Valo Corporate Presentation

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Valo

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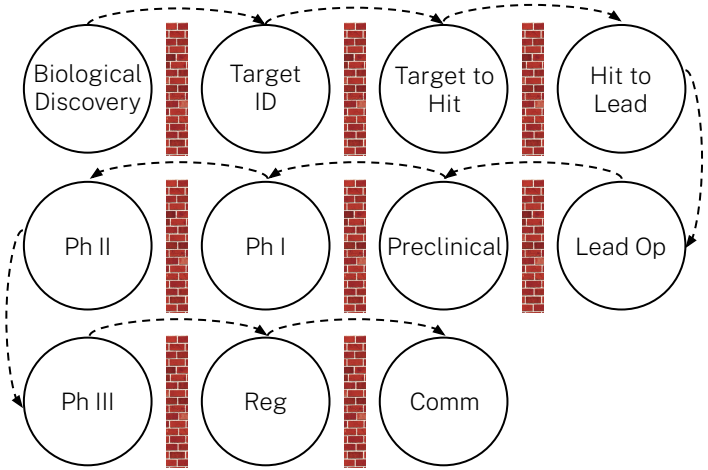
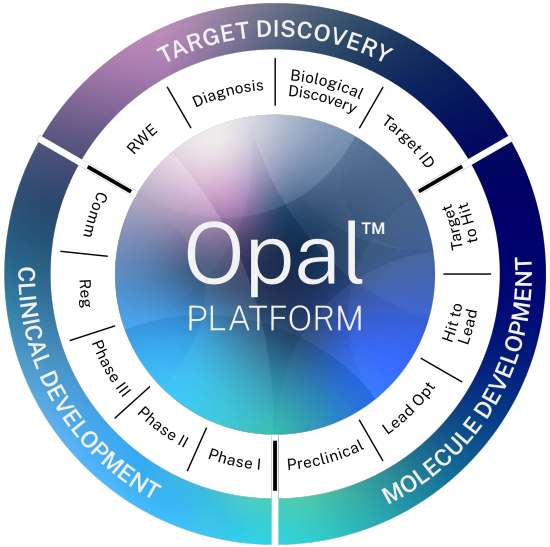
Valo is a technology company that is building a new, integrated approach to developing drugs

LEGACY BIOPHARMA MODEL

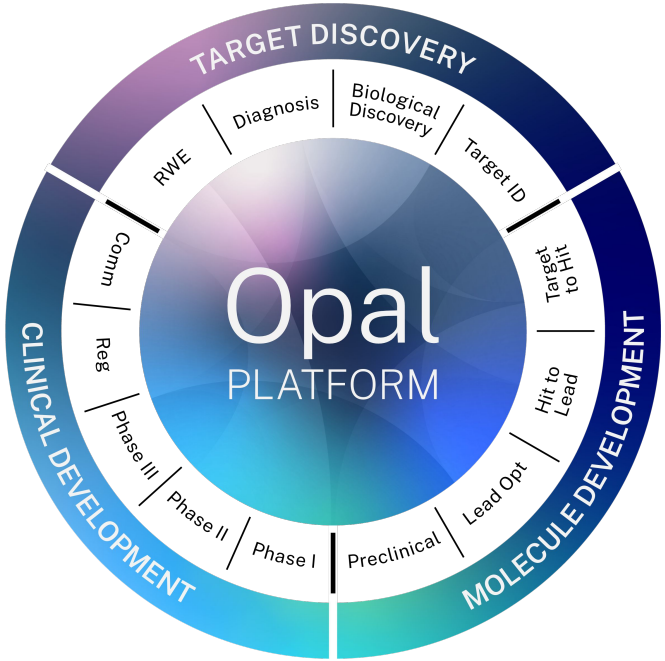


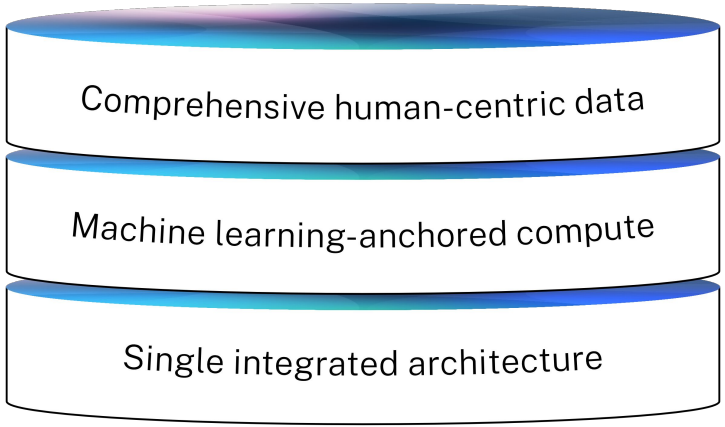
VALO DRUG ACCELERATION MODEL



The legacy biopharma model is built on successes of decades ago.
To usher in the next generation, to deliver what patients need:
We need a new model. Now.

Valo's Opal platform is a fully integrated target discovery and drug development capability uniquely anchored on human-centric data and machine learning





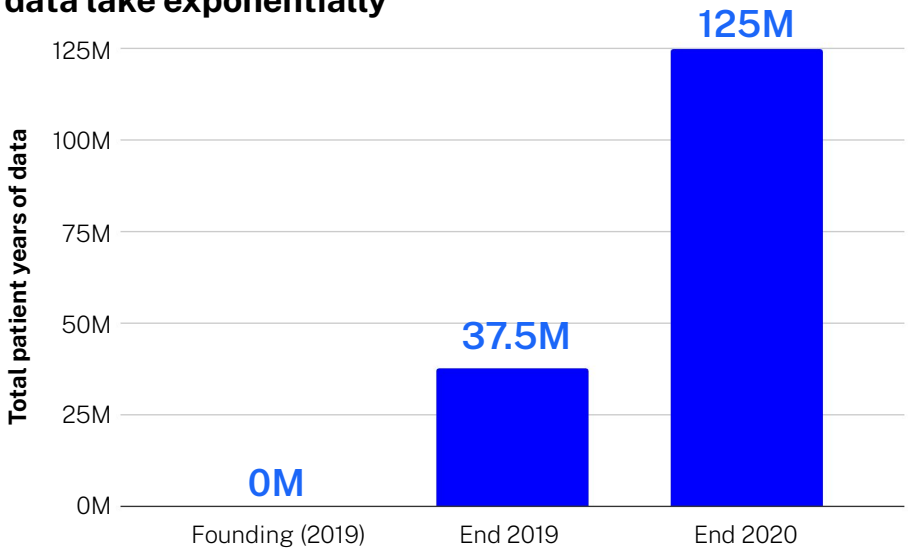
Valo is building **a systems optimized drug development capability** with a **single unified architecture** founded upon world-class human data and machine learning anchored computation. Opal is a proprietary, integrated, end-to-end target discovery and drug development platform accelerated by a **self-reinforcing data→drug→compute flywheel**

Valo's high-density human-centric data lake is unique, comprehensive and self-reinforcing

Over 125M patient-years of GDPR and HIPAA compliant data

>7 million longitudinal patients with >15 years of continuous comprehensive data

Valo has expanded its high-density human data lake exponentially



- **Unique data** sets coupling high quality, high density longitudinal data with large scale, deep multi-omic data
- **Three national scale data deals** with continuous updating
- **Near zero missingness rate** on patients
- **Integration of longitudinal and deep data** enables human-centric discovery and development
- **Self-reinforcing data model** to accelerate scale and impact

>300K patients
Tracked from healthy to neurodegenerative disease

>700K patients
Tracked from healthy to cardiovascular disease

>600K patients
Tracked from healthy to cancer

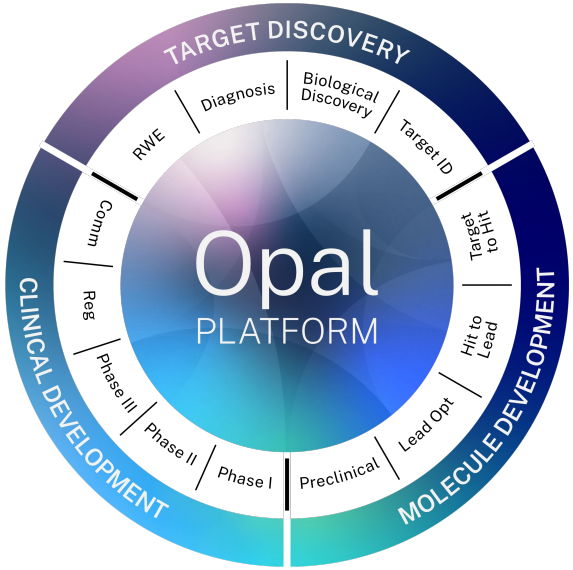
Opal is a fully unified, end-to-end platform with applications across the entirety of the discovery and development paradigm

TARGET DISCOVERY

Human data to identify human targets to treat human disease with **enhanced clinical development profiles** based on genotype-phenotype-causality linkages

CLINICAL DEVELOPMENT

Improve safety, efficacy, patient selection and disease selection for increased likelihood of success



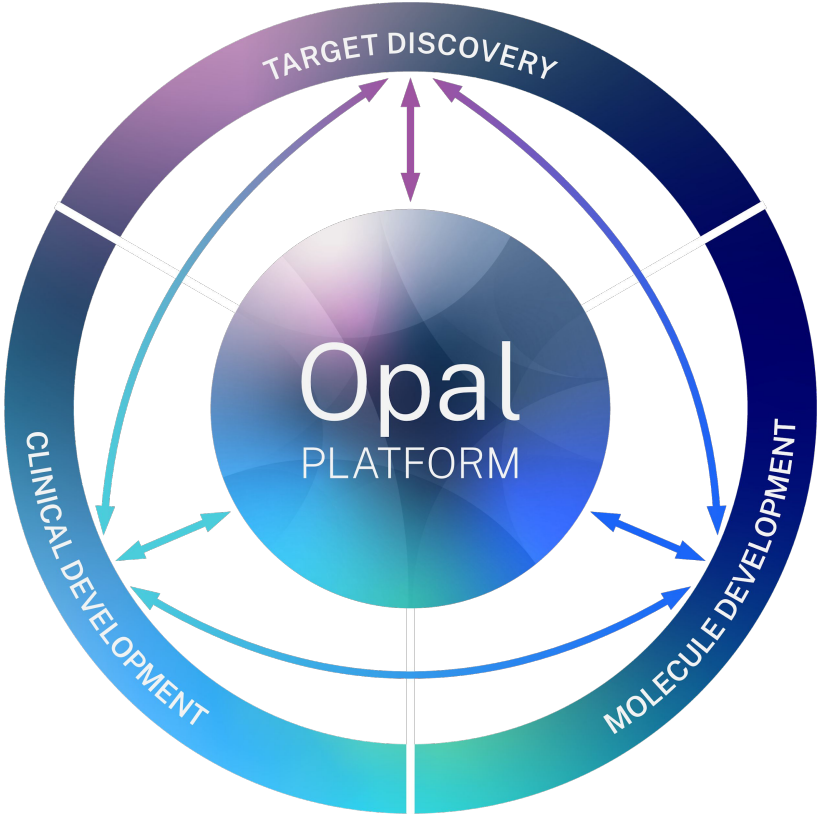
MOLECULE DEVELOPMENT

Active learning, **self-reinforcing, in silico - experimental platform** that rapidly iterates to design drugs, making targeted and specific small molecules 'engineerable'

Opal is built on a single integrated architecture enabling end-to-end human-centric insights and connecting the phases of development

Opal programs are:

- Built on a **common data framework and analytics capability** shared throughout development
- **Accelerated by the integration of data** across the end-to-end drug development continuum
- Enabled by **continuous, consistent decision-making** based on risk-reward ratio and probability of success without human bias
- **Optimized for overall success, informed by human data**, regardless of program maturity
- **Bolstered by Opal's data → compute → drug flywheel** which improves the platform with every cycle



Example platform validations: Opal has demonstrated an ability to substantially accelerate advancement of programs

OPAL		INDUSTRY
New target identification in ***days*** *(CV and ND targets discovered and statistically validated in less than a week)*	VS.	Average of ***6-12 months*** for typical target discovery using surrogates rather than humans
New molecule identification in ***days*** *(7 hits on novel target in 100 person hours)*	VS.	Average of ***1 - 2.5 years*** to move from target to hit to lead candidate
Lead optimization in ***weeks*** *(0 to LO in 6-12 weeks)*	VS.	Average of ***two years*** spent in lead optimization alone
Biomarker discovery in ***months*** *(0 to novel Parkinson's biomarker in 2 months)*	VS.	***Millions of person-hours*** to discover clinically relevant biomarkers

Opal is engineered to develop first/best-in-class therapeutic programs across major disease areas, faster, at lower cost and with higher confidence

Valo is actively developing a suite of preclinical programs across three therapeutic areas

Neurodegenerative

- Application of patient data analysis to discover novel target hypotheses
- Multiple novel preclinical programs expected in 2021

Oncology

- Acceleration of molecule design to treat underserved patient populations
- Multiple drug candidates expected in 2021

Examples from Valo active oncology pipeline

OPL-0001 (PARP1)

OPL-0015 (USP28)

Cardiovascular

- Application of causal modeling approaches to patient data to identify novel target hypotheses
- Clinical program launch expected in 2021

OPL-0001 (PARP1): Creating a best-in-class compound by design

THERAPEUTIC HYPOTHESIS

A **centrally penetrant PARP1** could be effective against **difficult-to-treat brain metastases and brain cancers,** with clinically proven class efficacy

STATE OF THE ART

Current PARP inhibitors are effective against **peripheral cancers**

MOLECULE DESIGN BASED ON AN IDEAL TPP

BRAIN PENETRANCE
Designing a PARP inhibitor to cross the blood-brain barrier to treat brain cancers

PARP1 SELECTIVITY
Designing to selectively target PARP1, not bind PARP2, and minimize any off-target activity

ENZYMATIC INHIBITION
Designing a molecule that inhibits the PARP enzyme to achieve efficacy

VALO INTEGRATED DEVELOPMENT

Designing a centrally-penetrant PARP inhibitor is a **global optimization problem**

Local optimization methodologies used by pharma today **cannot solve this problem**

VALO ADVANTAGE

Leverage **Opal modeling of target binding and ADME** to optimally design a centrally penetrant PARP1 inhibitor, maximizing therapeutic impact while reducing development time and cost

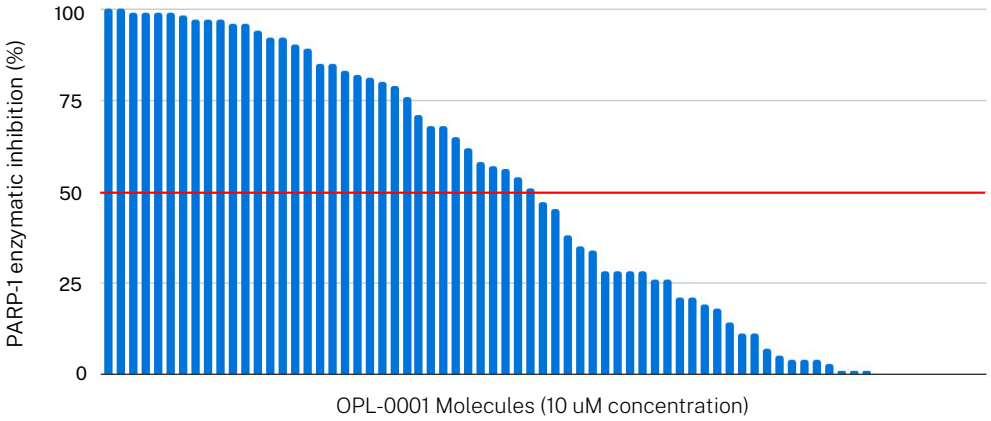
Opal enables the simultaneous co-optimization of multiple molecule features to design best in class molecules

OPL-0001 (PARP1): Fully integrated compound design, synthesis, and testing to rapidly optimize compound properties and efficacy

OPAL VALIDATION

~6 weeks from program start to **tier 1 ADME** screening results for **42 novel molecules: >50% TPP hit rate** on **first cycle,** with **best** observed central penetrance

PARP1 ENZYMATIC INHIBITION: >50% Hit Rate on First Cycle

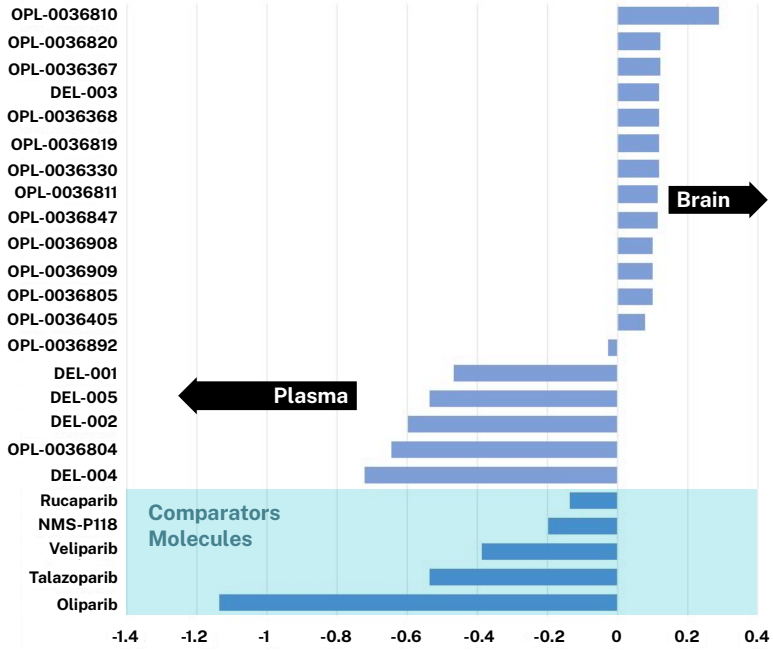


>50% hit rate on first cycle with 18 distinct chemotypes

DESIGNING A CNS-PENETRANT PARP1 INHIBITOR

Predicted in vivo biodistribution

Log([brain]/[plasma])

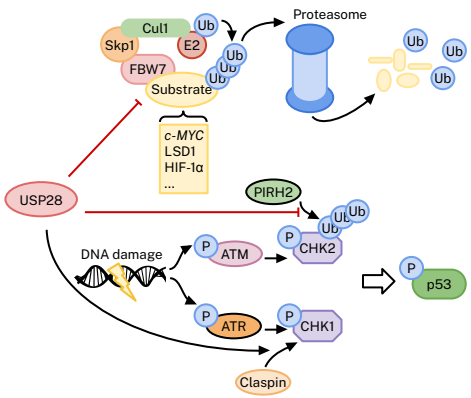


OPL-0015 (USP28): Creating a first-in-class highly selective deubiquitinating enzyme (DUB) as a means to unlock *c-Myc* inhibition

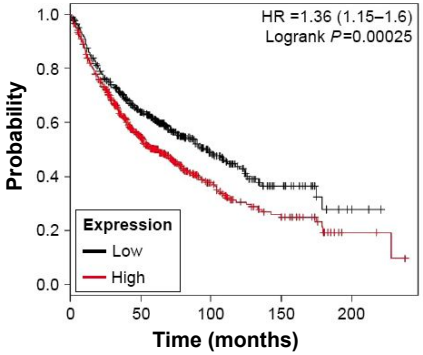
THERAPEUTIC HYPOTHESIS

A highly **specific USP28 inhibitor could precisely decrease *c-Myc* and LSD1 levels and activities in tumor cells** causing powerful anti-tumor effects in a well validated but intractable pathway

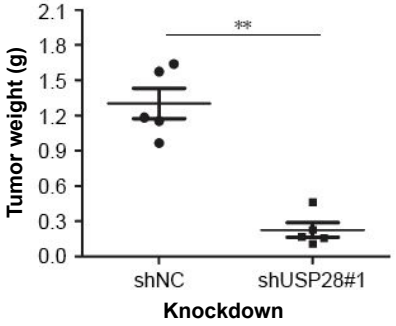
USP28 has been shown to be clinically relevant in lung cancer (NSCLC & SCC), but is considered undruggable



NSCLC patients with high USP28 expression see shorter survival



Knockdown of USP28 significantly inhibited NSCLC cell growth



- USP28 is required for MYC stability
- USP28 is found in high levels in various cancers; and its stabilization of MYC is essential for tumor growth
- USP28 is **widely considered to be undruggable** due to selectivity issues that have made previous attempts fail

VALO ADVANTAGE

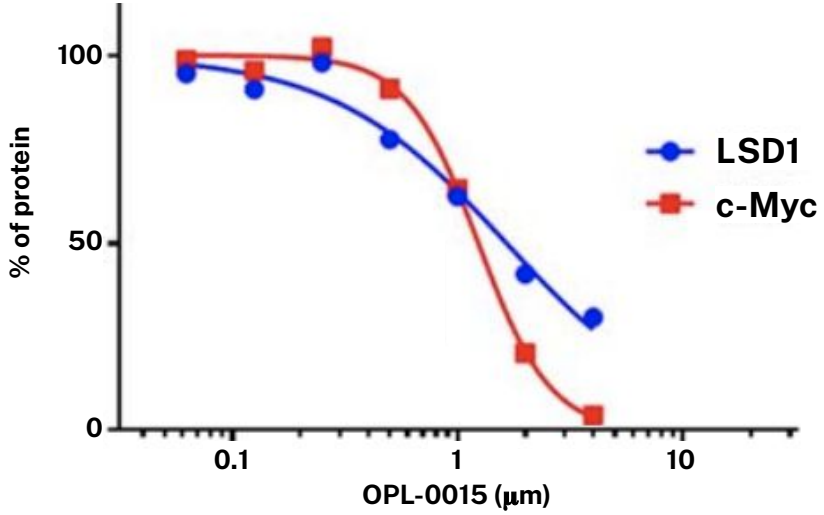
Opal enables the development USP28 selective molecule, co-optimized for efficacy as well as ADME and toxicology properties

OPL-0015 (USP28): Unlocking a first-in-class highly selective deubiquitinating enzyme (DUB) as a means to inhibit *c-Myc*

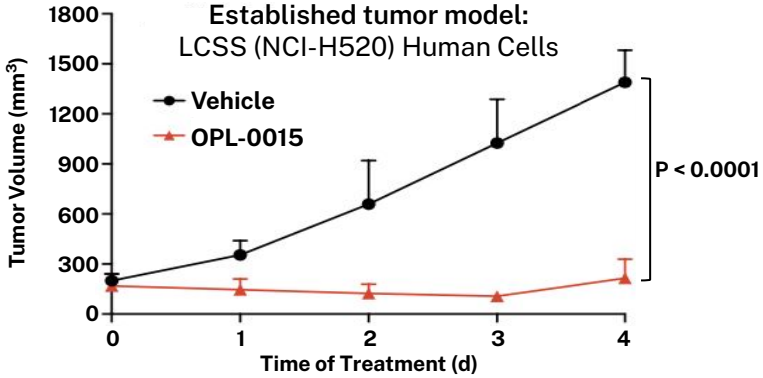
OPAL VALIDATION

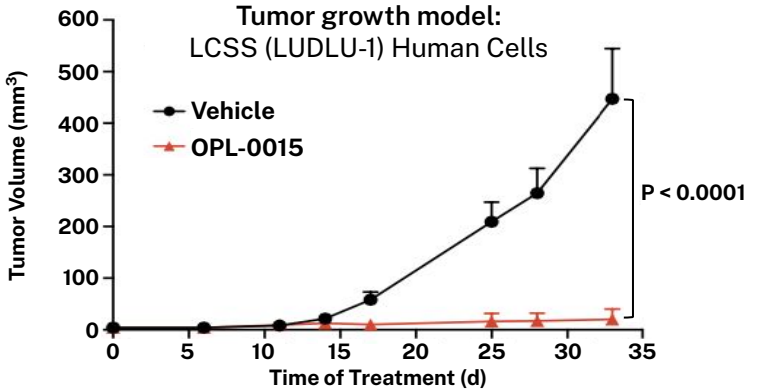
In only 3 months, **Opal identified multiple highly selective and potent compounds** driving precise, mechanistic *c-Myc* inhibition and tumor killing

OPL-0015 (USB28) inhibitor decreases *c-Myc* and LSD1 protein levels in cells



Strong anti-tumor signals demonstrated in murine lung squamous cell carcinoma (LSCC) models

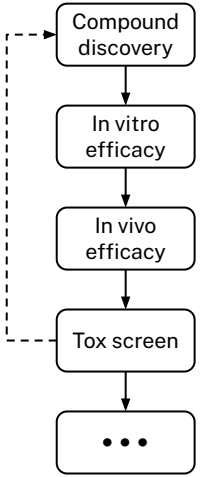




Safety prediction: Opal's toxicity prediction has proven to be 86% accurate (N=152) at predicting off-target safety issues in small molecules

- Machine learning driven screen to **anticipate interactions between any molecule and potential binding partners**
- **Validated with 86% accuracy on blinded, 3rd party review** of 152 compounds from 20 programs at a major pharma

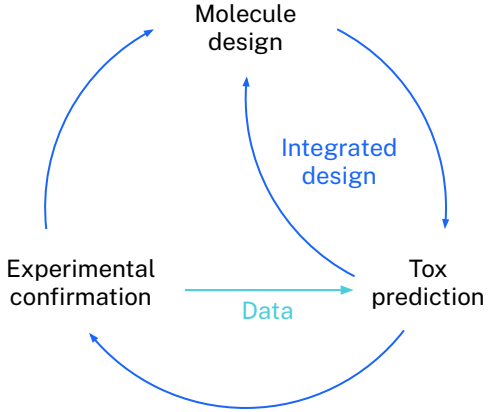
TRADITIONAL LINEAR DEVELOPMENT



Traditional molecule discovery methods screen for tox and modify compounds in a linear, iterative fashion

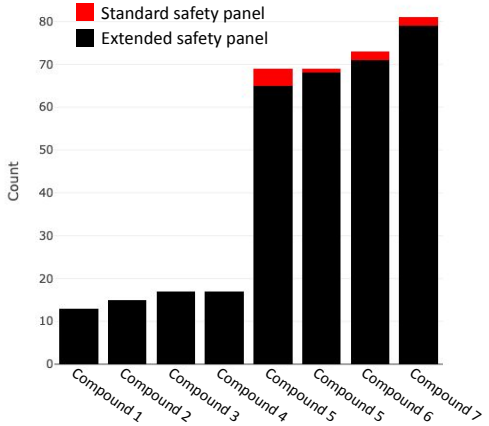
VALO INTEGRATED DEVELOPMENT

Molecule discovery



Valo's tox tool enables us to design molecules that are optimized for tox, by using computational predictions in parallel with molecule design generating safer, better optimized compounds in the first cycle

Clinical development



Valo's tox tool predicts human tox (rather than animal tox), enabling us to reduce Phase 1 risk and identify potential clinical safety issues while designing molecules prior even to animal tox

Valo is creating a risk-mitigated proprietary pipeline of breakthrough drug programs leveraging Opal to increase confidence and impact

FIRST-IN-CLASS THERAPEUTIC ASSETS PIONEERED BY OPAL

Opal-discovered and engineered therapeutics

- Unlocking undruggables
- Novel targets
- Fully integrated development from target discovery through clinical development on single programs
- Focus on large potential markets with biology risk offset by advancement of other programs
- Long term proprietary value creation

BEST-IN-CLASS FAST FOLLOWERS ENABLED BY OPAL

Opal-engineered best-in-class therapeutics

- Use proof of concept and proof of biology/mechanism from third parties to rule-in targets
- Focus on efforts where a key therapeutic (i.e. efficacy) advantage can be generated
- Leverages Opal's accelerated development in a de-risked manner
- Proprietary candidates with improved therapeutic profiles

EXISTING MOLECULES ACCELERATED BY OPAL

Opal-accelerated clinical and late preclinical assets

- Identify key responder populations, underappreciated mechanisms and beyond
- Focus on large potential markets with the potential for differentiation
- Unique "Valo-add" through Opal insights across multiple dimensions

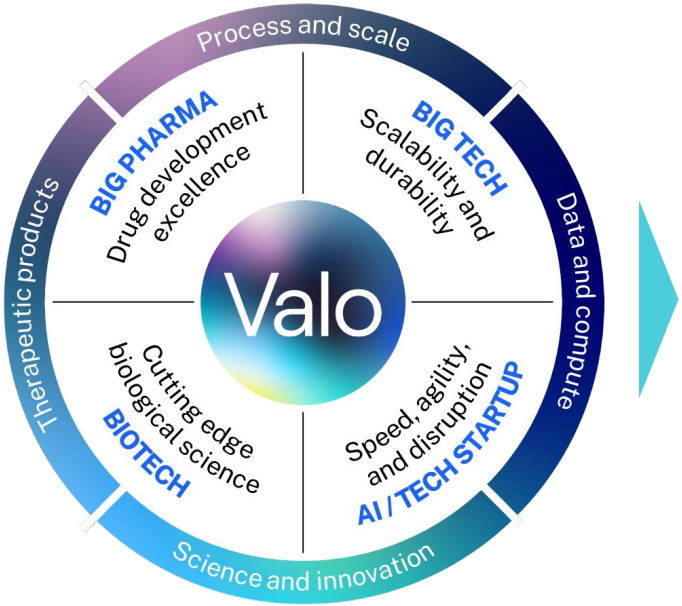
Transforming the value chain requires an organization built at the interface of life sciences and technology

>100
drug approvals[1]

>500
regulatory submissions[1]

>1,000
discovery and clinical programs[1]

>30,000
ML models deployed[1]



David Berry, MD, PhD
Founder, Chief Executive Officer
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Co-founder of >25 companies

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Founder, CSO of HemoShear, Cogen, and Kintai
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Hilary Malone, PhD
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Chief Regulatory Officer, Sanofi

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Graeme Bell, MBA, FCMA
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CFO, Tmunity / Intellia / Anacor
CFO, Merck U.S.

Moni Miyashita, MBA
Chief Strategy Officer
Partner, Innosight
VP, Corporate Development, IBM

Cissy Young, PhD
Chief People Officer
Managing Director, Russell Reynolds Associates
Director, Strategy & BD, Cerulean Pharma

[1] Valo data aggregates historical experience across Valo staff

Fueled by the Opal platform, Valo is positioned to achieve unprecedented growth in 2021 and beyond

With a recent **$300M Series B** financing, Valo's fundraising totals **>$450M** since 2019

Our 2021 plans will power the Opal flywheel:

- Accelerate and expand **self-reinforcing data model**
- Form **strategic sector partnerships** to reinforce drug acceleration model and launch a Valo-enabled ecosystem
- Launch **innovative clinical trials** enabled by Opal
- **10-15 therapeutic programs** accelerated by Opal to enable multiple additional clinical programs in 2022
- Proprietary Opal targets accelerating into preclinical programs to create **rapidly expanding pipeline to support 2022 programs**