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): September 5, 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 7.01. Regulation FD Disclosure.

On September 5, 2023, Recursion Pharmaceuticals, Inc. (the "Company") issued a press release announcing it has completed its Phase 1 Study for REC-3964 for Clostridioides Difficile Infection. The press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated into this Item 7.01 by reference.

Also on September 5, 2023, the Company released an updated investor presentation. The investor presentation will be used from time to time in meetings with investors. A copy of the presentation is attached hereto as Exhibit 99.2.

The information furnished in this Item 7.01 (including Exhibits 99.1 and 99.2), shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release of Recursion Pharmaceuticals, Inc. dated September 5, 2023.
99.2	Investor presentation of Recursion Pharmaceuticals, Inc. dated September 5, 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 September 5, 2023.

RECURSION PHARMACEUTICALS, INC.

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

Recursion Announces Completion of Phase 1 Study for REC-3964 for Clostridioides Difficile Infection

- REC-3964 has been well tolerated in healthy volunteers with no reported serious adverse events
- Recursion to explore initiating a Phase 2 proof-of-concept study in patients with recurrent Clostridioides difficile infection in 2024

SALT LAKE CITY, September 5, 2023 -- Recursion (NASDAQ: RXRX), a leading clinical stage TechBio company decoding biology to industrialize drug discovery, today announced it has completed the Phase 1 study for REC-3964 in healthy volunteers. The study achieved its primary objectives of assessing the safety, tolerability and pharmacokinetic profile of REC-3964. REC-3964 has been well tolerated with no serious adverse events (SAEs) reported.

“This is an important step in our efforts to rapidly translate our first new chemical entity into a safe and effective therapy that has the potential to address a significant unmet need,” said David Mauro, M.D., Ph.D., Chief Medical Officer of Recursion. “We are encouraged by the strong safety and tolerability profile and are actively exploring the most expeditious path to advance this program to patients.”

REC-3964 is a novel non-antibiotic small molecule inhibitor of *C. difficile* toxins that is being developed for the potential treatment of Clostridioides difficile (C. diff) infection, a bacterial disease that impacts more than 730,000 people in the US and EU5 every year. REC-3964 is Recursion’s first and most advanced new chemical entity, demonstrating the power of Recursion’s platform to rapidly identify, validate, optimize and translate novel insights into clinical candidates.

REC-3964 represents a novel small molecule approach designed to selectively inhibit the toxin produced by Clostridioides difficile in the gastrointestinal tract. This molecule has the potential, when used as part of a treatment regimen, to prevent recurrent disease and/or other forms of C. diff infection, which is a leading cause of antibiotic-induced diarrhea sometimes leading to significant morbidity and mortality. More than 29,000 patients die in the US every year from C. diff infection.

About the Trial
The Phase 1 study was designed as a first-in-human protocol evaluating single and multiple doses of orally administered REC-3964 in healthy volunteers. The study assessed the safety, tolerability and pharmacokinetic (PK) profile of REC-3964 and consisted of two parts: single ascending dose (SAD) and multiple ascending dose (MAD). Dosing levels for MAD were 100 mg (Cohort 1), 300 mg (Cohort 2), 500 mg (Cohort 3), and 900 mg (Cohort 4). In Cohort 1, 12 participants were randomized to receive either REC-3964 (N=10) or placebo (N=2) and in each Cohorts 2 through 4, 10 participants were randomized to receive either REC-3964 (N=8) or placebo (N=2) for a total of 42 participants for the MAD study. Participants were dosed with REC-3964 for 14 days.

PK analysis demonstrated that exposures (AUC) increased approximately dose-proportionally across the dose ranges tested and the half-life ranged from approximately 7 to 10 hours. As a result, twice-daily (BID) dosing is expected to reach targeted trough concentrations. Overall, REC-3964 was very well tolerated. Four participants (11.8%, N=34) experienced treatment-related adverse events, which were mild. Additionally, no treatment-related SAEs were observed, and there were no discontinuations due to a treatment-related adverse event. Based on these data, a Phase 2 proof-of-concept trial is expected to initiate in 2024 to further study the attributes of this molecule.

About Recursion
Recursion (NASDAQ: RXRX) is a clinical stage TechBio company leading the space by decoding biology to industrialize drug discovery. Enabling its mission is the Recursion OS, a platform built across diverse technologies that continuously expands one of the world's largest proprietary biological and chemical datasets. Recursion leverages sophisticated machine-learning algorithms to distill from its dataset a collection of trillions of searchable relationships across biology and chemistry unconstrained by human bias. By commanding massive experimental scale — up to millions of wet lab experiments weekly — and massive computational scale — owning and operating one of the most powerful supercomputers in the world, Recursion is uniting technology, biology, and chemistry to advance the future of medicine.

Recursion is headquartered in Salt Lake City, where it is a founding member of BioHive, the Utah life sciences industry collective. Recursion also has offices in Toronto, Montréal and the San Francisco Bay Area. Learn more at www.Recursion.com, or connect on Twitter and LinkedIn.

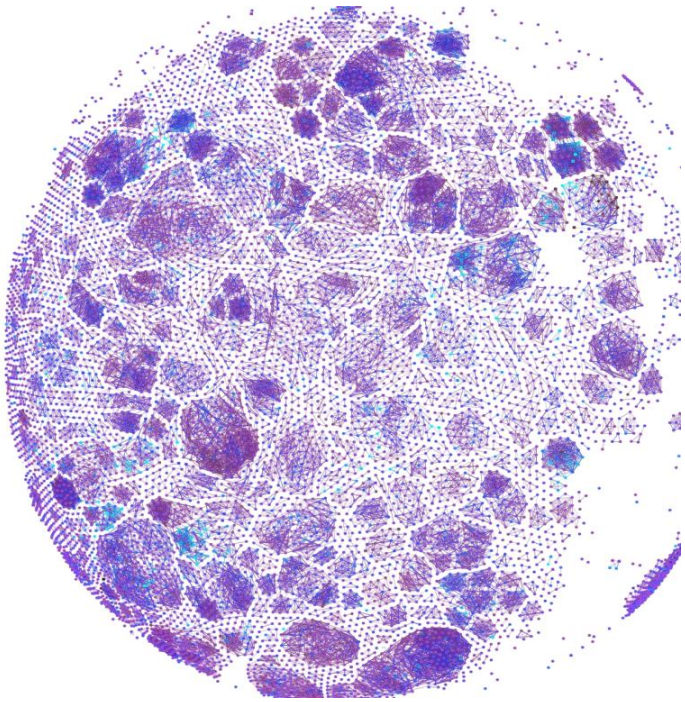
Media Contact
Media@Recursion.com

Investor Contact
Investor@Recursion.com

Forward-Looking Statements
This document contains information that includes or is based upon "forward-looking statements" within the meaning of the Securities Litigation Reform Act of 1995, including, without limitation, those regarding REC-3964 and other early and late stage discovery, preclinical, and clinical programs; licenses and collaborations; prospective products and their potential future indications and market opportunities; the Recursion OS and other technologies; business and financial plans and performance; and all other statements that are not historical facts. Forward-looking statements may or may not include identifying words such as "plan," "will," "expect," "anticipate," "intend," "believe," "potential," "continue," and similar terms. These statements are subject to known or unknown risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements, including but not limited to: challenges inherent in pharmaceutical research and development, including the timing and

results of preclinical and clinical programs, where the risk of failure is high and failure can occur at any stage prior to or after regulatory approval due to lack of sufficient efficacy, safety considerations, or other factors; our ability to leverage and enhance our drug discovery platform; our ability to obtain financing for development activities and other corporate purposes; the success of our collaboration activities; our ability to obtain regulatory approval of, and ultimately commercialize, drug candidates; our ability to obtain, maintain, and enforce intellectual property protections; cyberattacks or other disruptions to our technology systems; our ability to attract, motivate, and retain key employees and manage our growth; and other risks and uncertainties such as those described under the heading "Risk Factors" 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. All forward-looking statements are based on management's current estimates, projections, and assumptions, and Recursion undertakes no obligation to correct or update any such statements, whether as a result of new information, future developments, or otherwise, except to the extent required by applicable law.

Decoding Biology To Radically Improve Lives



Early September, 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 outcomes and benefits expected from the NVIDIA partnership and Cyclica and Valence Discovery acquisitions and the launch of Valence Labs, outcomes and benefits from licenses and collaborations, including option exercises by partners and additional partnerships; the occurrence or realization of any near or medium term potential milestones, the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical and clinical studies, including timelines for data readouts, 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. 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.

Table of Contents

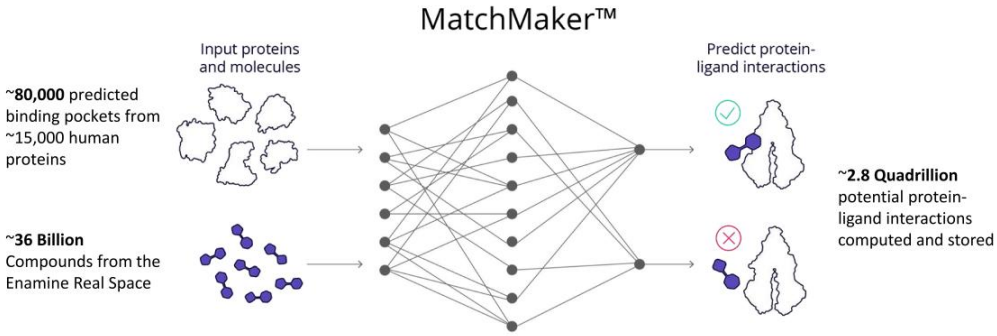
Maturing the TechBio value proposition – Early September, 2023

Pipeline - Added, accelerated or tightened guidance for clinical studies:
- **REC-3964 Ph1 C Diff** achieved primary objective of assessing safety, tolerability, and PK in **Q3, 2023, Ph2 initiation** expected in **2024**
- **REC-994 Ph2 CCM** top-line in **H2, 2024**
- **REC-2282 Ph2 NF2** safety & preliminary efficacy in **H2, 2024**
- **REC-4881 Ph2 FAP** safety & preliminary efficacy in **H1, 2025**
- **IND accepted** for ***AXIN1*** **or** ***APC*** **mutant cancers** with **Ph2 initiation** expected in **Q4, 2023**

Partnerships - Sector-leading partnerships across biopharma and tech:
- Announced a $50 million **investment and partnership** with **NVIDIA** to accelerate the construction, optimization and deployment of foundation models for biology and chemistry
- Advancing collaborations with **Roche-Genentech** and **Bayer:** $13B in potential milestones across 50+ possible programs plus royalties

Platform - Continued building on the strength of our Recursion OS:
- **Predicted** ligand-protein **interactions for ~36 billion compounds** in **Enamine REAL Space** (reported to be the world's largest searchable chemical library) **working with partners at NVIDIA**
- New pipeline programs now exclusively generated via Large Language Model (LLM) workflow
- Developing large-scale foundation models for drug discovery, based upon our massive proprietary dataset spanning biology and chemistry

Quick Update: Bridging Protein and Chemical Space with Massive Protein-Ligand Interaction Predictions



Computation at Scale

Recursion partnered with NVIDIA to integrate and optimize MatchMaker (acquired via CYCLICA) for massive scale GPU-based computation on BioHive-1 and the DGXCloud

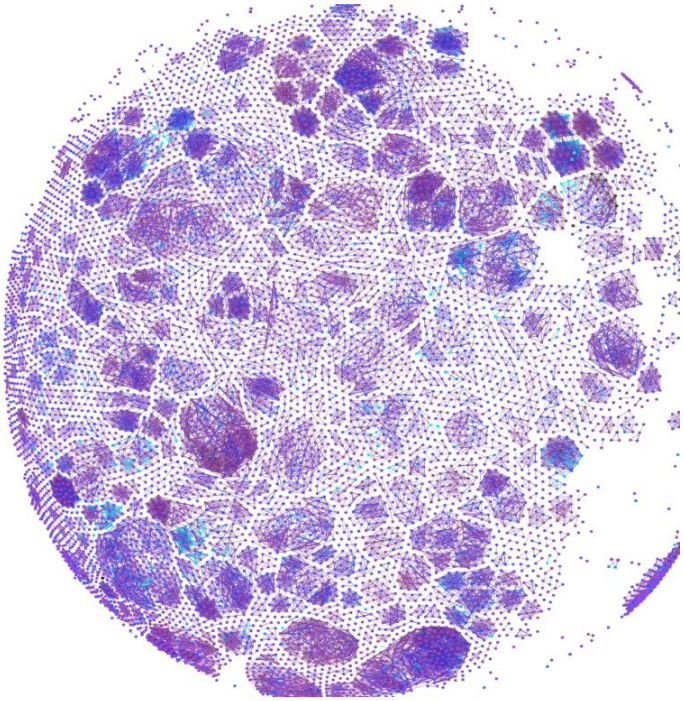
Computation at Speed

This tool was deployed to predict protein-ligand interaction for ~36 Billion compounds from the Enamine Real Space, less than 90 days post-acquisition of Cyclica and less than 30 days post-partnership with NVIDIA

Computation as a Data-Layer

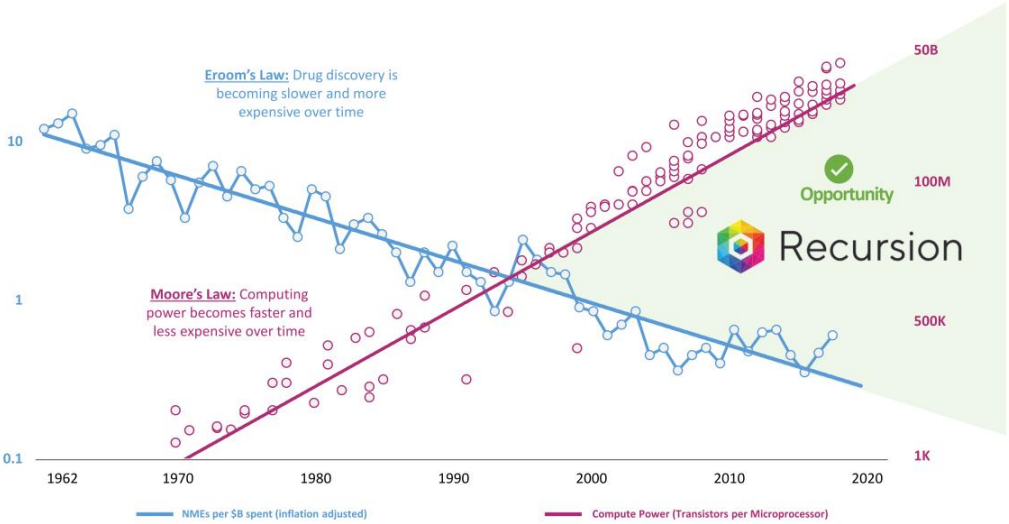
Recursion will use the predicted interactions as a data-layer in its multi-omic dataset for honing mechanistic predictions from its wet-labs and for accelerating SAR cycles through better predictions for its internal pipeline and within its partnerships

In Brief: The Recursion Value Proposition



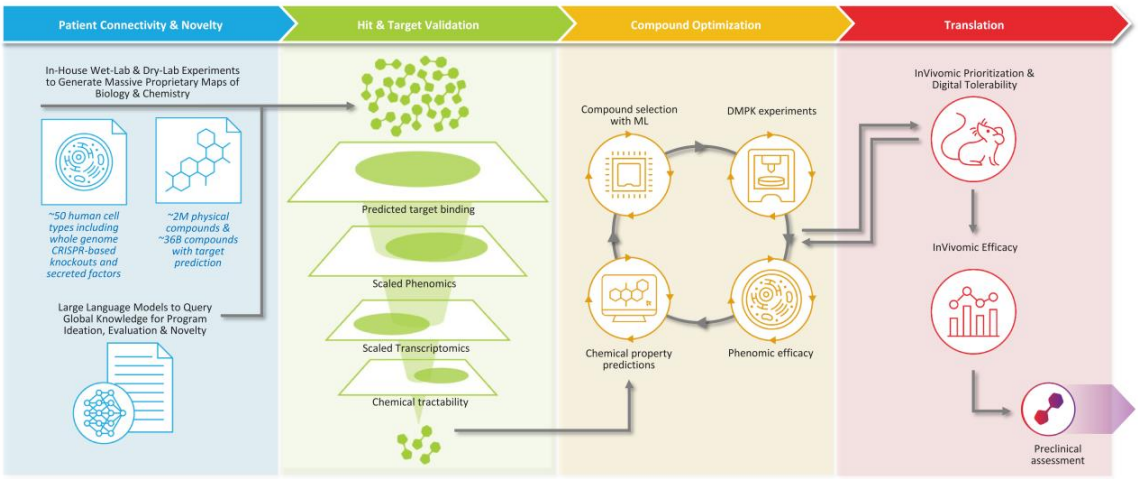
Recursion

Recursion leading a new TechBio sector at the intersection of technology and biology



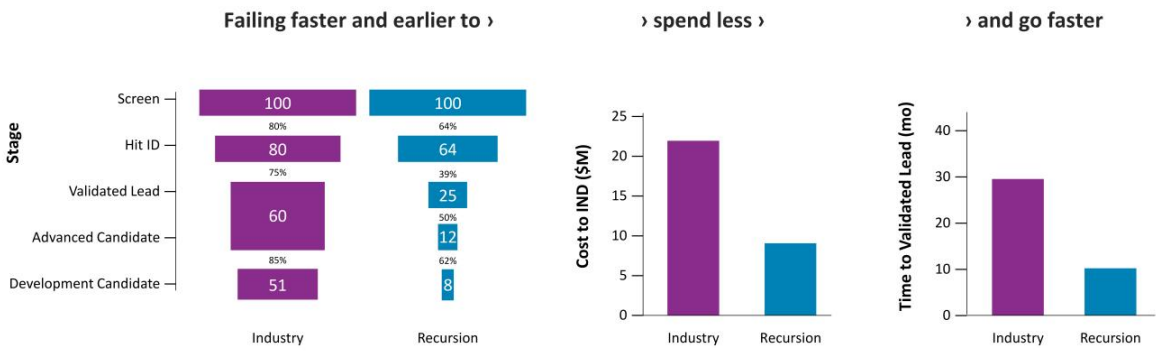
Adapted from Scannell, J et al (2012). Diagnosing the decline in pharmaceutical R&D efficiency. Nat Rev Drug Discov, 11, 191-200.

The Recursion OS today: Industrializing drug discovery to transform BioTech into TechBio



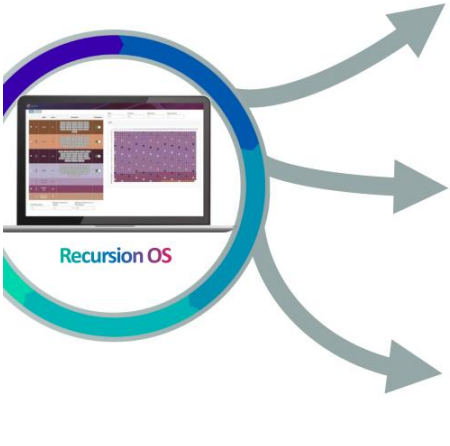
Recursion

Mapping and navigating the complex systems of biology and chemistry has demonstrated leading indicators of efficiency



Data shown is the average of all our programs since late 2017 through 2022. All industry data adapted from Paul, et al. Nature Reviews Drug Discovery. (2010) 9, 203–214

Harnessing value with a multi-pronged capital-efficient business strategy



Pipeline Strategy

Build internal 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***
- **Other large, intractable areas of biology**

Data Strategy

License subsets of data and key tools

Direct generation of new data internally **to maximize pipeline and partnership value-drivers**

- **Licensing**
- **Augment Recursion OS**

**Includes a single oncology indication from our Roche and Genentech collaboration.*

Our pipeline reflects the scale and breadth of our approach

More than a dozen additional early discovery and research programs in oncology or with our partners

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

Our existing partnerships represent some of the most significant scientific collaborations in TechBio across biopharma and tech

BAYER

(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**

Roche
Genentech
A Member of the Roche Group

(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**

NVIDIA®

(Announced July 2023)

Computation and ML/AI

- **$50M equity investment**
- Partnership on **advanced computation** (e.g., foundation model development)
- **Priority access** to compute hardware or **DGXCloud Resources**
- **Potential to house Recursion Tools on NVIDIA's BioNeMo Marketplace**

Relatable and scalable data is a key Recursion differentiator

Recursion Data Universe: >25 PB of proprietary biological and chemical data, spanning phenomics, transcriptomics, invivomics, and more

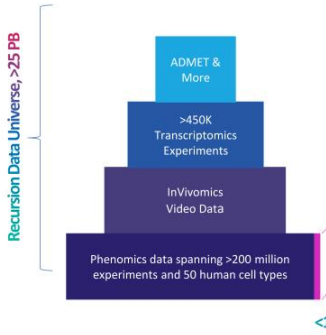
- We believe this is one of the largest such datasets **fit for the purpose of training large-scale ML models in biology**

RXRX3: CRISPR knockouts of most of the human genome, 1,600 FDA approved / commercially available bioactive compounds

- We believe the **largest public dataset of its kind**, <1% of Recursion Data Universe, what Recursion can generate in ~1 week

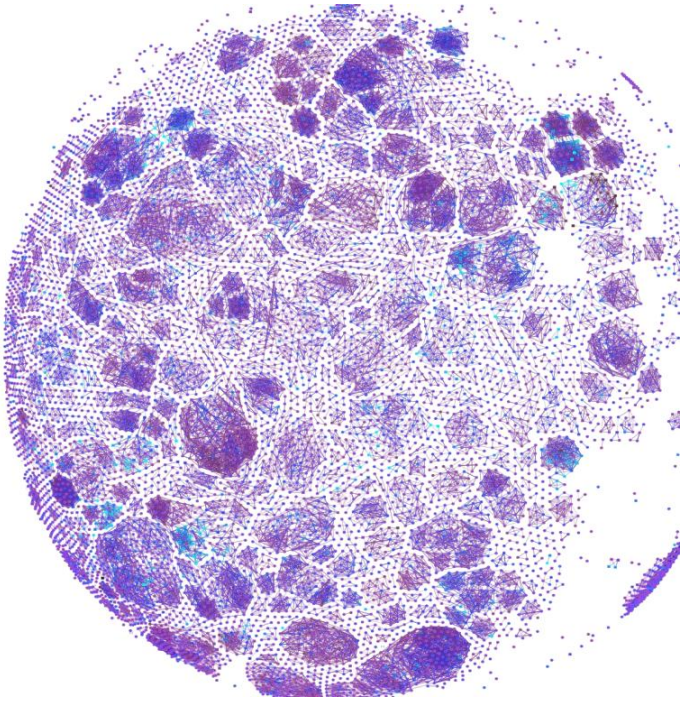
MolRec™: freemium web-based **application to explore compound and gene relationships** in RXRX3

Start working with RXRX3 and MolRec™: www.rxrx.ai



Dataset	Released	Number of Samples
Bio/Chem Phenomic Maps		
RxRx3	**2023**	**2.2M**
JUMPCP	2023	823,438
Autonomous Driving		
Waymo Open Dataset	2018	~105,000
nuScenes	2018	1,000
Image/Object recognition		
ImageNet (21k)	2009	14M
COCO	2014	330,000

How we build maps of biology and chemistry to turn drug discovery into a search problem

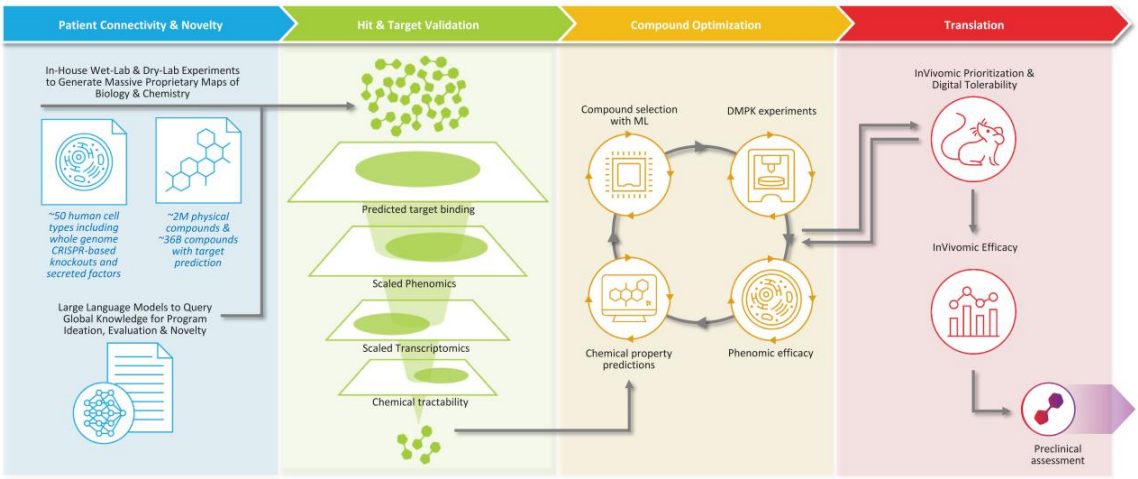


Recursion

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

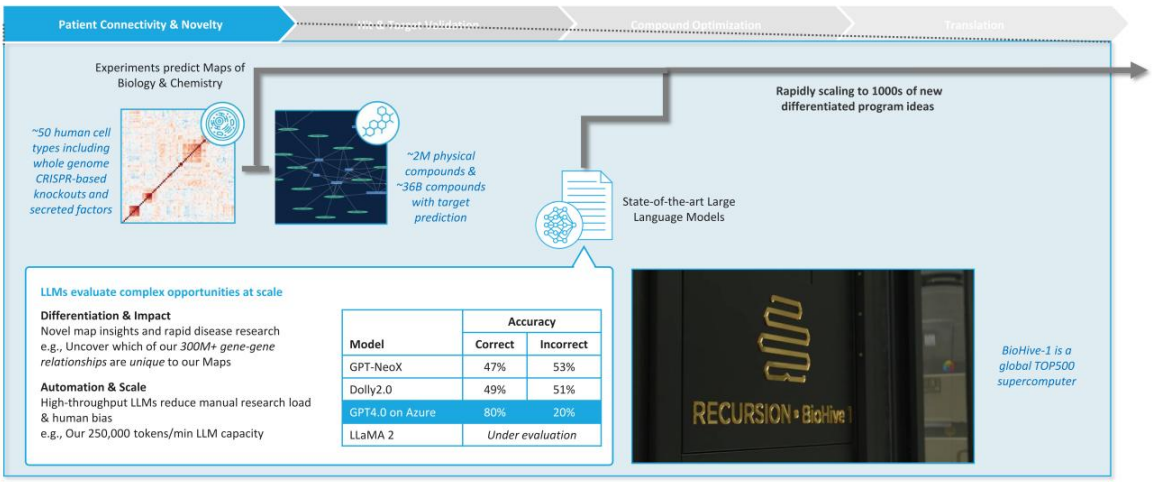
Traditional Drug Discovery		Recursion Approach
Literature drives discovery. *Informs target-based hypotheses*	vs	**Platforms** drive discovery. *Unbiased & target agnostic*
Data are an exhaust. *Limited to testing hypotheses*	vs	**Data** are our fuel. *Shape our hypotheses*
Disparate data generation. *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*

The Recursion OS today: Industrializing drug discovery to transform BioTech into TechBio

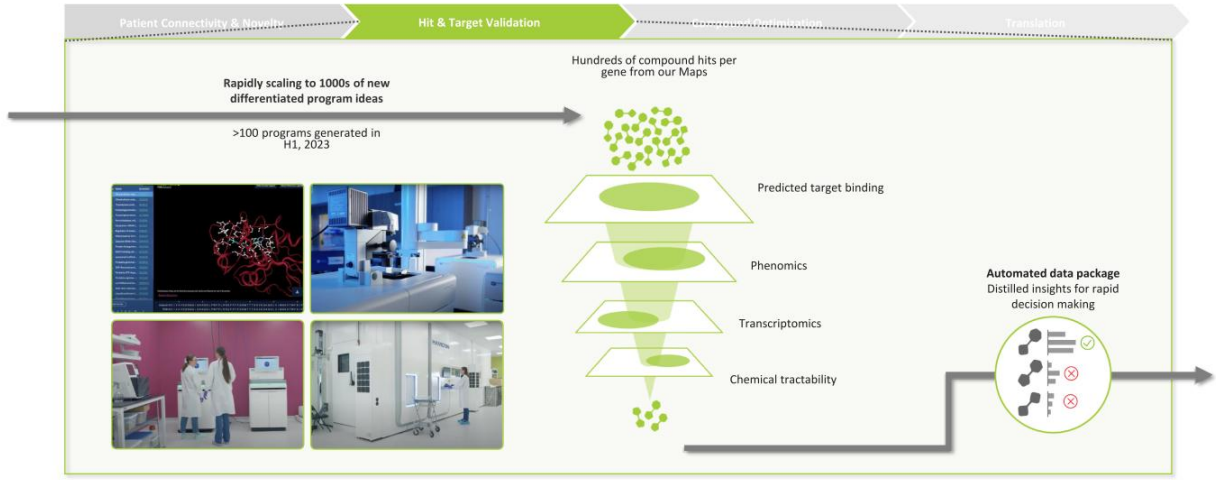


Recursion

Our maps encode ~4 trillion relationships & LLMs allow us to quickly distill the most promising novel ideas from this massive search space

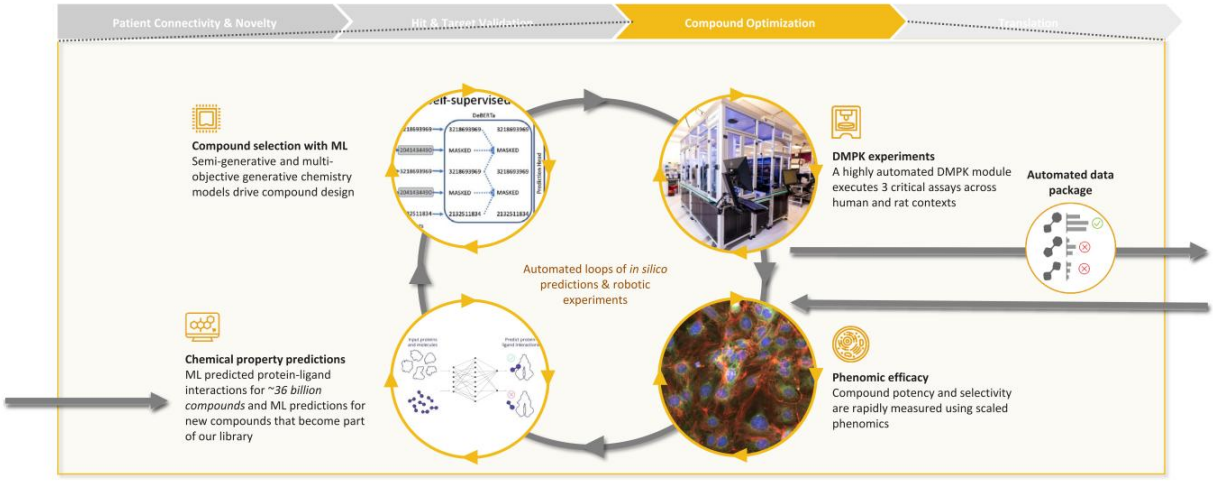


Automatic validation of map insights: we rapidly confirm novel predictions from our maps with automated, standardized, scaled -omics



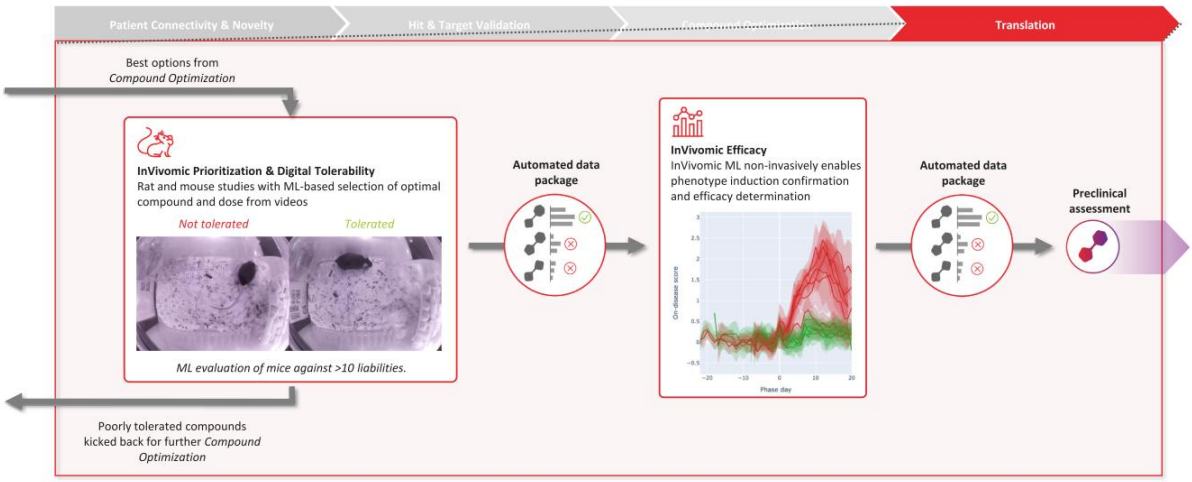
Recursion

Loops of experimental data & ML predictions rapidly accelerate hit to lead and lead optimization



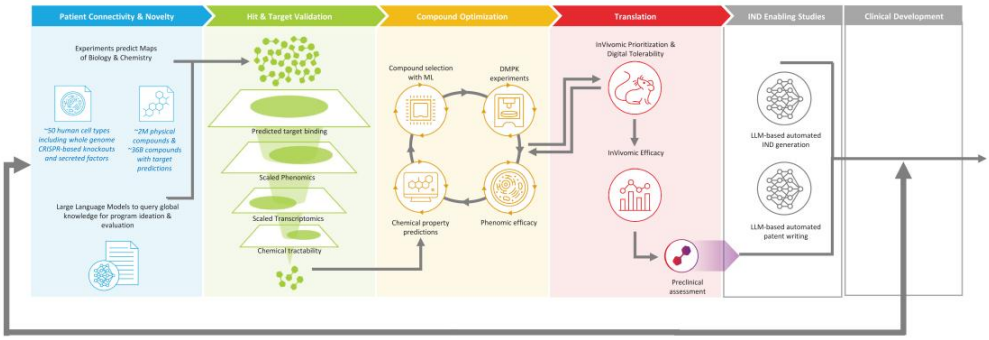
Recursion

InVivomics improves whole organism understanding to rapidly translate programs towards the clinic



Recursion

Roadmap: Addition of population-scale data will enable rapid, precise, automated program progression into clinical development at scale

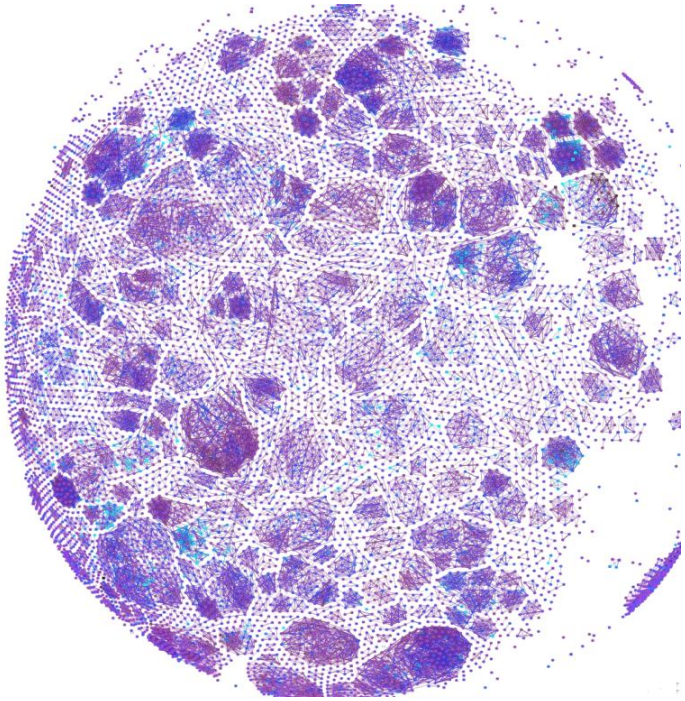


Public Population-Scale Patient – OMICS Data

Proprietary Population-Scale Patient – OMICS Data

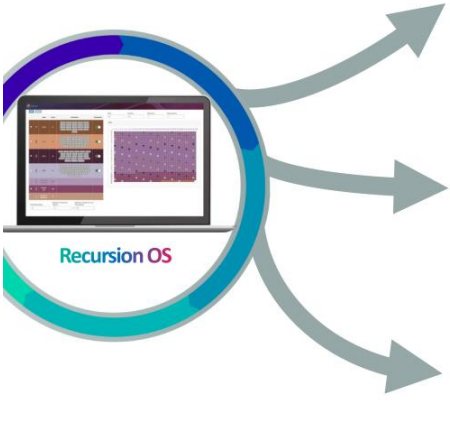
Recursion

How we create value using our maps of biology and chemistry



Recursion

Harnessing value with a multi-pronged capital-efficient business strategy



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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

SYCAMORE Clinical Trial : REC-994 for CCM Phase 2 Fully Enrolled

PREVALENCE & STANDARD OF CARE

~360,000

Symptomatic US + EU5, >1 million patients worldwide live with these lesions today

>5x larger US patient population than other rare diseases like Cystic Fibrosis (>31k patients)

No approved therapy

- Most patients receive no treatment or only symptomatic therapy
- Surgical resection or stereotactic radiosurgery not always feasible because of location and is not curative

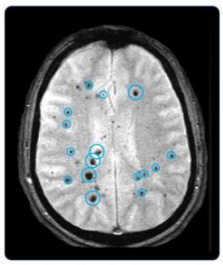
CAUSE

LOF mutations in genes *CCM1*, *CCM2* & *CCM3*, key for maintaining the structural integrity of the vasculature due to unknown mechanisms

PATHOPHYSIOLOGY & REASON TO BELIEVE

Vascular malformations of the CNS leading to focal neurological deficits, hemorrhage and other symptoms

Efficacy in Recursion OS as well as functional validation via scavenging of massive superoxide accumulation in cellular models; reduction in lesion number with chronic administration in mice



Vascular malformations (cavernomas)

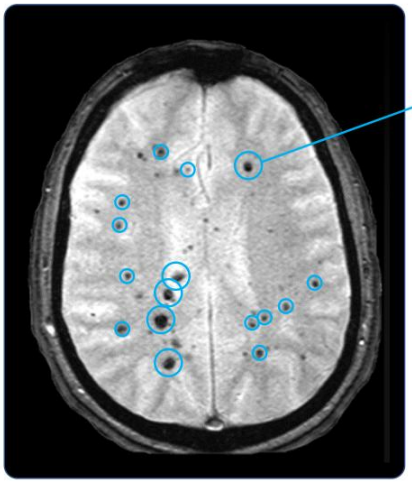
Julia – living with CCM

KEY ELEMENTS

- Targeting **sporadic and familial symptomatic CCM** patients with *CCM1*, *CCM2*, and *CCM3* mutations
- Superoxide scavenger, small molecule
- Phase 2 trial initiated in Q1 2022
- US & EU **Orphan Drug Designation**
- Oral dosing

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

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
- 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

Sources: 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

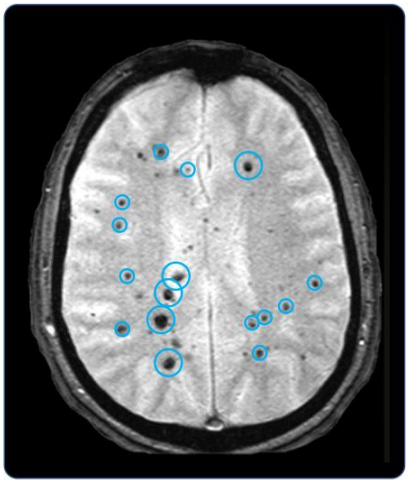
Disease Overview : CCM is an Under-Appreciated Orphan Disease

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

Sources: 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

Therapeutic Approach to Cerebral Cavernous Malformations (CCM)

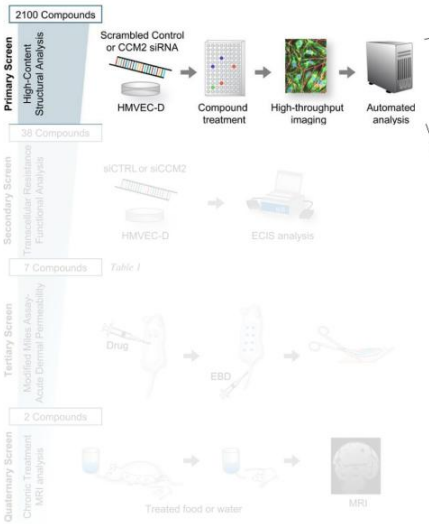


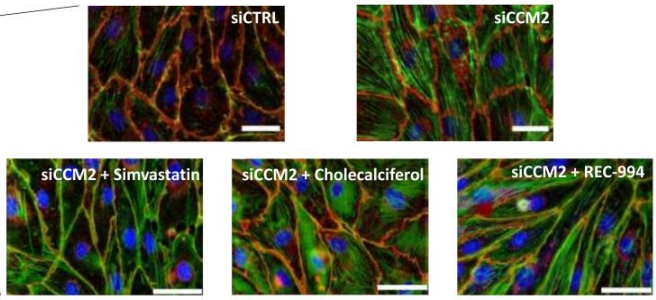
Novel therapeutic approach

- Symptoms associated with both increased size of lesions, but also inflammation or activation of lesions within the immunoprivileged 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

Clinical: CCM

CCM – Applied prototyping of the Recursion OS





Using an early version of our Recursion OS in an academic setting, we identified about 39 molecules out of 2,100 screened that according to a machine learning classifier rescued a complex unbiased phenotype associated with CCM2 loss of function.

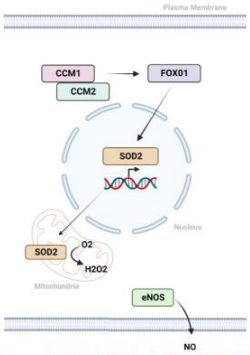
Through a set of follow-on confirmatory assays of increasing complexity, REC-994 stood out as one of two compounds we tested in a 5-month chronic CCM animal model where both compounds demonstrated significant benefit.

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

Clinical: CCM

REC-994 – Mechanism of Action

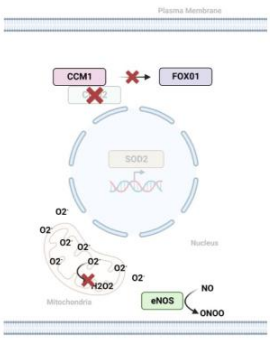
Healthy



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

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

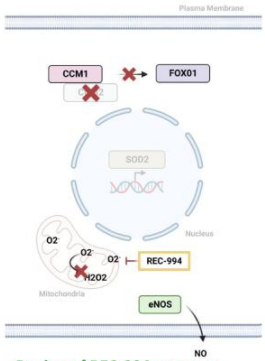
CCM



***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

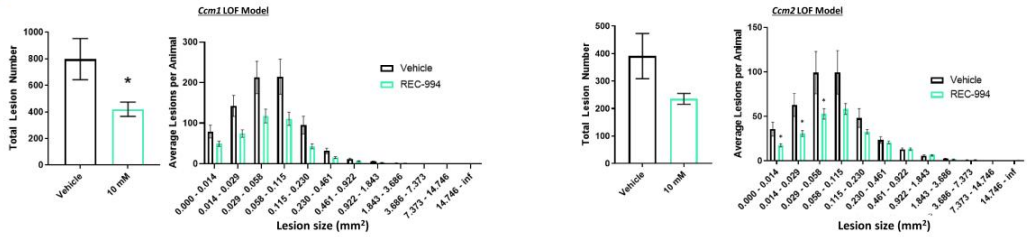
Adapted from REC-994 Investigator Brochure

Clinical: CCM

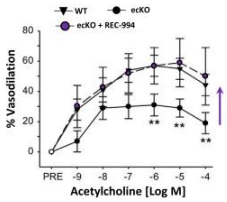
Further Confidence : Preclinical Studies Confirm Insight

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**

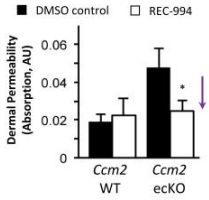


2 **Completely rescues acetylcholine-induced vasodilation defect**



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

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 for CCM Phase 2 Fully Enrolled

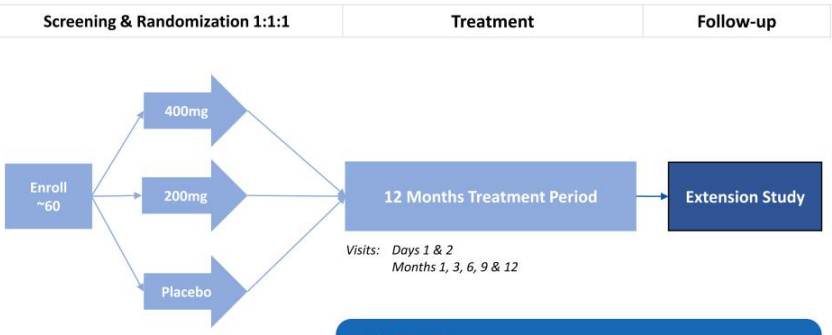
Phase 2 trial initiated in Q1, 2022

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 complete
- Several participants have completed twelve months of treatment and entered long-term extension study
- **Top-line data expected H2, 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

Clinical: NF2

POPLAR Clinical Trial : REC-2282 for NF2 Part A Underway

PREVALENCE & STANDARD OF CARE

~33,000 **Treatable US + EU**

No approved therapy

- There are 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

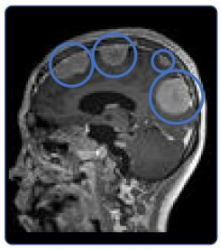
CAUSE

LOF mutations in NF2 tumor suppressor gene, leading to deficiencies in the tumor suppressor protein merlin

PATHOPHYSIOLOGY & REASON TO BELIEVE

Inherited rare **CNS tumor syndrome** leading to loss of hearing and mobility, other focal neurologic deficits

Efficacy in Recursion OS, cellular, and animal models; suppression of aberrant ERK, AKT, and S6 pathway activation in a Phase 1 PD Study in NF2 patient tumors



Intracranial meningiomas

Ricki – living with NF2

KEY ELEMENTS

- Targeting **familial and sporadic NF2 meningioma** patients
- HDAC inhibitor, small molecule
- Oral dosing
- Phase 2/3 trial initiated in Q2 2022
- **Fast-Track** and US & EU **Orphan Drug Designation**

Clinical: NF2

Disease Overview : Neurofibromatosis Type 2 (NF2)

Ricki – living with NF2

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

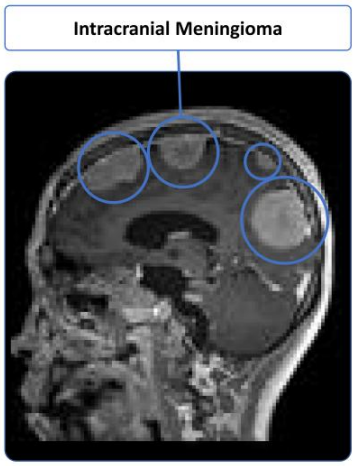
- **No approved drugs** for NF2
- **Surgery** is standard of care (when feasible)
- Location may make complete resection untenable, leading to hearing loss, facial paralysis, poor balance and visual difficulty

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

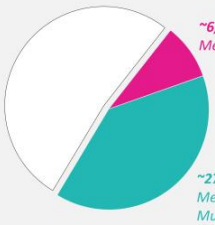
Clinical: NF2

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



>66,000 Patients have Meningiomas



***~6,000** NF2 Patients have Meningiomas (Familial)*

***~27,000** Patients who have Meningiomas that Harbor NF2 Mutations (Sporadic)*

~33,000

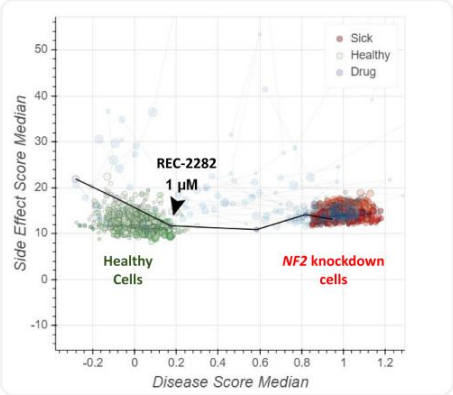
Treatable US + EU5 patients

- 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**

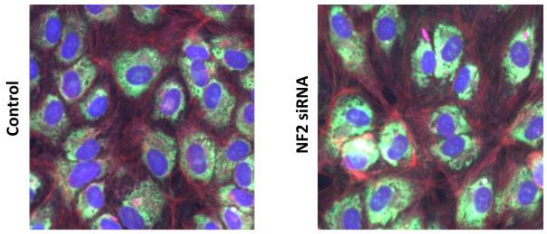
Source: Pemov, et al. Comparative clinical and genomic analysis of neurofibromatosis type 2-associated cranial and spinal meningiomas. Nature. 2020 Jul 28;10(12563). Doi: https://doi.org/10.1038/s41598-020-69074-z; NORD

Clinical: NF2

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



REC-2282 identified as rescuing HUVEC cells treated with NF2

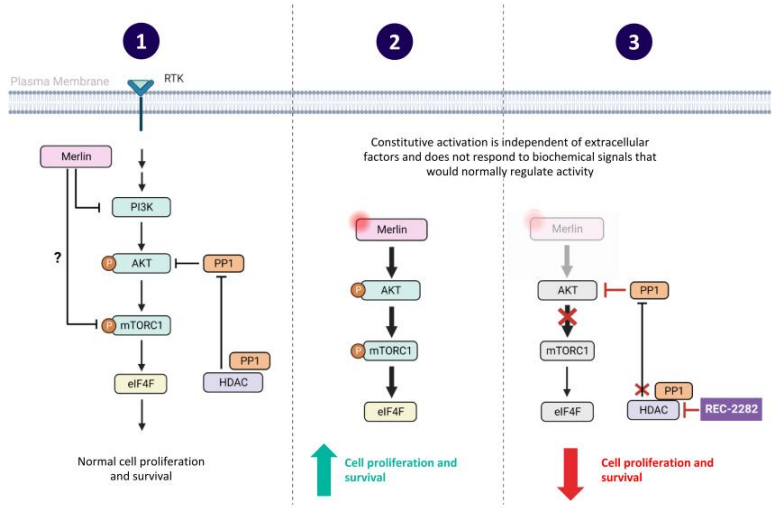


HUVEC, human umbilical vein endothelial cells; NF2, neurofibromatosis type 2; siRNA, small interfering RNA.

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

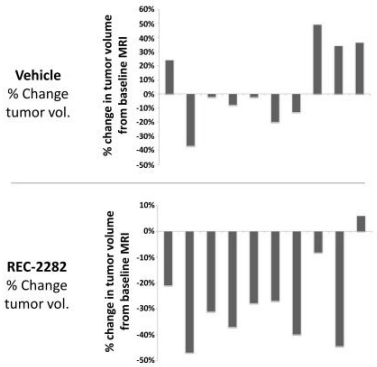
AKT, protein kinase B; eIF4F, eukaryotic initiation factor 4F; HDAC, histone deacetylase; mTor, mammalian target of rapamycin; mTORC1; mammalian target of rapamycin complex 1; NF2, neurofibromatosis type 2; PI3K, phosphoinositide 3-kinase; PP1, protein phosphate 1; Ras, reticular activating system.

Clinical: NF2

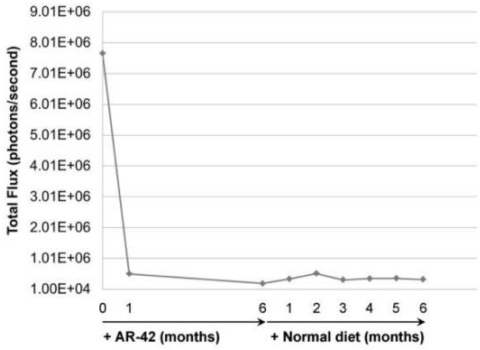
Further Confidence : Preclinical Studies Confirming Insight

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 Suggest 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

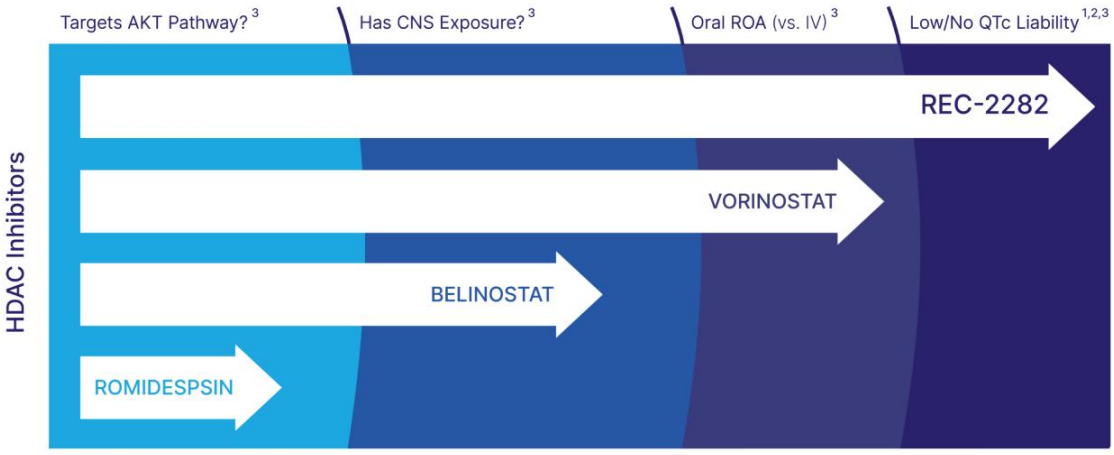
... with a drug-like profile

- 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 for NF2 Part A Underway

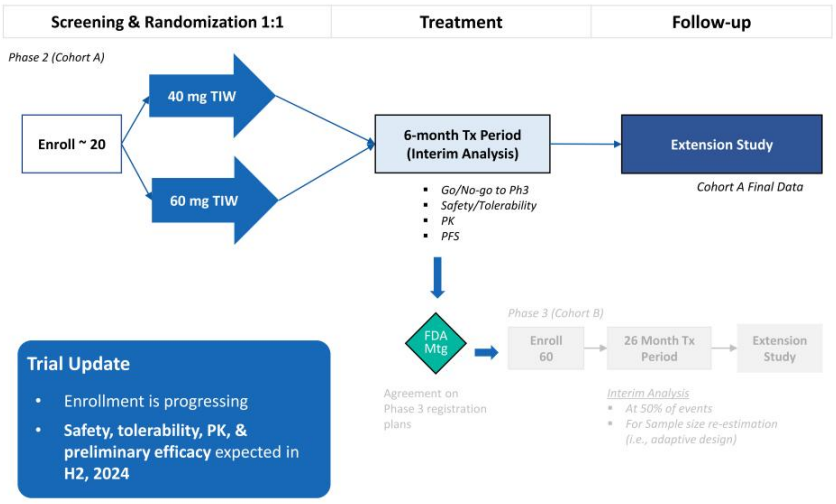
Phase 2/3 trial initiated in Q2, 2022

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
- **Safety, tolerability, PK, & preliminary efficacy** expected in **H2, 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

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

PREVALENCE & STANDARD OF CARE

~50,000 **Diagnosed US + EU5**

No approved therapy

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

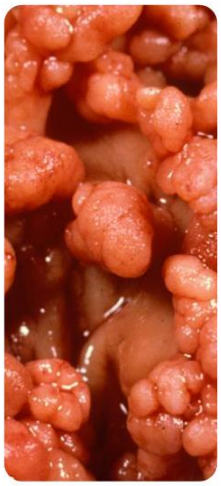
CAUSE

Inactivating mutations in the tumor suppressor gene *APC*

PATHOPHYSIOLOGY & REASON TO BELIEVE

Polyps throughout the GI tract with extremely high risk of malignant transformation

Efficacy in the Recursion OS showed specific MEK 1/2 inhibitors had an effect in context of *APC* LOF. Subsequent APC^{min} mouse model showed potent reduction in polyps and dysplastic adenomas



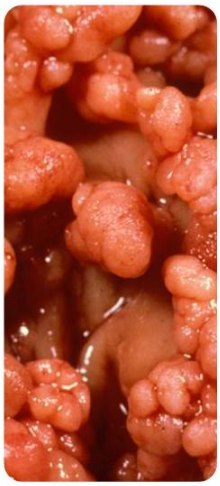
Polyps Found in Colon and Upper GI Tract

KEY ELEMENTS

- Targeting **classical FAP patients (with *APC* mutation)**
- MEK inhibitor, small molecule
- Oral dosing
- Phase 2 trial initiated in Q3 2022
- **Fast-Track** and US & EU **Orphan Drug Designation**

Clinical: FAP

Disease Overview : Familial Adenomatous Polyposis



Polyps Found in Colon and Upper GI Tract

Patient Population – Easily Identifiable

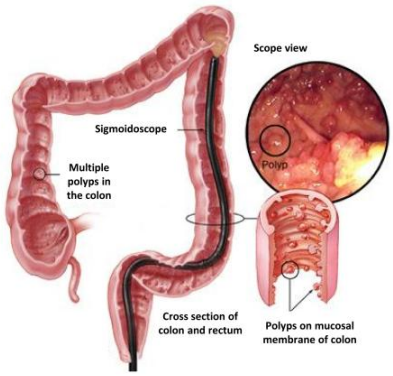
- Autosomal dominant tumor predisposition syndrome caused by a mutation in the APC gene
- Classic FAP (germline mutation) :
  - Hundreds to thousands of polyps in colon and upper GI tract
  - Extraintestinal manifestations (e.g., desmoid tumors)
  - 100% likelihood of developing colorectal cancer (CRC)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

~50,000 Diagnosed US + EU5 patients

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

Clinical: FAP

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"

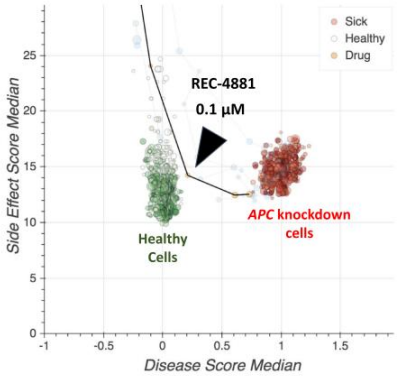
- **Niloy Jewel Samadder**, MD, Mayo Clinic

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



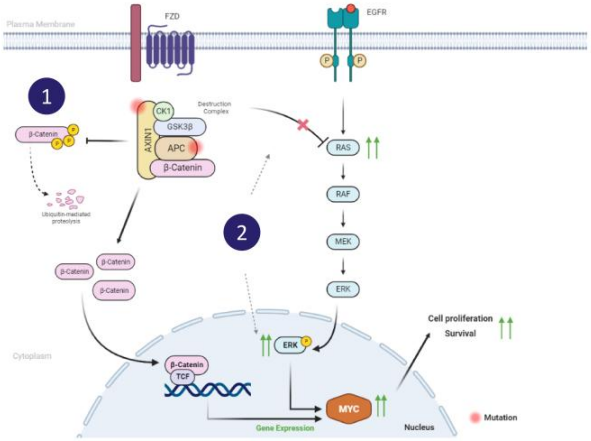
- Compared to thousands of other molecules tested, REC-4881 rescued phenotypic defects substantially better (including better rescue than other MEK inhibitors) for APC specific knockdown
- Findings validated in tumor cell lines and spheroids grown from human epithelial tumor cells with *APC* mutation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

Clinical: FAP

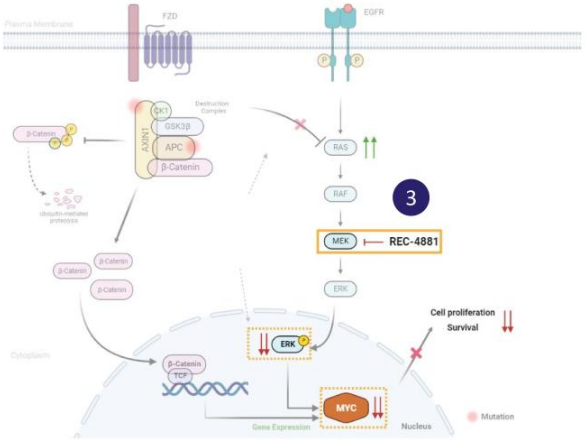
MoA : REC-4881 Blocks Wnt Mutation Induced MAPK Signaling

Orally Bioavailable, Small Molecule MEK Inhibitor

Disease State



REC-4881 Impact



3 REC-4881 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

Jeon, WJ, et al. (2018). Interaction between Wnt/β-catenin and RAS-ERK pathways and an anti-cancer strategy via degradations of β-catenin and RAS by targeting the Wnt/β-catenin pathway. npj Precision Oncology, 2(5).

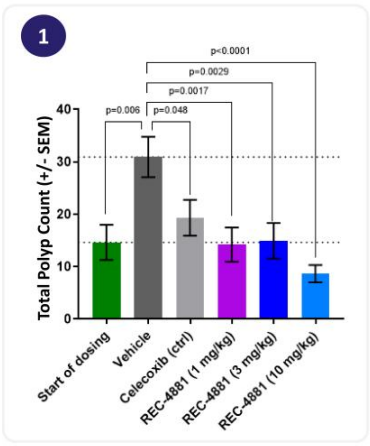
Clinical: FAP

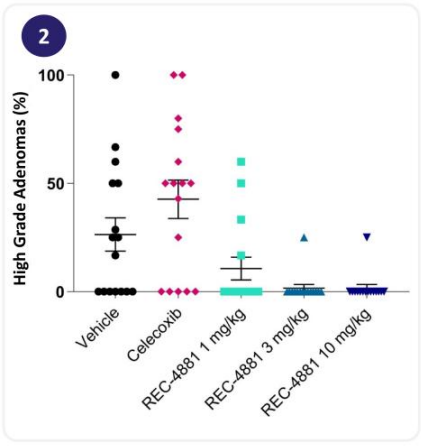
Further Confidence : Preclinical Studies Confirming Reduction in Polyp Count and High-Grade Dysplasia

- 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's formulation (molecule in-licensed from 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

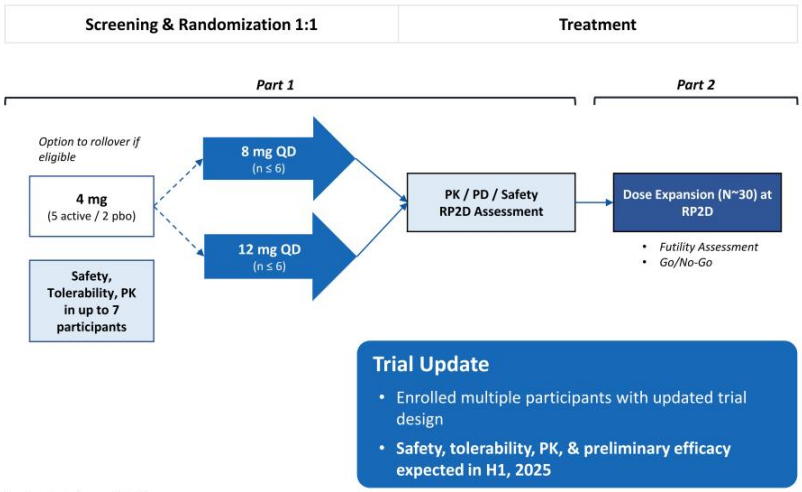
Phase 2 trial initiated in Q3, 2022

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: polyp burden (% change from baseline)
- Secondary:
  - Part 1: Safety & tolerability
  - Part 2: PK; PD; change from baseline in polyp number, histological grade, disease score



Trial Update

- Enrolled multiple participants with updated trial design
- **Safety, tolerability, PK, & preliminary efficacy expected in H1, 2025**

https://clinicaltrials.gov/ct2/show/NCT05552755, protocol amendments made to enhance quality and accelerate the pace of the trial

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

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

Clinical: AXIN1 or APC

Clinical Program : REC-4881 for *AXIN1* or *APC* Mutant Cancers

PREVALENCE & STANDARD OF CARE

~65,000 **Treatable US + EU5**

Substantial need for developing therapeutics for patients harboring mutations in *AXIN1* or *APC*, as **these mutations are considered undruggable**

To our knowledge, REC-4881 is the **only industry sponsored small molecule therapeutic** designed to enroll solid tumor patients harboring mutations in *AXIN1* or *APC*

CAUSE

LOF mutations in *AXIN1* or *APC* tumor suppressor genes

PATHOPHYSIOLOGY & REASON TO BELIEVE

Alterations in the WNT pathway are found in a **wide variety of tumors** and confer poor prognosis and resistance to standard of care

Efficacy in the Recursion OS and favorable results in PDX models harboring *AXIN1* or *APC* mutations vs wild-type leading to a significant PFS benefit in HCC and Ovarian tumors

KEY ELEMENTS

- Targeting ***AXIN1* or *APC* mutant cancers**
- MEK inhibitor, small molecule
- Oral dosing
- **IND accepted** by FDA
- Expect to **initiate Phase 2** study in **Q4, 2023**

Gross morphology of HCC

Clinical: AXIN1 or APC

Disease Overview : *AXIN1* or *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* or *APC* **leads to sustained Wnt signaling promoting** cancer progression and survival[1]
- *AXIN1* or *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*

Clinical: AXIN1 or APC

Disease Overview : *AXIN1* or *APC* Mutant Cancers

Tumor Type	*AXIN1* Mutation Frequency[1]	*APC* Mutation Frequency[1]	Treatable Population[2] (US+EU5)
CRC	3%	70%	27,450
LUAD	4%	11%	14,000
Prostate	2%	11%	6,700
Bladder	3%	8%	5,100
HCC	12%	5%	3,100
Endometrial	8%	12%	2,600
Esophageal	2%	7%	2,600
PDAC	1%	2%	1,500
Ovarian	1%	3%	1,400
TNBC	1%	2%	300
			~65,000

Flexible Patient Selection Strategy and Study Design

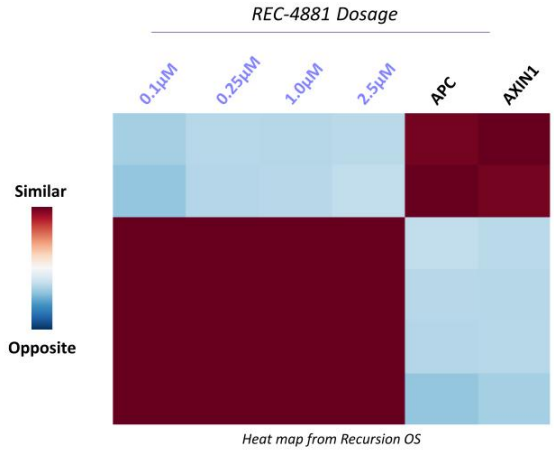
- *AXIN1* and *APC* genes covered by commercially available NGS panels and liquid biopsy detection assays
- FDA guidance supports utility of ctDNA as patient selection for the detection of alterations for eligibility criteria and as a stratification factor for trials enrolling marker-positive and marker-negative populations[3]
- 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] *Obtained from cbioportal.org.* [2] *Represents 2L treatable population estimates; obtained from DRG.* [3] *https://www.fda.gov/media/158072/download*

Clinical: AXIN1 or 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

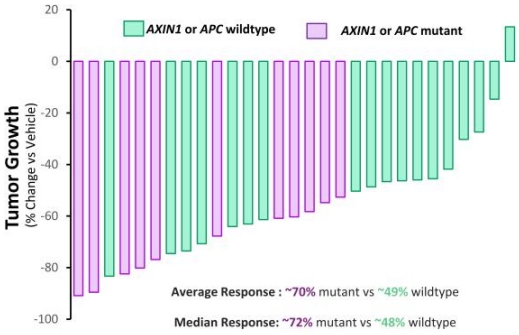
Recursion Differentiation: REC-4881 rescues tumor suppressor genes *APC* and *AXIN1*

- *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 or APC

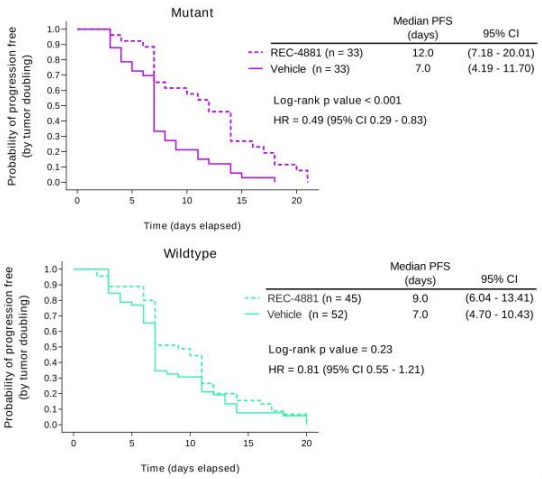
Further Confidence : Preclinical Studies Confirming Insight

Efficacy found in In Vivo Mice Models …



- Significantly greater antitumor activity observed with REC-4881 in mutant models versus wildtype
- Majority of mutant models ≥ 60% tumor growth inhibition, which is considered a benchmark for a response in the clinic[1]

… Led to Significant Progression Free Survival



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. [1] *Wong, H., et al. Clin Cancer Res, 2012, 18:14, pp.3846-3855*

Clinical: AXIN1 or APC

Phase 2 Trial Design : REC-4881 for *AXIN1* or *APC* Mutant Cancers

Expect Phase 2 initiation in Q4, 2023

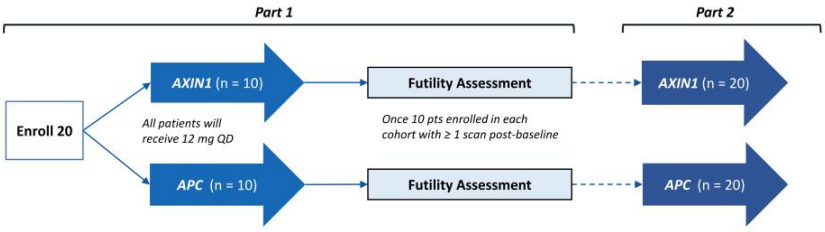
Enrollment Criteria

- Unresectable, locally advanced, or metastatic cancers
- *AXIN1* or *APC* mutation confirmed by NGS (tissue or blood)
- CRC patients must be *RAS / RAF* wildtype
- No MEK inhibitor treatment within 2 months of initial dose
- ≥ 1 prior line of therapy
- ECOG PS 0-1

Outcome Measures

- Primary
  - Safety/tolerability
  - ORR (RECIST 1.1)
- Secondary
  - PK
  - Additional efficacy parameters

Screening & Treatment



Trial Update

- First clinical trial for an oncology indication at Recursion
- **IND accepted by FDA**

REC-3964 for the Treatment of C. Difficile Infection

Target / MOA	Selective C. diff Toxin Inhibitor
Molecule Type	Small Molecule
Lead Indication(s)	C. Difficile Infection
Status	Phase 2
Source of Insight	Recursion OS

Clinical: C. Difficile

Clinical Trial : REC-3964 for C. Difficile Phase 1 study complete

PREVALENCE & STANDARD OF CARE

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

Standard of care includes antibiotic therapies which can further impair gut flora, and lead to relapse

CAUSE

C. difficile toxins from colonizing bacterium causes degradation of colon cell junction, toxin transit to bloodstream, and morbidity to host

KEY ELEMENTS

- Selective C. diff toxin inhibitor, small molecule
- **Non-antibiotic approach** with potential for combination with SOC and other therapies
- Designed for **selective antitoxin pharmacology** to target infection
- Phase 1 HV study complete

PATHOPHYSIOLOGY & REASON TO BELIEVE

Highly recurrent infectious disease with severe diarrhea, colitis, and risk of toxic megacolon, sepsis, and death

Recursion OS identified a new chemical entity for recurrent C. difficile infection and potentially prophylaxis via glycosyl transferase inhibition with potential to be orally active

TRIAL UPDATE

- **Phase 1 PK study complete**
- REC-3964 was **well tolerated** and all AEs were Grade 1
- Expect to **initiate Phase 2 proof-of-concept study** in **2024**

Colleen – lived with rCDI

Clinical: C. Difficile

Disease Overview : C. Difficile Infection (CDI)

Colleen – lived with rCDI

Patient Population – Large, Diagnosable and Easy to Identify

- Symptoms caused by clostridioides 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**

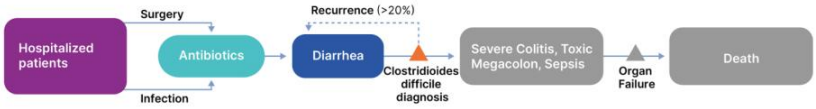
~730,000 **Diagnosed US + EU5 patients**

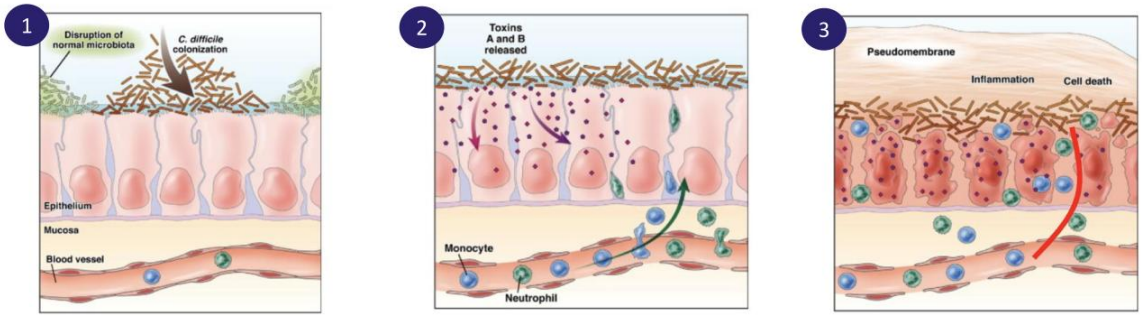
*Source, CDC *NAAT = Nucleic Acid Amplification Test; **rCDI = recurrent CDI*

Clinical: C. Difficile

Disease Overview : C. Difficile Infection (CDI)

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





Disruption of microbiota and colonization of *C. diff*

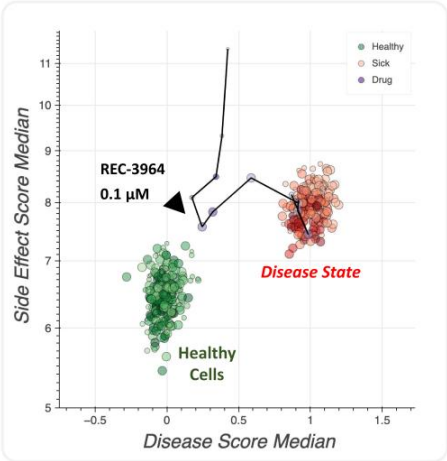
Release of C. diff toxins

Degradation of colon cell junction & toxin transit to bloodstream

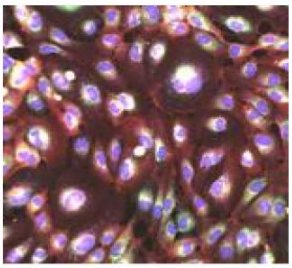
Source: McCollum, D., Rodriguez, JM . Detection, Treatment, and Prevention of Clostridium difficile Infection. Clinical Gastroenterology and Hepatology 2012 Mar 19. https://doi.org/10.1016/j.cgh.2012.03.008

Clinical: C. Difficile

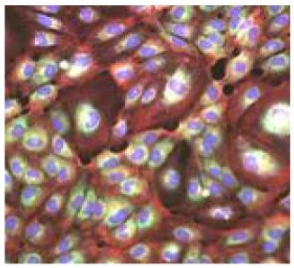
Insight from OS : REC-3964 Rescued Cells Treated with C. Difficile Toxins



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



C. diff toxin B phenotype

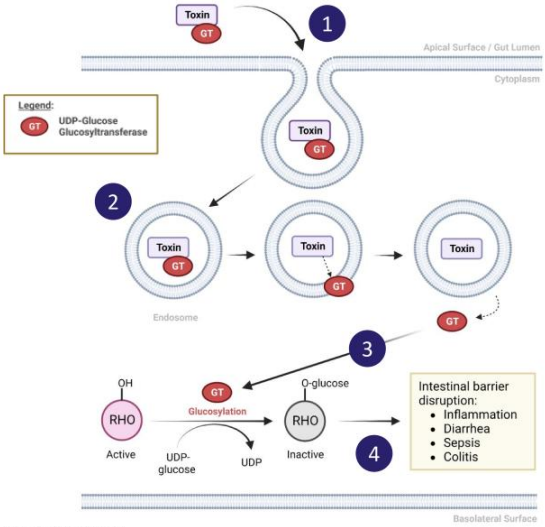


Healthy Control

Clinical: C. Difficile

REC-3964 : Selective Inhibitor of C. Difficile Toxins

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



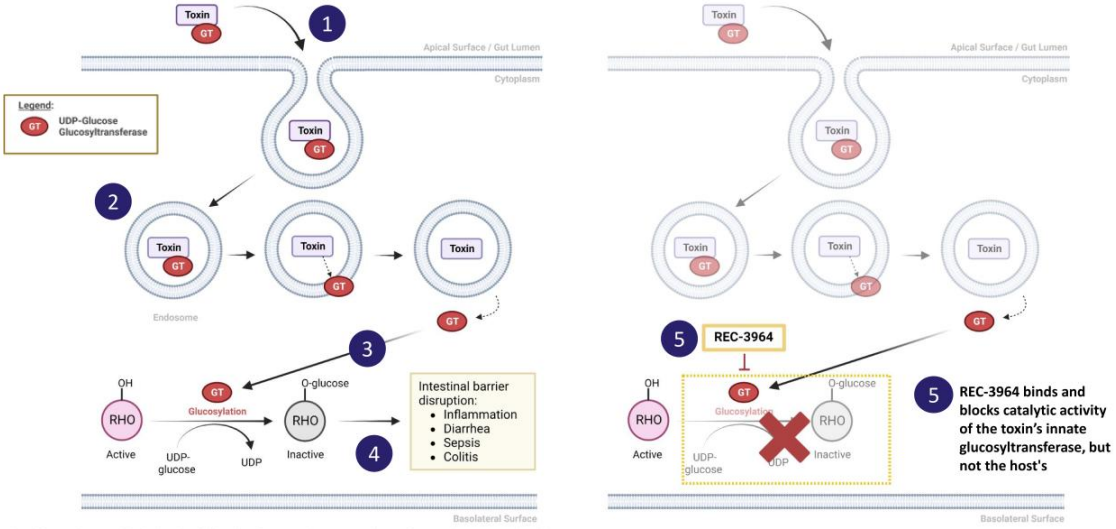
Adapted from Awad et al. 2014

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. Difficile

REC-3964 : Selective Inhibitor of C. Difficile Toxins

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

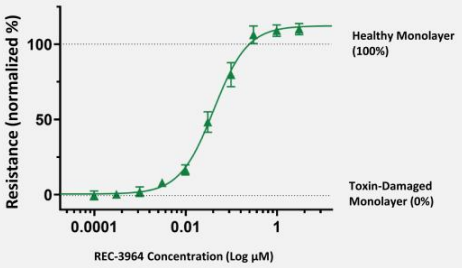


Adapted from Awad, MM. et al. (2014). Clostridium difficile virulence factors: Insights into an anaerobic spore-forming pathogen. Gut Microbes. 5(5), 579-593.

Clinical: C. Difficile

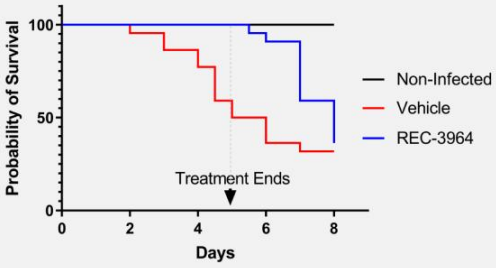
Further Confidence : Preclinical Studies Confirmed Recursion OS Insight

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. Difficile

Clinical Trial : REC-3964 for C. Difficile Phase 1 study complete

Trial Design
- Randomized, Double-blind Trial

Population
- Healthy Participants
- SAD (n = 48)
  - 36 participants treated with REC-3964
  - 12 participants treated with placebo
- MAD (n = 42)
  - 34 participants treated with REC-3964
  - 8 participants treated with placebo

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

Phase 1 Topline

- REC-3964 oral administration was **well tolerated** by all subjects tested
  - ✓ **3%** (n=1) of participants in SAD with drug-related AEs
  - ✓ **12%** (n=4) of participants in MAD with drug-related AEs
  - ✓ All AEs were deemed **Grade 1**
  - ✓ **No SAEs** were observed
  - ✓ **No discontinuations** related to treatment
- REC-3964 exhibited a **favorable PK profile**
  - ✓ Exposures (AUC) **increased approximately dose-proportionally** across the dose ranges tested (50 mg – 1200 mg)
  - ✓ Half-life ranged from **~7-10 hours;** BID dosing expected to reach targeted trough concentrations

Clinical: C. Difficile

Further Confidence : Clinical Studies Confirming Safety

REC-3964 was well-tolerated with no treatment-related SAEs

MAD Study	Placebo (N=8) n (%)	100 mg (N=10) n (%)	300 mg (N=8) n (%)	500 mg (N=8) n (%)	900 mg (N=8) n (%)	REC-3964 Overall (N=34) n (%)	MAD Overall (N=42) n (%)
Total Number of TEAEs	17	24	5	9	7	45	62
Total Participants with ≥ 1 TEAE	6 (75.0)	8 (80.0)	4 (50.0)	5 (62.5)	4 (50.0)	21 (61.8)	27 (64.3)
Relationship to Study Drug							
Not Related	4 (50.0)	6 (60.0)	3 (37.5)	4 (50.0)	4 (50.0)	17 (50.0)	21 (50.0)
Related	2 (25.0)	2 (20.0)	1 (12.5)	1 (12.5)	0	**4 (11.8)**	6 (14.3)
Abdominal Distension	2 (25.0)	1 (10.0)	1 (12.5)	1 (12.5)	0	3 (8.8)	5 (11.9)
Flatulence	0	1 (10.0)	0	0	0	1 (2.9)	1 (2.4)
Severity							
Grade 1	6 (75.0)	8 (80.0)	4 (50.0)	5 (62.5)	4 (50.0)	21 (61.8)	27 (64.3)
Grade 2	0	0	0	0	0	0	0
Grade ≥ 3	0	0	0	0	0	0	0
Total Number of SAEs	0	0	0	0	0	0	0
Discontinued Study Drug Due to AE	0	0	0	0	0	0	0

TEAEs = treatment emergent adverse events; Grade 1 = Mild, Grade 2 = Moderate, Grade 3 = Severe, Grade 4 = Life Threatening, Grade 5 = Fatal

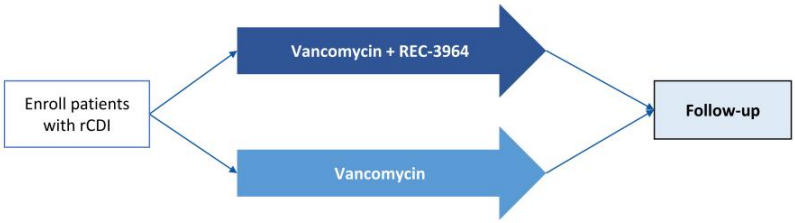
Clinical: C. Difficile

Planned Phase 2 Proof-of-Concept Trial Design

Development Approach

- Initial Phase 2 POC study to evaluate REC-3964 in combination with vancomycin
- Focus on subjects at risk for CDI with moderate to severe disease planning to receive SOC therapy
- Flexibility to assess effects of REC-3964 on both treatment and reduction of recurrence populations
- Potential to generate early evidence of economic value and model cost-effectiveness of REC-3964

Preliminary Phase 2 POC Design



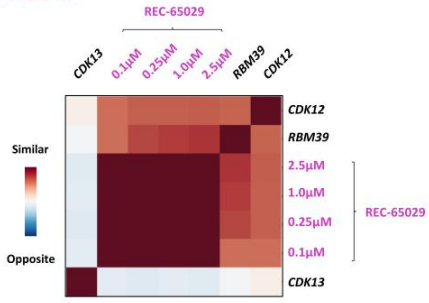
Trial Update

- Determination of optimal dose and sample size underway
- **Phase 2 initiation expected in 2024**

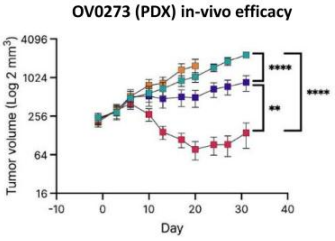
Preclinical: HR-Proficient Ovarian Cancer

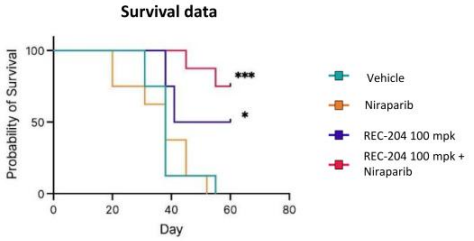
RBM39: Novel CDK12-Adjacent Target for HR-Proficient Ovarian Cancer

GOAL	Identify potential first-in-class tumor-targeted precision therapeutic NCE with novel MOA capable of potentially treating HR-proficient ovarian cancer
INSIGHT FROM OS	Inhibition of target RBM39 (previously referred to as Target γ) may mimic the inhibition of CDK12 while mitigating toxicity related to CDK13 inhibition
FURTHER CONFIDENCE	A Recursion-generated NCE showed single agent efficacy that is enhanced in combination with Niraparib in a BRCA-proficient PDX model
NEXT STEPS	IND-enabling studies are progressing



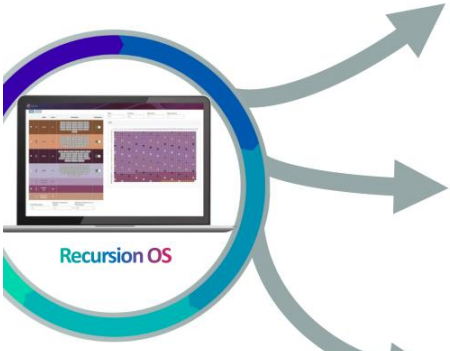
BRCA-proficient ovarian cancer PDX





*Note: in the OV0273 PDX model, mice were treated with a representative lead molecule REC-1170204 (100 mg/kg, BID, PO) ± Niraparib (40 mg/kg, QD, PO) for 32 days. Single agent REC-1170204 or in combination with Niraparib resulted in a statistically significant response vs either Niraparib or vehicle arms. In addition, there was a statistically significant improvement in survival > 30 days post final dose. *p<0.05, ** p<0.01, **** p<0.0001*

Harnessing value with a multi-pronged capital-efficient business strategy



Pipeline Strategy

Build internal 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***
- **Other large, intractable areas of biology**

Data Strategy

License subsets of data and tools

Direct generation of new data internally **to maximize pipeline and partnership value-drivers**

- Licensing
- Augment Recursion OS

*Includes a single oncology indication from our Roche and Genentech collaboration.

Our existing partnerships represent some of the most significant scientific collaborations in TechBio across biopharma and tech

BAYER

(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**

Roche
Genentech
A Member of the Roche Group

(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**

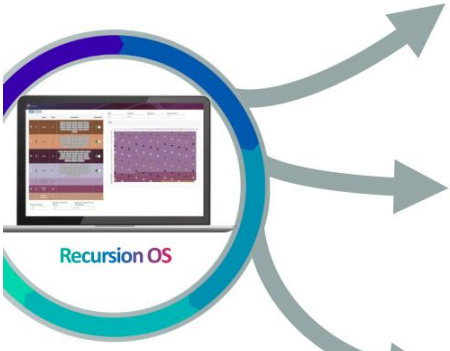
NVIDIA®

(Announced July 2023)

Computation and ML/AI

- **$50M equity investment**
- Partnership on **advanced computation** (e.g., foundation model development)
- **Priority access** to compute hardware or **DGXCloud Resources**
- **Potential to house Recursion Tools on NVIDIA's BioNeMo Marketplace**

Harnessing value with a capital efficient business strategy



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Data that is relatable and scalable is the Recursion differentiator

Recursion Data Universe: >25 PB of proprietary biological and chemical data, spanning phenomics, transcriptomics, invivomics, and more

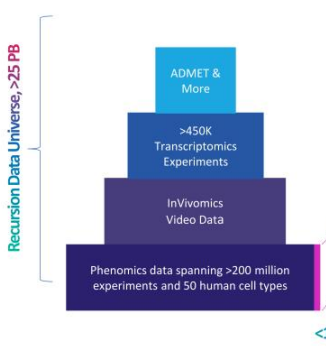
- We believe one of the largest biological and chemical datasets **fit for the purpose of training large-scale ML models**

RXRX3: CRISPR knockouts of most of the human genome, 1,600 FDA approved / commercially available bioactive compounds

- We believe the **largest public dataset of its kind**, <1% of Recursion Data Universe, what Recursion can generate in ~1 week

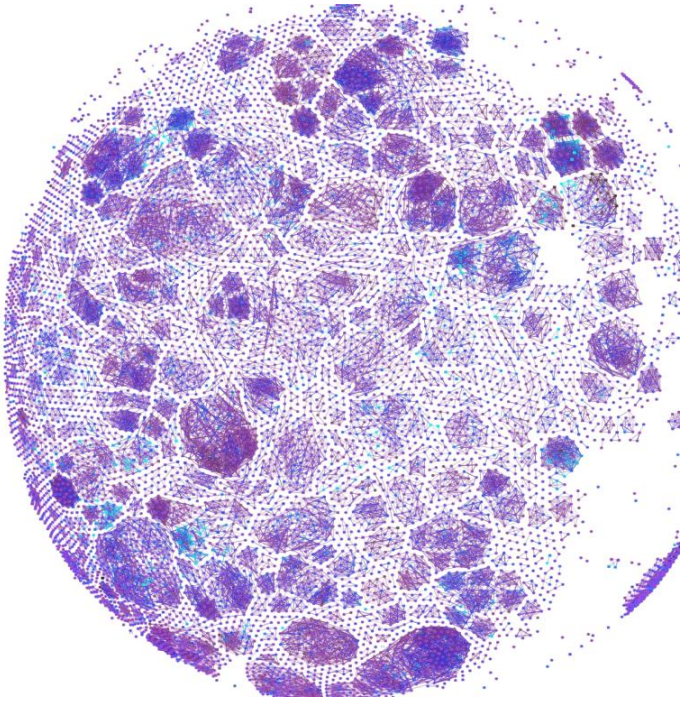
MolRec™: freemium web-based **application to explore compound and gene relationships** in RXRX3

Start working with RXRX3 and MolRec™: www.rxrx.ai



Dataset	Released	Number of Samples
Bio/Chem Phenomic Maps		
RxRx3	**2023**	**2.2M**
JUMPCP	2023	823,438
Autonomous Driving		
Waymo Open Dataset	2018	~105,000
nuScenes	2018	1,000
Image/Object recognition		
ImageNet (21k)	2009	14M
COCO	2014	330,000

Value driven by our team and our milestones



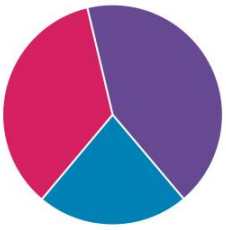
Recursion

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

Team Members

>550 **Employees**

>50% **Advanced degrees**



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

~43% Female ~56% Male ~1% Non-Binary

Parity Pledge Signer
gender parity and people of color parity

ESG Highlights

- ✓ ESG reporting on **Healthcare and Technology Metrics**
- ✓ **100% of electricity** powering our Biohive-1 supercomputer comes from renewable sources
- ✓ Learn more about Recursion's ESG stewardship: www.recursion.com/esg

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 SUSTAINALYTICS

MSCI ESG RATINGS A
CCC | B | BB | BBB | A | AA | AAA

Data shown reflective of Q2 2023 and includes Cyclica and Valence acquisitions, gender statistics include participating individuals

Our leadership team brings together experience & innovation to lead TechBio

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

Blake Borgeson, PHD
Co-Founder of RXRX

MIRI · BUILD A SIGN

Zachary Bogue, JD
Co-Founder & Partner of Data Collective

DC >C

Executive Team

Chris Gibson, PHD
Co-Founder & CEO

Tina Larson
President & COO

Roche · Genentech · ACHAOGEN

Michael Secora, PHD
Chief Financial Officer

LAURION

Shafique Virani, MD FRCS
Chief Business Officer

Roche · Genentech · bridgebio

David Mauro, MD PHD
Chief Medical Officer

CODIAK · CHECKMATE PHARMACEUTICALS

Heather Kirkby, MBA
Chief People Officer

intuit

Ben Mabey
Chief Technology Officer

Laura Schaevitz, PHD
SVP and Head of Research

vium

Kristen Rushton, MBA
SVP of Business Operations

Myriad genetics

Nathan Hatfield, JD MBA
Chief Legal Officer

WILSON SONSINI

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**
- **Ph2 initiation** for **AXIN1 or APC mutant cancers** program expected in **Q4, 2023**
- Potential to **accelerate value creation** with **proprietary foundation models** for biology and chemistry
- Potential to open-source data and tools for non-commercial use and **license data and tools to biopharma and other commercial users**

Medium-Term

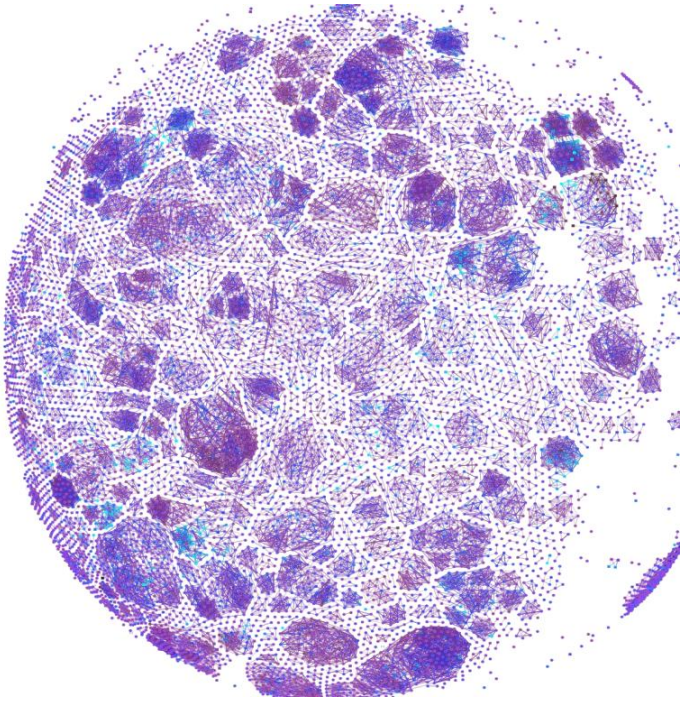
- Multiple **Ph2 readouts** for AI-discovered programs
  - **CCM** top-line data expected **H2, 2024**
  - **NF2** & **FAP** safety & preliminary efficacy expected **H2, 2024** & **H1, 2025**, respectively
- **Ph2 initiation** for **C. difficile Infection** program in **2024**
- Potential for **additional 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 **~$406M in cash** at the end of **Q2, 2023** (does ***not*** include **$50M NVIDIA investment**)

Cash refers to cash and cash equivalents

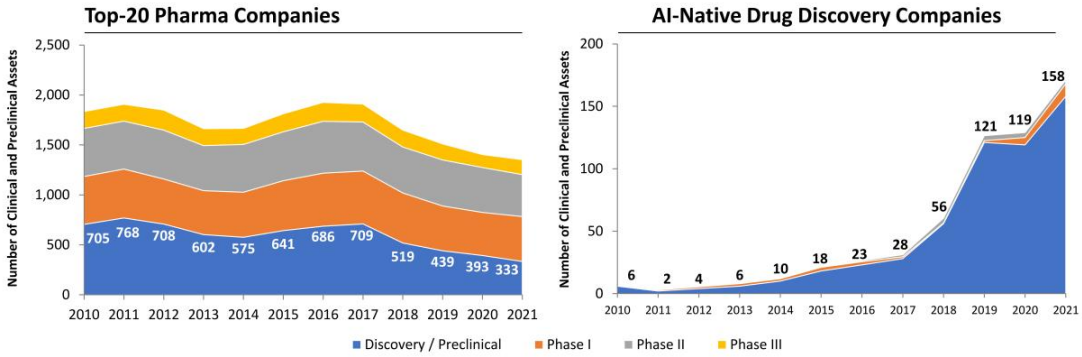

Impact
RECURSION

Additional scientific and business context



Recursion

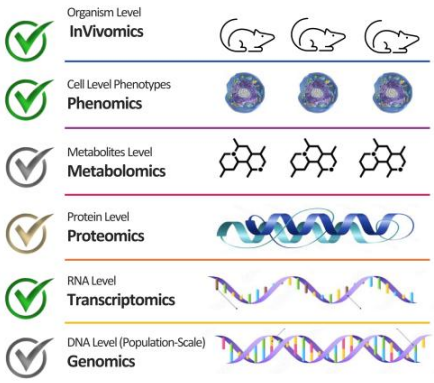
The biopharmaceutical industry faces pressure amidst declining efficiency in drug discovery



AI-enabled drug discovery efforts have proliferated alongside the declining efficiency of traditional approaches

Images adapted from Jayatunga, M., et al. Nature Reviews Drug Discovery 2022.

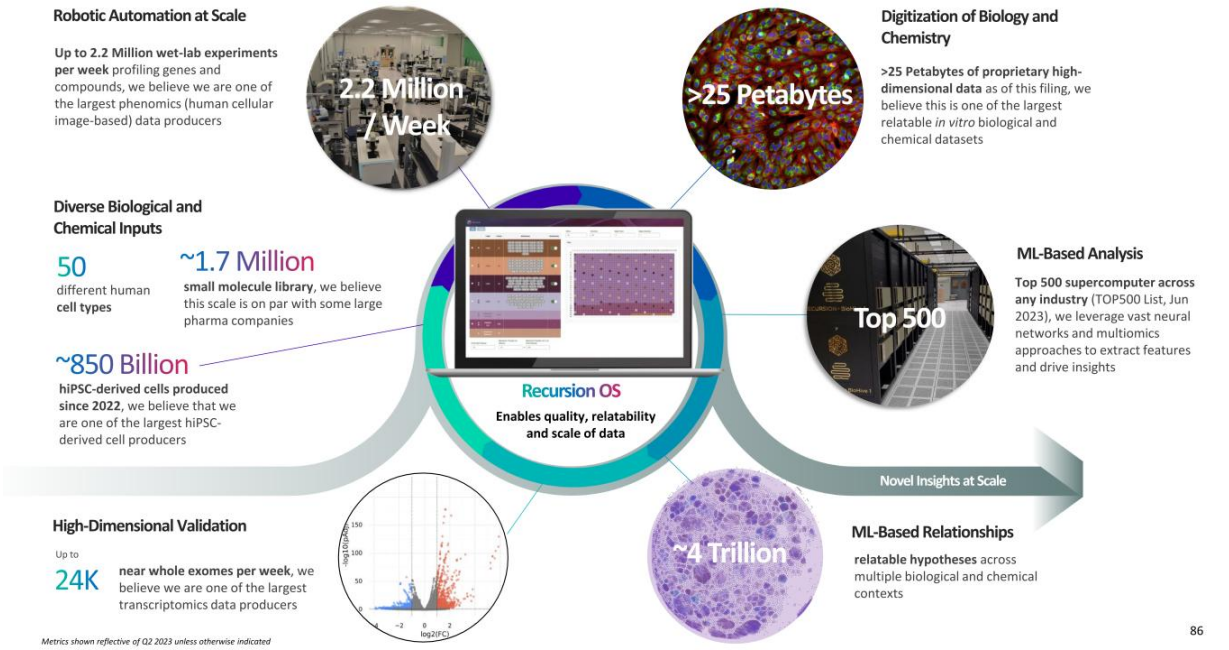
We build biological and chemical datasets to map relationships across scales and understand the connectivity of the system



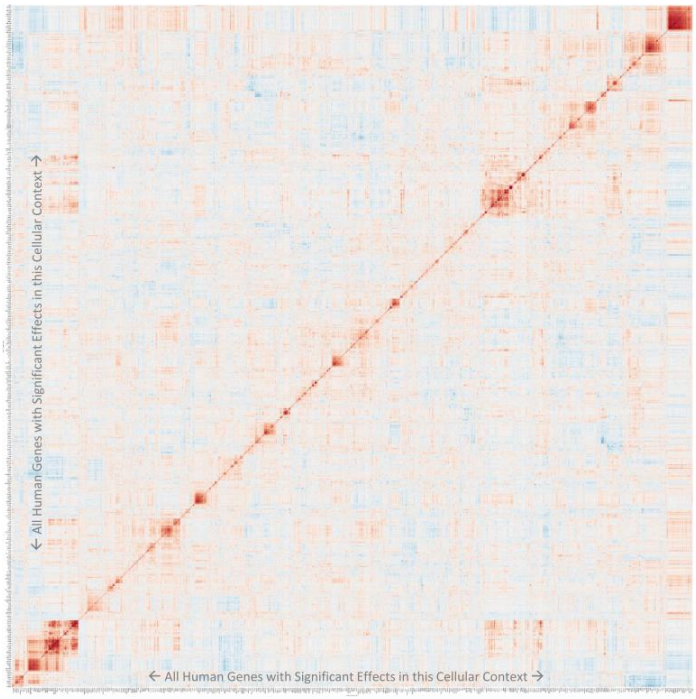
Built and scaled **Exploratory** **Aspirational**

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

Like digital maps of Earth, **connections within and between layers add useful context**. Similarly, Recursion is **mapping different multiomic layers of biology** and identifying connections within and between layers to **better understand biology at scale**.



Metrics shown reflective of Q2 2023 unless otherwise indicated



Recursion

Genome-scale mapping

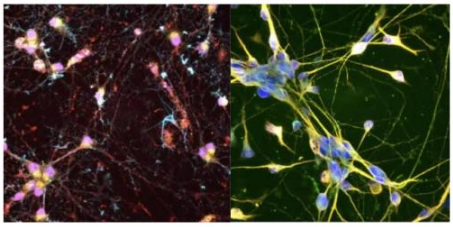
This is a **whole-genome arrayed CRISPR knock-out Map** generated in primary human endothelial cells

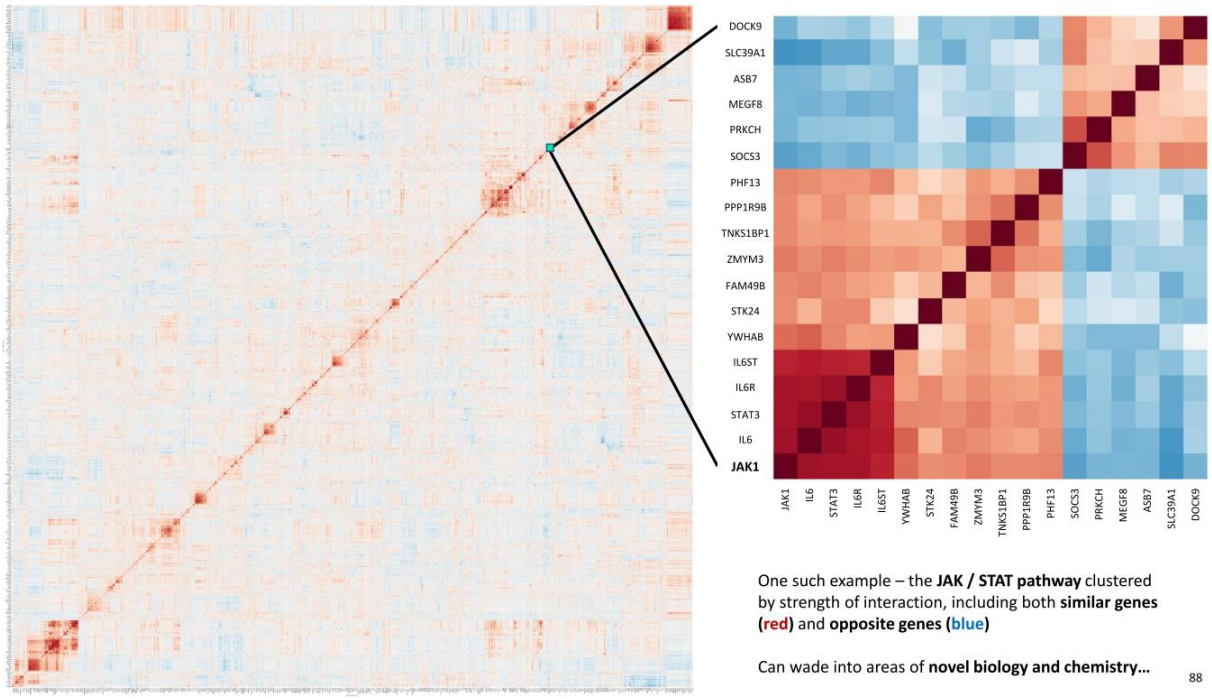
Every gene is represented in a pairwise way (each is present in columns and rows)

Dark Red indicates phenotypic similarity according to our neural networks while **Dark Blue** indicates phenotypic anti-similarity (which in our experience often suggests negative regulation)

We can add the phenotypes of hundreds of thousands of small molecules at multiple doses and query and interact with these maps using a web application

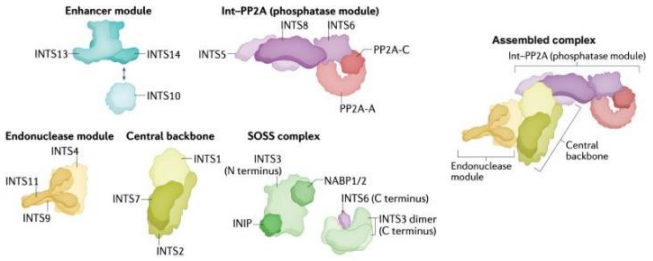
Thousands of examples of known biology and chemistry



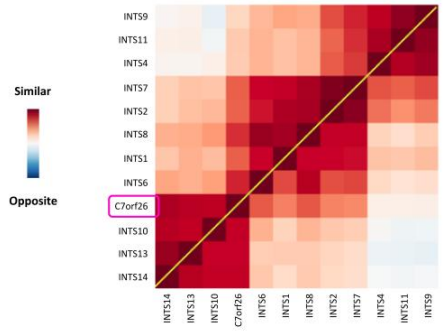


One such example – the **JAK / STAT pathway** clustered by strength of interaction, including both **similar genes (red)** and **opposite genes (blue)**

Can wade into areas of **novel biology and chemistry…**



Phenomics TVN (below diagram) vs. Centerscale (above diagram)



Maps reveal known and novel biology

- In 2022, new independent research identified a previously unknown gene, C7orf26, as part of the Integrator complex
- Maps jointly developed by Recursion and Genentech replicated this same result
- Demonstrates accuracy and consistency across different map building approaches

Recursion

Genentech
A Member of the Roche Group

Competitive Benchmarking – Technology Enabled Drug Discovery

	Recursion	AbCellera Biologics	Exscientia	Insitro	Schrodinger
Multiple Large-Scale Partnerships[1]	✓	✓	✓	✓	✓
Significant Internally Developed Pipeline of Early Programs[2]	✓	✓	✓		
Multiple Internally Developed Ph2 or Ph3 Clinical Programs[3]	✓				
Large-Scale Proprietary Biological and Chemical Datasets[4]	✓				

This analysis was performed on a best effort basis leveraging publicly available databases including company websites, press releases, and public filings as of May 1, 2023. (1) Companies with at least two large-scale partnerships with pharmaceutical companies (potential milestones up to or exceeding $1 billion per partnership). (2) Companies providing clear details on at least ten in-house programs from discovery to preclinical. (3) Companies with at least three programs in either Phase 2 or Phase 3. (4) Companies providing clear details on large-scale proprietary biological and chemical datasets built in-house using internal laboratory capabilities (>20 petabytes).

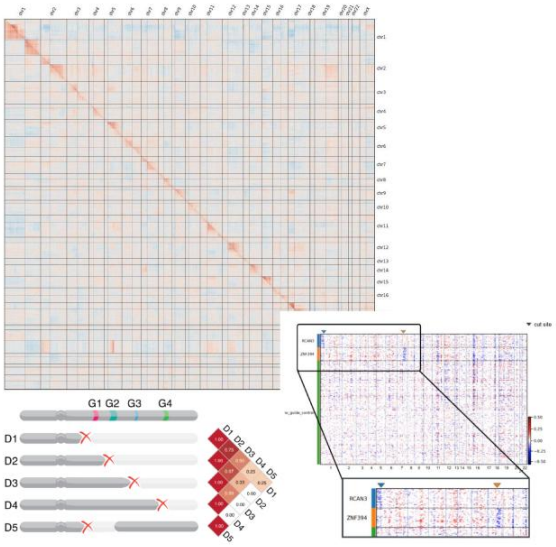
Source: Frost & Sullivan

Biology and chemistry are complex – data that is reliable, relatable, and scalable is the Recursion differentiator

Year	2018	2019	2020	2021	2022
Total Phenomics Experiments (Millions)	8	24	56	115	175
Total Transcriptomics Experiments (Thousands)	NA	NA	2	91	258
Data (PB)	1.8	4.3	6.8	12.9	21.2
Cell Types	12	25	36	38	48
Unique Compounds Physically Housed at Recursion[1] (Millions)	0.02	0.1	0.7	1.0	1.7
In Silico Chemistry Library (Billions)	NA	0.02	3	12	>1,000
Predicted Biological and Chemical Relationships[2] (Trillions)	NA	NA	0.01	0.2	3.1

[1] *Includes approximately 500,000 compounds from Bayer's proprietary library.*
[2] *'Predicted Relationships' refers to the number of Unique Perturbations that have been predicted using our maps.*

CRISPR proximity bias revealed using genome-wide phenomics screens



- Recursion demonstrated that **CRISPR-Cas9 editing induces chromosome arm-scale truncations** across the genome
- **Creates a proximity bias** in CRISPR screens which can confound some gene-gene relationships
- Recursion **demonstrated a correction method** leveraging public CRISPR-Cas9 knockout screens to **mitigate bias**
- Read "High-resolution genome-wide mapping of chromosome-arm-scale truncations induced by CRISPR-Cas9 editing" at www.biorxiv.org
- Already in the **top 5% of research outputs** in online engagement www.altmetric.com

COVID-19 research

Drug	Prediction	Correct?
Hydroxychloroquine	x	✓
Lopinavir	x	✓
Ritonavir	x	✓
Remdesivir	✓	✓
Baricitinib	✓	✓
Tofacitinib	✓	✓
Ivermectin	x	✓
Fluvoxamine	x	✓
Dexamethasone	x	x

- Recursion conducted several AI-enabled experiments in April 2020 to investigate therapeutic potential for COVID-19
  - Included FDA-approved drugs, EMA-approved drugs, and compounds in late-stage clinical trials for the modulation of the effect of SARS-CoV-2 on human cells
- Experiments were compiled into the **RxRx19 dataset** (860+ GB of data) and **made publicly available** to accelerate the development of methods and pandemic treatments.
- **Recursion OS correctly predicted 8 of 9 clinical trials** associated with early and late-stage COVID-19

https://www.biorxiv.org/content/10.1101/2020.04.21.054387v1

Transformational collaborations provide multiple potential value inflection points

Illustrative example of potential value inflection points