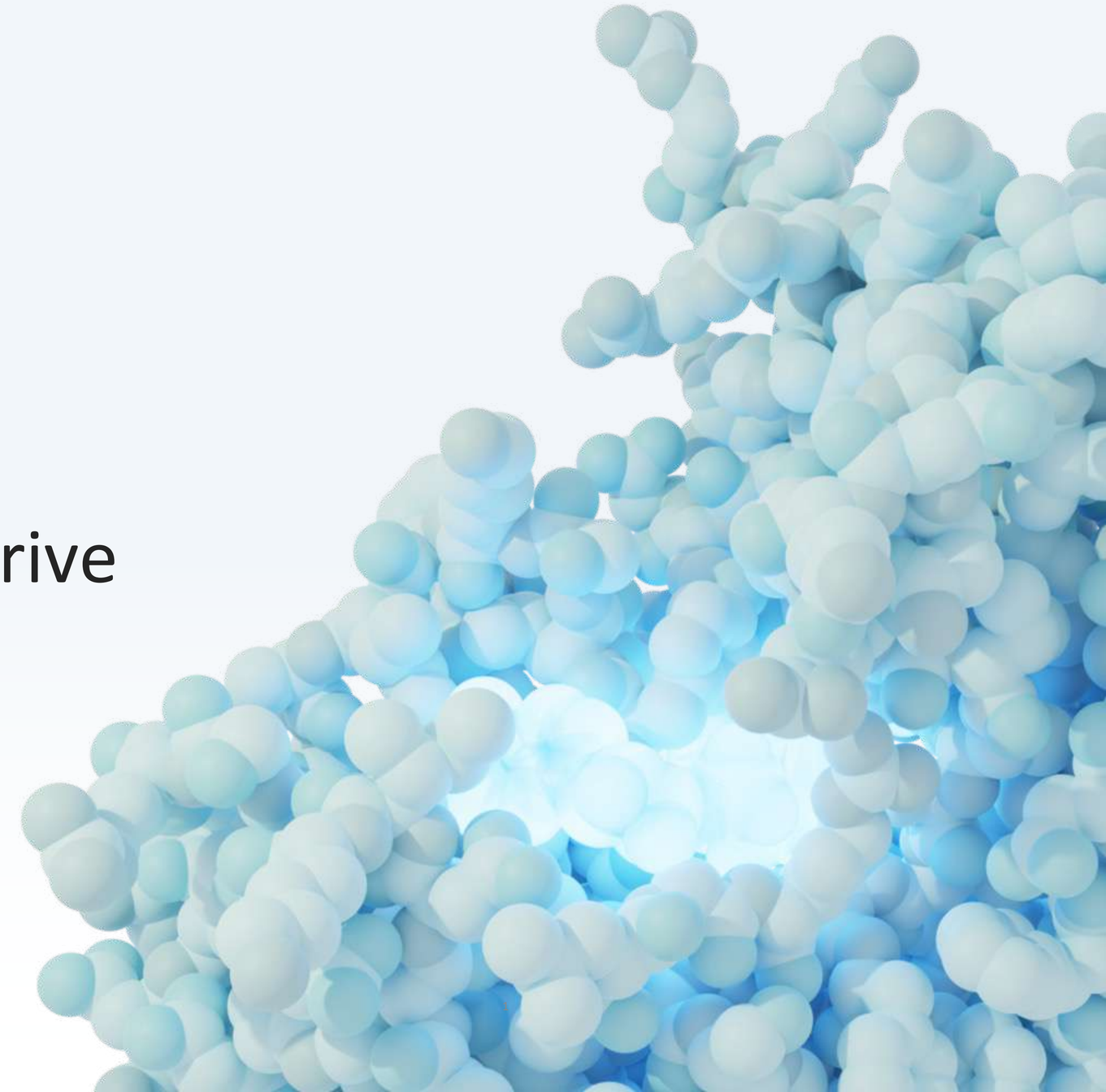
Iambic

From Models to Medicines: How Iambic Technologies Drive Discovery



Delivering on AI-driven drug discovery

Technology



Industry-leading technologies for drug-discovery: structure prediction, molecular optimization, and laboratory automation

Clinical Data



AI-DD: some of the first, fastest, strongest clinical data

IAM1363 (HER2): anti-tumor activity, safety, combinability

Pipeline



New INDs in 2026: KIF18A & CDK2/4

Multiple additional internal programs, driven by Iambic platform

Partnerships



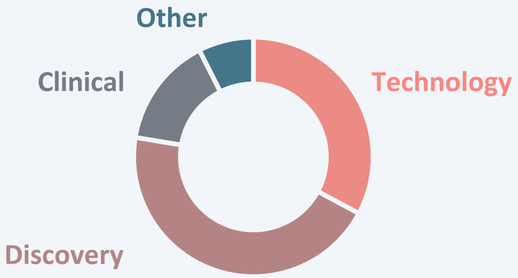
Spanning discovery, technology enablement, clinical research

Four partnerships signed in the past year

In 2026, Iambic will expand on the thesis:
better technology leads to better medicines

Iambic at a Glance

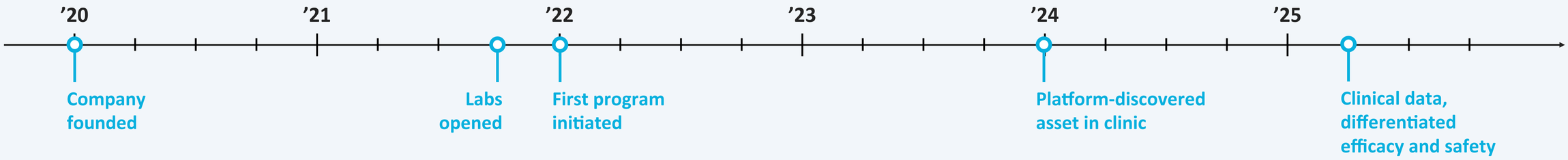
>100
EMPLOYEES



>$300M
RAISED IN CAPITAL

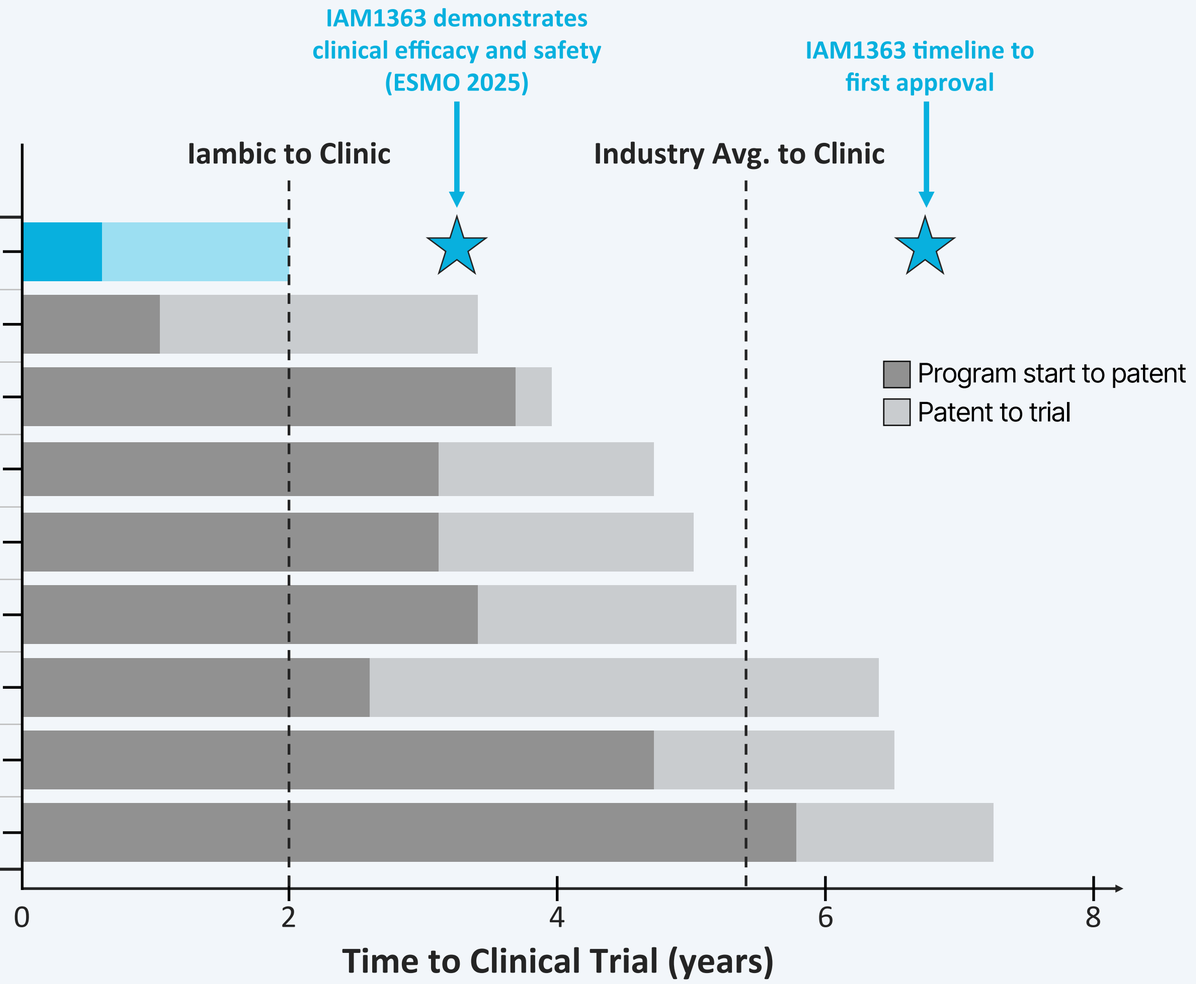
Global
SAN DIEGO BASED





Realizing the impact of AI for patients

Company	Development Candidate	Target
Iambic	**IAM1363**	**HER2**
Relay	RLY-1971	SHP2
Relay	RLY-4008	FGFR2
Exscientia	EXS-21546	A2A Receptor
Pharos iBio	PHI-101	CHK2
Exscientia	DSP-1181	5-HT1a Receptor
Nimbus	NDI-010976	Acetyl-CoA Carboxylase
Exscientia	DSP-0038	5-HT1a/5-HT2a Receptor
BenevolentAI	BEN-2293	pan-TRK

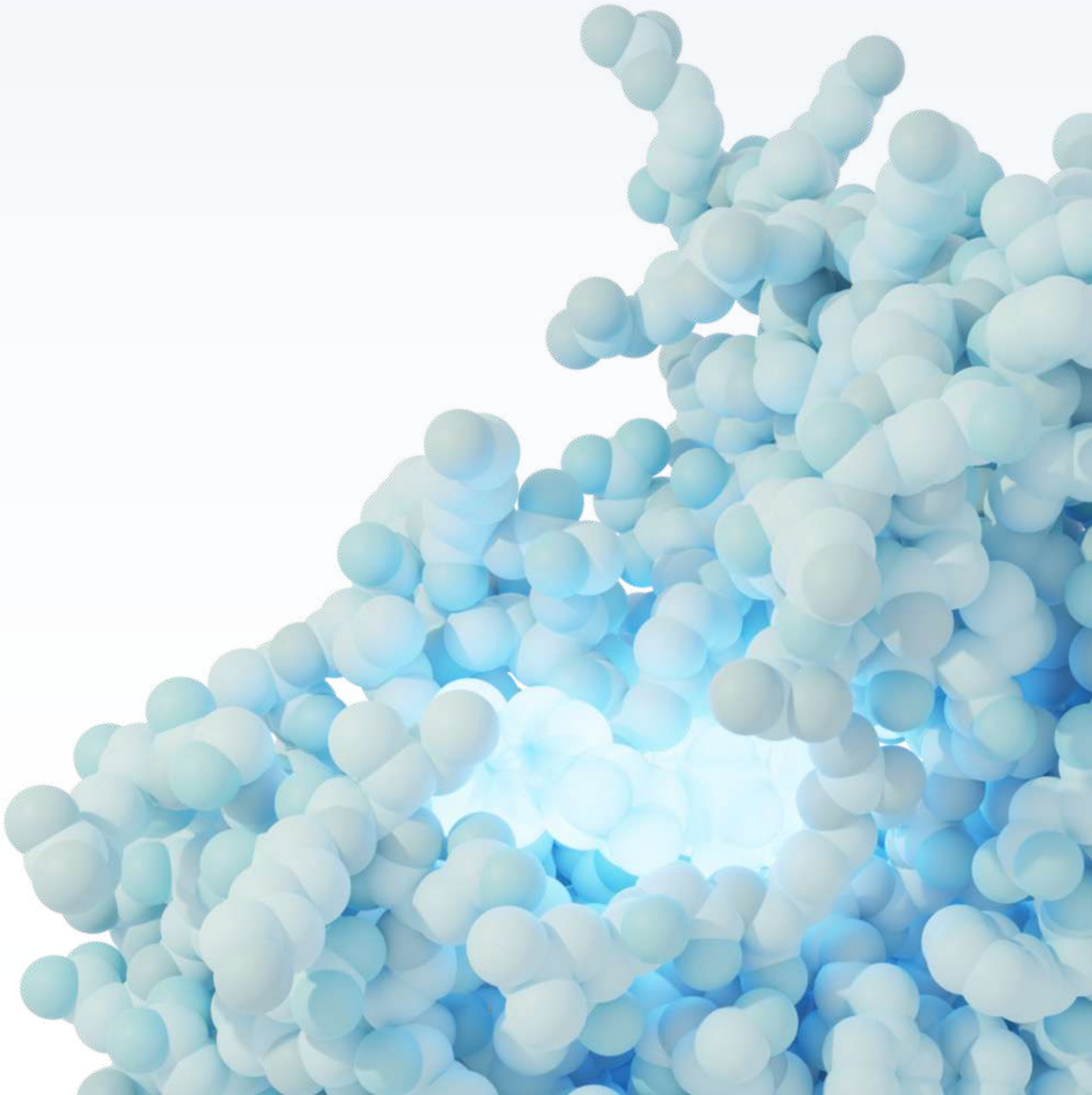


Adapted from Boston Consulting Group analysis: Nature Reviews: Drug Discovery (2022) https://doi.org/10.1038/d41573-022-00025-1.
Abbreviations: 5-HT1A, serotonin 1A receptor; A2A, adenosine A2A receptor; CHK2, checkpoint kinase 2; FGFR2, fibroblast growth factor receptor 2; HER2, human epidermal growth factor receptor 2; SHP2, src homology 2 domain-containing phosphatase 2; TRK, tropomyosin receptor kinase.

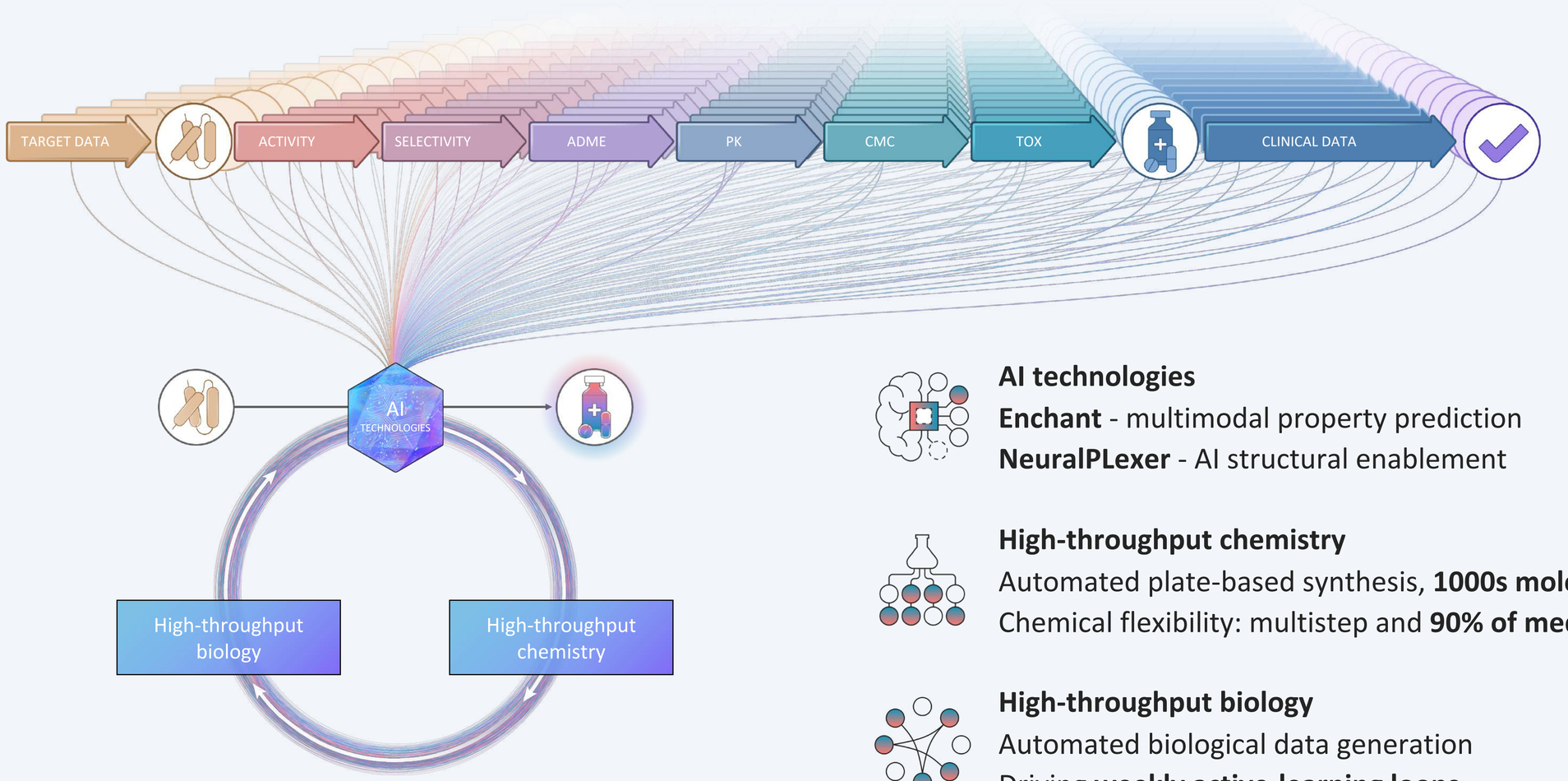
Iambic

Technology

Integrated Experimental &
Computational Activities



The Iambic Discovery Platform



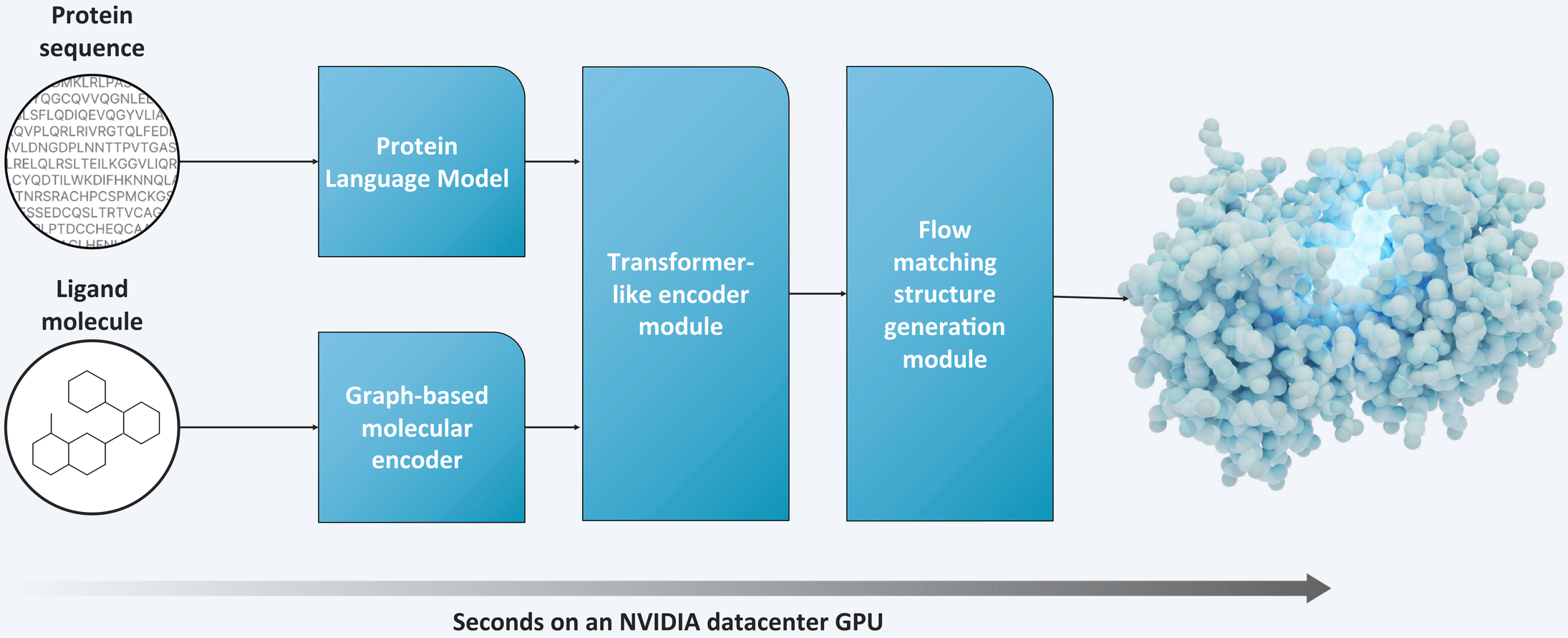
AI technologies
Enchant - multimodal property prediction
NeuralPLexer - AI structural enablement

High-throughput chemistry
Automated plate-based synthesis, **1000s molecules/week**
Chemical flexibility: multistep and **90% of medchem reactions**

High-throughput biology
Automated biological data generation
Driving **weekly active-learning loops**

IN COLLABORATION WITH Caltech NVIDIA

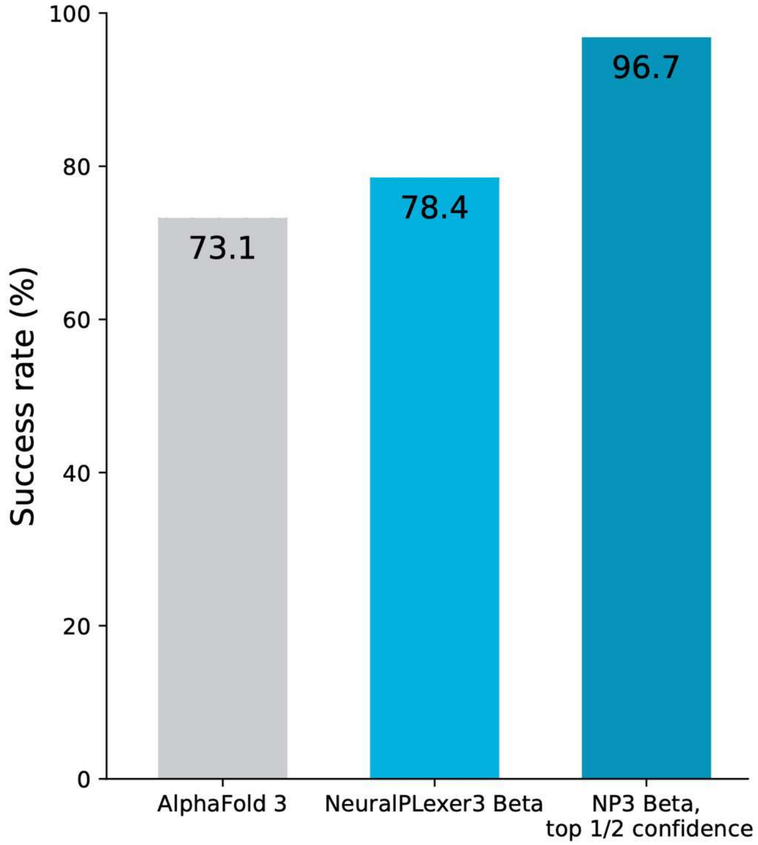
Iambic NeuralPLexer



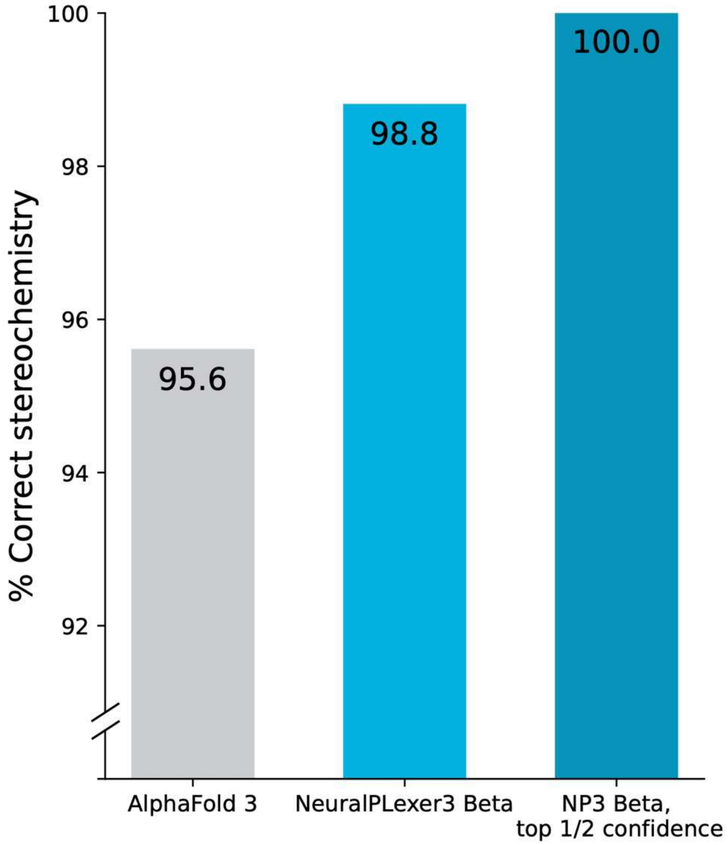
Z Qiao, et al., Nature Mach. Int. (2024); Z Qiao, et al., arXiv 2412.10743v2 (2024)

NeuralPLexer: Best-in-class Protein-ligand Prediction

PoseBusters V2, no ground-truth structure provided

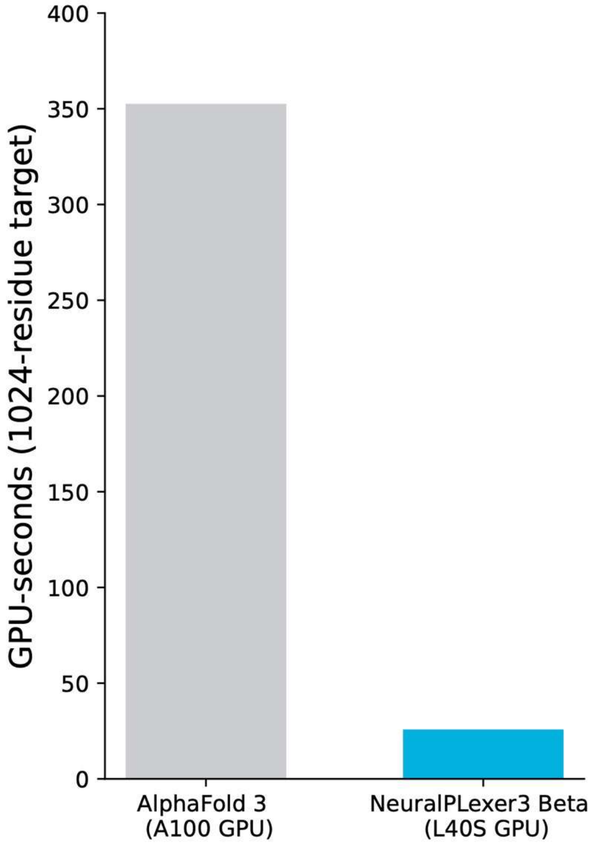


More accurate structures…



Better Physics…

Inference time



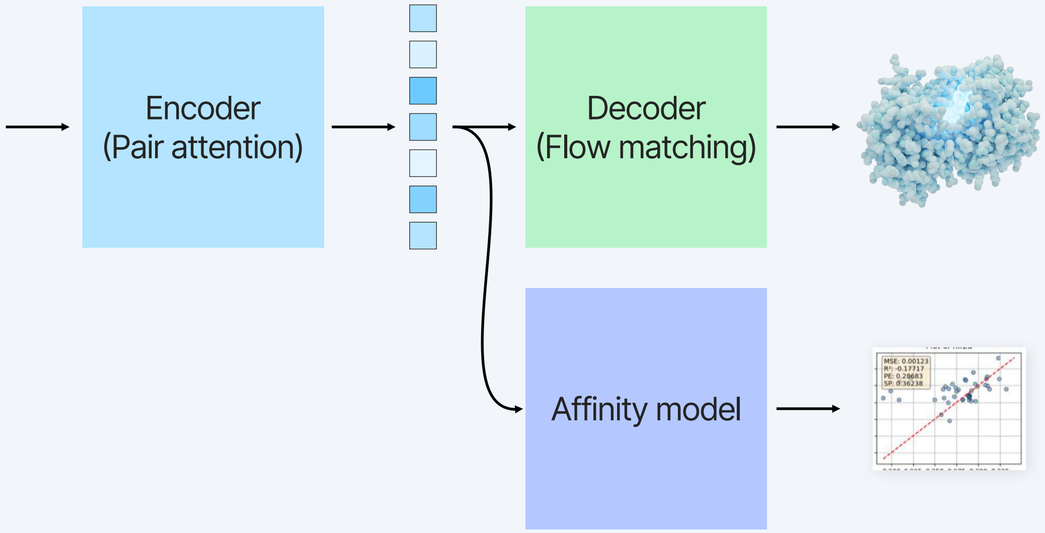
And much faster.

Z Qiao, et al., arXiv:2412.10743v2 (2024) with open-source benchmarking

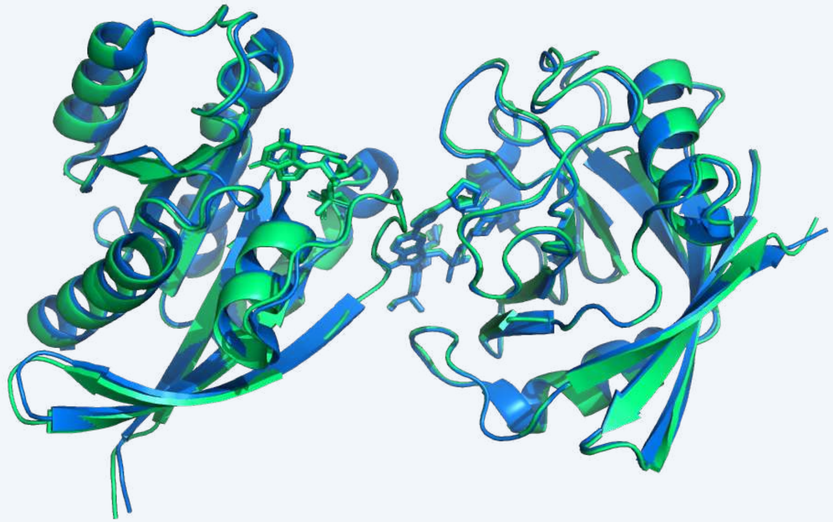
Abbreviations: AF3, AlphaFold 3; NP2, NeuralPLexer; NP3, NeuralPLexer; PB-valid, protein block valid; RMSD, root mean square deviation.

Structural enablement that drives real programs

Affinity prediction that delivered unprecedented control of polypharmacology in our CDK2/4 development candidate



Structurally enabling molecular glue design for partners, and in our own pipeline



Revolution Medicines

Public domain example
Held-out reference: 8TBM
Protein RMSD: 0.48Å
Ligand RMSD: 0.76Å

Enchant: a Multimodal Transformer for Drug Discovery



- Enchant is a large multimodal transformer model
- We achieve scale by broadening the scope of what is considered “data”
- Enchant trained at scale achieves an exciting thing:

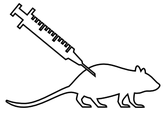
Enchant’s ability to predict a given property can be improved by providing on more data on a different property

https://openreview.net/pdf?id=Ya5OHw7lZ8

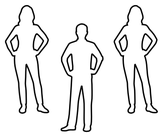
Enchant learns to…



predict expensive assays
using data from
cheaper assays
(on different molecules)

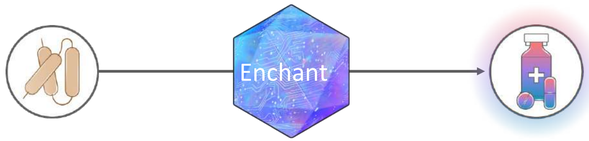


predict *in vivo* properties
using data from
in vitro assays
(on different molecules)

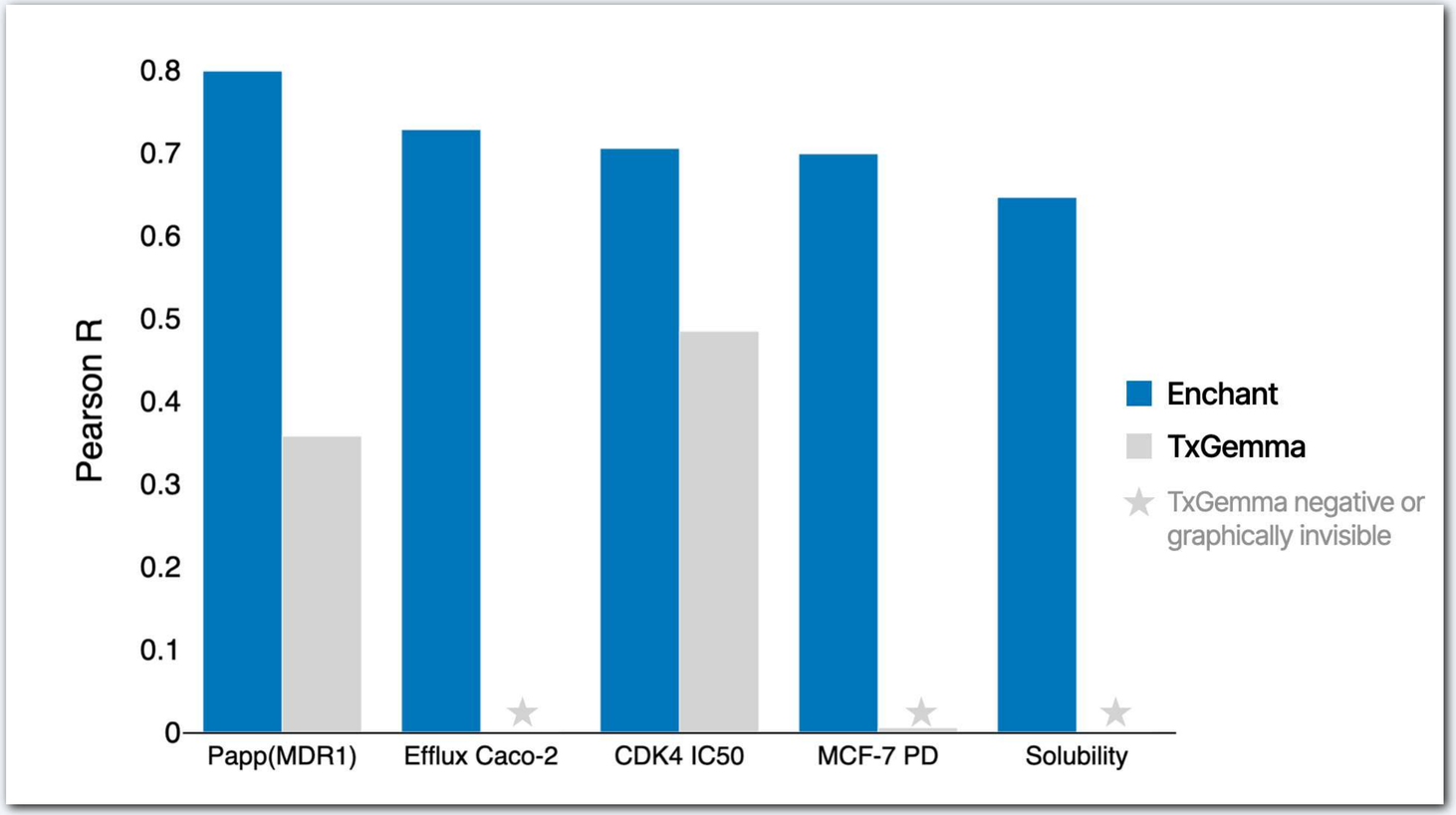


predict clinical properties
using data from
pre-clinical studies
(on different molecules)

Enchant drives drug discovery decisions, making predictions on properties that span the discovery and development process



Enchant is one of one. Fine-tuning an LLM is not the same.



- Enchant models outperform competitors in predicting properties of drugs
- Enchant performance cannot be approached by starting from an LLM and fine-tuning on drug-discovery tasks, as illustrated by the wide margin between Enchant and DeepMind's TxGemma model.

Benchmarks on Iambic-generated experimental data across a range of drug discovery examples. Papp(MDR1) is cellular permeability in MDCK cells with overexpression of MDR1 (P-gp). CDK4 IC50 refers to biochemical enzyme inhibition of CDK4. MCF-7 PD is a cellular pharmacodynamics endpoint. Solubility is kinetic solubility in simulated gut fluid. Highly impactful predictions are made on these and dozens of other endpoints, based on models that are fine-tuned each week. Negative Pearson R coefficients are not shown.

https://www.iambic.ai/post/enchantv2

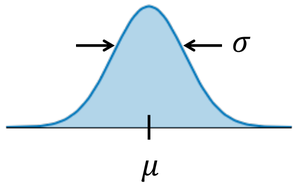
Integrated across our entire discovery portfolio

Fine-tuned on over 50 properties

- Biological activities
- Physicochemistry
- ADME properties
- Pharmacokinetics
- Safety properties
- DDI liabilities
- Clinical properties

Robust uncertainty quantification

- State-of-the-art UQ
- Converts predictions to actionable statements about probability



Integrated with HTE data generation

- Deeply integrated active-learning loops with powerful automated HTE workflows



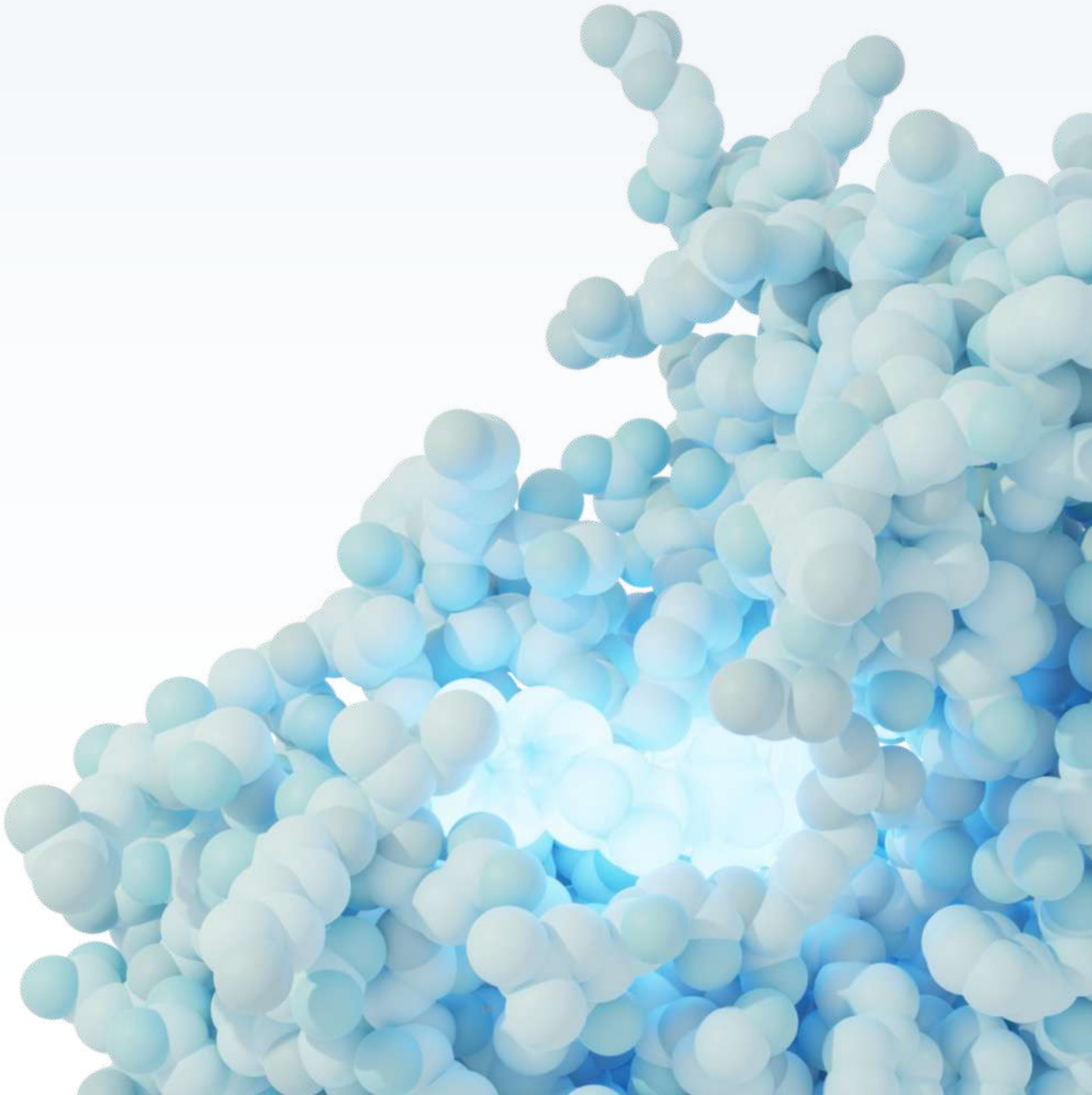
A scalable technology opportunity

- More compute yields better models
- That scaling is not slowing down
- 2026 will see the arrival of Enchant v3, an even larger and more powerful model

Iambic

Value Creation

Partnerships and Pipeline



Entering Multiple Partnerships in past year

Discovery

Iambic advancing novel therapeutics,
validates platform execution

Technology

Iambic building leading AI models,
expands platform innovation

Tech Enablement

Iambic deploying AI technology to partner,
validates platform innovation

Clinical Trials

Iambic receiving drug product for combinations,
validates clinical execution

Our Pipeline

Development Candidate	Target MOA/Indication	Discovery	Preclinical	Phase 1 / 1b
IAM1363	**HER2** Highly selective, brain penetrant, WT + pan-mutant inhibitor	**Phase 1/1b trial – compelling data shown at ESMO & World Lung**		
IAM-K1	**KIF18A** Allosteric inhibitor, mitotic kinesin target			
IAM-C1	**CDK2/4** Selective dual inhibitor			
	Undisclosed Neurological indication		Lundbeck	
	Undisclosed Multiple wholly owned program			

Abbreviations: CDK, cyclin-dependent kinase; GPCR, G protein-coupled receptor; HER2, human epidermal growth factor receptor 2; KIF18A, kinesin family member 18A; MOA, mechanism of action; WT, wild type.

IAM1363: Selective, Pan-Mutant, Brain-Penetrant HER2 Inhibitor

Patient Need

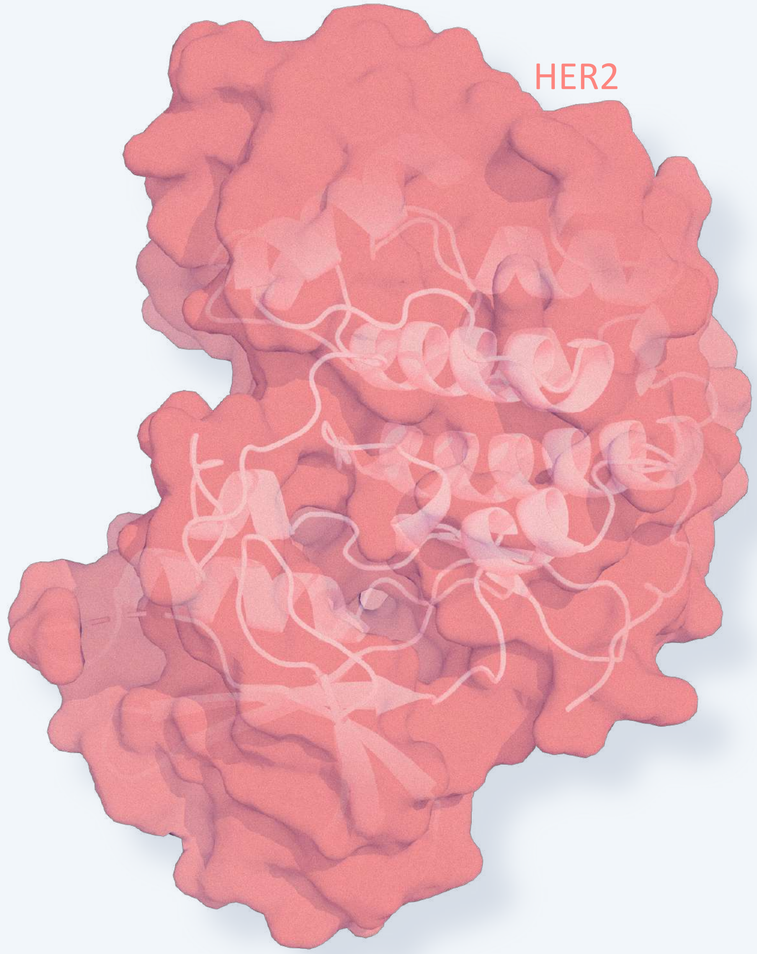
- HER2 aberrations: mutation, overexpression, amplification
- Multiple solid tumors indications: breast, lung, colon, gastric, …
- US+EU+UK incidence: 200k / year
- Tens of thousands of patients with metastatic disease each year

Differentiation of IAM1363

- Only known Type II HER2 TKI
- Unrivaled selectivity (1000x wrt EGFR)
- Activity >20 oncogenic mutants, expanding indications
- Brain penetrant with efficacy in preclinical intracranial models

Status in Clinic

- Ph 1/1b data presented at ESMO in October 2025
- Efficacy and favorable safety profile observed
- Additional data coming in 2026



Abbreviations: EGFR, epidermal growth factor receptor;
HER2, human epidermal growth factor receptor 2; TKI, tyrosine kinase inhibitors.

IAM1363 Stands Alone in HER2 Competitive Landscape

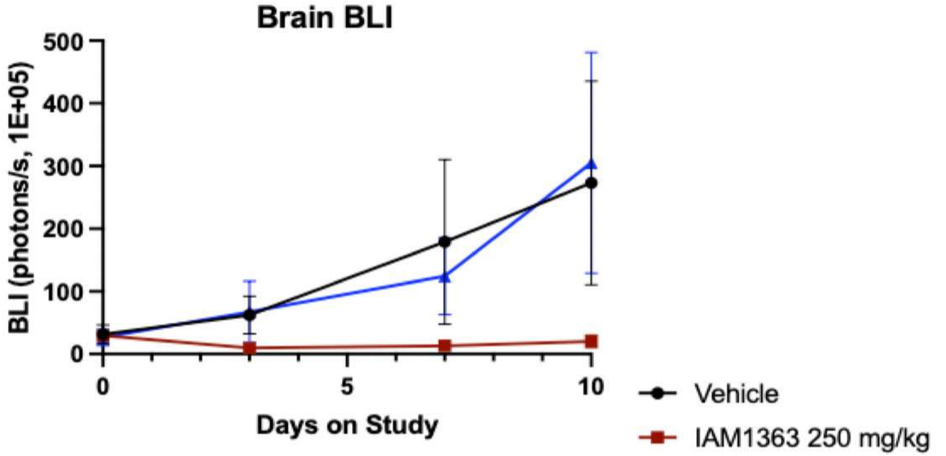
			In Vivo Selectivity[1]	
Drug (manufacturer)	**Brain Penetrant**	**Active on Exon 20 Mutations**	**Cell pHER2 vs. pEGFR[5]**	**Biochemical HER2 vs EGFR[6]**
Tucatinib (Pfizer)	Marginal	No[3]	2160	-
Zongertinib (BI)	No[4]	Yes	62.4	24
NVL-330 (Nuvalent)[2]	Yes	Yes	96[7,8]	-
Sevabertinib (Bayer)[2]	No[4]	Yes[9]	<100[7]	-
IAM1363 (Iambic)	Yes	Yes	3790	5200

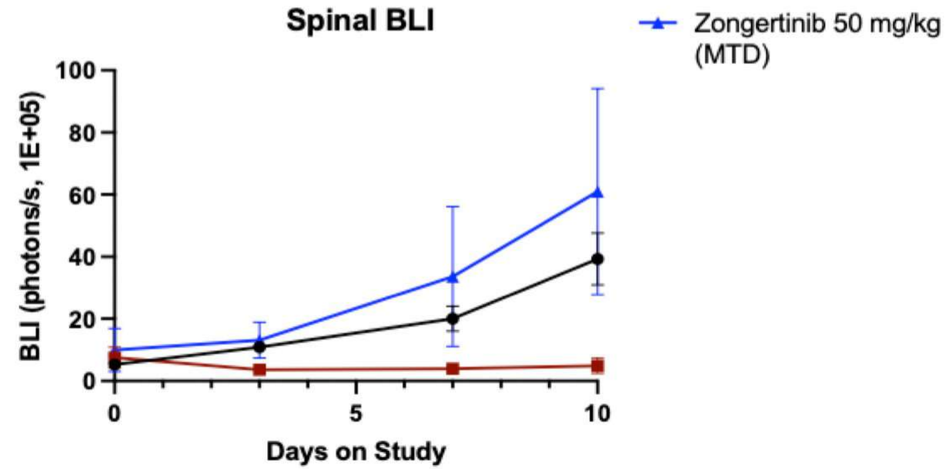
- A safe and effective HER2 TKI demands >1000-fold selectivity vs EGFR
- IAM1363 achieve this safety window, while expanding addressable population with intracranial and pan-mutant activity

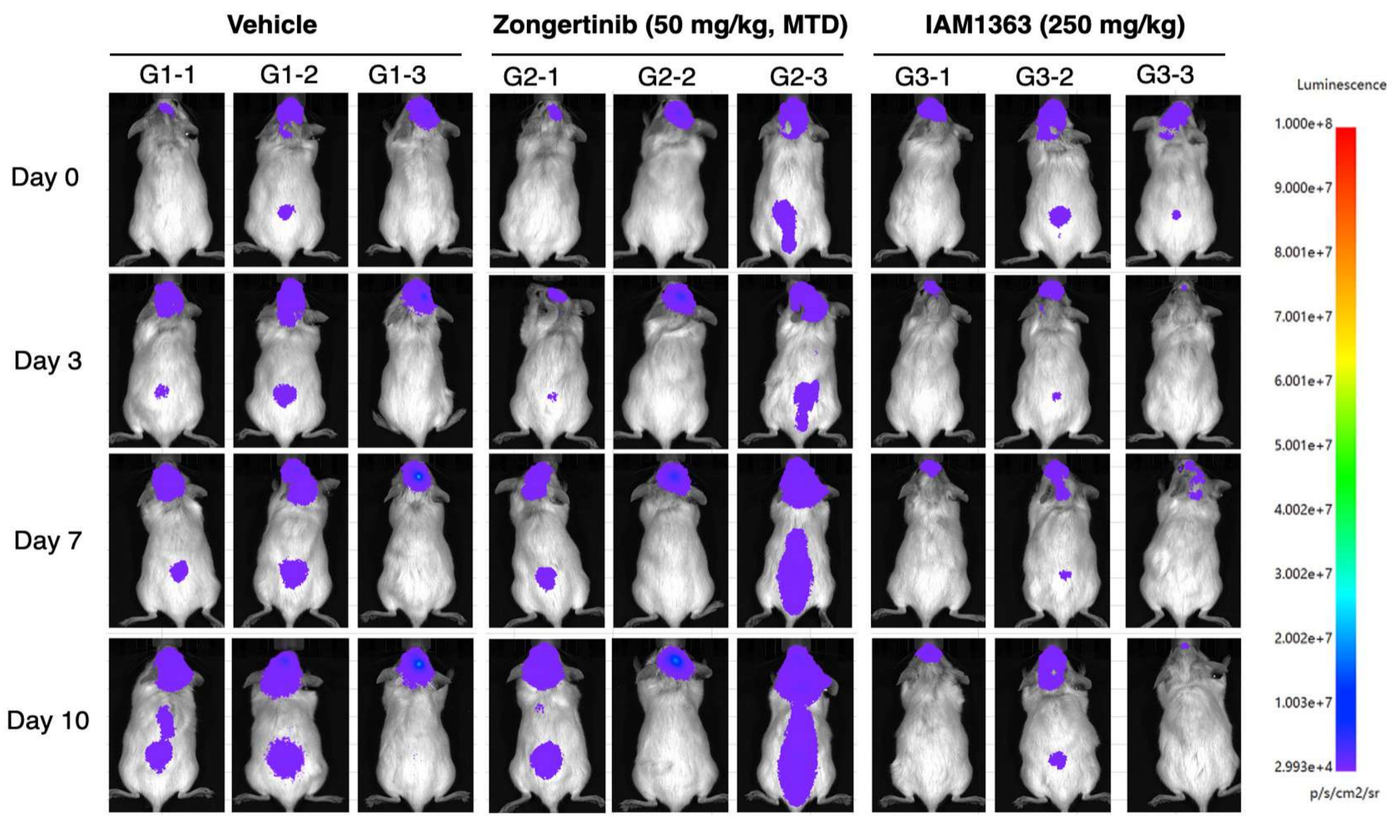
1. Includes relative tumor as measured by tumor/plasma $AUC_{0\text{-}12h}$ ratio (data reported in Iambic/Entos AACR 2023 poster), unless otherwise specified; 2 Public data unless otherwise specified; 3. IC50 > 200 nM in Ba/F3 HER2YVMA; 4. Brain Kp 0.01 (zongertinib) and 0.03 (sevabertinib), internal data; 5. BT-474 (pHER2) and A431 (pEGFR) internal data unless otherwise specified; 6. Covalent kinetic analysis (kinact/Ki), internal data; 7. Tumor/plasma $AUC_{0\text{-}12h}$ ratio is unknown, assumed 1; 8. NCI-N87 (pHER2) from public data; 9. Clinical development is limited to HER2 and EGFR mutant NSCLC

IAM1363 Active for a Brain and Spinal Metastatic NSCLC Model

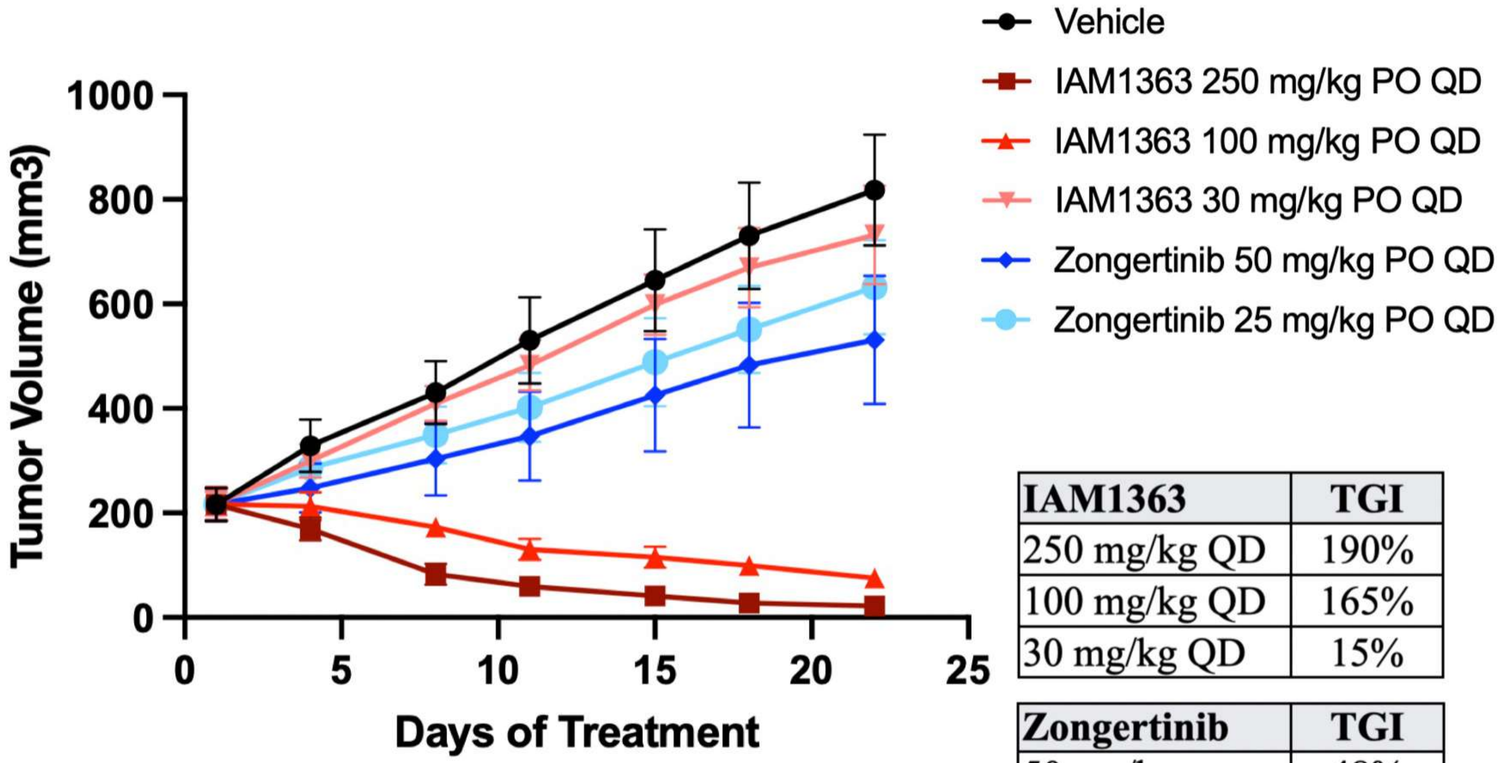
NOD SCID mice intracranially implanted with HER2-mut NCI-H1781-luciferase cells





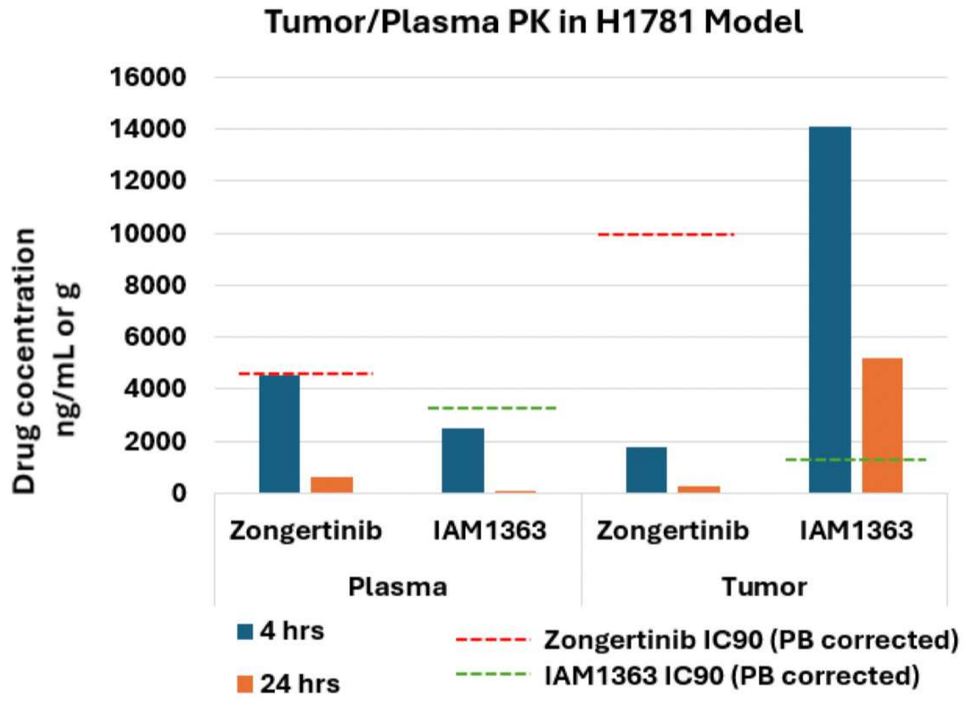


IAM1363 Superior Activity to Zongertinib in HER2 Exon20 VC-mut NSCLC Xenograft Model



IAM1363	TGI
250 mg/kg QD	190%
100 mg/kg QD	165%
30 mg/kg QD	15%

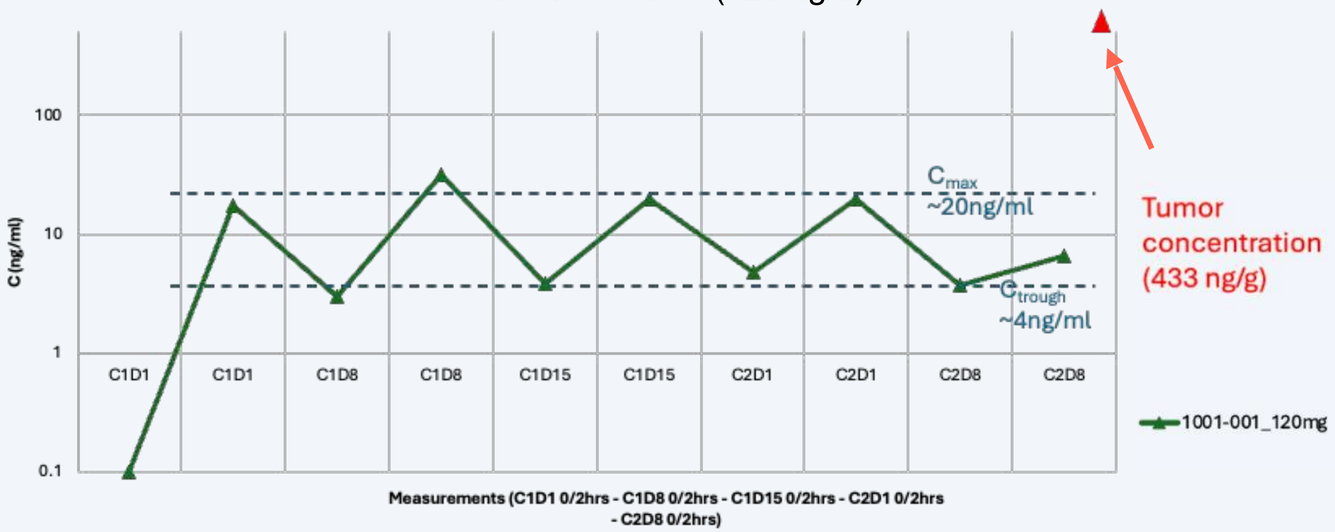
Zongertinib	TGI
50 mg/kg	48%
25 mg/kg	31%



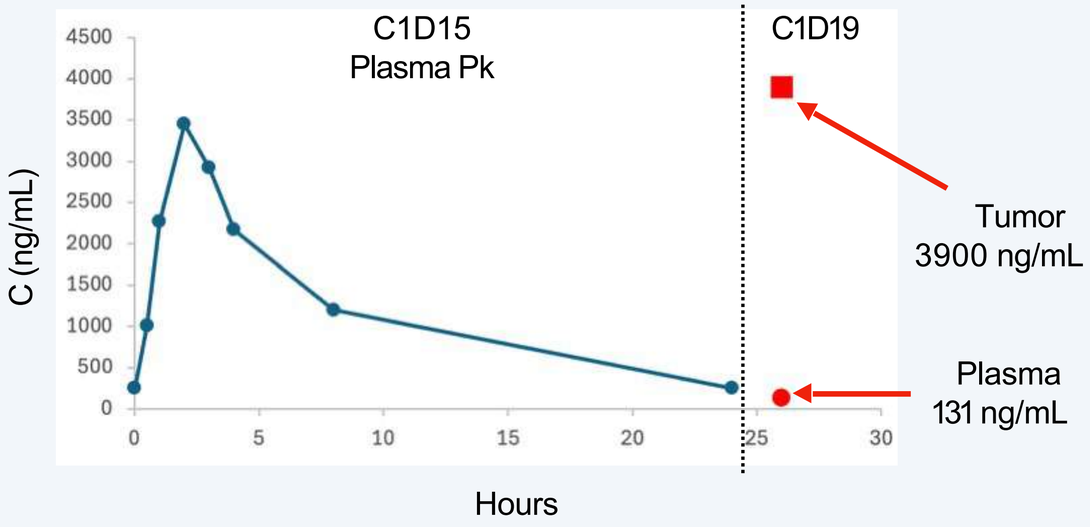
IAM1363 demonstrates superior tumor enrichment for target coverage and efficacy in the H1781 HER2-mutant model compared to zongertinib, supporting the potential of IAM1363 in more treatment refractory tumors.

Plasma vs Tumor Pk in IAM1363 Study Patients

Plasma C_{max}/C_{trough} and Tumor Pk
for Pt 1001-001 (120mg/d)



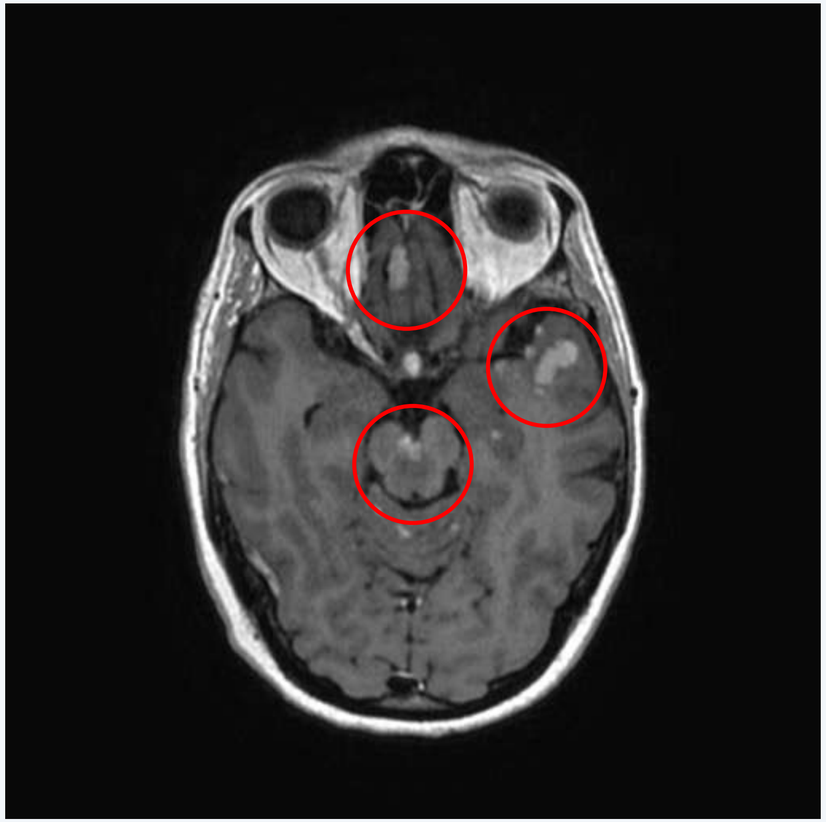
Plasma C_{max}/C_{trough} and Tumor Pk
for Pt 1009-01 (1560 mg/d)



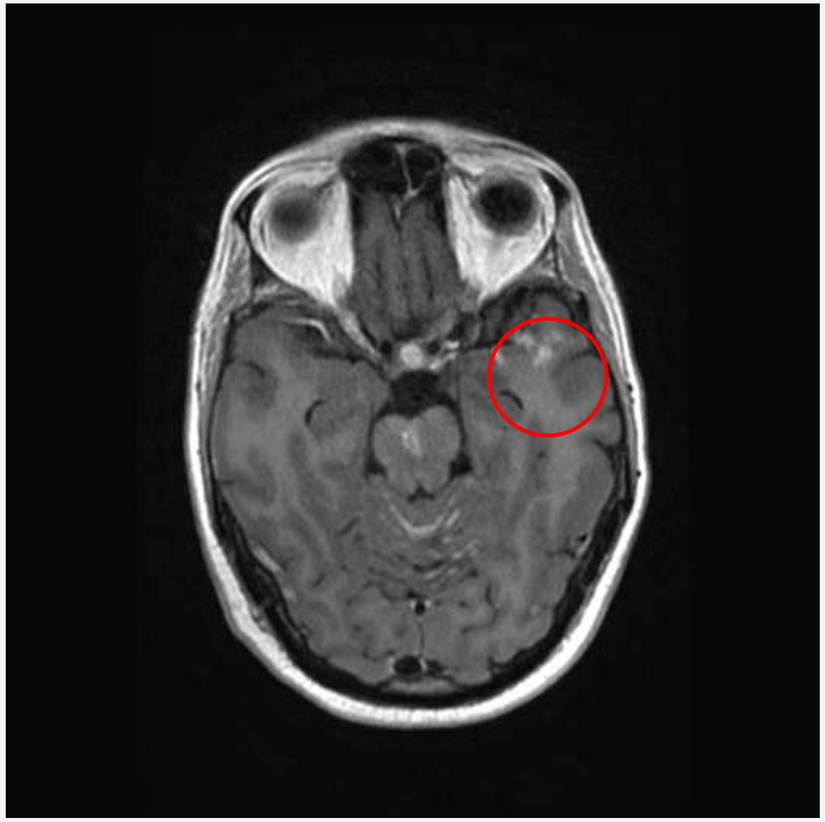
>30X Enrichment of Tumor vs Plasma C_{trough} levels of IAM1363

IAM1363 Shows Activity in CNS Disease Including LMD

Baseline



After 2 Cycles



66 yo F with breast cancer HR+ HER2 3+ by IHC; **metastases to bone, brain and LMD**; multiple lines of treatment, including THP, T-DM1, T-DXd and Tucatinib, Capecitabine and Trastuzumab

Clinical Data Reported at ESMO 2025

Dose escalation complete

Broad activity in late-line patients

18 patients with targetable mutations received ≥ 960mg/d

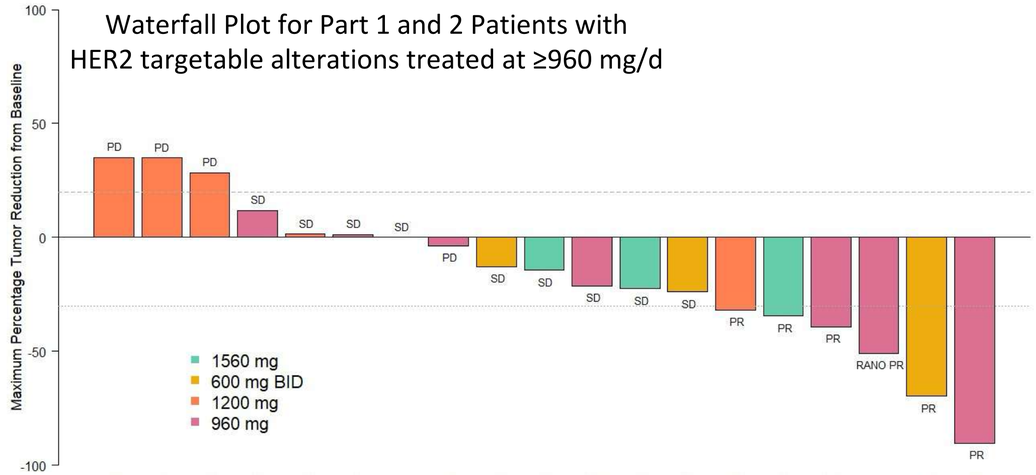
- 5 RECIST PRs: ORR = 28%
- 1 RANO-BM PR: ORR = 33%
- 1 pt with LMD remains on Tx with SD (-12% TLs) for >7 mos

Differentiated safety

- **Competitor agents have more rash and liver toxicity than IAM1363**
- **Safety is a critical factor, given the opportunities to combine with ADCs**

Upcoming readouts

- Completion of dose optimization
- Breast cancer combination cohorts for IAM1363 + zanidatimab (post T-DXd)

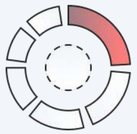


Cancer Type:	En	CRC	Pa	BC	En	Oth	CRC	Pr	NSC	BC	BC	BC	NSC	RCC	GEA	NSC	BC	Ov	NSC
HER2 Status:	**3+**	**Mut**	**Amp**	**3+**	**Amp**	**Mut**	**Mut**	**3+**	**Mut**	**3+**	**3+**	**Mut**	**Mut**	**Mut**	**Amp**	**Mut**	**3+**	**Amp**	**Amp**
Prior HER2 Therapies:	T, X	–	X	P, T, X, M, U	–	–	Inv	–	A, X	P, T, X, M, U	P, T, X, U	T, M, U	X	–	T, X	X	L, P, T, X, M, U	–	X

Cancer Type legend:
BC, breast cancer; CRC, colorectal cancer; En, endometrial cancer; GEA, gastric and gastroesophageal cancers; NSCLC, non-small lung cancer; Oth, other; Ov, ovarian cancer; Pa, pancreatic; Pr, prostate cancer; RCC, renal cell carcinoma.
Prior HER2 Therapies legend:
A, afatinib; I, investigational; L, lapatinib; M, T-DM1; P, pertuzumab; T, trastuzumab; U, tucatinib; X, T-DXd; NA, none.

12Sep2025 data cut; subject to change

IAM-K1: Best-in-Class KIF18A Inhibitor Development Candidate



Therapeutic Area

- Triple-negative breast cancer
- Ovarian cancer
- Other solid-tumor indications



Differentiated Profile

- Excellent ADME and PK properties
- Clean DDI profile relative to competitors
- Brain penetrant

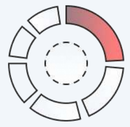


Opportunity

- Strong anti-tumor activity
- Differentiated clinical path based on comprehensive biomarker strategy
- Anticipated efficacy in patients with brain metastases

IND submission in near term

IAM-C1: Iambic Selective Dual CDK2/4 Inhibitor



Therapeutic Area

- HR+ HER2– Breast Cancer
- Cell-cycle dysregulation driven by cyclin D and/or E
- $10B market



Unique Profile

- Iambic compounds potently inhibit CDK2 and CDK4, sparing CDK1, CDK6, CDK7, and CDK9
- Achieved through novel structural engagement



Opportunity

- Improved tolerability and response durability vs. CDK4/6 inhibitors
- Overcoming cyclin-E driven resistance to CDK4/6 inhibitors

IND submission in near term

What to Expect From Iambic in 2026



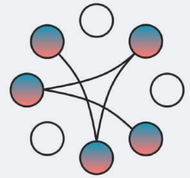
Lead clinical program poised to initiate registrational trials



Three wholly owned clinical-stage programs in oncology



Deep pipeline spanning multiple therapeutic areas



Expanded technology leadership in AI-driven DD, with additional partnerships

In 2026, Iambic will expand on the thesis:
better technology leads to better medicines