MTAI-1025 is Highly Selective Versus Approved NRF2 Therapeutics for Safe Chronic Dosing

Safety Profile

CRITERIA	THRESHOLD	Montai DC
		MTAI-1025
hERG (IC50)	> 30 µM	> 30 µM
AMES (DEREK)	Negative	Negative
CYP Inhibition (IC50)	≥10 µM	≥10 µM
BSEP/BCRP/ OATP/PGP Inhibition (IC50)	>10uM	>10 µM

Selectivity vs Approved NRF2 Agonists

Family (Gene)	Montai Development Candidate		SKYCLARYS	
	MTAI-1025 (µM)		Omaveloxolone (µM)	
	Agonist (EC50)	Antagonist (IC50)	Agonist (EC50)	Antagonist (IC50)
α1A-adrenergic receptor	>50	>50	>50	1.92
α2A-adrenergic receptor	>50	>50	2.19	>50
β1-adrenergic receptor	>50	>50	>50	0.80
β2-adrenergic receptor	>50	>50	>50	1.36
Cannabinoid receptor CB2	>50	>50	0.240	>50
Dopamine receptor D1	>50	>50	>50	0.92
Dopamine receptor D2	>50	>50	2.20	>50
Endothelin receptor A	>50	>50	>50	4.71
Histamine H1 receptor	>50	>50	>50	1.62
Histamine H2 receptor	>50	>50	>50	1.32
Muscarinic acetylcholine receptor M1	>50	>50	>50	2.86
Muscarinic acetylcholine receptor M2	>50	>50	1.90	>50
δ-type opioid receptor	>50	>50	1.32	>50
κ-type opioid receptor	>50	>50	5.30	>50
μ-type opioid receptor	>50	>50	4.18	>50
5-HT1A	>50	>50	3.94	>50
5-HT2A	40.62	>50	>50	5.04
Vasopressin V1A receptor	>50	>50	>50	2.18
Androgen receptor	>50	9.55	>50	0.18
Glucocorticoid receptor	>50	8.21	>50	0.31

Good

Moderate

Poor

Biologic Replacement Example

CONNECTA® AI Unlocked Precision Targeting of Undrugged

CHALLENGES

High value hard to drug target **without known binding pockets** for small molecules



OUTCOME

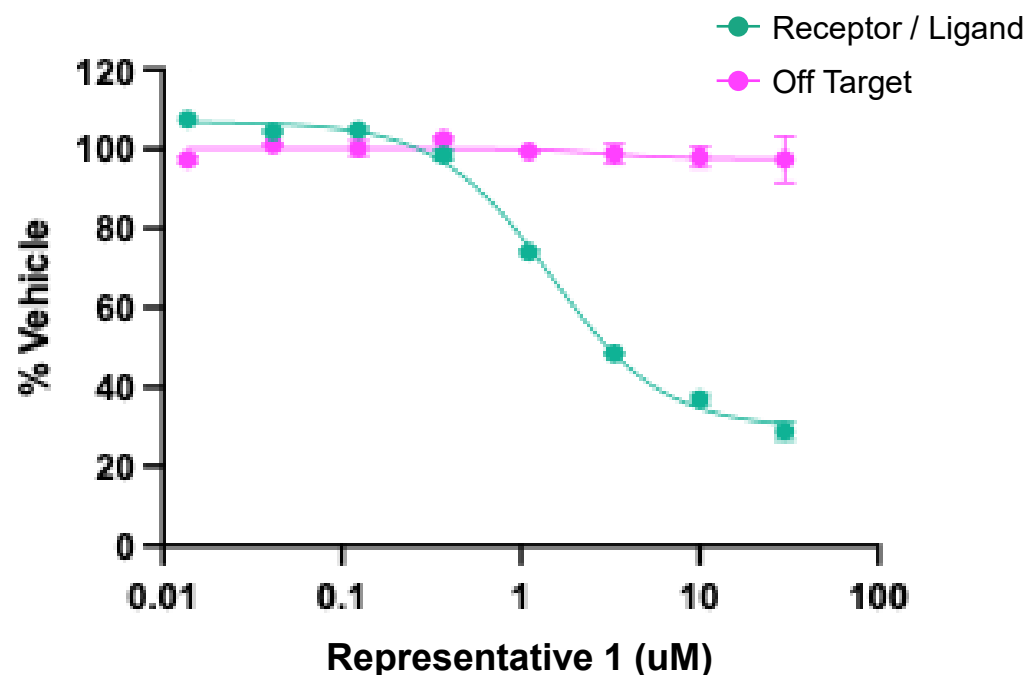
Precision ranked chemistry that blocked downstream pathway activation

Multiple MoAs including a series of novel PPI inhibitors

Biologic Replacement | Unoptimized FIC Compound Shows Disruption of Ligand / Receptor Interaction in Multiple Assays

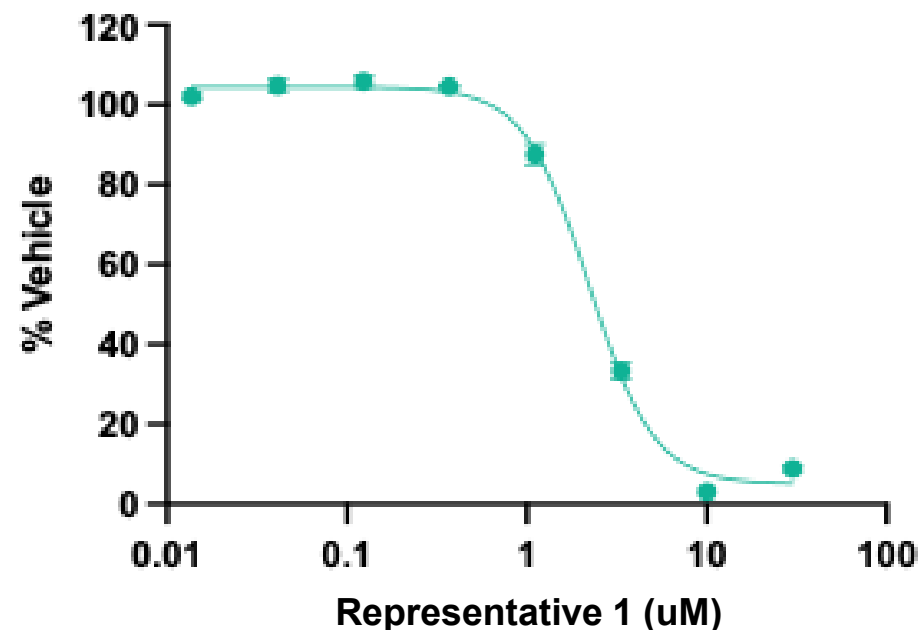
Biologic Replacement PPI Antagonism

Biochemical Assay



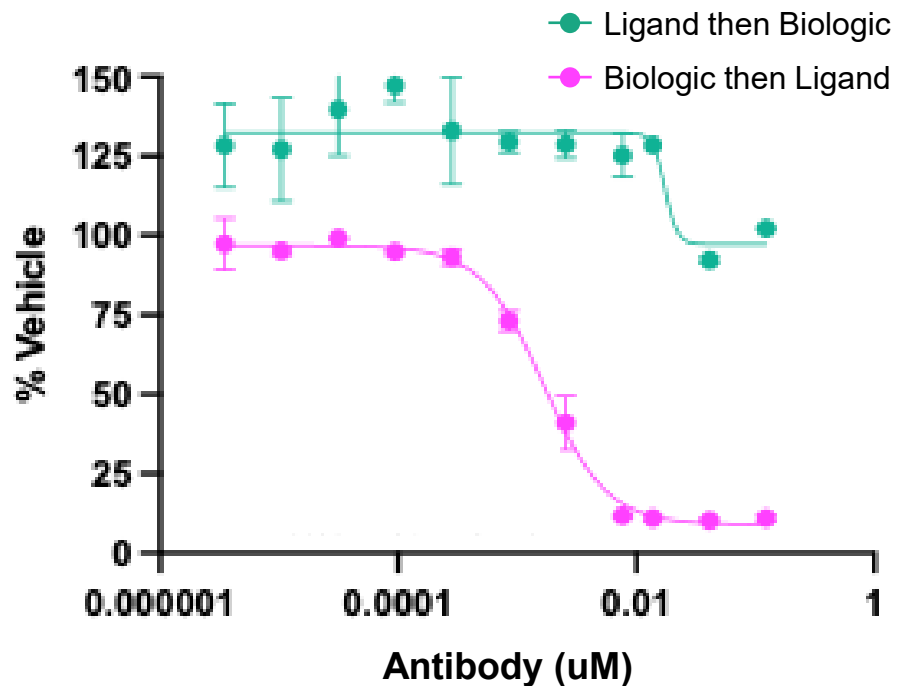
Biologic Replacement PPI MoA

Cellular Assay

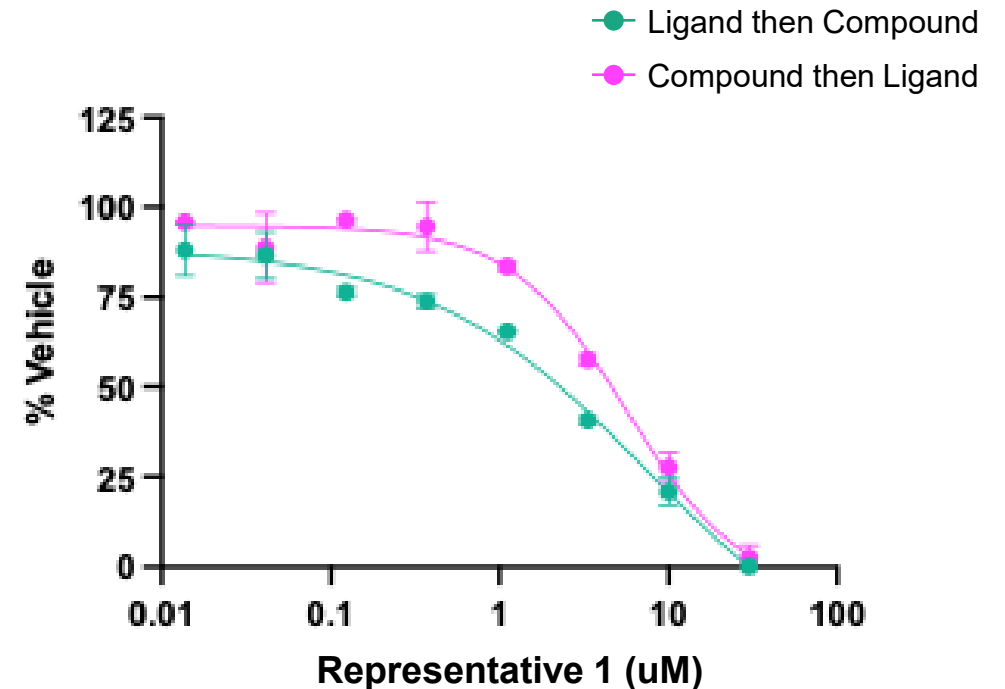


Biologic Replacement | FIC Compound can Antagonize Bound Ligand, something the Biologic cannot Achieve

Biologic



Unoptimized CONECTA® Molecule



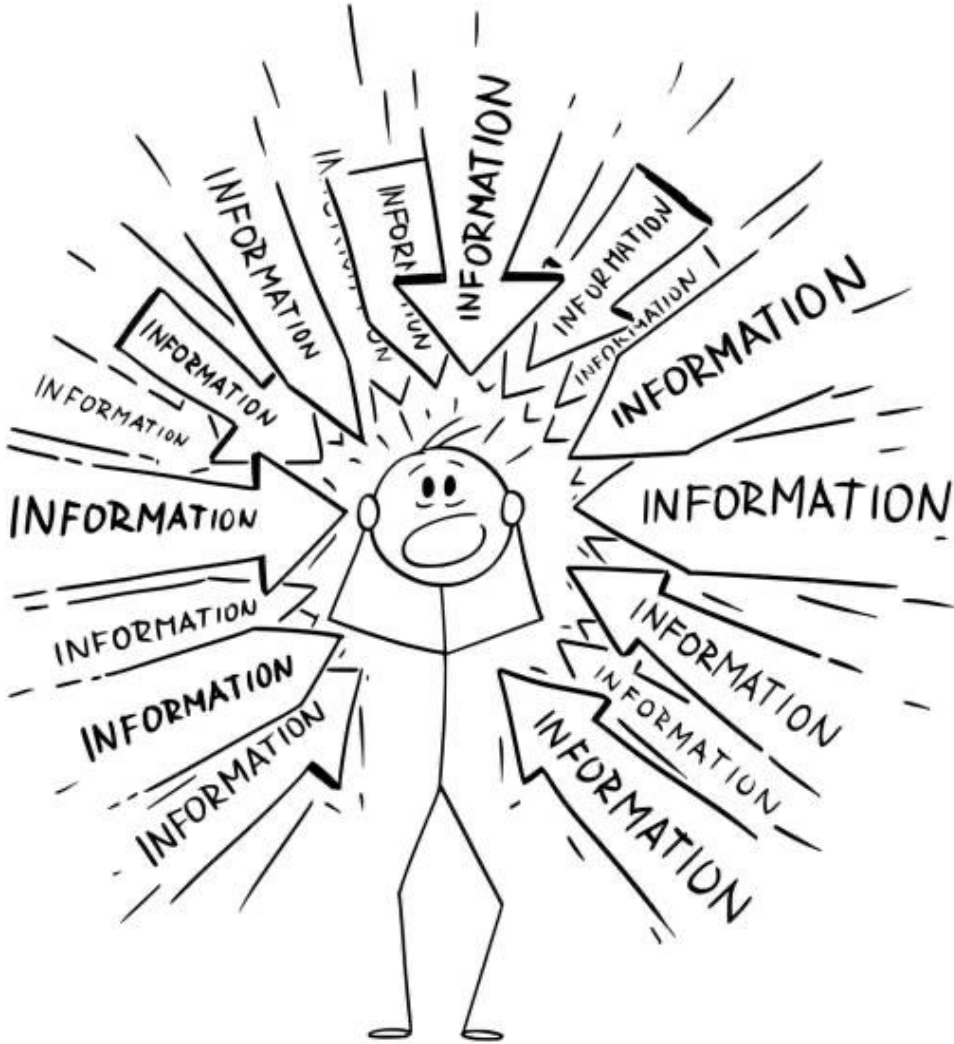
Learnings on Making AI/ML Work in Drug Discovery

Define the right objective function end-to-end

Focus on decisions vs. information or models

Team and culture are critical

Information Does Not Move Programs Forward - Decisions Do



**Clear criteria for decision making –
must-have vs. nice to have**

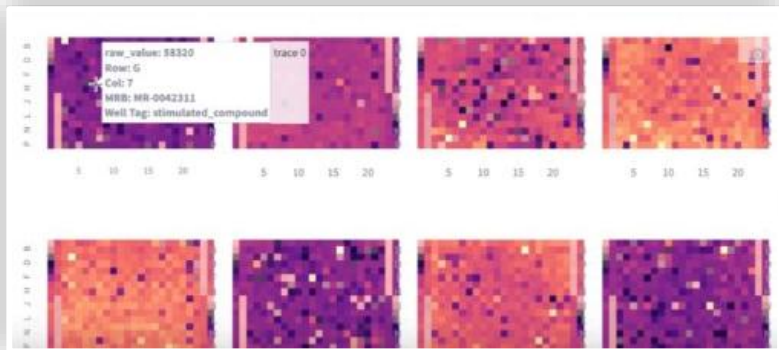
**Focus on how modeling can support or
de-risk the must-haves**

**Continuous learning on the outcomes of
decisions to improve models and tools**

CONNECTA[®] Automation Unlocks Productivity Across Tech and R&D Teams with Integrated Decisioning Tools

AUTOMATED DATA HANDLING

Saves **90%** of Time



OPTIMIZED AND AUTOMATED ML

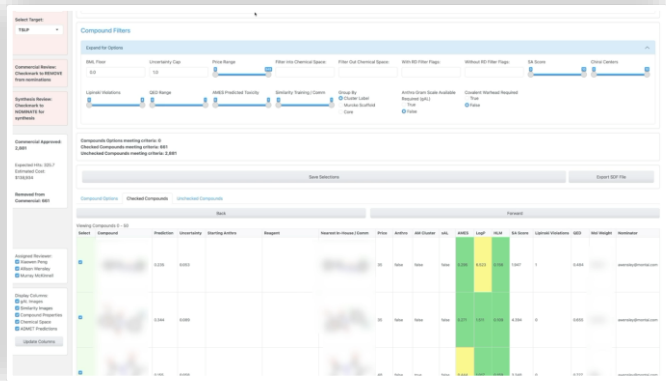
20x More Efficient

1,500,000
SPEED:
Compound predictions
per minute

0.00003¢
EFFICIENCY:
Compute cost
per prediction

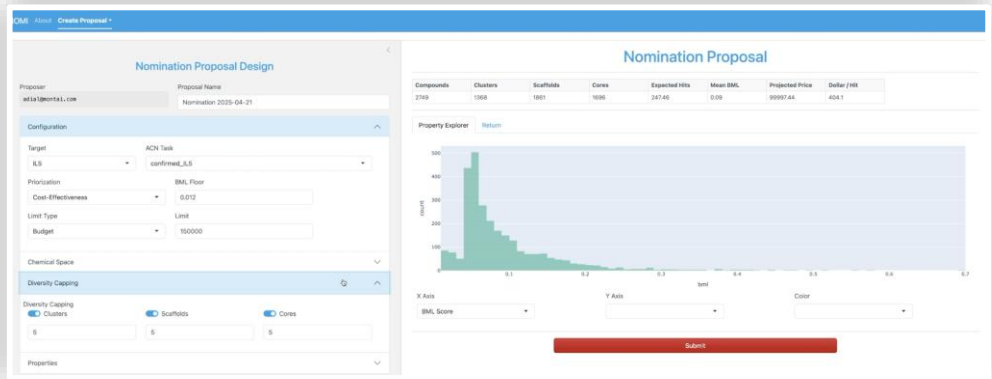
DATA ANALYSIS AND REVIEW TOOLS

Enables Rapid Expert Feedback Integration and Power ML



DECISION SUPPORT TOOLS

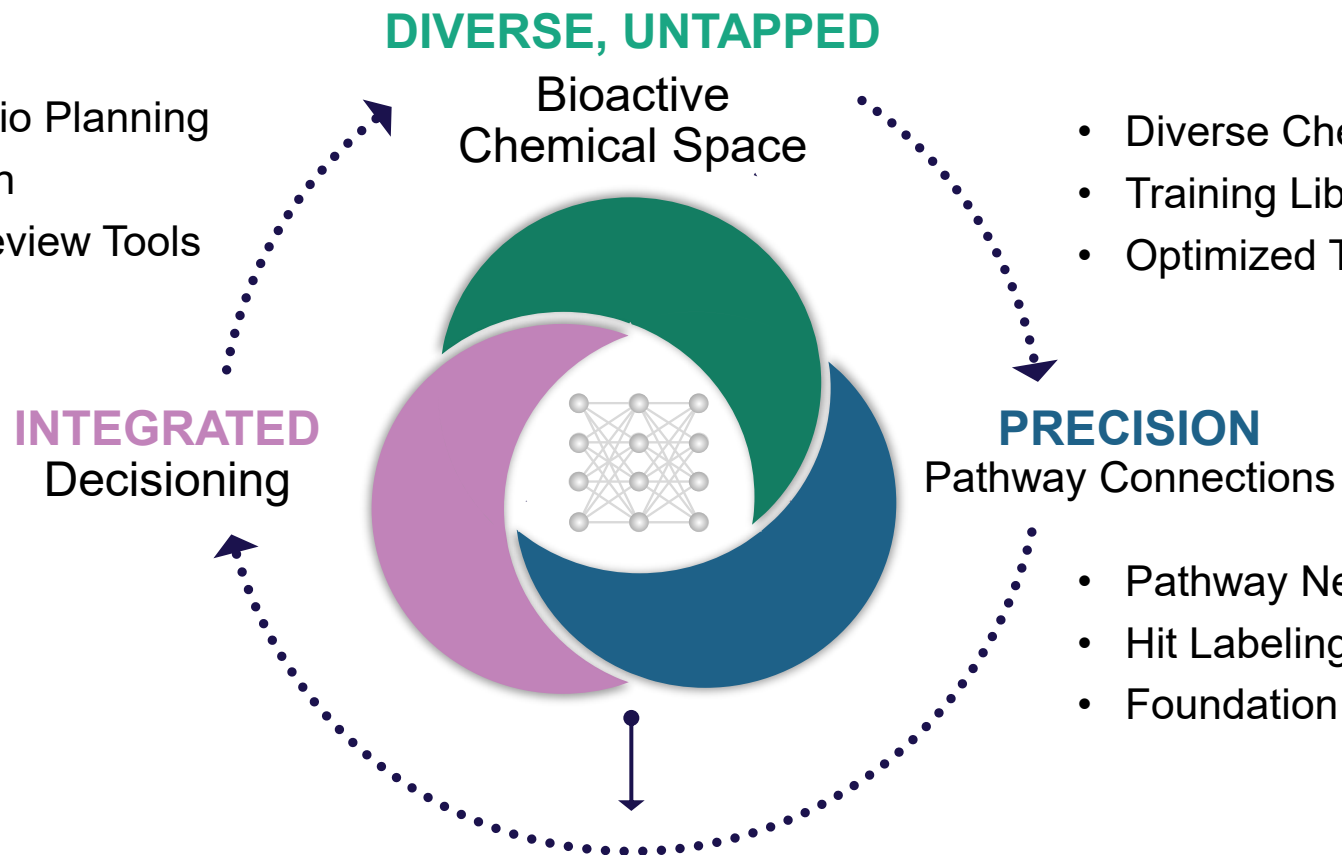
Enables Real-time Scenario Planning and Optimization - Nomination



CONNECTA[®] Continuous Learning Drives Gains in Chemistry, Ranking and Decisioning

INTEGRATED

- Multi-factorial Scenario Planning
- Enhanced Automation
- Data Analysis and Review Tools
- Medchem Assist



- Diverse Chemical Space Expansion
- Training Library Optimization
- Optimized Target/Assay Selection

- Pathway Network and MoA Data
- Hit Labeling/Ensembling Strategies
- Foundation Models Gains

✓
Increases PoS

✓
Improves Efficiency

✓
Self Reinforcing

Learnings on Making AI/ML Work in Drug Discovery

Define the right objective function end-to-end

Focus on decisions vs. information or models

Team and culture are critical

Building a Cross-Functional Culture is Critical



Source: https://blog.kainexus.com/hubfs/teamwork_-_puzzle.jpg

Shared, written understanding of goals and objectives

Shared glossary and task chain

Cross functional core program teams to improve communications

Opportunities for shared learning and evaluation

Proven Leadership Team...

AI Platform Builders



Margo Georgiadis
Co-Founder and CEO,
Board Director

30+ yrs. executive leadership;
4x CEO/President
across industries



Hok Hei Tam, PhD
Co-Founder and CTO

8+ yrs. venture creation,
founded 4 companies,
13+ years scientific software;
2x AI/ML CTO



William Hayes, PhD
VP, Head of Data Science
& Systems Biology

20+ yrs. life science
digital technologist



Matt Davis, PhD
Head of Machine Learning

10+ yrs. leading advanced AI/ML
teams across industries



45+

Drugs to
the Clinic

14

Drugs
Approved

4

Modalities
Innovated

Leaders
in ML

Drug Developers



Lamya Shihabuddin, PhD
CSO

25 yrs. pharma and biotech
R&D leadership;
2x CSO



Annie Chen, MD, MPH
Consulting CMO

22+ yrs. Immunology,
oncology, and biotech
leadership



Kyle Chiang, PhD
COO

15+ yrs. public/private biotech;
3x COO/CSO



Craig Correll, PhD
VP, Head of Early
Discovery & Immunology

25+ yrs. small molecule
drug discovery experience



Alan Collis, PhD
VP, Preclinical Development

38+ yrs. Development &
Discovery – DMPK, PK-PD,
CMC



Murray McKinnell, PhD
SVP, Drug Discovery

20+ yrs. Drug development,
medicinal chemistry



Thank you
