UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 25, 2023

RECURSION PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-40323**	**46-4099738**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

41 S Rio Grande Street
Salt Lake City, UT 84101
(Address of principal executive offices) (Zip code)

(385) 269 - 0203
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Class A Common Stock, par value $0.00001 per share	RXRX	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

On January 25, 2023, Recursion Pharmaceuticals, Inc. released an updated investor presentation. The investor presentation will be used at its Download Day presentation and from time to time in meetings with investors. A copy of the presentation is attached hereto as Exhibit 99.1.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

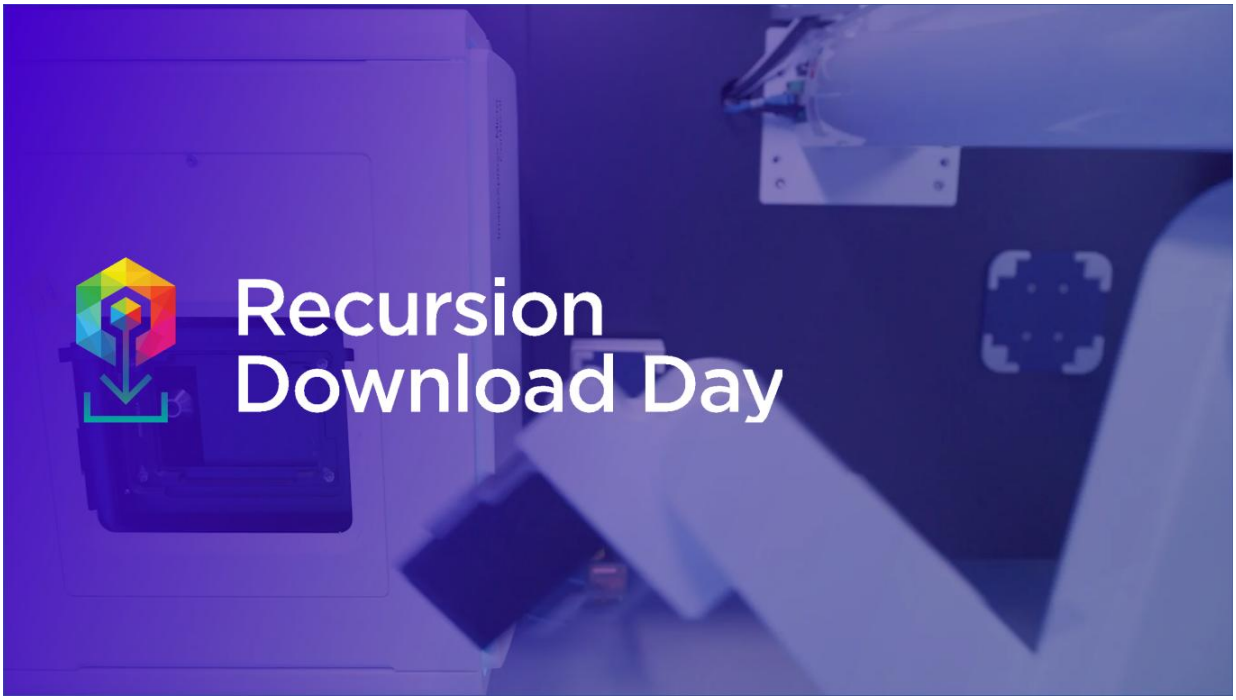
Exhibit Number	Description
99.1	Investor presentation of Recursion Pharmaceuticals, Inc. dated January 25, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized on January 25, 2023.

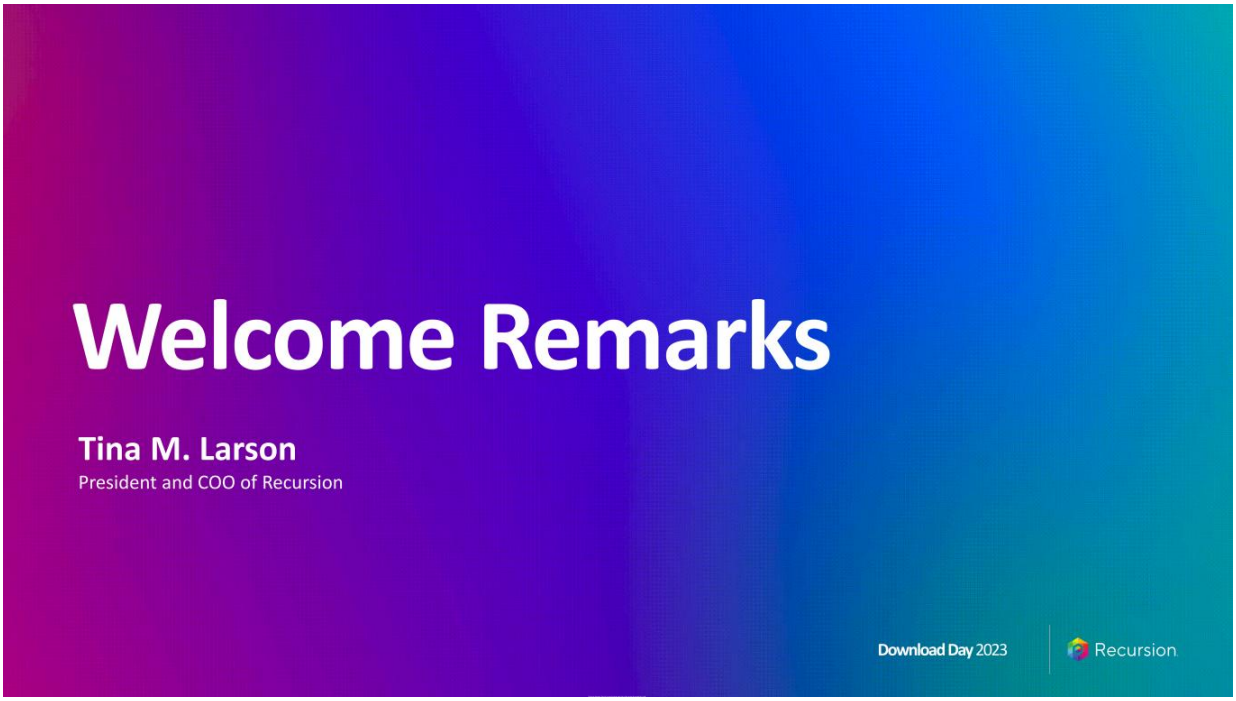
RECURSION PHARMACEUTICALS, INC.

By: /s/ Christopher Gibson
Christopher Gibson
Chief Executive Officer


Recursion
Download Day

Agenda

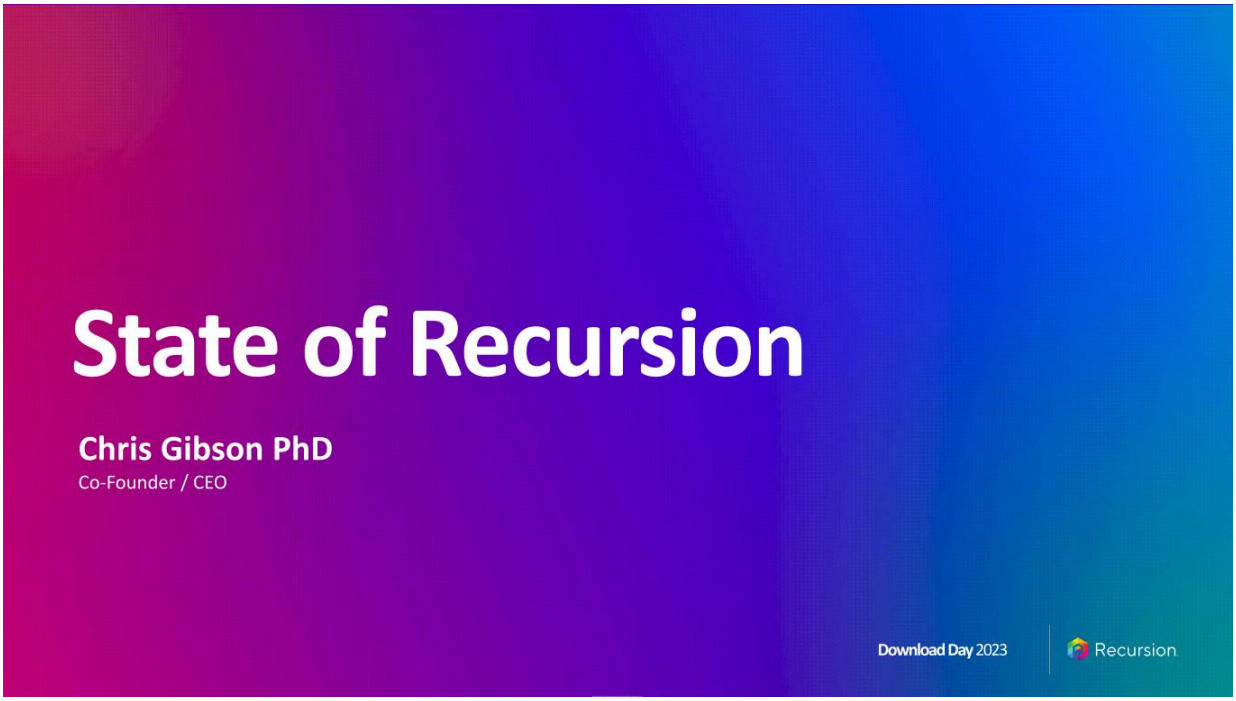
Breakfast (8:30 – 9:30 AM)	
Welcome	**Tina Larson**, President & COO **R. Martin Chavez PhD**, Chairman
State of Recursion	**Chris Gibson PhD**, Co-Founder & CEO
Recursion OS	**Imran Haque PhD**, VP of Data Science **Lina Nilsson PhD**, VP of Product
Pre-Clinical Opportunities	**Laura Schaevitz PhD**, SVP and Head of Research
Tours & Demos	**Ben Mabey**, Chief Technology Officer
Lunch (12:00 – 1:00 PM)	
Welcome Back	**Heather Kirkby**, Chief People Officer **Dean Li MD PhD**, Co-founder and Board Member
Clinical Programs	**Shafique Virani MD**, Chief Business Officer and Interim Chief Medical Officer
Partnerships	**Matt Kinn**, SVP of Business Development
Financials & Potential Milestones	**Michael Secora PhD**, Chief Financial Officer
Closing	**Chris Gibson PhD**, Co-Founder & CEO **Zavain Dar**, Board Member
Reception, Tours & Demos (3:30 – 4:30 PM)	


Welcome Remarks
Tina M. Larson
President and COO of Recursion
Download Day 2023
Recursion

Welcome Remarks

R. Martin Chavez PhD
Chairperson of Recursion

Download Day 2023 | Recursion


State of Recursion
Chris Gibson PhD
Co-Founder / CEO
Download Day 2023
Recursion

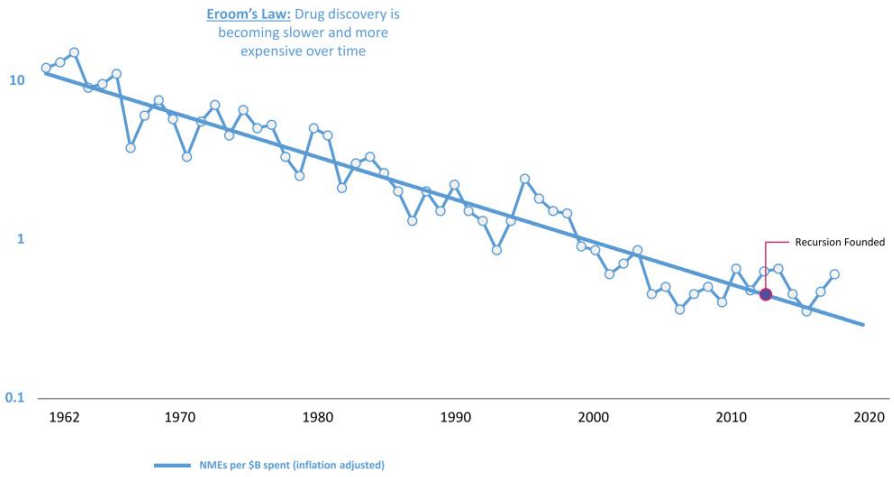
Disclaimers

This presentation and any accompanying discussion and documents contain information that includes or is based upon "forward-looking statements" within the meaning of the Securities Litigation Reform Act of 1995. These forward-looking statements are based on our current expectations, estimates and projections about our industry and our company, management's beliefs and certain assumptions we have made. The words “plan,” “anticipate,” “believe,” “continue,” “estimate,” “expect,” “intend,” “may,” “will” and similar expressions are intended to identify forward-looking statements. Forward-looking statements made in this presentation include statements about Recursion's use of the proceeds from its private placement, the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, the potential size of the market opportunity for our drug candidates, our ability to identify viable new drug candidates for clinical development and the accelerating rate at which we expect to identify such candidates, our expectation that the assets that will drive the most value for us are those that we will identify in the future using our datasets and tools, and many others. Forward-looking statements made in this presentation are neither historical facts nor assurances of future performance, are subject to significant risks and uncertainties, and may not occur as actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. For a discussion of factors that could affect our business, please refer to the "Risk Factors" sections in our filings with the U.S. Securities and Exchange Commission, including our most recent Quarterly Report on Form 10-Q and our Annual Report on Form 10-K. This presentation does not purport to contain all the information that may be required to make a full analysis of the subject matter. We undertake no obligation to correct or update any forward-looking statements, whether as a result of new information, future events or otherwise.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the company’s own internal estimates and research. While the company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while the company believes its own internal research is reliable, such research has not been verified by any independent source.

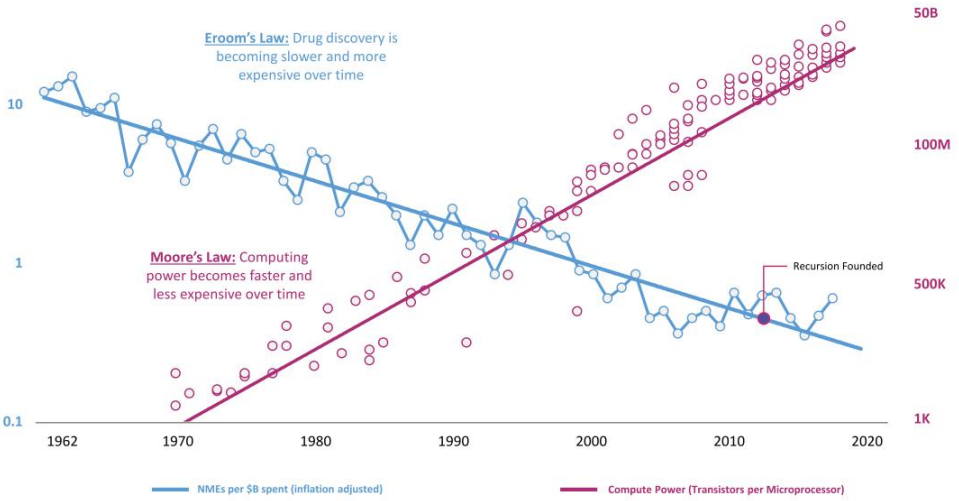
Any non-Recursion logos or trademarks included herein are the property of the owners thereof and are used for reference purposes only.

The biopharmaceutical industry faces pressure amidst declining efficiency in drug discovery…



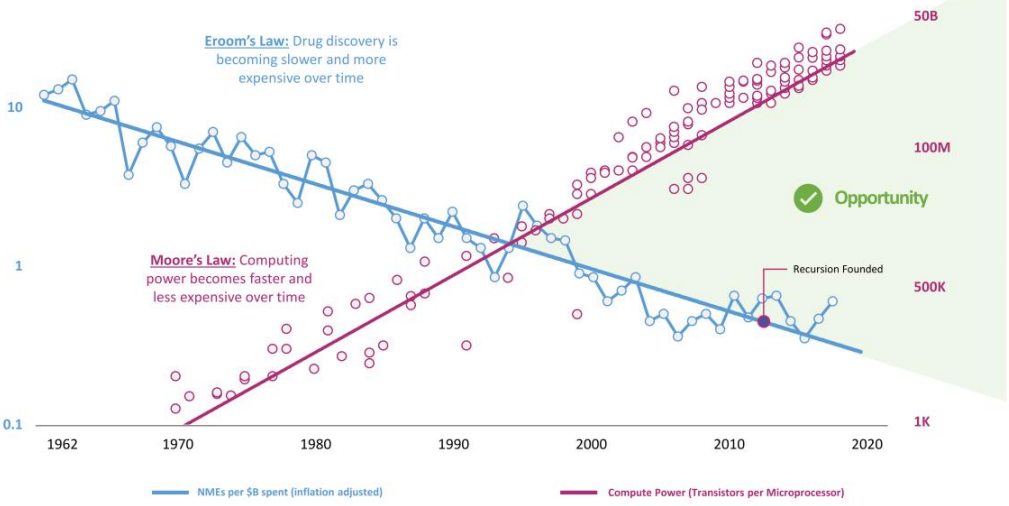
Adapted from Scannell et al and Our World in Data

The biopharmaceutical industry faces pressure amidst declining efficiency in drug discovery…



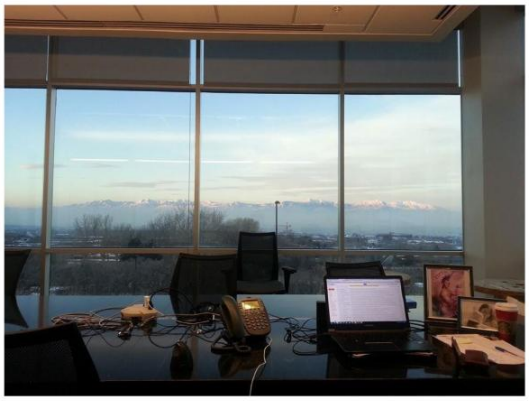
Adapted from Scannell et al and Our World in Data

Recursion was founded to conduct an experiment: determine whether technology can create an inflection in the discovery efficiency curve



Adapted from Scannell et al and Our World in Data

An experiment from the beginning…

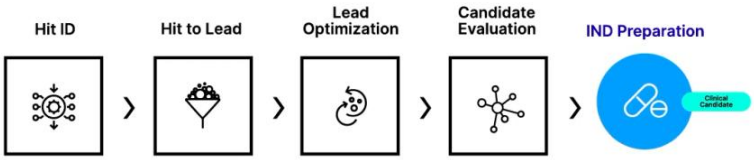


Hypothesis 1: ***In biology, structure suits function; by applying sophisticated analysis techniques to images of human cells, a new scale of biological insight can be unlocked***

An experiment from the beginning…

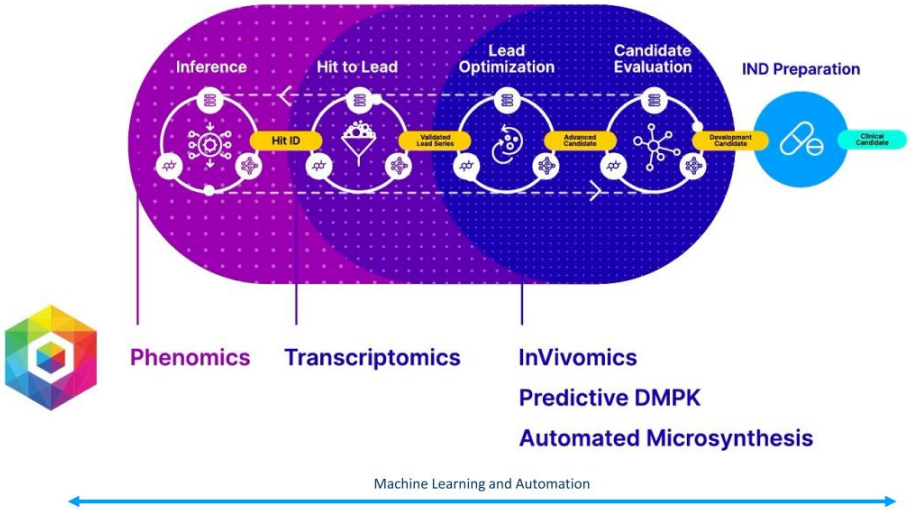
Hypothesis 2: ***By industrializing a small number of extraordinarily data-rich assays using automation and computation, biology and chemistry can be mapped and navigated, turning drug discovery into an efficient search problem***

Continuing to mature the TechBio value proposition – multiple cycles of learning and iteration



Machine Learning and Automation

Continuing to mature the TechBio value proposition – multiple cycles of learning and iteration



Phenomics

Transcriptomics

InVivomics

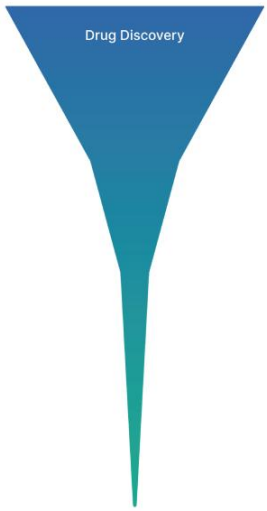
Predictive DMPK

Automated Microsynthesis

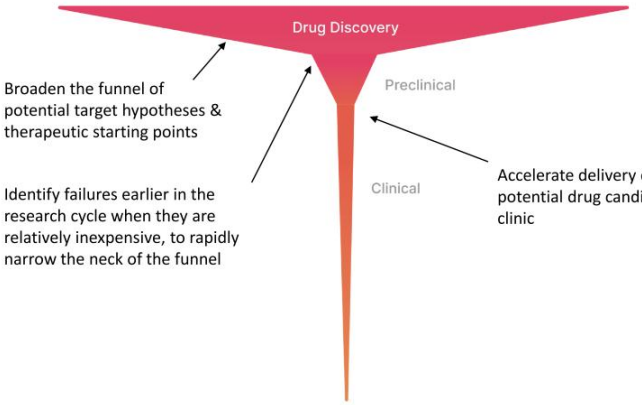
Machine Learning and Automation

Recursion is designed to impact drug discovery productivity…

Traditional discovery pipeline



Ideal discovery pipeline

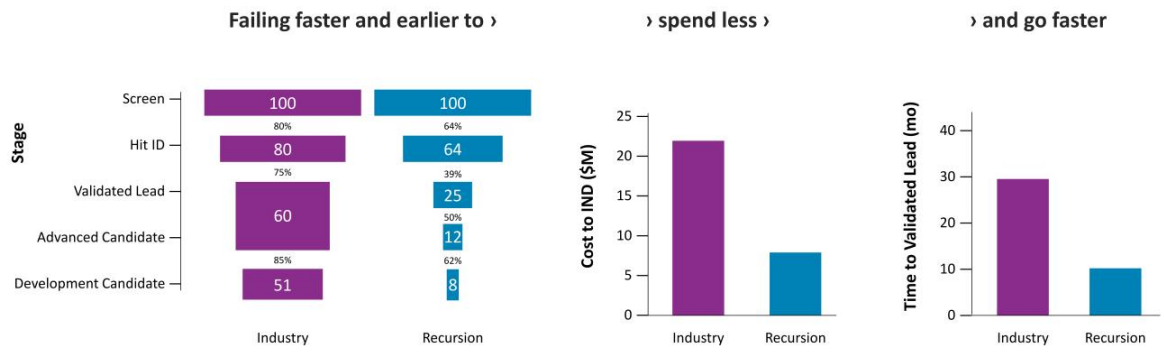


Broaden the funnel of potential target hypotheses & therapeutic starting points

Identify failures earlier in the research cycle when they are relatively inexpensive, to rapidly narrow the neck of the funnel

Accelerate delivery of high-potential drug candidates to the clinic

...Which Recursion has demonstrated with leading indicators of efficiency



Preliminary data shown is the average of all our programs since late 2017. All industry data adopted from Paul, et al. Nature Reviews Drug Discovery. (2010) 9, 203–214

Maturing the TechBio value proposition in 2022

Initiated 5 clinical trials in 2022 (3 Ph2, 2 Ph1)
- Includes Ph1 FAP study completed by Recursion

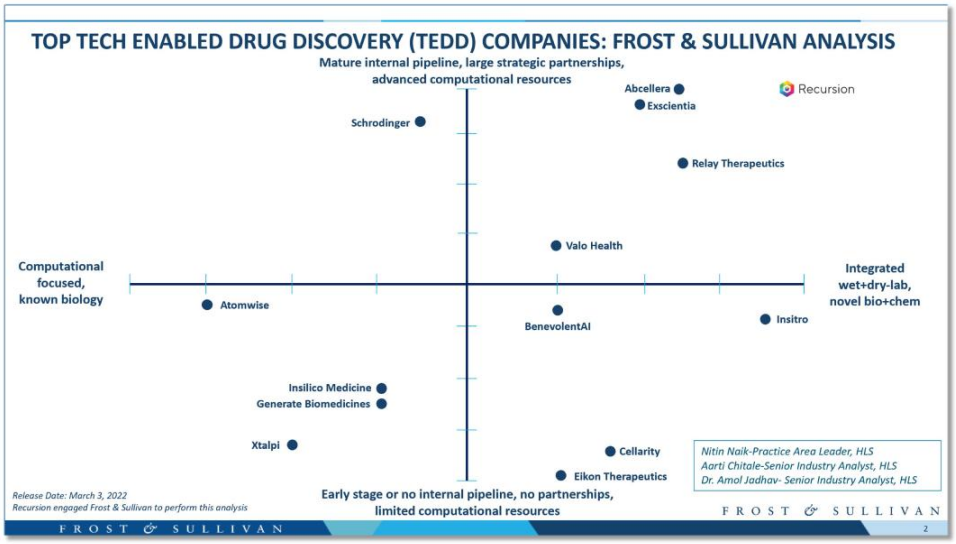
Planning a **6th clinical trial** to initiate (Ph1b/2)

Novel oncology programs (Target Alpha, Target Gamma) nearing **IND-enabling studies**

Advancing collaborations in **Fibrosis (Bayer)** and **Neuroscience (Roche-Genentech)**
- $13B in potential milestones across 50+ possible programs plus royalties

We believe that we have built one of the **largest proprietary & relatable** in-vitro biological and chemical **datasets on Earth**
- >21 petabytes of data and
  >3 trillion searchable relationships

Recursion leads the rise of AI-enabled drug discovery



New today

Pipeline

- Guidance on top-line readout for Ph2 CCM program
- Guidance on interim Ph2 safety readout for NF2 program
- Guidance on Ph1 C diff readout
- Trial update on Ph2 FAP program
- Guidance on Ph1b/2 AXIN1/APC trial start
- Target disclosure for Project Gamma

Partnerships

- Update on Bayer collaboration including state of partnered pipeline
- Update on Roche/Genentech collaboration

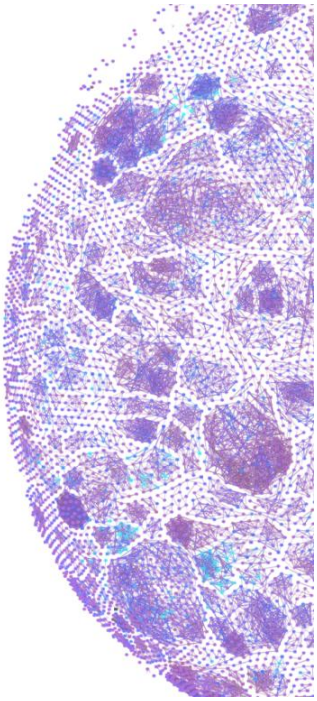
Platform

- Announcement of RXRX3 and MolRec dataset releases

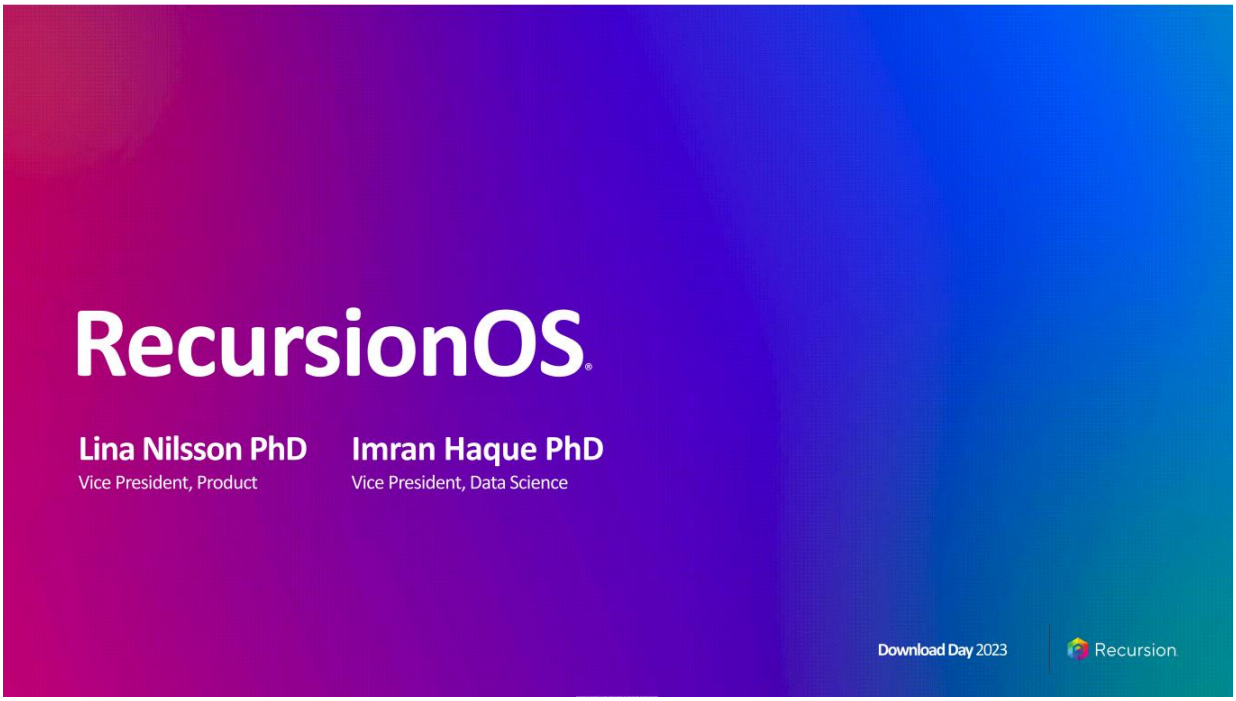
Strong Financials **~$550M in cash** and cash equivalents at the **end of 2022** with **potential for increased revenue** in the near term

Our Mission:

Decode Biology to
Radically Improve Lives




Impact


RecursionOS
Lina Nilsson PhD
Vice President, Product
Imran Haque PhD
Vice President, Data Science
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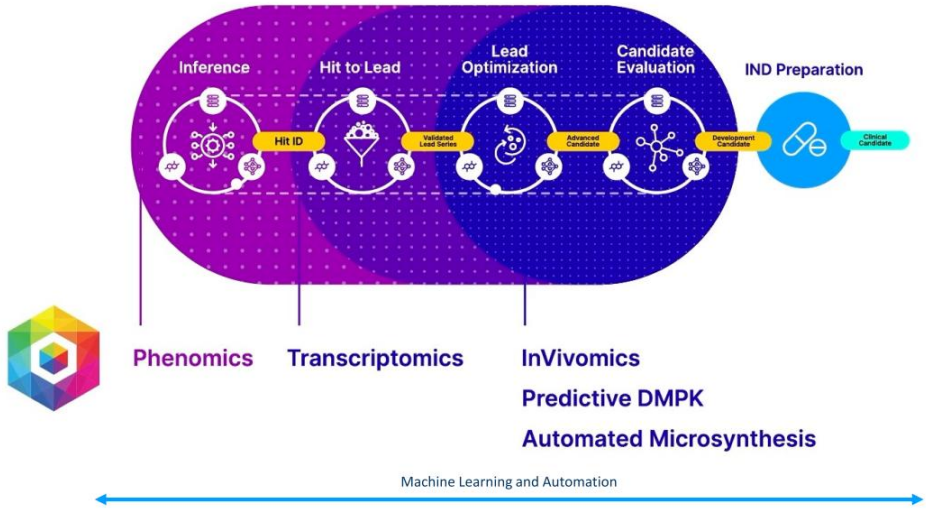
Recursion

Recursion's map-based approach is designed to set the standard for drug discovery in the 21st century

Traditional Drug Discovery		Recursion Approach
Literature drives discovery. *Informs target-based hypotheses*	vs	**Platforms** drive discovery. *Unbiased & target agnostic*
Data are an exhaust. *Limited to testing hypotheses*	vs	**Data** are our fuel. *Shape our hypotheses*
Disparate data generation. *Siloed to individual programs and diseases*	vs	**Connected data** across programs. *Relatable high-dimensional data*
Linear process. *Little cross-program learning or iteration*	vs	**Virtuous cycles** of atoms & bits. *Iterative feedback accelerates learning*
Bespoke processes. *Low-dimensional assays & biomarkers*	vs	**Industrialized** to scale. *Automation & standardization*

Industrializing drug discovery at Recursion: The big picture



Phenomics

Transcriptomics

InVivomics

Predictive DMPK

Automated Microsynthesis

Machine Learning and Automation

Recursion OS enables scale, reliability and relatability of datasets

Biological Tools

Automation Tools

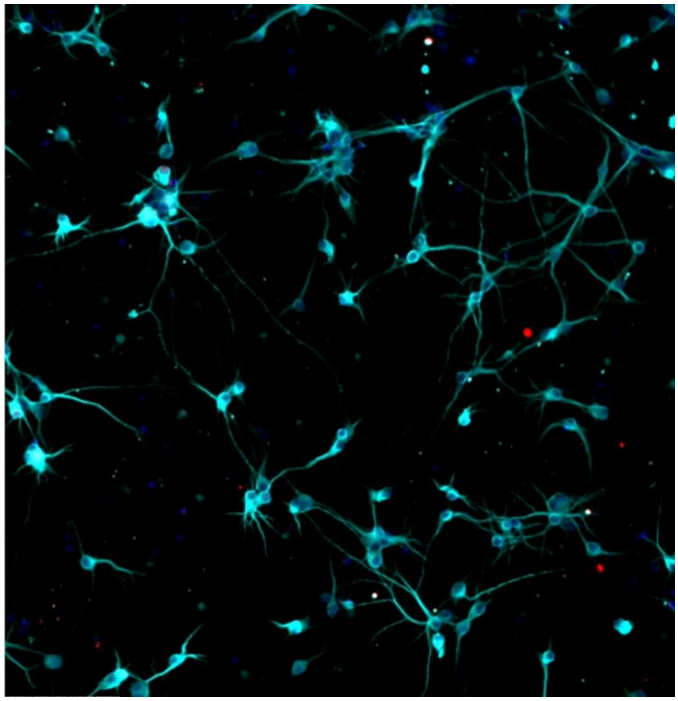
Computational Tools

Recursion OS
Biological Tools

Model and manipulate disease biology

>500 Billion

High-quality neurons produced in-house in 2022 using completely novel techniques.



Recursion OS
Automation Tools

Create scalable, repeatable and reliable laboratory processes

Up to

2.2 Million

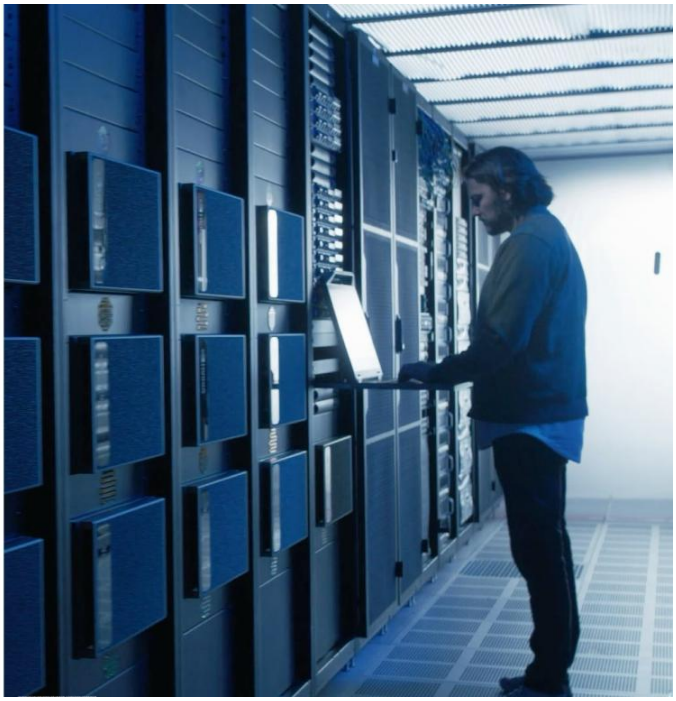
Wet-lab experiments per week

Recursion OS
Computational Tools

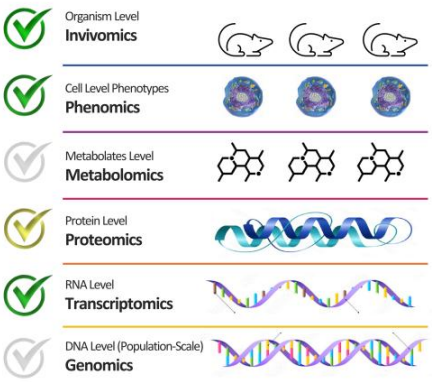
Extract, organize and analyze highly structured data

>21 Petabytes

Proprietary high-dimensional data

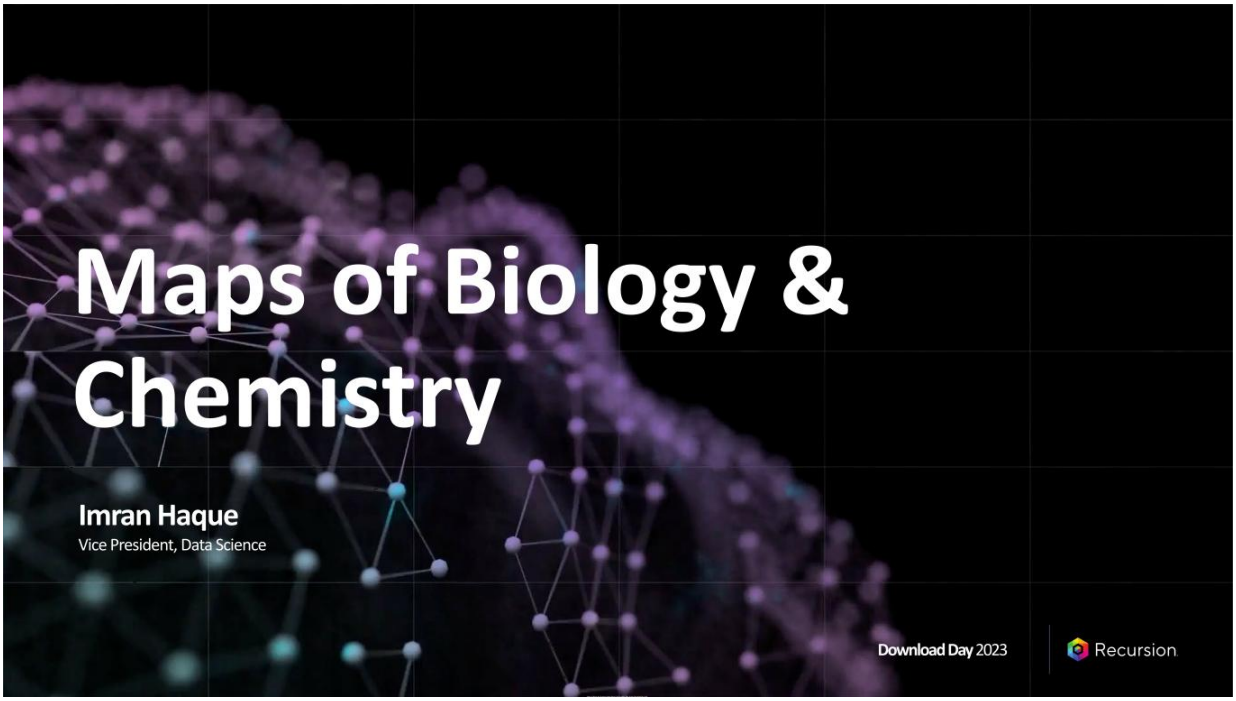


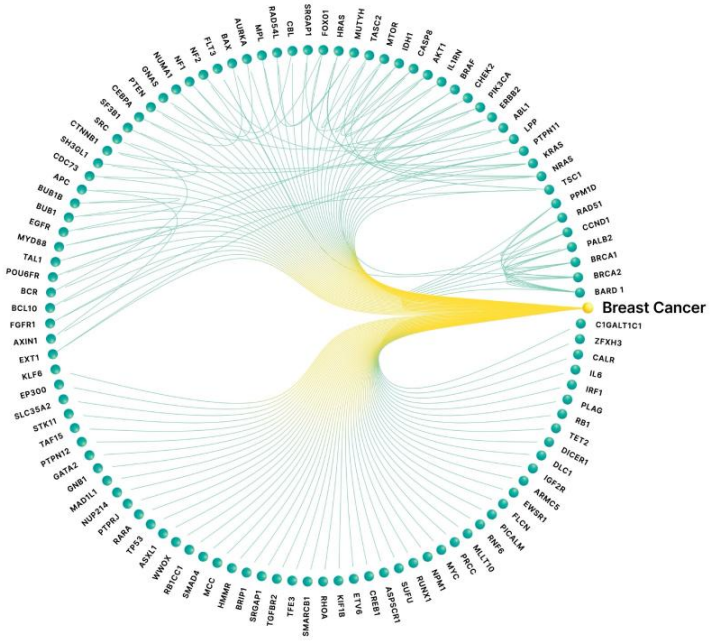
We build biological and chemical datasets to map relationships across scales and understand the connectivity of the system

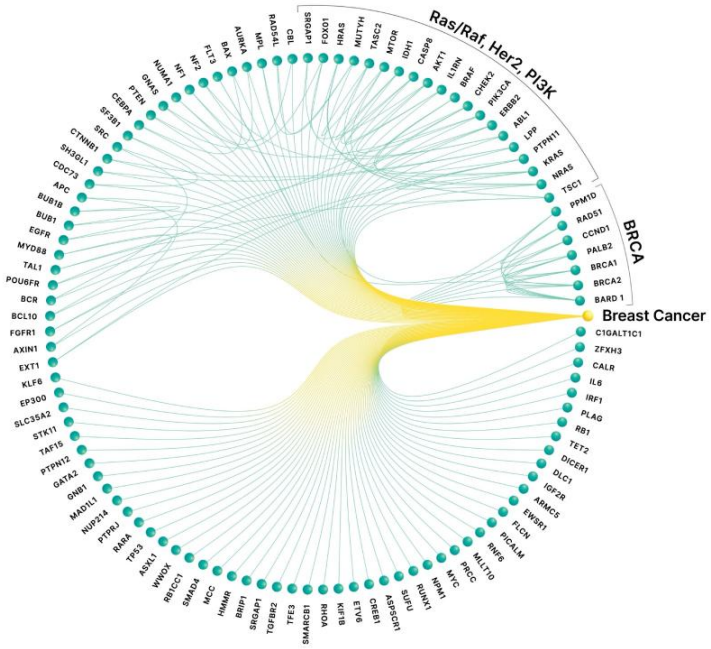


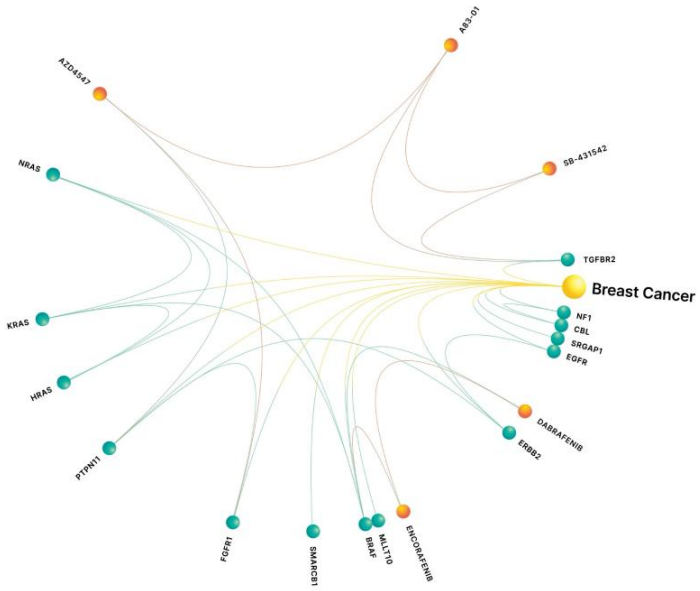
Built and scaled Exploratory Aspirational

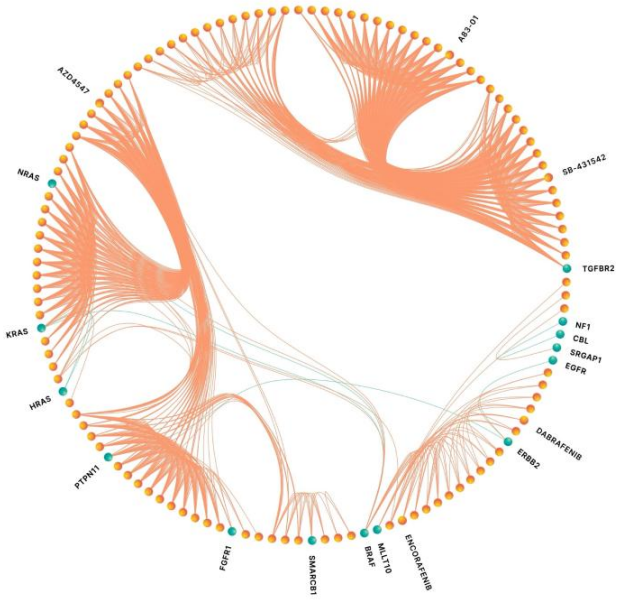
Image adapted from D'Orazio, M., et al. Nature Scientific Reports 2022.


Maps of Biology & Chemistry
Imran Haque
Vice President, Data Science
Download Day 2023
Recursion

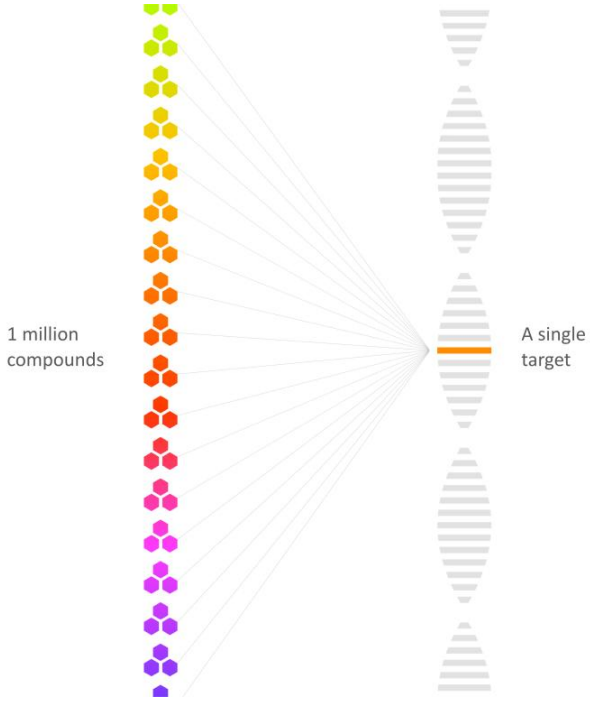

Breast Cancer
BARD 1
BRCA2
BRCA1
PALB2
CCND1
RAD51
PPM1D
TSC1
KRAS
HRAS
PTPN11
LPP
ABL1
ERBB2
PIK3CA
CHEK2
BRAF
IL1RN
AKT1
CASP8
IDH1
MTOR
TASC2
MUTYH
HRAS
FOXO1
SRGAP1
CBL
RAD54L
MPL
AURKA
BAX
FLT3
NF2
NF1
NUMA1
GNAS
PTEN
CEBPA
SF3B1
SRC
CTNNB1
SH3GL1
CDC73
APC
BUB1B
BUB1
EGFR
MYD88
TAL1
POU6F1
BCR
BCL10
FGFR1
AXIN1
EXT1
KLF6
EP300
SLC35A2
STK11
TAF15
PTPN12
GATA2
ONB1
MAD1L1
NUP214
PTPRJ
RARA
TP53
ASXL1
WWOX
RB1CC1
SMAD4
MCC
HMMR
BRIP1
SRGAP1
TGFBR2
TFE3
SMARCB1
NONO
KIF1B
ETV6
CREBB1
ASPSCR1
SUFU
RUNX1
NPM1
MYC
PRCC
MLLT10
RNF6
PICALM
FLCN
EWSR1
ABMC6
IGF2R
DLC1
DICER1
TET2
RB1
PLAG
IRF1
IL6
CALR
ZFXH3
C1GALT1C1


Ras/Raf, Her2, PI3K
BRCA
Breast Cancer
SRGAP1
FOXO1
HRAS
MUTYH
TASC2
MTOR
IDH1
CASP8
AKT1
IL1RN
BRAF
CHEK2
PIK3CA
ERBB2
ABL1
LPP
PTPN11
KRAS
NRAS
TSC1
PPM1D
RAD51
CCND1
PALB2
BRCA1
BRCA2
BARD 1
C1GALT1C1
ZFXH3
CALR
IL6
IRF1
PLAG
RB1
TET2
DICER1
ILC1
IGF2R
ARMC5
EWSR1
FLCN
PICALM
RNF6
MLLT10
PRCC
MYC
NBN1
RUNX1
SUFU
ASPSCR1
CREB1
ETV6
KIF1B
NOTCH
SMARCB1
TFE3
TGFBR2
SRGAP1
BRIP1
HMMR
MCC
SMAD4
RB1CC1
WWOX
ASXL1
TP53
RARA
PTPN13
NUP214
MAD1L1
ONS1
GATA2
PTPN12
TAF15
STK11
SLC35A2
EP300
KLF6
EXT1
AXIN1
FGFR1
BCL10
BCR
POU6F1
TAL1
MYD88
EGFR
BUB1
BUB1B
APC
CDC73
SH3GL1
CTNNB1
SRC
SF3B1
CEBPA
PTEN
GNAS
NUMA1
NF1
NF2
FLT3
BAX
AURKA
MPL
RAD54L
CBL


A83-01
AZD4547
SB-431542
NRAS
TGFBR2
Breast Cancer
KRAS
NF1
CBL
SRGAP1
EGFR
HRAS
DABRAFENIB
ERBB2
PTPN11
FGFR1
SMARCB1
BRAF
MLLT10
ENCORAFENIB

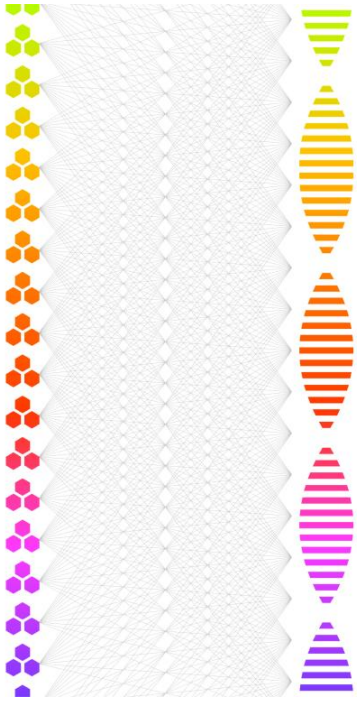

AZD4547
AR3-01
SB-431542
NRAS
TGFBR2
KRAS
NF1
CBL
SRGAP1
EGFR
HRAS
DABRAFENIB
ERBB2
PTPN11
FGFR1
SMARCB1
MLLT10
BRAF
ENCORAFENIB

Traditional target-based screens



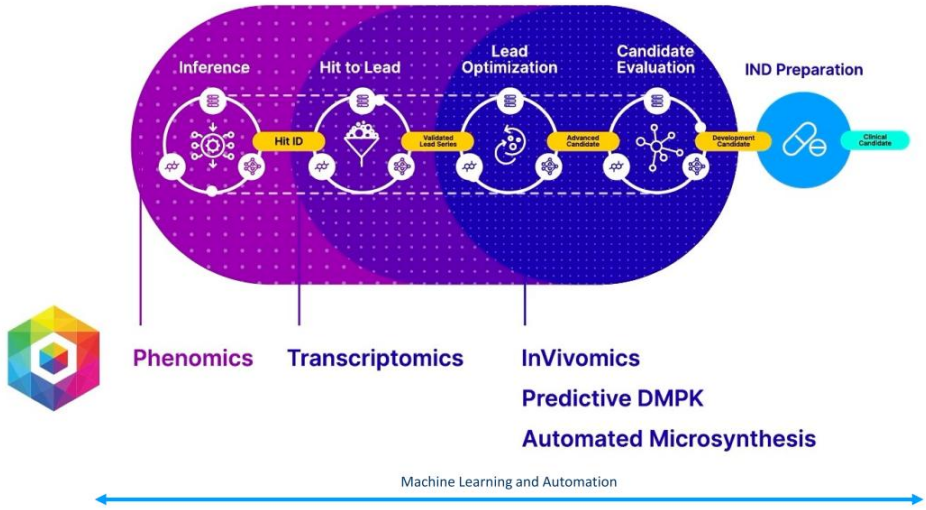
Recursion is generating exponentially more insights

1 million compounds



The entire genome

Industrializing drug discovery at Recursion: The big picture



Phenomics

Transcriptomics

InVivomics

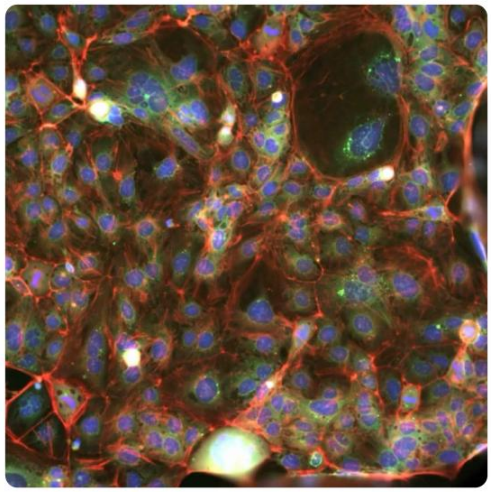
Predictive DMPK

Automated Microsynthesis

Machine Learning and Automation

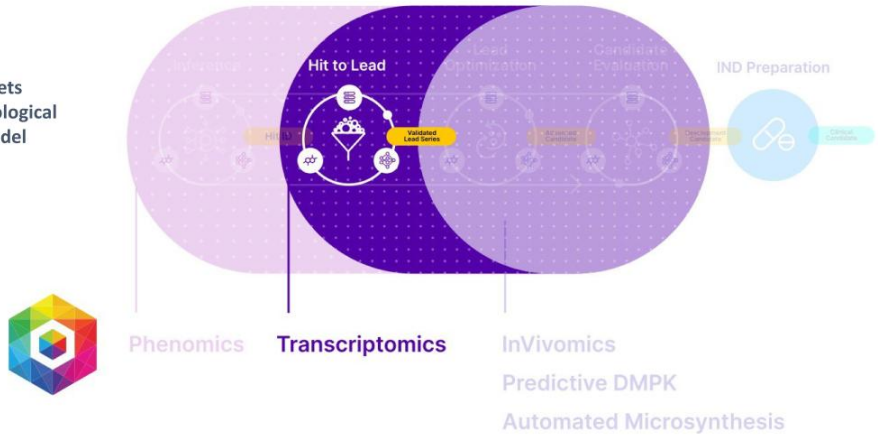
Hit ID with phenomics

- Model diseases with diverse biological and chemical tools
- Capture holistic and high-dimensional snapshots of cellular states
- Detect and analyze subtle changes using ML algorithms
- Combine datasets to reveal known & novel relationships in our Maps of Biology



Industrialized program generation and hit to lead

Multiple high-dimensional datasets validate and expand the total biological understanding of the disease model and hits



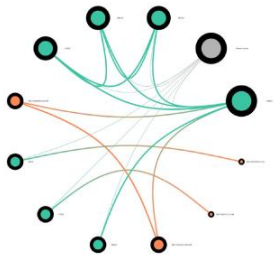
Phenomics **Transcriptomics** InVivomics

Predictive DMPK

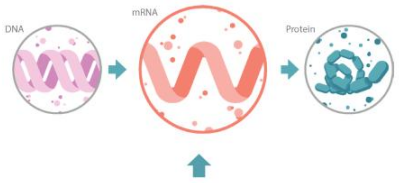
Automated Microsynthesis

Transcriptomics validates initial phenomic insights at scale

1 Relationships revealed in our maps become 'hits' for potential programs

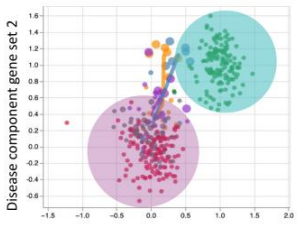


2 Transcriptomic assays validate a hypothesis with additional high-dimensional, unbiased data



Up to
15K Transcriptome profiles every week

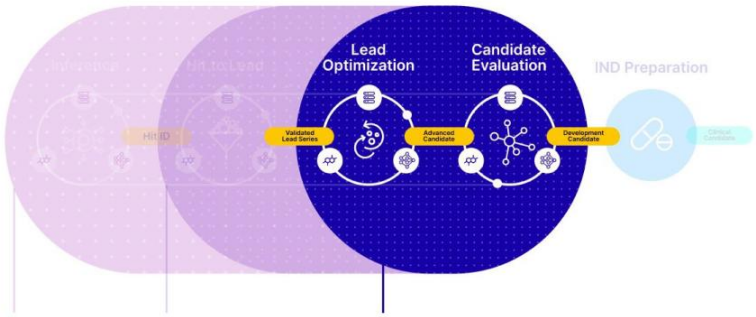
3 Detects more relationships between disease-relevant genes and each compound



Internal Myotonic Dystrophy Program

Industrialized Program Progression

Digital animal studies build high-dimensional signatures of animal behavior and health



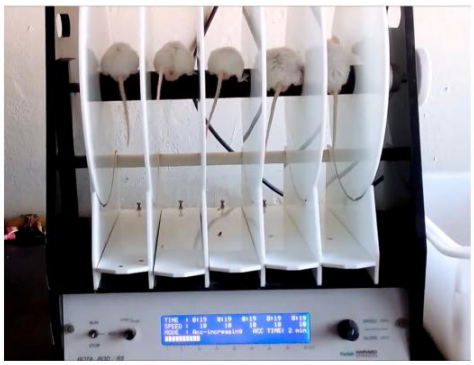
Phenomics Transcriptomics **InVivomics**

Predictive DMPK

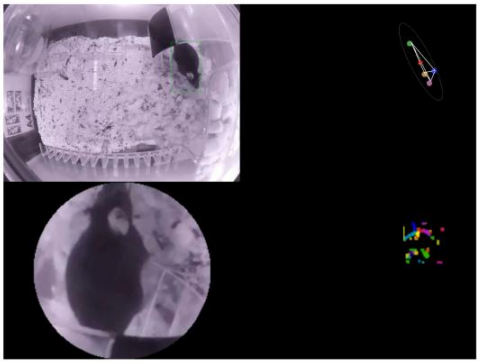
Automated Microsynthesis

InVivomics measures animal behavior with less bias and more data

Traditional Animal Studies



Recursion's Digital Animal Studies



InVivomics measures animal behavior with less bias and more data

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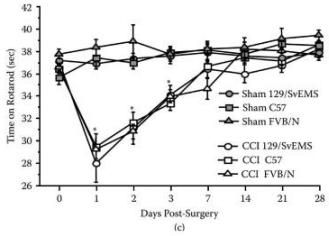
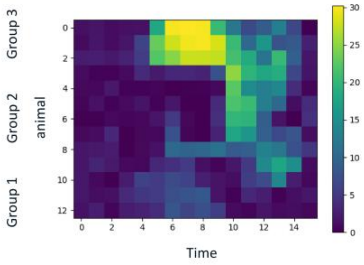


- Limited data generation
- Low-dimensional assays
- Influenced by human intervention
- Time-consuming
- Expensive

Recursion's Digital Animal Studies

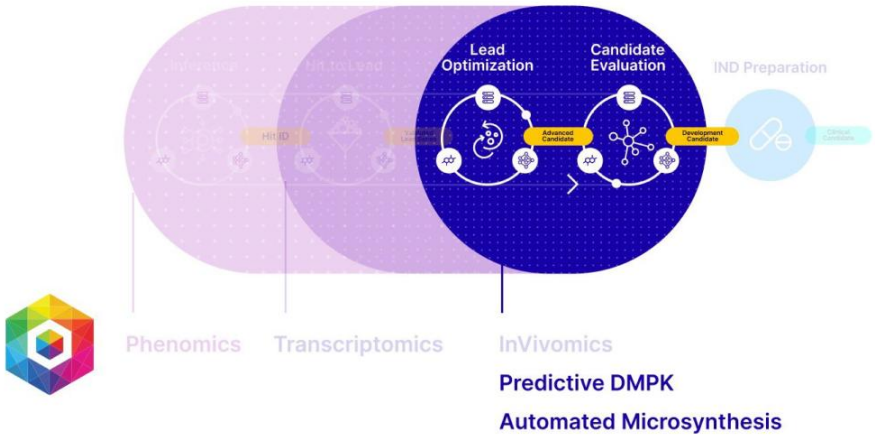


- Continuous data generation
- High-dimensional assays
- Unbiased
- Faster
- Cost-effective

InVivomics enables faster readouts for critical animal studies

	Industry Standard		Recursion
Disease Induction	1 year	vs.	~2 months
Digital Tolerability	1 week	vs.	Real-time
Liability InVivomics	6-8 weeks	vs.	<1 week

Industrialized Optimization



Phenomics Transcriptomics InVivomics

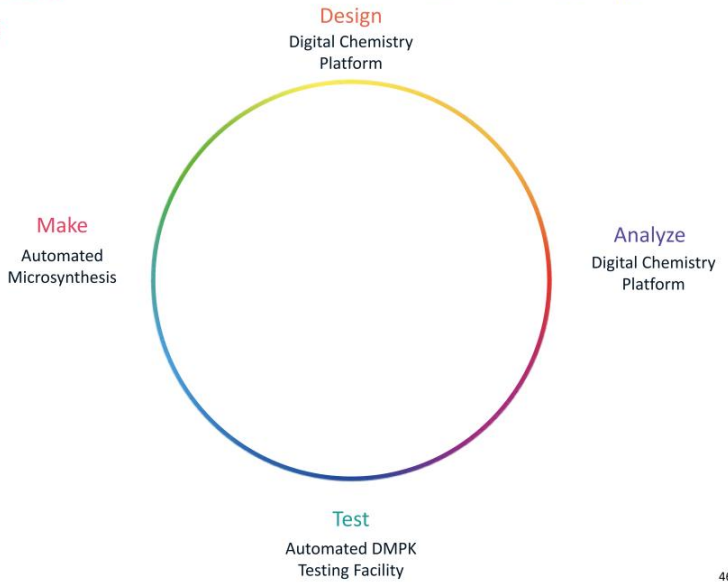
Predictive DMPK

Automated Microsynthesis

Our vision to integrate digital and robotic chemistry operations

The Impact:
Reduce time to candidate selection from months to weeks

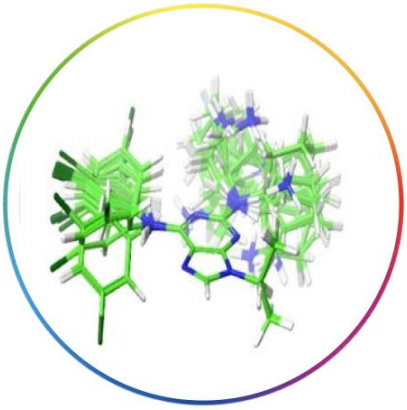
Our approach will improve the efficiency of the DMTA chemistry cycle, **reducing** the number of cycles, **shrinking** the time required, and **increasing** throughput for each cycle.



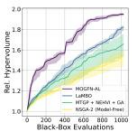
Our vision to integrate digital and robotic chemistry operations

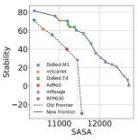
Design

Digital Chemistry Platform



Multi-Objective GFlowNets





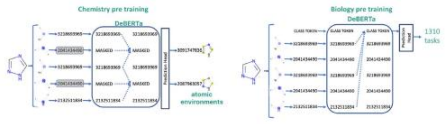
Algorithm	Diversity (↑)
NSGA-2	0.07 ± 0.03
MTGP + NEHVI + GA	0.12 ± 0.02
LaMBO	0.18 ± 0.03
MOGFN	0.25 ± 0.00

Multi-objective generative chemistry

MOGFNs outperform other benchmarked algorithms in numerous multi-objective settings in chemistry.

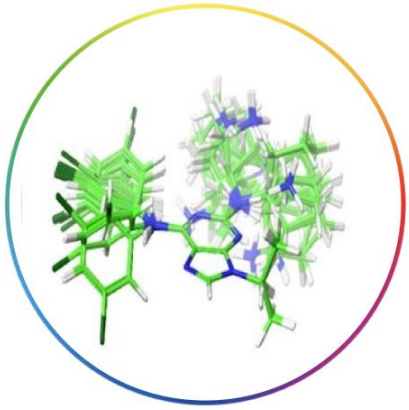
Our vision to integrate digital and robotic chemistry operations

MolE: a molecular foundation model for drug discovery



Foundation models for low-data prediction

MolE achieves #1 or #2 performance on 14 of 22 Therapeutics Data Commons ADMET tasks, including all distribution and metabolism tasks, and #1 in 9 of 22.



Analyze
Digital Chemistry Platform

Our vision to integrate digital and robotic chemistry operations

Automated DMPK Testing

Recursion proprietary DMPK module designed to test up to 500 compounds / week on three critical DMPK assays, to drive programs and fuel machine learning.

Test

Automated DMPK Testing Facility

Our vision to integrate digital and robotic chemistry operations

Robotic Synthesis

Automation of chemical synthesis will enable broader SAR and faster turnaround time for active learning cycles.

Make

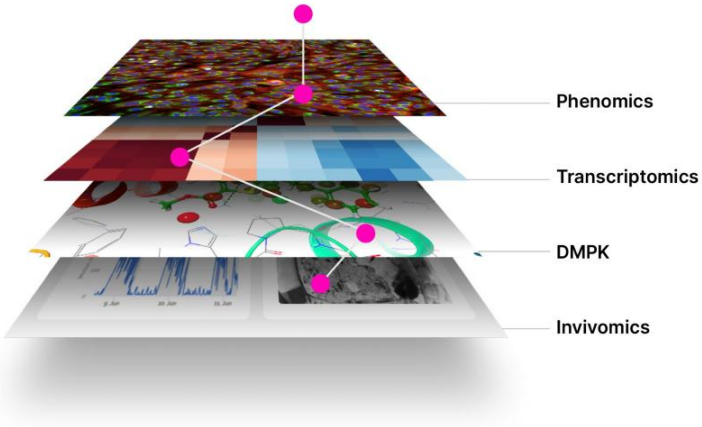
Automated Microsynthesis

Empowering scientists with multi-modal maps

Scalable

Reliable

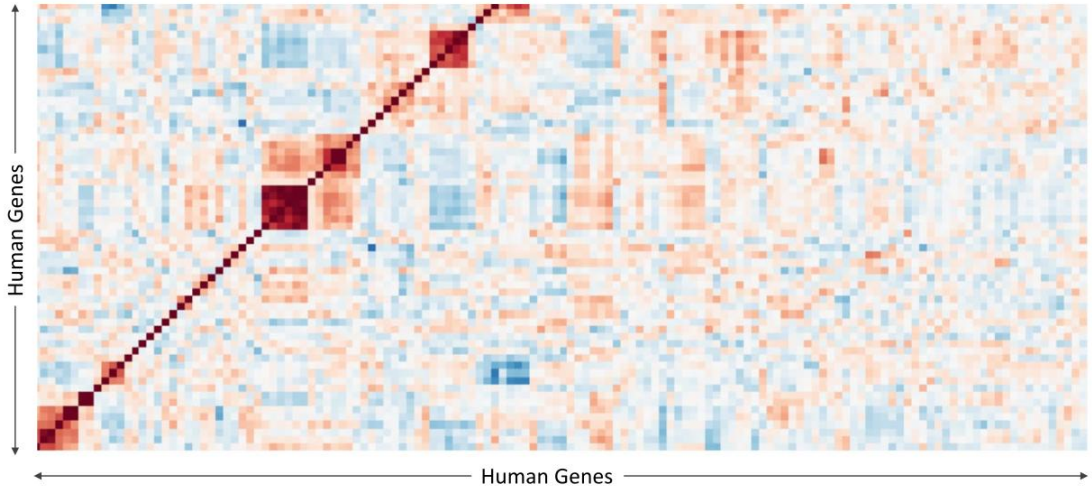
Relatable



Pre-clinical Opportunities

Laura Schaevitz PhD
Senior Vice President, Head of Research

The Recursion OS enables a differentiated capacity to interrogate...



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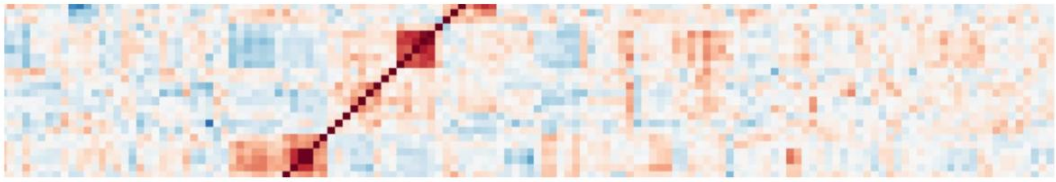
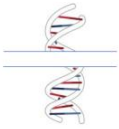


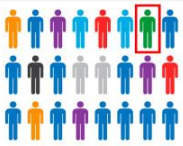
... Challenging biology

Undruggable targets

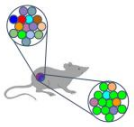


Recovery of function

... Complex datasets

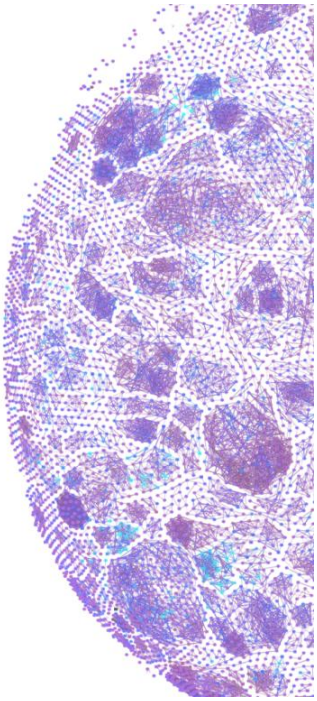


Patient genetics



Complex genetic screens

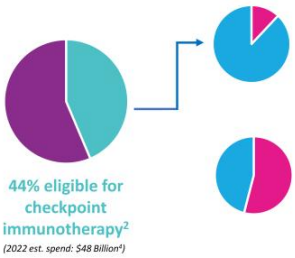
Target Alpha:
Potential first-in-class NCE with novel MOA to enhance anti-PD-(L)1 response



Pre-clinical: Target α

Ideal immunotherapy combination improves patient response and minimizes immune-related adverse events (IRAE)

1.9M US patients diagnosed with cancer in 2022[1]

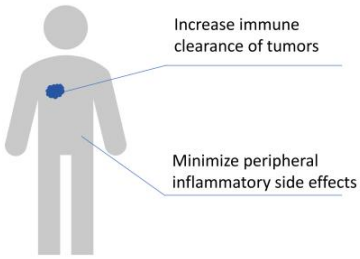


44% eligible for checkpoint immunotherapy[2]
(2022 est. spend: $48 Billion[4])

No response in 88% of patients

High proportion of treatment-limiting IRAE (Ex: 46%-melanoma[3])

Recursion's Goal

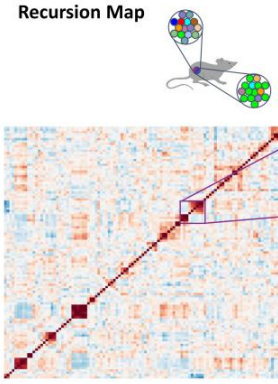


1. Cancer.gov 2. Haslam, A.; et al. JAMA Netw Open. 2019, 2, e192535. 2. Valentin,J.; et al. Journal of Oncology, Volume 2021, Article ID 5524685. 3. Ghisoni,E.; et al. European Journal of Cancer 149, 2021, 153; 4. Evaluate Pharma

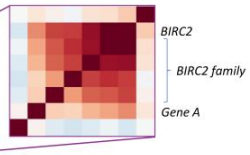
Pre-clinical: Target α

Potential first-in-class NCE with novel MOA to enhance anti-PD-(L)1 response

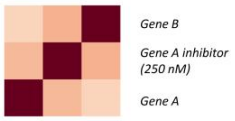
1 **Evaluation of 110 sensitization and resistance markers from public pooled CRISPR screens[1] in the Recursion Map**



2 **Identification of an unexpected, druggable gene similar to *BIRC2***



New target identified for annotated Gene A inhibitor



3 **Identification of novel dual-targeting checkpoint modifier**

Monitor local immune engagement:
Show immune-based clearance and associated cytokines

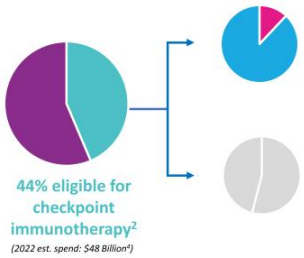
Measure peripheral inflammation:
Show reduced inflammatory risk

1 Manguso et al., 2017, Lawson et al., 2020

Pre-clinical: Target α

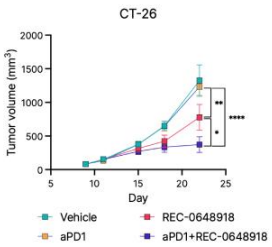
Alpha series achieves in vivo tumor response while minimizing peripheral inflammation

1.9M US patients diagnosed with cancer in 2022[1]

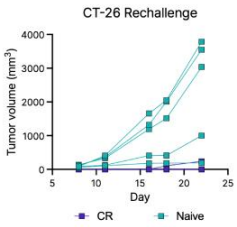


In vivo response: tumor clearance

Potentiation of immunotherapy



Immunological memory



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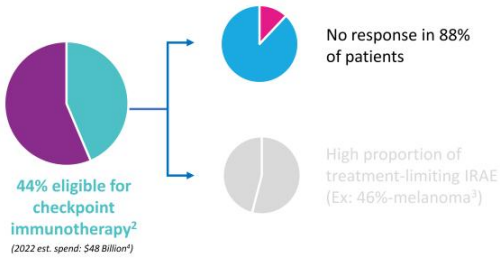

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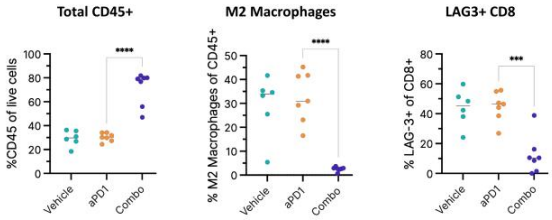

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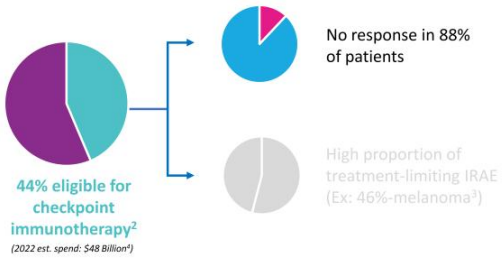

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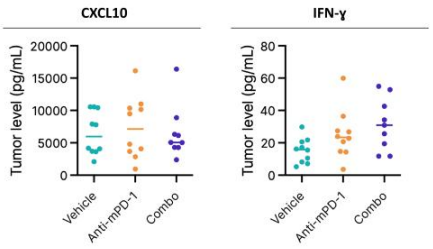
In vivo response: cytokine



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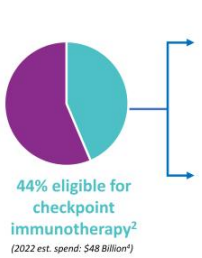

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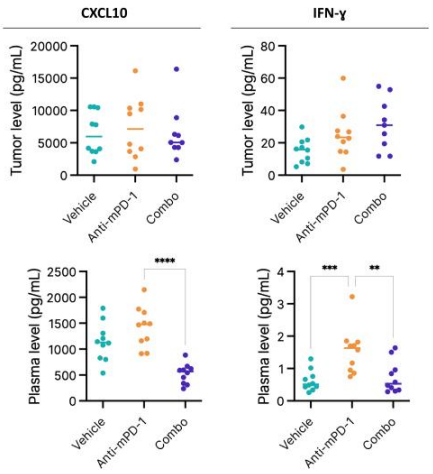

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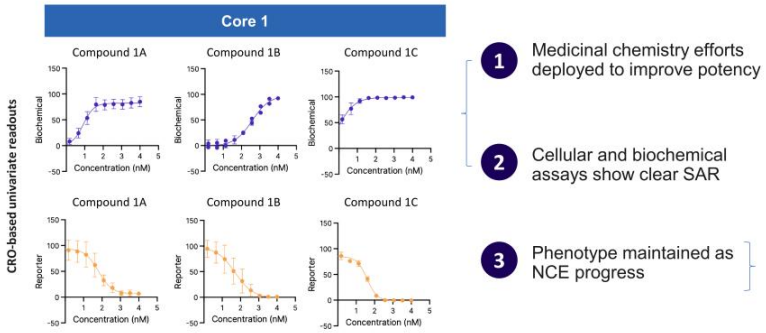
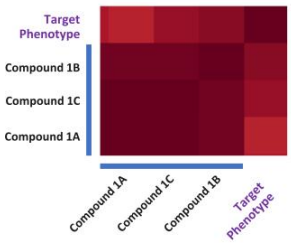
Pre-clinical: Target α

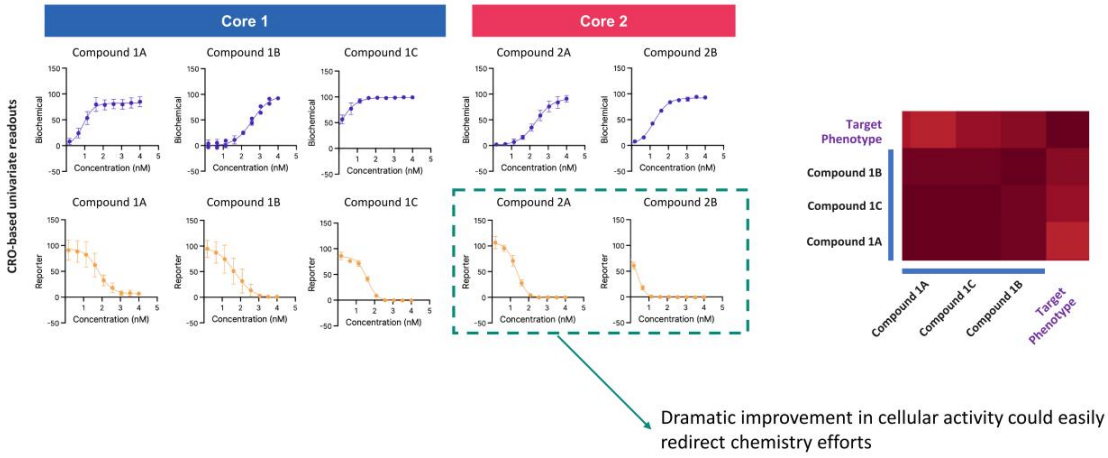
Map-guided compound optimization



1. Medicinal chemistry efforts deployed to improve potency
2. Cellular and biochemical assays show clear SAR
3. Phenotype maintained as NCE progress



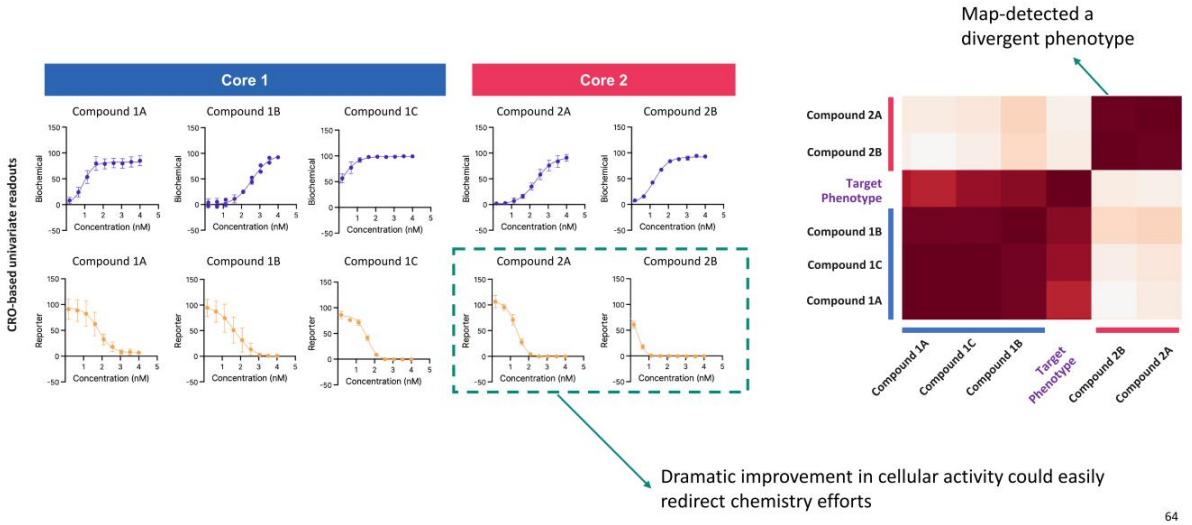
Phenomics captures total polypharmacologic activity of compounds and uncovers dramatic changes missed by univariate assays



Dramatic improvement in cellular activity could easily redirect chemistry efforts

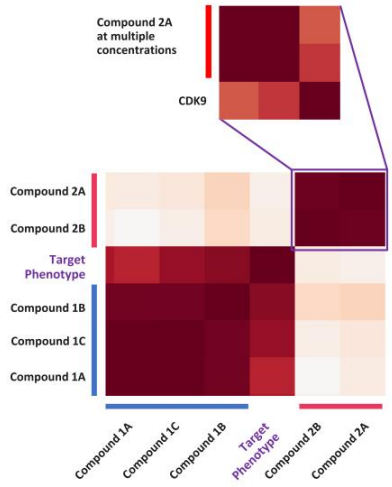
Pre-clinical: Target α

Phenomics captures total polypharmacologic activity of compounds and uncovers dramatic changes missed by univariate assays



Pre-clinical: Target α

Phenotype immediately redirects series away from unwanted activity



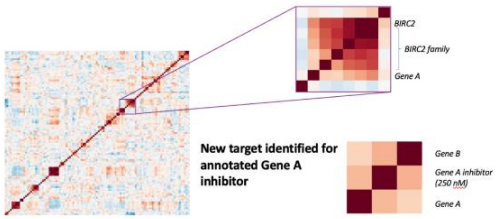
Immediately-deprioritized series

1. Despite activity in target and cellular assays, the compound series generated a clearly separate phenotype
2. Synthesis efforts immediately realigned on original series core
3. New series annotated as CDK9 inhibitor by map inference and confirmed by biochemical assay

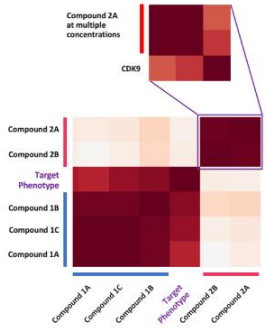
Pre-clinical: Target α

Recursion OS essential to discovering program insights and driving efficient compound optimization

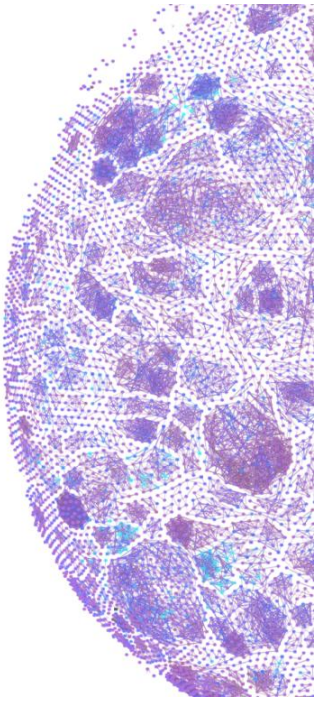
1. Unbiased discovery of an exciting dual targeting compound that appears to both enhance anti-PD1 response, while also decreasing peripheral inflammation



2. Recursion OS augmented our medicinal chemistry team enabling efficient optimization efforts on a molecule with essential polypharmacology



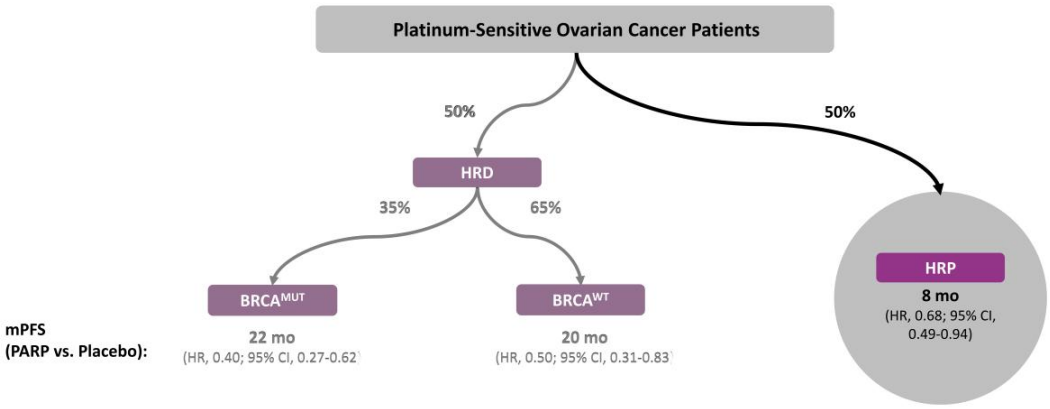
Target Gamma:
Novel CDK12-adjacent target, RBM39, for potentially treating HRD-negative ovarian cancer



Pre-clinical: Target γ

Clinical benefit of PARP inhibitors is limited in HRD-negative (HR-proficient) ovarian cancer patients

Data from cohort analysis of Phase 3 PRIMA trial for niraparib

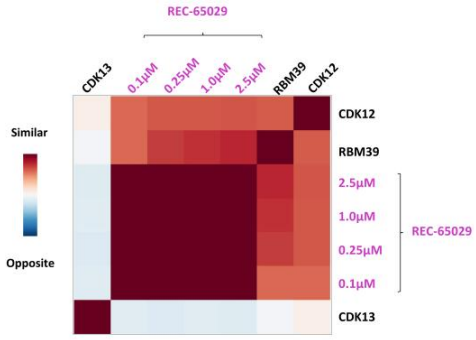


NCT02655016; N=733 patients with newly diagnosed, advanced ovarian cancer who responded to frontline platinum-based chemotherapy 2:1 to receive niraparib (n = 487) or placebo (n = 246). Niraparib is the only approved PARP in Ovarian cancer patients with HRP disease
HRD: Homologous Recombination Repair Deficient
HRP: Homologous Recombination Repair Proficient

Pre-clinical: Target γ

Novel CDK12-adjacent target, RBM39, for potentially treating HR-proficient ovarian cancer

- CDK12 has been advanced as a target to improve response in the HR-proficient setting
- Selective inhibition of CDK12 over other CDKs, especially CDK13, is very challenging
- Inhibition of target RBM39 (for example, with REC-65029) may mimic inhibition of CDK12 while mitigating toxicity due to CDK13 inhibition

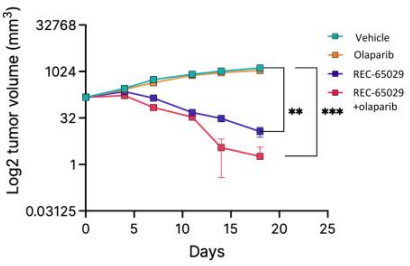


Pre-clinical: Target γ

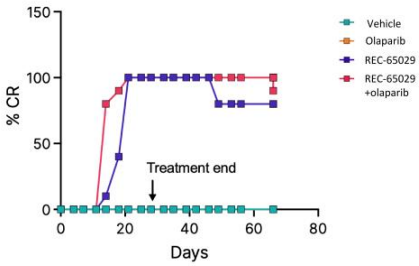
Novel CDK12-adjacent target, RBM39, induces tumor regression alone or in combination with PARPi in vivo

HR-*proficient* ovarian cancer PDX

Tumor volume



Increase in rate to CR, durability in combination

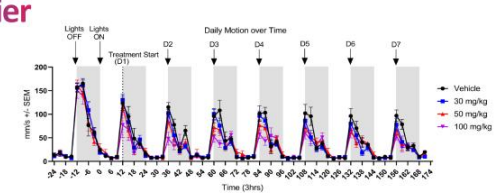


*OV0273 PDX – REC-65029 dosed at 85 mg/kg PO, BID, olaparib dosed at 90mg/kg PO QD; ** p<0.01 **** p<0.0001 relative to vehicle*

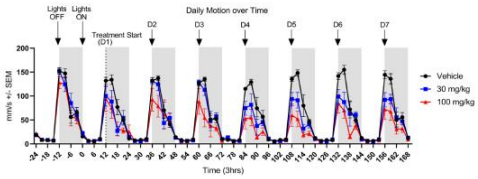
Pre-clinical: Target γ

Recursion OS-guided digital tolerability with InVivomics minimized unexpected safety risk earlier

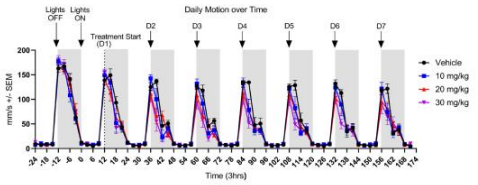
1. REC-0065029 is tolerated at an efficacious dose

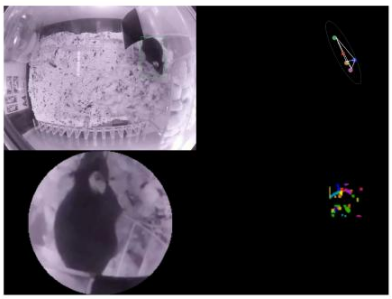


2. Digital tolerability uncovers safety concern for REC-1170204 at an efficacious dose



3. REC-1321245 demonstrates improved tolerability at efficacious doses

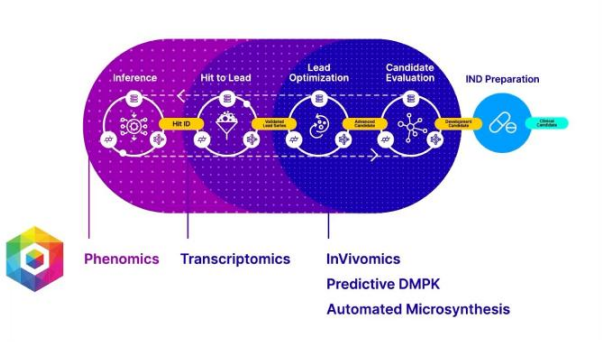




Pre-clinical

Looking ahead to 2023 and beyond

- Target Alpha and Gamma reaching IND-enabling studies in 2023
- Continuing to augment our digital chemistry and predictive capabilities (property assessment, DMPK, ADMET, etc.)
- Continuing to drive potential first-in-disease or first-in-class programs at greater automation and scale



RxRx3 Dataset & MolRec Application

Ben Mabey
Chief Technology Officer

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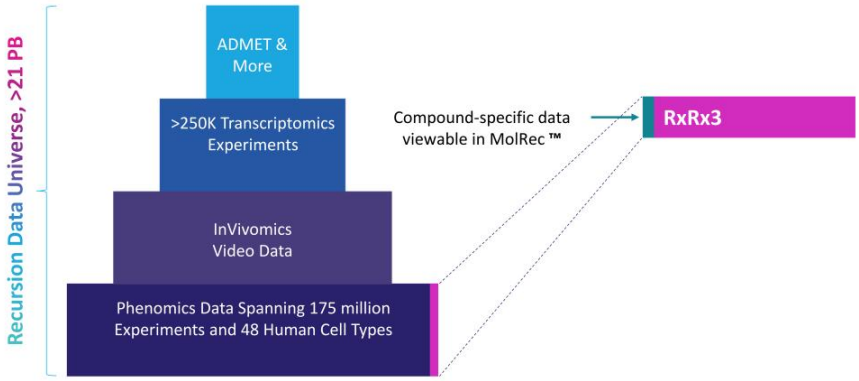
Leading the field in open science – RxRx3

RxRx3: Phenomics Map of Biology

- Spans CRISPR knockouts of most of the human genome, ~17k genes
- 1,600 FDA approved and commercially available bioactive compounds at 8 concentrations and tens of thousands of control images
- 2.2 million images and deep learning embeddings of HUVEC cells, over 100TB
- Recursion's 5th major public dataset release,
  - **100 times larger than our previous datasets *combined***

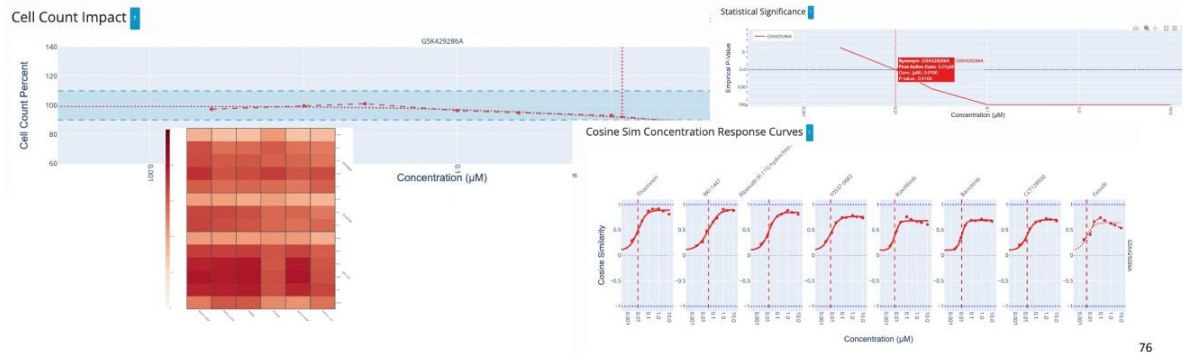
RxRx3: <1% of Recursion's phenomic data



Leading the field in open science – MolRec™ using RxRx3

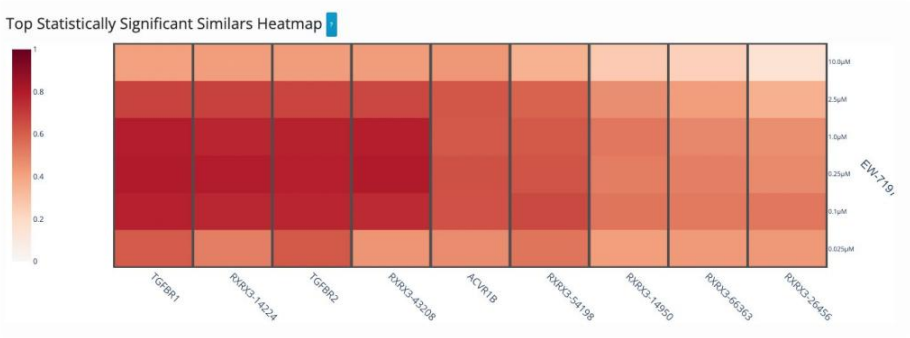
MolRec™ is a *simplified* version of one of Recursion's internal compound intelligence tools

- A demo/freemium app to illustrate what can be done with this data. This is not our flagship internal Map App.
- We are providing this tool for basic exploration of compound/compound and compound/gene relationships across ~1,600 FDA approved and commercially available bioactive compounds
- All plots and driven by this single dataset highlighting the power and flexibility of our phenomics-based platform

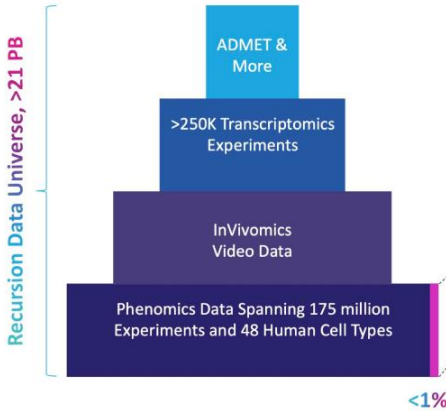


Offer a glimpse to pique interest with potential partners

The majority of the genes (~16k) are anonymized / blinded to facilitate a "sneak peek"



RxRx3: Transformational for the ML field



~10 0 TB

~1-5 TB

10 GB - ~1 TB

Dataset	Released	# of Samples
Bio/Chem Phenomic Maps		
RxRx3	**2023**	**2.2M**
JUMPCP	2023	823,438
Autonomous Driving		
Waymo Open Dataset	2018	~105,000
nuScenes	2018	1000
Computer Vision		
ImageNet (21k)	2009	14M
COCO	2014	330,000

Goals of releasing RxRx3 & MolRec™

- Offer a glimpse of the power of Recursion's internal data and tools to pique the interest of potential partners
- Provide the largest dataset of its kind to date to enrich the field and foster the next generation of computational biologists
- Discover new methods and bright talent that we can bring in house

Clinical Programs

Shafique Virani MD
Chief Business Officer &
Interim Chief Medical Officer

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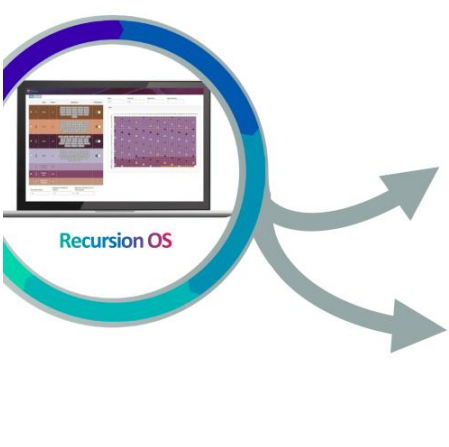
How we create value using our maps of biology and chemistry



Pipeline strategy

Build wholly-owned pipeline in indications with potential for **accelerated path** to approval

- **Precision Oncology**
- **Rare Disease**

Partnership strategy

Partner in **complex therapeutic areas** requiring large financial commitment and competitive market dynamics

Leverage partner knowledge and clinical development capabilities

- **Fibrosis**
- **Neuroscience**
  *and a single oncology indication
- **Other large, intractable areas of biology**

Our pipeline reflects the scale and breadth of our approach

More than a dozen early discovery and research programs in oncology, neuroscience, inflammation & immunology, and rare disease

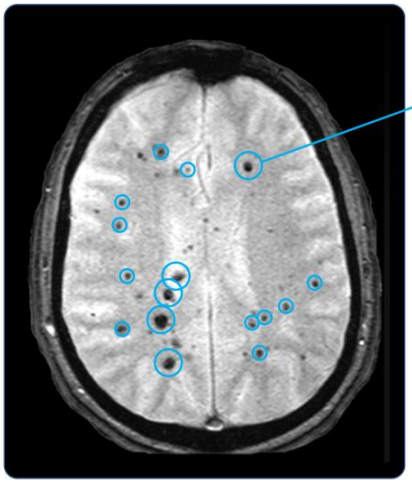
All populations defined above are US and EU5 incidence unless otherwise noted. EU5 is defined as France, Germany, Italy, Spain and UK. (1) Our program has the potential to address a number of indications driven by MYC alterations, totalling 54,000 patients in the US and EU5 annually. We have not finalized a target product profile for a specific indication. (2) Our program has the potential to address a number of indications in this space. (3) Prevalence for hereditary and sporadic symptomatic population. (4) Annual US and EU5 incidence for all NF2-driven meningiomas.

REC-994 for the Treatment of Symptomatic Cerebral Cavernous Malformations (CCM)

Target / MOA	Superoxide Scavenger
Molecule Type	Small Molecule
Lead Indication(s)	Cerebral Cavernous Malformations
Status	Phase 2
Designation(s)	US & EU Orphan Drug
Source of Insight	Recursion OS

Clinical: CCM

Disease Overview : Cerebral Cavernous Malformations (CCM)



Description

- Large unmet need for a novel nonsurgical treatment
- Vascular malformations (cavernomas) in the brain and spinal cord
- High-risk for hemorrhage creates “ticking time bomb”
- Progressive increase in CCM size and number over time in those with familial disease
- Debilitating symptoms, including intractable seizure, intracerebral hemorrhage, focal neurological deficits

“Historically, cavernomas have been managed primarily with observation, surgical resection, and occasionally radiotherapy. However, for a number of reasons, many patients with cavernomas must endure a life with neurologic symptoms”

- **Ryan Kellogg**, MD, Investigator at the University of Virginia

Clinical: CCM

CCM is an Under-Appreciated Orphan Disease

Non-oncology Orphan Indication	Product	U.S. + EU5 Prevalence
Cerebral cavernous malformation (CCM)	**REC-994 (Recursion)**	**>1,800,000 (Symptomatic: ~360,000)**
Idiopathic pulmonary fibrosis (IPF)	Esbriet (pirfenidone)	>160,000
Cystic fibrosis (CF)	VX-669/ VX-445 + Tezacaftor + Ivacaftor - Vertex	>55,000
Spinal muscular atrophy (SMA)	SPINRAZA (nusinersen)	>65,000

Source: Angioma Alliance ; Flemming KD, et al . Population-Based Prevalence of Cerebral Cavernous Malformations in Older Adults: Mayo Clinic Study of Aging. JAMA Neurol. 2017 Jul 1;74(7):801-805. doi: 10.1001/jamaneurol.2017.0439. PMID: 28492932; PMCID: PMC5647645 ; Spiegler S, et al Cerebral Cavernous Malformations: An Update on Prevalence, Molecular Genetic Analyses, and Genetic Counselling. Mol Syndromol. 2018 Feb;9(2):60-69. doi: 10.1159/000486292. Epub 2018 Jan 25. PMID: 29593473; PMCID: PMC5836221; Maher T, et al Global incidence and prevalence of idiopathic pulmonary fibrosis. Respir Res. 2021 Jul 7;22(197). Doi: 10.1186/s12931-021-01791-z. PMID: 34233665. DRG 2022 Solutions, Report: Epidemiology, Cystic Fibrosis. CDC: SMA

Clinical: CCM

Disease Overview : Cerebral Cavernous Malformations (CCM)

Julia – living with CCM

Patient Population – Large and Diagnosable

- **>1 million patients** worldwide live with these lesions today
- Caused by loss of function mutation in one of three genes: *CCM1 (60%), CCM2 (20%),* and *CCM3 (20%)*
- Inherited autosomal dominant mutation in 30-40%; or sporadic
- US symptomatic population is more than 5 times larger than other rare diseases like **Cystic Fibrosis** (>31k patients) and **Spinal Muscular Atrophy** (>33k patients)

No Approved Medical Therapy

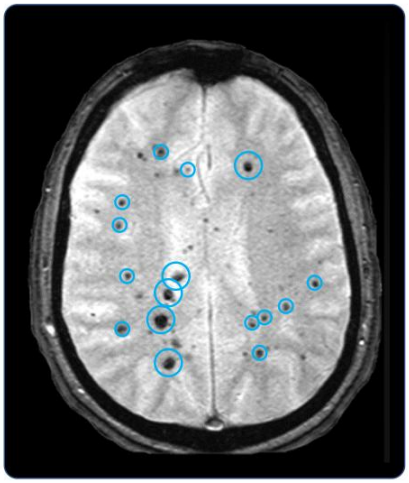
- **No approved drugs** for CCM and *no other* potential therapeutic in industry-sponsored clinical development
- Most patients receive **no treatment** or only **symptomatic therapy**
- Surgical resection or stereotactic radiosurgery not always feasible because of location of lesion and is not curative

~360,000 Symptomatic US + EU5 patients

Source: Angioma Alliance ; Flemming KD, et al . Population-Based Prevalence of Cerebral Cavernous Malformations in Older Adults: Mayo Clinic Study of Aging. JAMA Neurol. 2017 Jul 1;74(7):801-805. doi: 10.1001/jamaneurol.2017.0439. PMID: 28492932; PMCID: PMC5647645 ; Spiegler S, et al Cerebral Cavernous Malformations: An Update on Prevalence, Molecular Genetic Analyses, and Genetic Counselling. Mol Syndromol. 2018 Feb;9(2):60-69. doi: 10.1159/000486292. Epub 2018 Jan 25. PMID: 29593473; PMCID: PMC5836221.

Clinical: CCM

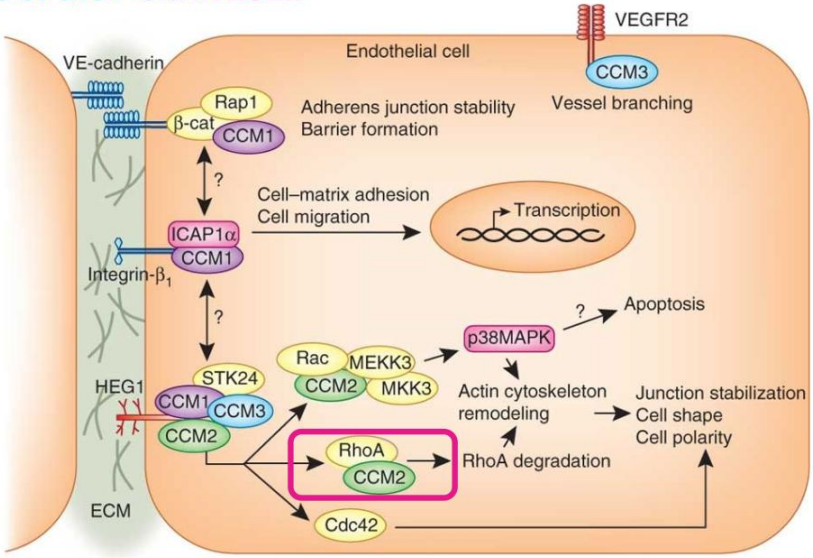
Therapeutic Approach to Cerebral Cavernous Malformations (CCM)



Novel therapeutic approach

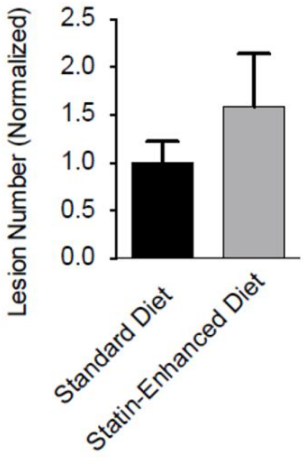
- Symptoms associated with both increased size of lesions, but also inflammation or activation of lesions within the immunopriviledged environment of the brain
- Lesions arise from the capillary bed and are not high-pressure (e.g. the lesion growth is unlikely to be primarily driven by the *law of Laplace*)
- *The Recursion Vascular Stability Hypothesis:*
  - Eliminating the lesions may not be required for significant patient benefit
  - Slowing or halting the growth of the lesions while mitigating lesion leakiness and endothelial cell activation to halt the feed-forward inflammatory reaction *may* mitigate some symptoms and be beneficial to patients

CCM – State of the Field in 2011



Storkebaum, et al. Cerebrovascular disorders: molecular insights and therapeutic opportunities. Nature Neuroscience, 2011

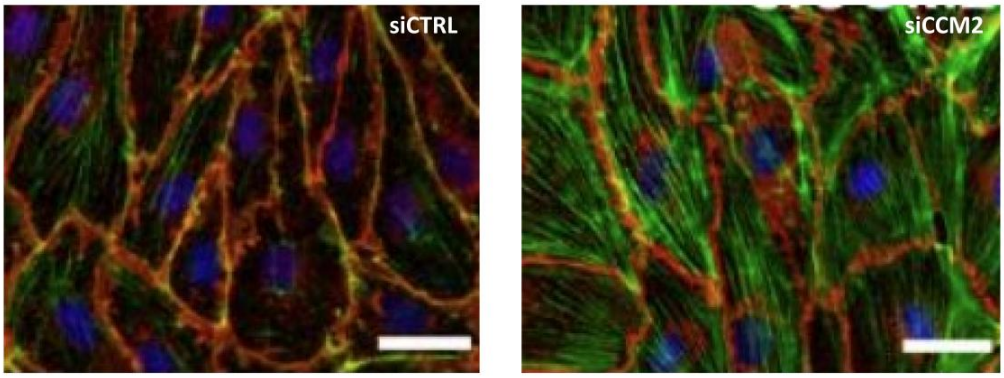
CCM – A Traditional Approach Fails



Gibson, et al. Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation, 2015

Clinical: CCM

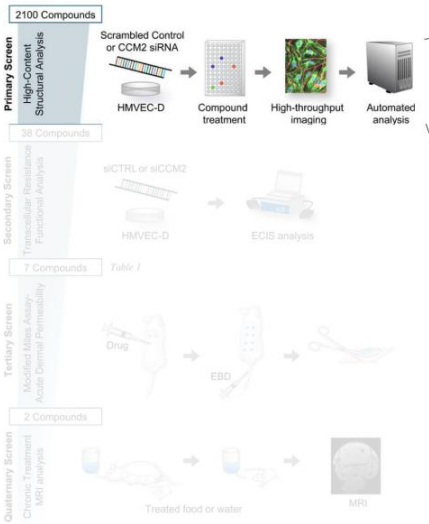
CCM – An Unbiased Approach Using ML on Cellular Images?

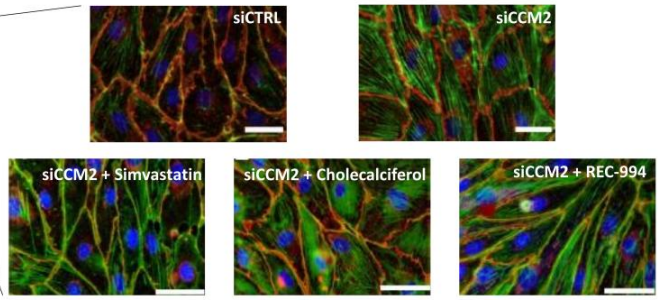


Gibson, et al. Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation, 2015

Clinical: CCM

CCM – Applied prototyping of the RecursionOS





To the human eye, Simvastatin looks like the only potential *rescue* in this panel. However, we already know that at the doses tested it did *not* rescue the translational animal model…

…but according to a basic machine-learning classifier trained on images, cholecalciferol, REC-994 and other molecules show image-based *rescue.*

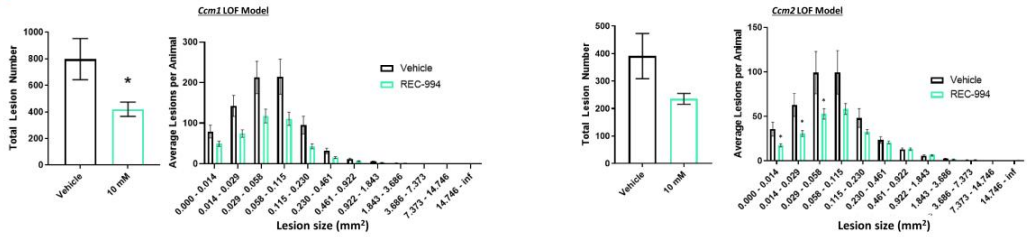
Gibson, et al. Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation, 2015

Clinical: CCM

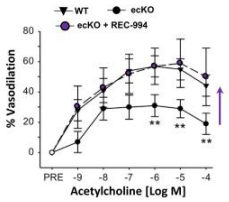
Further Confidence : Preclinical Studies Confirm Insight

Preclinical Studies: REC-994 reduces lesion burden and ameliorates vascular defects in genetic mouse models of CCM

1 **Reduces lesion number and size in *Ccm1* and *Ccm2* LOF mouse models**

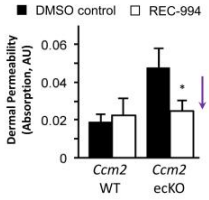


2 **Completely rescues acetylcholine-induced vasodilation defect**



REC-994 stabilizes the integrity of vasculature against challenges to permeability

3 **Rescues dermal permeability defect in CCM2 mice**



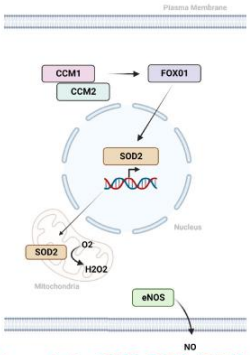
Vascular permeability is a clinically relevant feature of CCM lesions

Source:: Data above from Gibson, et al. Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation, 2015 or Recursion internal data (Ccm1 mouse model)

Clinical: CCM

REC-994 – Mechanism of Action

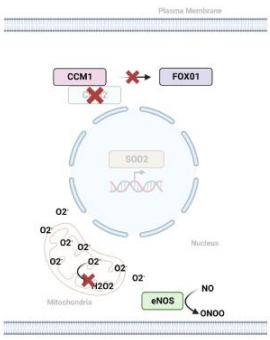
Healthy



By regulating SOD2, CCM1 (KRIT1) & CCM2 suppress:

- Endothelial cell activation
- Smooth muscle proliferation
- Leukocyte adhesion
- Platelet aggregation

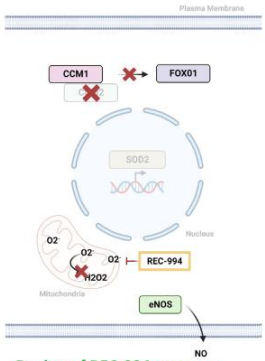
CCM



***CCM1* or *CCM2* loss of function leads to activated endothelium:**

- Decreased cell-cell junctional integrity and increased monolayer permeability
- Impaired vasodilation
- Cavernous angioma formation

REC-994 Impact



Dosing of REC-994 restores normal function:

- Normalized ROS balance
- Restores quiescent endothelial cell state
- Stabilizes endothelial barrier function

Adapted from REC-994 Investigator Brochure

Clinical: CCM

Further Confidence : Clinical Studies Confirming Safety

REC-994 Phase 1 Studies - well-tolerated with no dose-dependent adverse events in SAD and MAD

MAD Study	Placebo	50 mg	200 mg	400 mg	800 mg
Total Number of TEAEs	5	0	10	4	15
Total Subjects with ≥ one TEAE	4	0	3	3	4
Severity					
Mild	3	0	3	3	3
Moderate	1	0	0	0	1
Severe	0	0	0	0	0
Relationship to Study Drug					
None	3	0	0	2	1
Unlikely	1	0	1	1	2
Possibly	0	0	0	0	0
Likely	0	0	2	0	1
Definitely	0	0	0	0	0
Total Number of SAEs	0	0	0	0	0
Total Subject with ≥ one TEAE	0	0	0	0	0
Discontinued Study Drug Due to AE	0	0	0	0	0

Source: REC-994 for the Treatment of Symptomatic Cerebral Cavernous Malformation (CCM) Phase 1 SAD and MAD Study Results. Oral Presentation at Alliance to Cure Scientific Meeting. 2022 Nov 17

Clinical: CCM

SYCAMORE Clinical Trial : REC-994 Phase 2 Underway

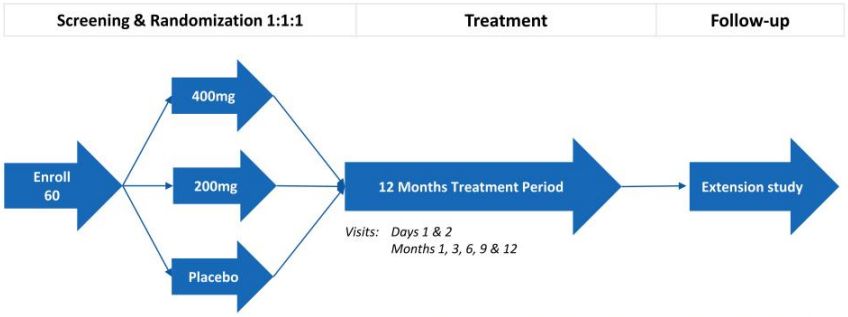
Phase 2 trial initiated in Q1 2022

Enrollment Criteria

- MRI-confirmed CCM lesion(s)
- Familial or sporadic
- Symptoms directly related to CCM

Outcome Measures

- Primary: Safety and tolerability
  - Adverse events & symptoms
- Secondary: Efficacy
  - Clinician-measured outcomes (CGI and PGI)
  - Imaging of CCM lesions – number, size & rate of change
  - Impact of acute stroke (mRS, NIHSS)
  - Patient reported outcomes (SMSS, PROMIS-29, CCM HI, symptom questionnaires)
- Exploratory: Biomarkers



Trial Update

- Enrollment is progressing
- Top-line data expected 2H 2024

Source: https://www.clinicaltrials.gov/ct2/show/NCT05130866?term=recursion&draw=2&rank=3; https://www.SycamoreCCM.com/

REC-2282 for the Treatment of Progressive Neurofibromatosis Type 2 (NF2) Mutated Meningiomas

Target / MOA	HDAC Inhibitor
Molecule Type	Small Molecule
Lead Indication(s)	NF2 Mutated Meningiomas
Status	Phase 2/3
Designation(s)	Fast Track; US and EU Orphan Drug
Source of Insight	Recursion OS

Disease Overview : Neurofibromatosis Type 2 (NF2)

Ricki – living with NF2

Source: https://rarediseases.org/rare-diseases/neurofibromatosis-2

Patient Population – Large and Diagnosable

- Rare autosomal dominant tumor syndrome resulting from biallelic inactivation of the *NF2* gene which leads to deficiencies in the tumor suppressor protein merlin
- **NF2 can be inherited or spontaneous** (>50% of patients represent new mutations); up to 1/3 are mosaic
- CNS manifestations: meningiomas and vestibular schwannomas; mean age at presentation: **~20 years**

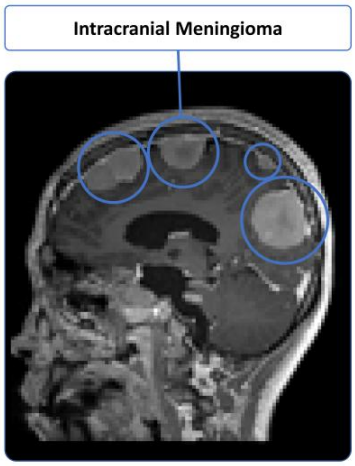
No Approved Medical Therapy

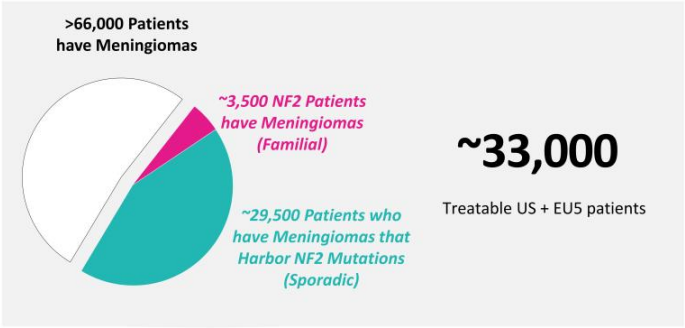
- **No approved drugs** for NF2
- **Surgery** is standard of care (when feasible)
- Location may make complete resection untenable, leading to hearing loss, facial paralysis, poor balance and visual difficulty

Clinical: NF2

Disease Overview : Neurofibromatosis Type 2 (NF2) Meningiomas

- Most tumors are benign and slow growing but location in CNS leads to serious morbidity or mortality
- Prognosis is adversely affected by early age at onset, a higher number of meningiomas and having a truncating mutation



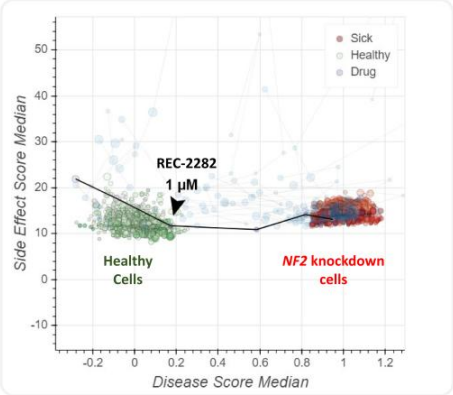


- Threatens mortality; if amenable, surgical excision is primary intervention
- Many patients have multiple meningiomas that exhibit heterogenous behavior and asynchronous growth
- **Stasis or shrinkage of tumor could improve prognosis**

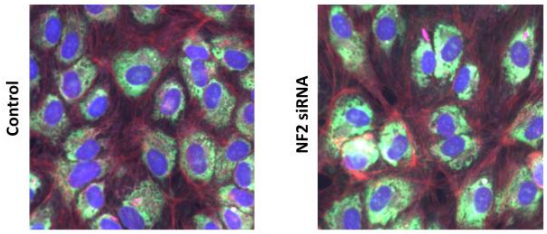
Source: Pemov, et al. Comparative clinical and genomic analysis of neurofibromatosis type 2-associated cranial and spinal meningiomas. Nature. 2020 Jul 28;10(12563). Doi: https://doi.org/10.1038/s41598-020-69074-z; NORD

Clinical: NF2

Insight from OS : REC-2282 Rescued Loss of *NF2*



REC-2282 identified as rescuing HUVEC cells treated with NF2

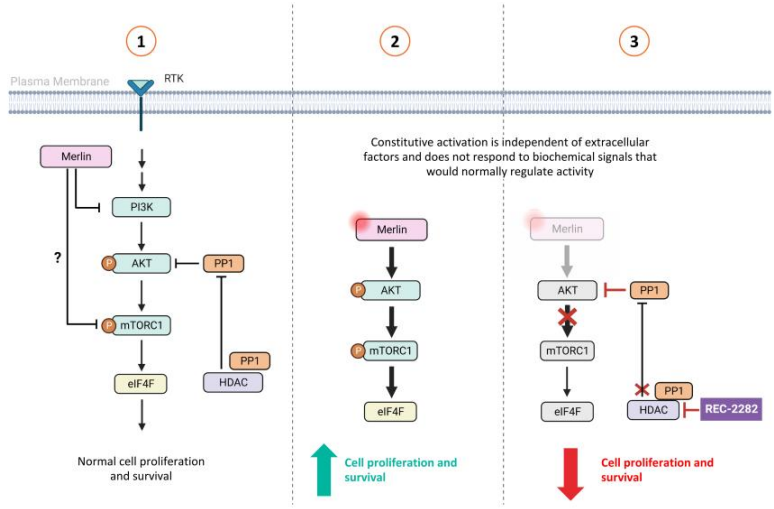


HUVEC, human umbilical vein endothelial cells; NF2, neurofibromatosis type 2; siRNA, small interfering RNA.

Clinical: NF2

REC-2282 – Mechanism of Action

Orally Bioavailable, CNS-penetrating, Small Molecule HDAC Inhibitor



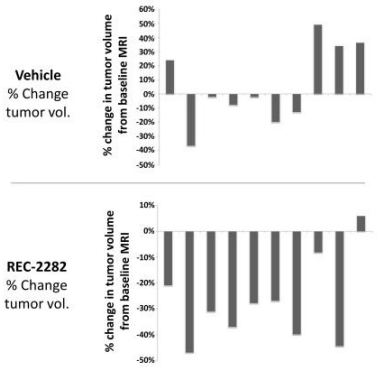
1. NF2 encodes for the protein Merlin and negatively regulates mTOR signaling
2. Loss of Merlin leads to increased signaling in the PI3K/AKT/mTOR pathway
3. Oncogenic mTOR signaling arrested with HDAC inhibitors

AKT, protein kinase B; eIF4F, eukaryotic initiation factor 4F; HDAC, histone deacetylase; mTor, mammalian target of rapamycin; mTORC1; mammalian target of rapamycin complex 1; NF2, neurofibromatosis type 2; PI3K, phosphoinositide 3-kinase; PP1, protein phosphate 1; Ras, reticular activating system.

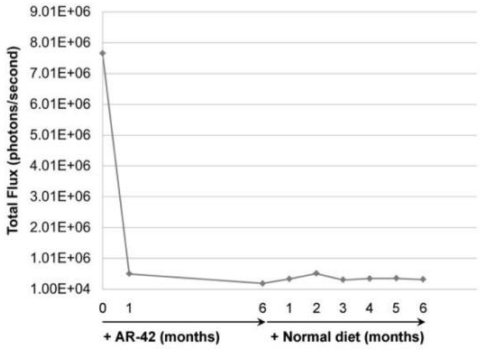
Further Confidence : Preclinical Studies Confirming Insight

REC-2282 preclinical studies demonstrated clear in-vivo efficacy in multiple NF2 tumor types

1 Shrinks vestibular schwannoma xenografts in nude mice



2 Prevents growth & regrowth of NF2-deficient meningioma model in mice



https://link.springer.com/article/10.1007/s00280-020-04229-3

Clinical: NF2

Further Confidence : Prior Studies Suggestive of Potential Therapeutic Benefit

- **Evaluable Patients: CNS Solid Tumors: NF2 N=5; Non-CNS Solid Tumors: N=10**
- PFS: CNS solid tumors = **9.1** months; Non-CNS solid tumors = **1.7** months
- Best overall response = **SD in 8/15 patients** (53%; 95% CI 26.6–78.7)
- Longest duration of follow-up without progression: > **27 months** (N=1)
- Most common AEs: **cytopenia, fatigue, nausea**

Well understood clinical safety ...

- Multiple investigator-initiated studies in oncology indications
- Lengthy human clinical exposure in NF2 – multiple patients on drug for several years
- Well-characterized side effect profile

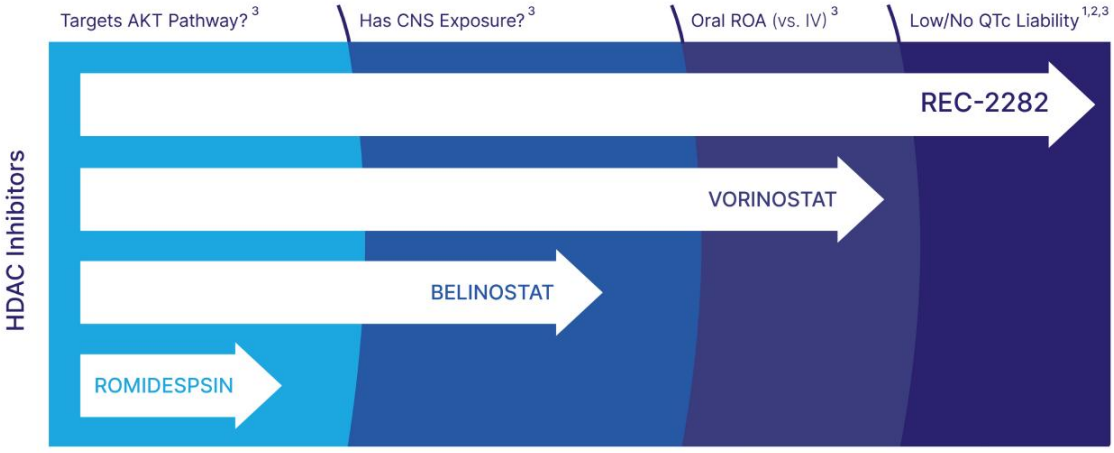
... with a drug-like profile

- Established and scalable API manufacturing process
- Multiple cGMP batches of 10mg and 50mg tablets have been manufactured
- Excellent long-term stability

Clinical: NF2

REC-2282 Appears Well Suited for NF2 vs. Other HDAC inhibitors

REC-2282 Would be First-In-Class HDAC Inhibitor for Treatment of NF2 Meningiomas



[1]Sborov DW, et al. A phase 1 trial of the HDAC inhibitor AR-42 in patients with multiple myeloma and T- and B-cell lymphomas. Leuk Lymphoma. 2017 Oct;58(10):2310-2318.
[2]Collier KA, et al. A phase 1 trial of the histone deacetylase inhibitor AR-42 in patients with neurofibromatosis type 2-associated tumors and advanced solid malignancies. Cancer Chemother Pharmacol. 2021 May;87(5):599-611.
[3] Prescribing information of Vorinostat/Belinostat/Romidepsin respectively

Clinical: NF2

POPLAR Clinical Trial : REC-2282 Phase 2/3 Underway

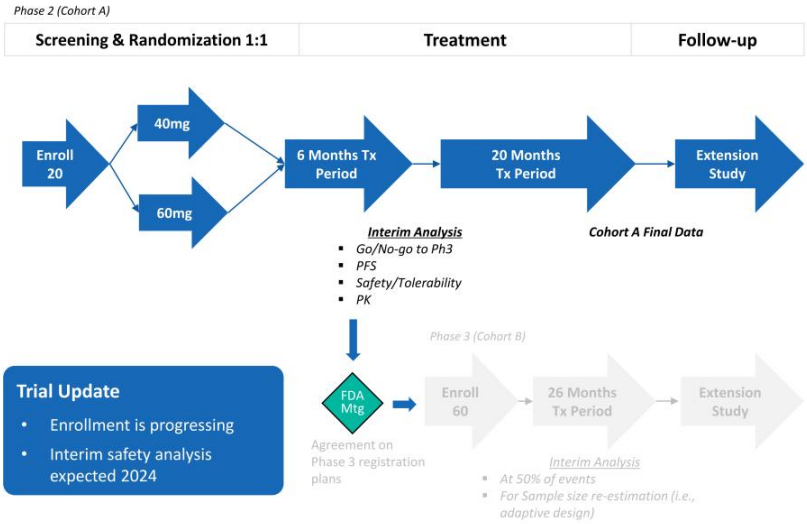
Phase 2/3 trial initiated in Q2 2022

Enrollment Criteria

- MRI-confirmed progressive meningioma
- Either of the below
  - Sporadic meningioma with confirmed NF2 mutation
  - Confirmed diagnosis of NF2 disease

Outcome Measures

- Primary: Safety and tolerability
  - Progression-free survival
  - Time to progression
  - Duration of response
  - Overall response rate



Trial Update

- Enrollment is progressing
- Interim safety analysis expected 2024

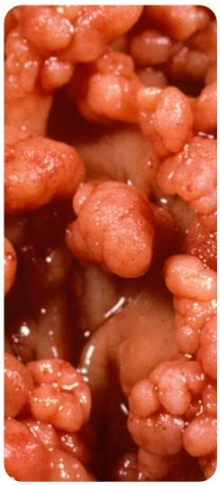
https://clinicaltrials.gov/ct2/show/NCT05130866

REC-4881 for the Treatment of Familial Adenomatous Polyposis (FAP)

Target / MOA	MEK Inhibitor
Molecule Type	Small Molecule
Lead Indication(s)	Familial Adenomatous Polyposis
Status	Phase 2
Designation(s)	Fast Track; US and EU Orphan Drug
Source of Insight	Recursion OS

Clinical: FAP

Disease Overview : Familial Adenomatous Polyposis



Polyps Found in Colon and Upper GI Tract

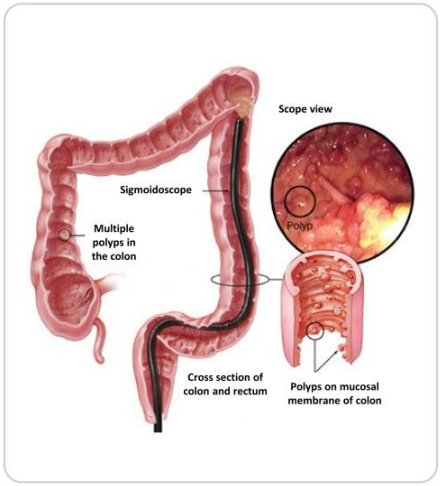
Patient Population – Easily Identifiable

- Autosomal dominant tumor predisposition syndrome caused by a mutation in the APC gene
- Classic FAP (germline mutation) :
  - Hundreds to thousands of polyps in colon and upper GI tract
  - Extraintestinal manifestations (e.g. desmoid tumors)
  - 100% likelihood of developing colorectal cancer (CRC) before age 40, if untreated

~50,000 Diagnosed US + EU5 patients

https://www.hopkinsmedicine.org/health/conditions-and-diseases/familial-adenomatous-polyposis

Disease Overview : Familial Adenomatous Polyposis – Standard of Care



No Approved Medical Therapy

- Standard of care: colectomy during adolescence (with or without removal of rectum)
- Post-colectomy, patients still at significant risk of polyps progressing to GI cancer
- Significant decrease in quality-of-life post-colectomy: continued endoscopies and surgical intervention

"Despite progress with surgical management, the need for effective therapies for FAP remains high due to continued risk of tumors post-surgery"

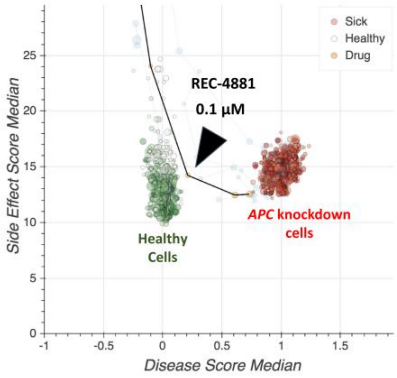
- **Niloy Jewel Samadder**, MD, Mayo Clinic

https://www.hopkinsmedicine.org/health/conditions-and-diseases/familial-adenomatous-polyposis

Clinical: FAP

Insight from OS : Rescued Loss of *APC*, Inhibited Tumor Growth

REC-4881 rescued phenotypic defects of cells with APC knockdown



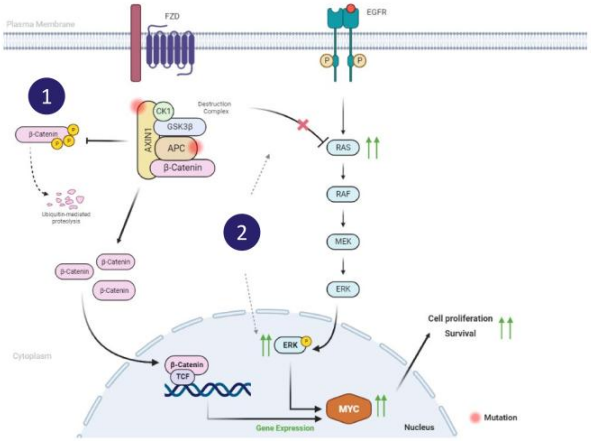
- Compared to thousands of other molecules tested, REC-4881 rescued phenotypic defects substantially better (including better rescue than other MEK inhibitors) for APC specific knockdown
- Findings validated in tumor cell lines and spheroids grown from human epithelial tumor cells with *APC* mutation
  - 1,000x more selectivity in tumor cell lines with *APC* mutation
  - Inhibited growth and organization of spheroids

Clinical: FAP

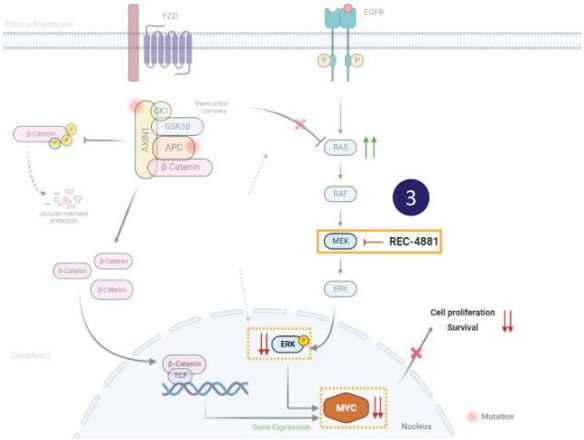
MoA : REC-4881 blocks Wnt mutation induced MAPK signaling

Orally Bioavailable, Small Molecule MEK Inhibitor

Disease State



REC-4881 Impact



3 REC-4481 inhibits MEK 1/2 and recovers the destabilization of RAS by the β-Catenin destruction complex, restoring the cell back to a Wnt-off like state

Goitre et al., PLoS ONE, 2010.

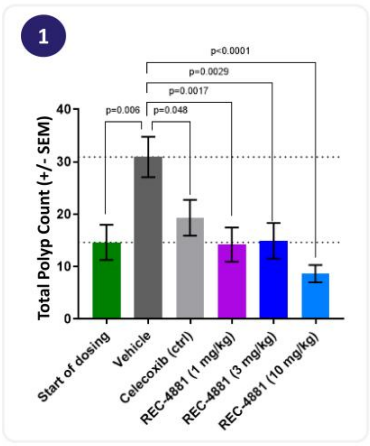
Clinical: FAP

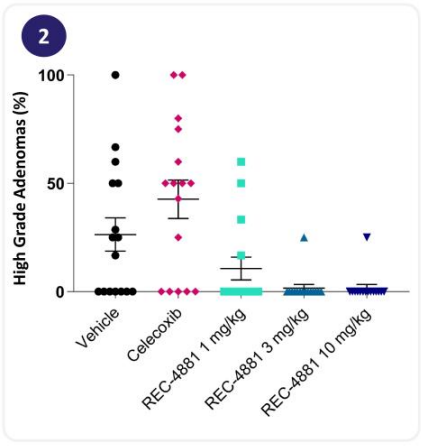
Further Confidence : Preclinical Studies Confirming Reduction in Polyp Count and High-Grade Dysplasia

- In-vivo efficacy in APCmin mouse model
- Apc^{min} = FAP disease model
- Mice treated once daily for 8 weeks

After 8 weeks of treatment:

1. ↓ Polyp Count
2. ↓ High-Grade Dysplasia





APC, adenomatosis polyposis coli; ERK, extracellular signal-regulated kinase; FAP, familial adenomatous polyposis.

Clinical: FAP

Further Confidence : Clinical Data Generated by Recursion

REC-4881-101: Single-center, double-blind, placebo-controlled, dose-escalation study in healthy volunteers

- Group 1 (n=13): Food effect crossover (REC-4881 4 mg/PBO [fed/fasted]), followed by single dose REC-4881 8 mg/PBO [fed]
- Group 2 (n=12): Matched single ascending dose (REC-4881 4 mg/PBO; REC-4881 8 mg/PBO; REC-4881 12 mg/PBO)

Accomplished

- Recursion formulation yields exposures comparable to Takeda
- No food effect
- Dose proportional increases in exposure
- Similar to C20001 study, observed pERK inhibition (i.e. target engagement) at 8 mg and 12 mg doses
- Acceptable safety profile

Note: AE, adverse event; MEK, mitogen-activated protein kinase; NHV, normal healthy volunteer; pERK, phosphorylated extracellular signal-regulated kinase; SAE, serious adverse event.

Clinical: FAP

TUPELO Clinical Trial : REC-4881 for FAP Phase 2 Underway

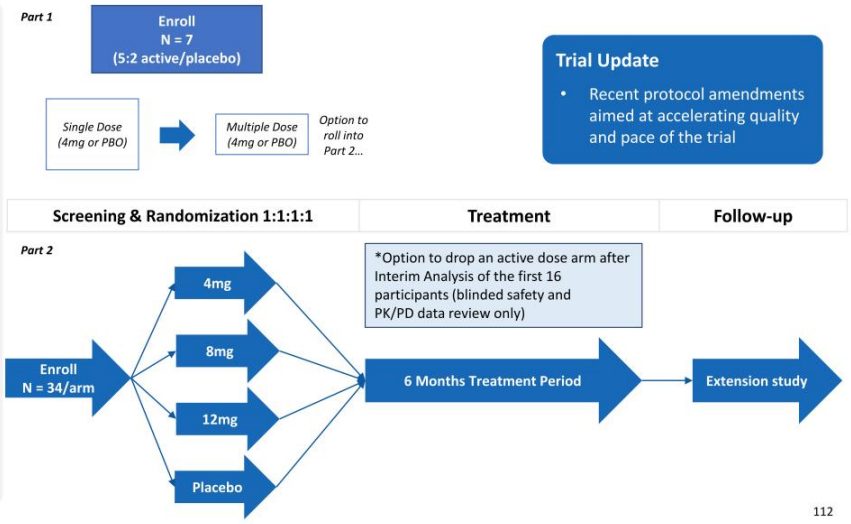
Phase 2 trial initiated in Q3 2022

Enrollment Criteria

- Confirmed *APC* mutation
- Post-colectomy/proctocolectomy
- No GI cancer present
- Polyps in either duodenum (including ampulla of Vater) or rectum/pouch

Outcome Measures

- Primary:
  - Part 1: PK
  - Part 2: % Change from Baseline in Polyp Burden
- Secondary:
  - Part 1: Safety & Tolerability
  - Part 2: PK; PD; Change from Baseline in Polyp Number, Histological grade, disease scoring
- Exploratory:
  - Part 1: PD
  - Part 2: Time to first occurrence of FAP-related event; Change from baseline in extent of Desmoid Disease



https://clinicaltrials.gov/ct2/show/NCT05552755

REC-4881 for the Treatment of Solid Tumors with AXIN1/APC Mutant Cancers

Target / MOA	MEK Inhibitor
Molecule Type	Small Molecule
Lead Indication(s)	Solid Tumors with AXIN1/APC Mutant Cancers
Status	Phase 1b/2
Source of Insight	Recursion OS

Clinical: AXIN1/APC

Disease Overview : *AXIN1/APC* mutant cancers

Gross morphology of HCC tumor

- **Sustained Wnt signaling** is a frequent driver event found across a wide variety of solid tumors
- Dysregulation of β-catenin destruction complex due to inactivating mutations in *AXIN1/APC* **leads to sustained Wnt signaling promoting** cancer progression and survival[1]
- *AXIN1/APC* **mutant solid tumors** are considered clinically aggressive and resistant to standard treatments

"Nothing in HCC has immediate therapeutic relevance and the most common mutations are TERT, TP53, and Wnt (CTNNB1/AXIN1/APC) and combined these alterations define almost 80% of patients and are not targetable"

- KOL, Clinical Investigator, Texas

[1]Bugter, J.M., et al. Nat Rev Cancer, 2021, **21**, pp.5-21

Disease Overview : *AXIN1/APC* mutant cancers

Tumor Type	Alteration Frequency[1]	Treatable Population[2,3] (US+EU5)
LUAD	11%	10,000
HCC	12%	7,600
Prostate	11%	5,600
Bladder	8%	3,700
Esophageal	7%	2,000
Endometrial	12%	1,500
PDAC	2%	1,000
Ovarian	1%	350
TNBC	2%	200
		~32,000

Flexible Patient Selection Strategy and Study Design

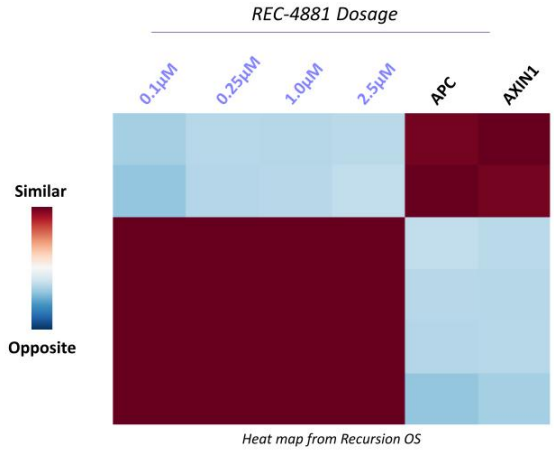
- *AXIN1* and *APC* genes covered by commercially available NGS panels and liquid biopsy detection assays
- FDA guidance supports utility of ctDNA as patient selection for the detection of alterations for eligibility criteria and as a stratification factor for trials enrolling marker-positive and marker-negative populations[4]
- Multiple tumor types will inform study design and patient selection

Preclinical data with REC-4881 at clinically relevant exposures in HCC and Ovarian PDX mouse models gives confidence to pursue other mutant cancer types

[1]Represents higher of either AXIN1 or APC alteration frequency; obtained from cbioportal.org. [2]Represents 2L prevalance estimates; obtained from DRG. [3]HCC treatable population includes potential 1L treatment regimen.
[4] https://www.fda.gov/media/158072/download

Clinical: AXIN1/APC

Insight from OS : Novel Insight around Established MoA



Heat map from Recursion OS

Hypothesis: Rescue of *AXIN1* may impact tumor progression and/or restore checkpoint sensitivity in cancers driven by *AXIN1* loss

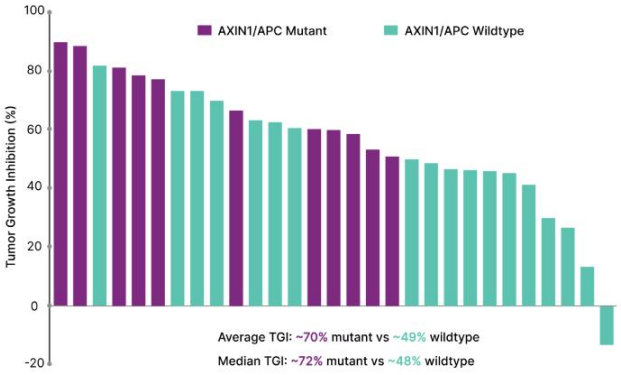
Recursion Differentiation: REC-4881 rescues tumor suppressor genes *APC* and *AXIN1*

- *APC* and *AXIN1* are negative regulators of Wnt signaling
- Both proteins form part of the B-catenin destruction complex. Strong clustering suggests map recapitulation of this biology

Clinical: AXIN1/APC

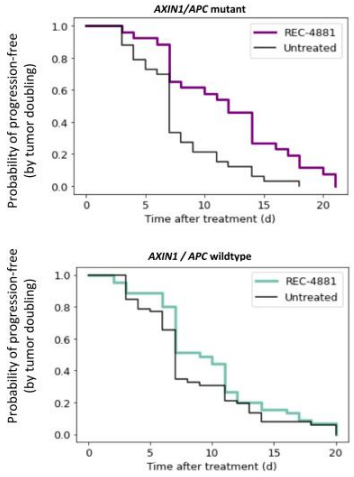
Further Confidence : Preclinical Studies Confirming Insight

Efficacy found in In Vivo Mice Models …



Note: REC-4881 dosed at 3 mg/kg QD for up to 21 days. 3 mice per treatment per model (3 x 3 x 3) design

… Led to Significant Progression Free Survival



Clinical: AXIN1/APC

Next Steps

- Finalize design of a Phase 1b/2 biomarker-enriched trial
- Initiate Phase 1b/2 trial in select tumor types in early 2024
- Identify suitable partners for genetic testing capabilities
- Evaluate REC-4881 in combination with targeted and/or immune modulating agents

REC-3964 for the Treatment of Clostridium Difficile Infection

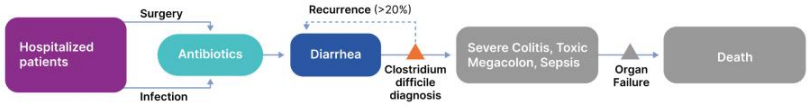
Target / MOA	Selective C. diff Toxin Inhibitor
Molecule Type	Small Molecule
Lead Indication(s)	Clostridium Difficile Infection
Status	Phase 1
Source of Insight	Recursion OS

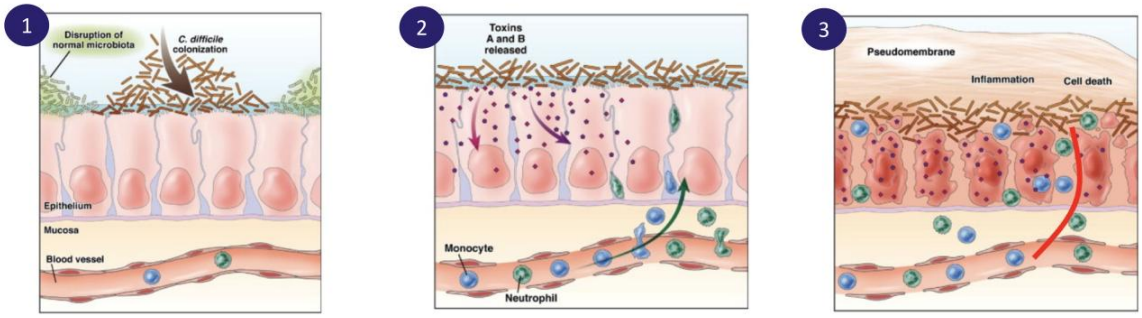
Clinical: C. *diff*

Disease Overview : Clostridium Difficile Infection (CDI)

C.diff is the leading cause of antibiotic-associated diarrhea

(over 500,000 annual cases)





Disruption of microbiota and colonization of *C. diff*

Release of C. diff toxins

Degradation of colon cell junction & toxin transit to bloodstream

Source: McCollum, D., Rodriguez, JM . Detection, Treatment, and Prevention of Clostridium difficile Infection. Clinical Gastroenterology and Hepatology 2012 Mar 19. https://doi.org/10.1016/j.cgh.2012.03.008

Clinical: C. *diff*

Disease Overview : Clostridium Difficile Infection (CDI)

Colleen – lived with rCDI

Patient Population – Large, Diagnosable and Easy to Identify

- Symptoms caused by clostridium difficile tissue-damaging toxins released in the colon
- Patients who experience >3 unformed stools are diagnosed via NAAT* for toxin gene or positive stool test for toxins
- Patients who are at highest risk are those on antibiotics, and frequently visit hospitals or are living in a nursing home
- More than **80% of cases** occur among patients **age 65** or older

Large, Unmet Need with Significant Cost Burden

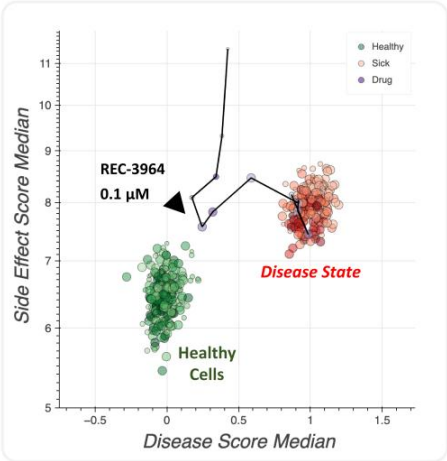
- RCDI** occurs in **20-30% of patients treated with standard of care**
  - 40% of those patients will continue to recur with 2+ episodes
- **>29,000 patients** die in the US each year from CDI
- Cost burden of up to **$4.8bn annually**

~730,000 **Diagnosed US + EU5 patients**

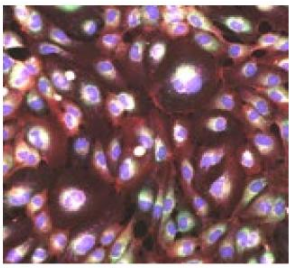
*Source, CDC. *NAAT = Nucleic Acid Amplification Test; **rCDI = recurrent CDI*

Clinical: C. *diff*

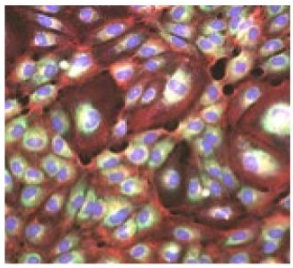
Insight from OS : REC-3964 Rescued Cells Treated with C. diff Toxins



REC-3964 identified as a NCE that demonstrated strong rescue in HUVEC cells treated with C. diff toxin



C. diff toxin B phenotype

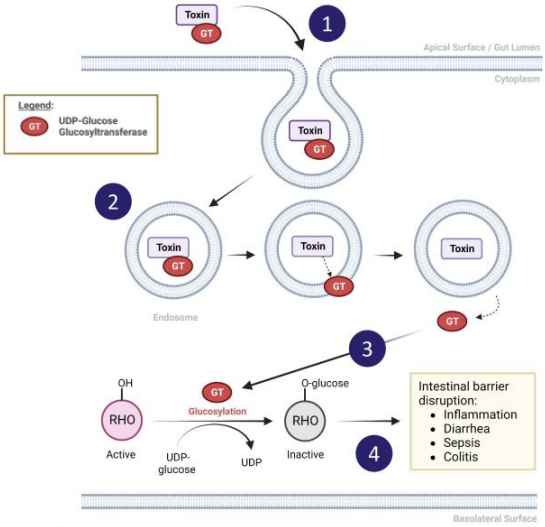


Healthy Control

Clinical: C. *diff*

REC-3964 : Selective Inhibitor of C. diff Toxins

REC-3964 is Recursion's 1st Small Molecule NCE to Reach the Clinic



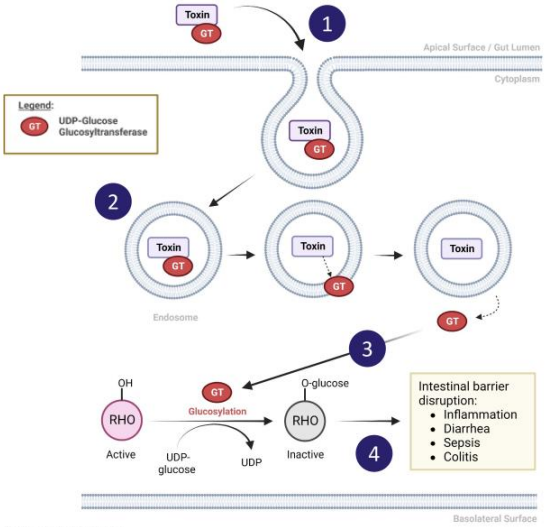
Adapted from Awad et al, 2014

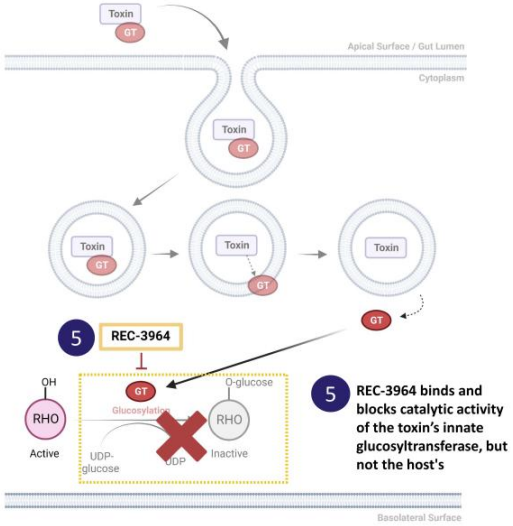
1. C.diff toxins bind to cell surface receptors and trigger endocytic event
2. Autocatalytic cleavage event releases C.diff toxin's glucoyltransferase enzymatic domain into the cytosol of the infected cell
3. The glucosyltransferase locks Rho family GTPases in the inactive state
4. Inactivation of Rho GTPases alters cytoskeletal dynamics, induces apoptosis, and impairs barrier function which drives the pathological effects of C.diff infection

Clinical: C. *diff*

REC-3964 : Selective Inhibitor of C. diff Toxins

REC-3964 is Recursion's 1st Small Molecule NCE to Reach the Clinic



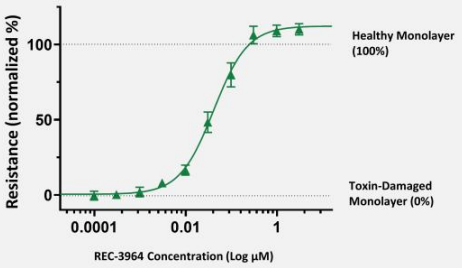


Adapted from Awad et al, 2014

Clinical: C. *diff*

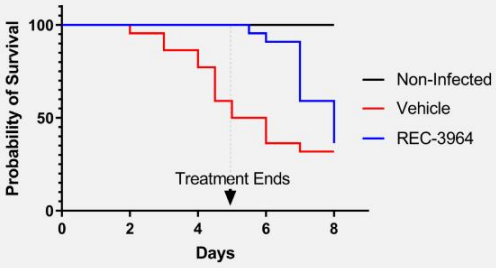
Further Confidence : Preclinical Studies Confirmed Recursion OS Insight

REC-3964 rescues barrier integrity with increasing concentrations



✓ REC-3964 restores gut epithelial barrier integrity, which when disrupted causes inflammation and diarrhea

REC-3964 improved probability of survival in a hamster model of C. difficile infection



✓ Improved probability of survival beyond treatment completion

Clinical: C. *diff*

Clinical Trial : REC-3964 Phase 1 Study Underway

Phase 1 FIH SAD/MAD Trial initiated in Q3 2022

Trial Design
- Randomized, Double-blind Trial

Population
- Healthy Subjects
- SAD (n = 56)
- MAD (n = 50)

Primary Objectives

✓ Assess the safety & tolerability of SAD and MAD of REC-3964

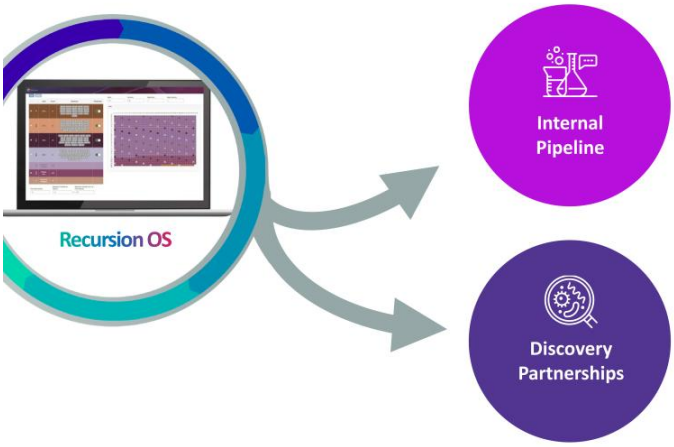
✓ Evaluate the PK profile of REC-3964 after single and multiple doses

Trial Update
- Enrollment is progressing
- In several SAD cohorts and at least one MD cohort, REC-3964 has been extremely safe and well tolerated
- **Complete safety and PK data readout expected 2H 2023**

Partnerships

Matt Kinn
Senior Vice President of Business Development

How we create value using our maps of biology and chemistry



Pipeline strategy

Build wholly-owned pipeline in indications with potential for **accelerated path** to approval

- **Oncology**
- **Rare Disease**

Partnership strategy

Partner in **complex therapeutic areas** requiring large financial commitment and competitive market dynamics

Leverage partner knowledge and clinical development capabilities

- **Fibrosis**
- **Neuroscience**
  *and a single oncology indication
- **Other large, intractable areas of biology**

Our existing partnerships represent some of the most significant scientific collaborations in biopharma

(Announced Sep 2020; Expanded Dec 2021)

Fibrosis

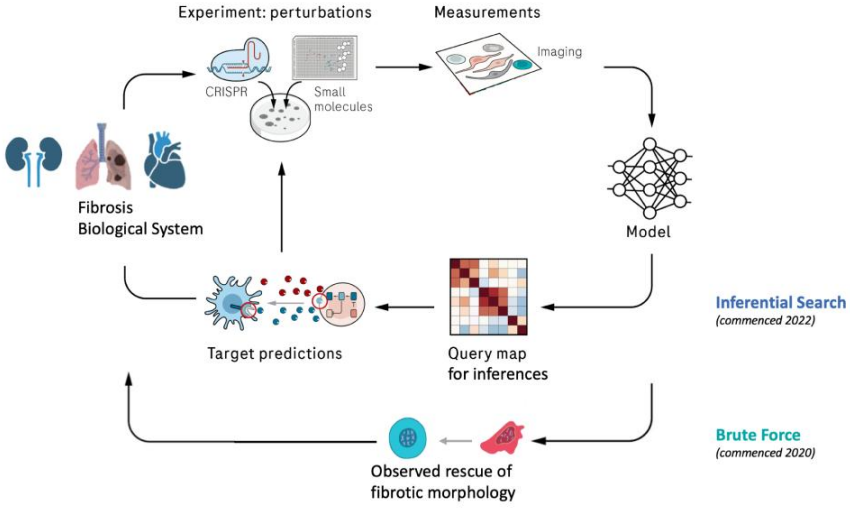
- $30M upfront and $50M equity investment
- Up to or exceeding $1.2B in milestones for up to or exceeding 12 programs
- Mid single-digit royalties on net sales
- Recursion owns all algorithmic improvements

(Announced Dec 2021)

Neuroscience
*and a single oncology indication

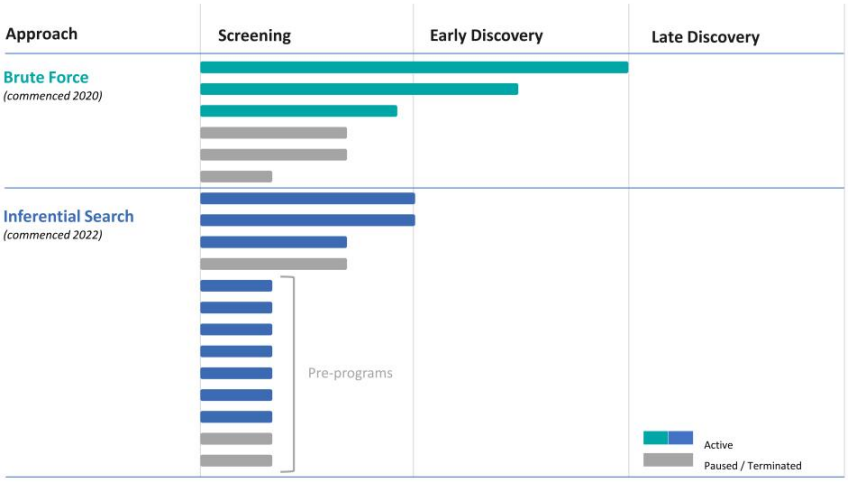
- $150M upfront and up to or exceeding $500M in research milestones and data usage options
- Up to or exceeding $300M in possible milestones per program for up to 40 programs
- Mid to high single-digit tiered royalties on net sales
- Recursion owns or co-owns all algorithmic improvements

We are leveraging the Recursion OS in multiple ways to identify novel fibrosis-relevant biology



Multiple programs advancing in parallel to near-term milestones

Transition to Inferential Search has accelerated new program initiation in 2022




8
Projects initiated;
4 in 2022
40 million
experiments performed
2 PB
of data generated
>500,000
Phenoprints
Mapped
~100
fibrosis-relevant genes
ready for further study
100%
of projects to be sourced from
inferential search in 2023

Our existing partnerships represent some of the most significant scientific collaborations in biopharma

(Announced Sep 2020; Expanded Dec 2021)

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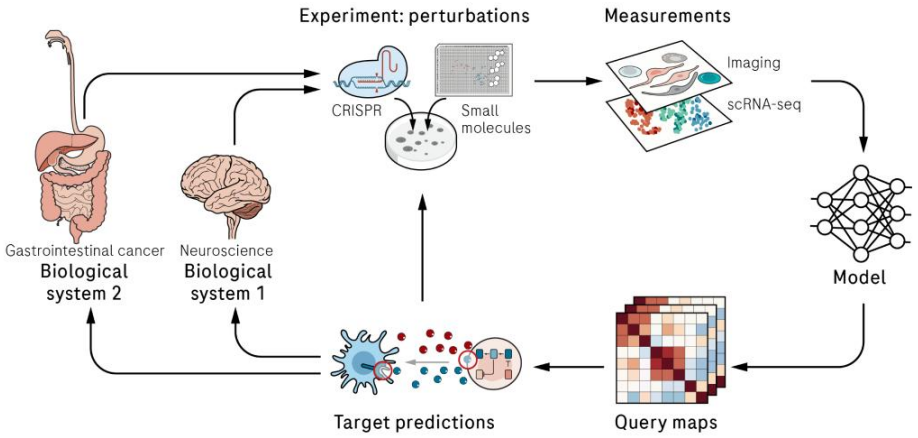
Under our collaboration with Roche & Genentech, we are creating multi-modal maps of cellular biology to elucidate novel targets and starting points



Financials & Milestones

Michael Secora PhD
Chief Financial Officer

Financial position – strong yet prudent expansion

- **Cash and cash equivalents**
  - Currently projecting **~$550M at the end of 2022**
- **Operating costs and expenses**
  - Currently projecting **~$275-295M in 2022**
  - Based on current operations, we project relatively **flat operating costs and expenses** in the near term
- **Revenue**
  - Currently projecting **~$30-45M in 2022**
  - **Potential for increased revenue** in the near-term from the following sources:
    - Potential **partnership option exercises**
    - Potential **additional partnership(s)**
    - **Revenue recognition** from existing partnerships

Condensed Consolidated Statements of Operations

	Three months ended September 30		Nine months ended September 30	
(Unaudited, in thousands)	**2022**	**2021**	**2022**	**2021**
Revenue				
Operating revenue	$ 13,053	$ 2,500	$ 26,005	$ 7,500
Grant revenue	107	34	162	145
Total revenue	**$ 13,160**	**$ 2,534**	**$ 26,167**	**$ 7,645**
Operating costs and expenses				
Cost of revenue	$ 15,409	-	$ 37,435	-
Research and development	40,836	33,246	111,716	86,979
General and administrative	19,488	15,690	61,761	38,481
Total operating expenses	**$ 75,733**	**$ 48,936**	**$ 210,912**	**$ 125,460**
Loss from operations	**($62,573)**	**($46,402)**	**($184,745)**	**($117,815)**
Other income (loss), net	2,128	(1,026)	2,761	(3,731)
Net loss	**($60,445)**	**($47,428)**	**($181,984)**	**($121,546)**

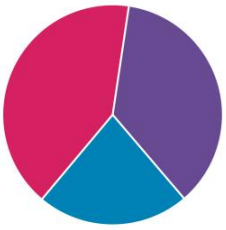
Funding history – uniting the worlds of tech and bio investing

What it takes to make this happen – a new kind of team and culture

Team Members

~500 **Employees**

43% **Advanced degrees**



- Life Sciences – biology, chemistry, development, etc.
- Technology – data science, software engineering, automation, etc.
- Strategic Operations

43% Female | 55% Male | 1% Non-Binary

Parity Pledge Signer - gender parity and people of color parity

ESG Highlights

- ✓ Inaugural ESG report in 2022 – reporting on **Healthcare and Technology Metrics**
- ✓ **100% of electricity** powering our Biohive-1 supercomputer comes from renewable sources

Community Impact

altitude lab
Founding Partner,
Life Science Accelerator

biohive
Founding Member,
Life Science Collective

Committed to ESG Excellence

Corporate ESG Performance Prime
RATED BY ISS ESG

Rated
MORNINGSTAR | SUSTAINALYTICS

Data shown reflective of Q4 2022 and Recursion's 2022 ESG report

Our leadership team brings together experience & innovation to lead TechBio

Executive Team

CHRIS GIBSON, PHD
Co-Founder & CEO

TINA LARSON
President & COO
Roche Genentech ACHAOGEN

SHAFIQUE VIRANI, MD FRCS
Chief Business Officer & Interim CMO
Roche Genentech bridgebio

MICHAEL SECORA, PHD
Chief Financial Officer
LAURION

HEATHER KIRKBY, MBA
Chief People Officer
intuit

LAURA SCHAEVITZ, PHD
SVP and Head of Research
vium

BEN MABEY
Chief Technology Officer

KRISTEN RUSHTON, MBA
SVP of Business Operations
Myriad genetics

NATHAN HATFIELD, JD MBA
SVP and Head of Legal
WILSON SONSINI

Board of Directors

R. MARTIN CHAVEZ, PHD
Chairman of RXRX,
Board Member of Alphabet,
Vice-Chairman of 6th Street,
Former CFO/CIO of GS
Alphabet 6 SIXTH STREET Goldman Sachs

CHRIS GIBSON, PHD
Co-Founder & CEO

DEAN LI, MD/PHD
Co-Founder of RXRX,
President of Merck Research Labs
MERCK THE UNIVERSITY OF UTAH

ZAVAIN DAR
Co-Founder & Partner of Dimension
DIMENSION LUX+

TERRY-ANN BURRELL, MBA
CFO & Treasurer,
Beam Therapeutics
Beam THERAPEUTICS J.P.Morgan

ROB HERSHBERG, MD/PHD
Co-Founder/CEO/Chairman of HilleVax,
Former EVP/CSO/CBO of Celgene
Celgene

BLAKE BORGESON, PHD
Co-Founder of RXRX
MIRI BUILD A SIGN

ZACHARY BOGUE, JD
Co-Founder & Partner of Data Collective
DC >C

What to watch for at Recursion

Upcoming Potential Milestones

Near-Term

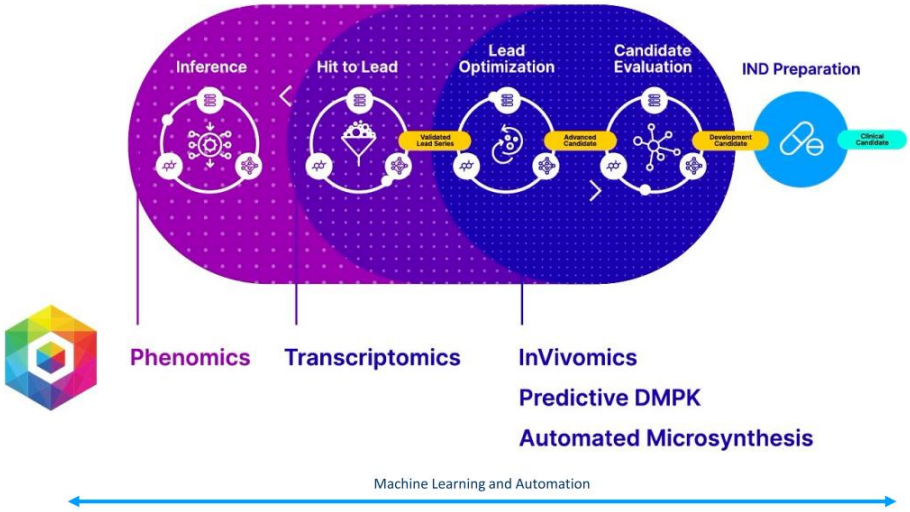
- Potential **option exercises** for partnership **programs**
- Potential **option exercises** for **map building** initiatives or data sharing
- Potential for **additional partnership(s)** in large, intractable areas of **biology and / or technological innovation**
- **Ph1 clinical trial readout** for **Clostridium difficile Colitis** program expected **2H 2023**
- Potential for **additional INDs and clinical starts**, including **Ph1b/2 trial initiation** for **AXIN1/APC** program
- Potential for consolidation of **technologies, talent and assets** to accelerate the Recursion OS

Medium-Term

- Multiple **POC readout(s)** for AI-discovered programs
  - **NF2 interim safety** analysis expected **2024**
  - **CCM** top-line data expected **2H 2024**
- Potential for **additional INDs and clinical starts**
- Potential **option exercises** for partnership **programs**
- Potential **option exercises** for **map building** initiatives or data sharing
- Potential **additional partnership(s)** in large, intractable areas of **biology and / or technological innovation**
- Recursion OS moves towards **autonomous map building and navigation** with digital and micro-synthetic chemistry

Strong Financials **~$550M in cash** and cash equivalents at the **end of 2022** with **potential for increased revenue** in the near term

Continuing to mature the TechBio value proposition – multiple cycles of learning and iteration



Phenomics

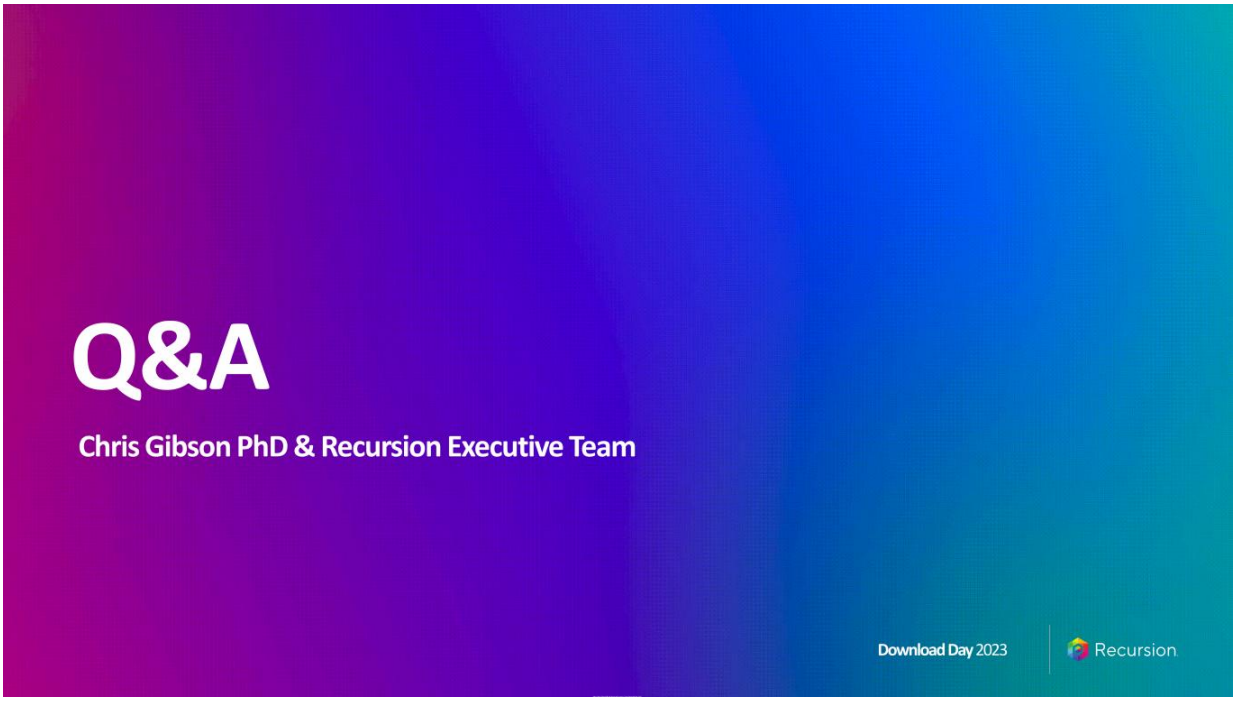
Transcriptomics

InVivomics

Predictive DMPK

Automated Microsynthesis

Machine Learning and Automation


Q&A
Chris Gibson PhD & Recursion Executive Team
Download Day 2023
Recursion

Closing Remarks

Zavain Dar
Director of Recurison