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): November 9, 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 1.01. Entry into a Material Definitive Agreement.

Tempus Master Agreement

On November 3, 2023, Recursion Pharmaceuticals, Inc. (the "Company") and Tempus Labs, Inc. ("Tempus") entered into a Master Agreement (the "Tempus Agreement") pursuant to which Tempus may provide certain services and deliverables to Company and/or license certain data to Company. The term of the Tempus Agreement is five years from the effective date of the Tempus Agreement (the "Term").

Under the terms of the Tempus Agreement, the Company is granted a limited right to access Tempus's proprietary database of de-identified clinical and molecular data for certain therapeutic product development purposes, including to develop, train, improve, modify, and create derivative works of Company's machine learning/artificial intelligence models for the purposes of therapeutic product development. The Company is permitted to download a maximum number of de-identified records at any one time, subject to an aggregate cap in the total unique records that can be downloaded over the course of Term, and to retain each downloaded record for a period of 180 days from the date of download. After such 180 day period, Company may elect to license such downloaded records for a longer period subject to additional terms and the payment of additional fees.

In exchange for these rights, Company will pay Tempus an initial license fee in an amount equal to $22.0 million (the "Initial License Fee") and annual license fees during the Term ranging between $22.0 million and $42.0 million, which, together with the Initial License Fee, totals up to $160.0 million over the Term, subject to Company's early termination, which may be triggered only following the third anniversary of the Master Agreement's effective date, and payment by Company of an early termination fee (as further discussed below). The Initial License Fee and each annual license fee shall be payable at the Company's option either in the form of (x) cash, (y) shares of Class A Common Stock of the Company ("Class A Common Stock"), or (z) a combination of cash and shares of Class A Common Stock in such proportion as is determined by the Company in its sole discretion; provided that (a) the aggregate number of shares of Class A Common Stock that the Company may issue in connection with all payments under this Agreement shall not exceed 19.9% of the aggregate total of shares of Class A Common Stock and the Company's Class B Common Stock outstanding on November 2, 2023 or the date immediately preceding the date of any shares of Class A Common Stock issued pursuant to the Tempus Agreement, whichever is less (the "Share Maximum").

In the event that all or any portion of the Initial License Fee or any annual license fee is payable in the form of shares of Class A Common Stock, the Company shall, subject to the Share Maximum, issue to Tempus a number of shares of Class A Common Stock equal to (1) the amount of such fee divided by (2) the volume weighted average price of Class A Common Stock for the seven trading day period ending on the trading day immediately preceding (and including) the date that is five business days before the date on which such fee is paid (any shares so issued, the "Tempus Shares").

The Company has agreed to use commercially reasonable efforts to prepare and file a registration statement (or a prospectus supplement to an effective registration statement on Form S-3ASR that will become automatically effective upon filing with the SEC pursuant to Rule 462(e)) with the Securities and Exchange Commission (the "SEC") as soon as practicable but in no event later than 30 days after each issuance of Tempus Shares under the Tempus Agreement, and to use its commercially reasonable efforts to have the registration statement declared effective as promptly as possible but in any event within 30 days following initially filing (or up to 90 days in the event of full SEC review). After such registration, the

Company has agreed to use commercially reasonable efforts to keep such registration statement effective until such date that all Tempus Shares covered by such registration statement have been sold thereunder or may be sold without restriction or volume limitation under Rule 144 as promulgated by the SEC under the Securities Act of 1933, as amended (the "Securities Act").

The Tempus Agreement also grants Company the right to access and use Tempus' LENS software that permits the viewing and analysis of clinical, molecular, and other health data maintained by Tempus. Company will pay Tempus a six figure annual license fee for the duration of the Term for the use of such software.

In addition to mutual rights to terminate for an uncured breach of the Tempus Agreement, the Company may terminate the Tempus Agreement for convenience after three years upon 90 days prior notice, subject to payment by the Company of an early termination fee equal to (a) an amount per unique record that Company has downloaded prior to termination less (b) the sum of any annual license fees paid prior to termination, which could result in early payment of the aggregate annual license fees contemplated by the Tempus Agreement to the extent all records made available under the Tempus Agreement have been downloaded.

Either party may assign its rights under the Tempus Agreement subject to limited restrictions, but Company may not assign the Tempus Agreement without Tempus's consent if the proposed assignee is a large pharmaceutical company.

The foregoing description of the Tempus Agreement is not complete and is qualified in its entirety by reference to the full text of such agreement. The Company intends to file the Tempus Agreement as an exhibit to its Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2023.

Restated Bayer Agreement

As previously disclosed, on August 28, 2020, Recursion Pharmaceuticals, Inc. (the "Company") and Bayer AG ("Bayer"), entered into a Research Collaboration and Option Agreement, as expanded on December 1, 2021 (as amended, the "Original Agreement") for research and collaboration on a certain number of projects related to fibrosis. On November 8, 2023, the parties amended and restated the Original Bayer Agreement (the "Restated Agreement") to re-align the Original Agreement with Bayer's strategic shift in focus to oncology, as further described below. As a result, the parties will wind down their joint work in fibrosis and the exclusivities with respect to the field of fibrosis will terminate.

Under the Restated Agreement, the Company will collaborate with Bayer for the remainder of the five-year period under the Original Agreement (extendable by up to 2 years to enable completion of certain research activities) (the "Collaboration Term"), to initiate up to seven programs in oncology (each, an "Oncology Project"). During certain agreed time periods within the Collaboration Term, the Company is prohibited from conducting certain research and development activities with respect to certain identified genes of relevance in oncology outside of the collaboration, either by ourselves or together with third parties. However, the Company may continue research and development activities for any such identified genes that the Company has initiated prior to the date of identification of such gene.

Under each Oncology Project, the Company will work with Bayer to identify potential lead candidates for development. Under the Restated Agreement, Bayer has the first option to license potential candidates; each such license could potentially result in option exercise fees and development and commercial milestones paid to the Company with an aggregate value of up to approximately $210.0 million for one license and up to approximately $1.5 billion if each program is licensed, as well as tiered royalties for each such license, ranging from low- to mid-single digit percentages of sales, depending on commercial success. Royalty periods for each license are on a country-by-country basis, and the duration of each such period is tied to the duration of patent or regulatory exclusivity in each country (with a minimum term of 10 years each).

If Bayer does not exercise its option with respect to a lead candidate or otherwise discontinues an Oncology Project prior to completion, within a specified period of time, the Company may exercise an option to negotiate with Bayer in good faith to obtain an exclusive license under Bayer's interest in any lead series developed pursuant to the Oncology Project and backup compounds related to thereto, as well as a non-exclusive license under Bayer's background intellectual property necessary for the Company's use of the project results related to such compounds.

Bayer may terminate the collaboration at any time without cause. Either party may terminate the agreement for a material breach by the other party. The term of each license agreement continues on a product-by-product and country-by-country basis until the later of (a) the expiration of the last to expire valid claim of the licensed patents covering such product in such country, (b) the expiration of any applicable regulatory exclusivity period for such product in such country and (c) ten years after the first commercial sale of such product in such country. Bayer may terminate each such license agreement at any time without cause. Either party may terminate each such license agreement for the other party's uncured material breach.

The foregoing description of the Restated Agreement is not complete and is qualified in its entirety by reference to the full text of such agreement. The Company intends to file the Restated Agreement as an exhibit to the periodic report covering the period during which the Restated Agreement was executed.

Item 2.02. Results of Operations and Financial Condition.

On November 9, 2023, the Company issued a press release announcing its results of operations and financial condition for the third quarter September 30, 2023. A copy of the press release is furnished as Exhibit 99.1 and is incorporated herein by reference.

Item 3.02. Unregistered Sales of Equity Securities.

The information contained above under Item 1.01, to the extent applicable, is hereby incorporated by reference herein. Based in part upon the representations of Tempus in the Tempus Agreement, the offering and sale of the Tempus Shares was made in reliance on the exemption afforded by Section 4(a)(2) of the Securities Act and Rule 506 of Regulation D under the Securities Act and corresponding provisions of state securities or "blue sky" laws. The Tempus Shares have not been registered under the Securities Act or any state securities laws and may not be offered or sold in the United States absent registration with the SEC or an applicable exemption from the registration requirements. The sale of the Tempus Shares did not involve a public offering and was made without general solicitation or general advertising.

Neither this Current Report on Form 8-K nor any exhibit attached hereto is an offer to sell or the solicitation of an offer to buy shares of Class A common stock or other securities of the Company.

Item 7.01. Regulation FD Disclosure.

On November 9, 2023, the Company issued a press release announcing two updates with collaborators NVIDIA and Bayer and a new collaboration with Tempus Labs. The press release is attached as Exhibit 99.2 to this Current Report on Form 8-K and incorporated into this Item 7.01 by reference.

Also on November 9, 2023, the Company released an updated corporate presentation to the investor section of the Company's website. A copy of the presentation is attached hereto as Exhibit 99.3 to this Current Report on Form 8-K and incorporated into this Item 7.01 by reference.

The information furnished pursuant to Item 2.02 (including Exhibit 99.1) and 7.01 (including Exhibits 99.2 and 99.3) on this Form 8-K, 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 into any other filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Forward Looking Statements

The Company cautions you that statements contained in this report includes or is based upon "forward-looking statements" within the meaning of the Securities Litigation Reform Act of 1995, including, without limitation, those regarding all actions and anticipated performance under the Tempus Agreement and the Restated Agreement, 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 such as those described under the heading "Risk Factors" in the Company's filings with the SEC, including the Company's most recent Annual Report on Form 10-K and all subsequently filed Quarterly Reports on Form 10-Q. All forward-looking statements are based on management's current estimates, projections, and assumptions, and the Company 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.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Press release issued by the Company. dated November 9, 2023
99.2	Press release issued by the Company dated November 9, 2023
99.3	Company presentation dated November 9, 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 November 9, 2023.

RECURSION PHARMACEUTICALS, INC.

By: /s/ Michael Secora
Michael Secora
Chief Financial Officer

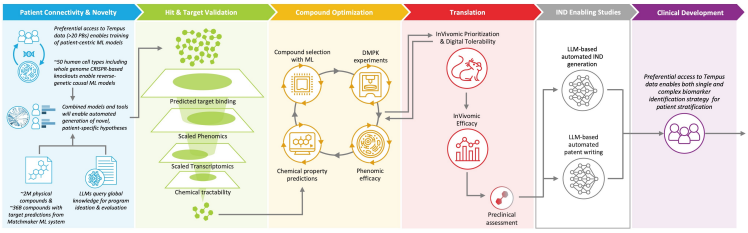
Exhibit 99.1

Recursion Provides Business Updates and Reports Third Quarter 2023 Financial Results

- Entered into a collaboration with Tempus giving Recursion access to over 20 petabytes of multimodal oncology data for the purpose of training causal AI models together with Recursion's proprietary data and for designing biomarker and patient stratification strategies for clinical programs
- Expansion of Recursion's in-house supercomputer, BioHive-1, with NVIDIA H100 GPUs will likely make it the most powerful computer wholly owned or operated by any biopharma company and among the 50 most powerful supercomputers on the Top500 List
- Updated collaboration with Bayer to deliver against their thematic focus in precision oncology with higher per program milestones and broader use of Recursion's OS

SALT LAKE CITY, November 9, 2023 — Recursion (Nasdaq: RXRX), a leading clinical stage TechBio company decoding biology to industrialize drug discovery, today reported business updates and financial results for its third quarter ending September 30, 2023.

“Since our founding we have led TechBio with a belief that the next generation of biopharma leaders would operate at the intersection of scaled datasets and accelerated computing," said Chris Gibson, Ph.D., Co-founder and CEO of Recursion. "Today, we are thrilled to share our plans to continue leading the field forward at this nexus in order to advance a growing pipeline of both wholly owned and partnered programs towards impact for patients. First, on the data front, we are excited to announce a collaboration with Tempus, giving us access to over 20 PB of proprietary data in precision oncology. I believe these forward-genetic data, combined with Recursion's multimodal reverse-genetic data, will continue strengthening our data-advantage. Second, on the compute front, we are pleased to announce a significant commitment to expand our BioHive-1 supercomputer to advance the exploration and construction of large AI models across our ever-growing proprietary biological data more rapidly and reliably. And finally, the evolution of our collaboration with Bayer and the recent exercise of our first oncology program option from Roche and Genentech highlights the growing appreciation of our Recursion OS by world-class teams in biopharma. We could not be more inspired about the future and are confident that the Recursion OS will continue to lead the transformation of BioTech into TechBio.”

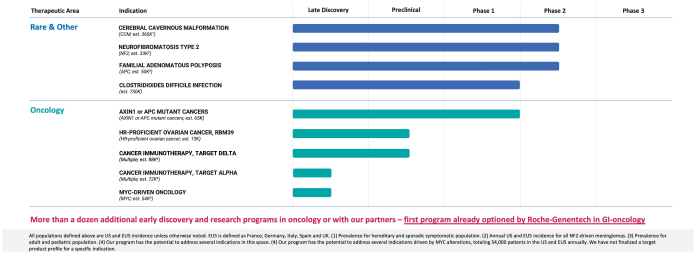


Recursion OS: Industrializing drug discovery to transform BioTech into TechBio

Summary of Business Highlights

- **Platform**
  - **Tempus Collaboration**
    - **Oncology-Focused, Precision Medicine Data:** Tempus has built one of the world's largest oncology-focused clinical and DNA/RNA molecular observational datasets. Our new collaboration with Tempus gives Recursion preferred access to these data. When combined with Recursion's proprietary dataset of over 25 petabytes of interventional biological and chemical data, Recursion will now have approximately 50 petabytes of proprietary data fit for the purpose of machine learning at its disposal, enabling us to improve the training of causal AI/ML models of biology. When applied to our genome-wide reverse genetics platform, these data could facilitate the discovery of novel associations and mechanisms not otherwise identifiable in the clinical and forward genetics data from Tempus. Additionally, this patient-linked data will be used to support translating innovative therapeutics from Recursion's platform directly to patients using novel biomarker and patient stratification strategies.
    - **Terms of the Tempus Collaboration:** Recursion entered into an agreement with Tempus to access its patient-centric data as part of a 5-year licensing agreement. Recursion will make annual payments to Tempus in cash or equity ranging between $22.0 million and $42.0 million each year, up to $160.0 million in aggregate, over the next 5 years in exchange for continued and updated data access and use rights for therapeutic development purposes.
  - **Supercomputer Expansion:** We have committed to working with NVIDIA to expand BioHive-1, our on-premise supercomputer. After the expansion, which will be completed in the first half of 2024, BioHive-1 computational capacity will increase by over 4x(adding more than 500 NVIDIA H100 GPUs to the more than 300 NVIDIA A100s already in place). We project that upon completion and benchmarking, BioHive-1 will be in the top 50 most powerful supercomputers in the world across any industry (according to the Top500 list) and will be the most powerful supercomputer owned and operated by any biopharma company. These additional computational resources will continue to support the construction of the largest foundation models across biology and chemistry using Recursion's vast datasets and data generation capabilities as well as tools based on interactive large language models and autonomous agents.
  - **Foundation Models:** Our supercomputer expansion is meant to build on the deployment of our first Phenomics Foundation Model, PHENOM-1, which is a vision transformer utilizing hundreds of millions of parameters trained on billions of biological images from our proprietary phenomics library. PHENOM-1 demonstrated the scaling hypothesis within a biological context, namely that larger models trained on more diverse datasets lead to increased performance

and emergent properties. With our recent acquisitions of digital chemistry company Cyclica and the deep-learning research team at Valence Discovery (now Valence Labs), the vast patient-centric data from Tempus and our own growing proprietary multi-omic datasets, we anticipate the construction and application of more foundation models and large language models across biology, chemistry and translation. Together, we believe these increasingly sophisticated models will enable us to drive new, better programs into clinical development both in our own pipeline and with our current and future partners at scale.



- **Pipeline**
  - **Cerebral Cavernous Malformation (CCM) (REC-994):** Our Phase 2 SYCAMORE clinical trial is a double-blind, placebo-controlled safety, tolerability and exploratory efficacy study of this drug candidate in participants with CCM. This study was fully enrolled as of June 2023 with 62 participants and the vast majority of participants who have thus far finished their first year of treatment have enrolled in the long-term extension study. We expect to share Phase 2 proof-of-concept data in H2 2024.
  - **Neurofibromatosis Type 2 (NF2) (REC-2282):** Our Phase 2/3 POPLAR clinical trial is a two part study of REC-2282 in participants with progressive NF2-mutated meningiomas due either to syndromic disease or initiating mutations in the meningiomas. Part 1 of the study is ongoing and is exploring two doses of REC-2282 in approximately 23 adults and 9 adolescents.We expect to share Phase 2 safety, tolerability, pharmacokinetics and preliminary efficacy in H2 2024.
  - **Familial Adenomatous Polyposis (FAP) (REC-4881):** Our Phase 2 TUPELO clinical trial is a two part study of REC-4881 in participants with FAP. Evaluation of three dose levels is ongoing, thereafter a dose expansion phase will commence evaluating the recommended Phase 2 dose in approximately 30 participants. We expect to share Phase 2 safety, tolerability, pharmacokinetics and preliminary efficacy in H1 2025.
  - **AXIN1 or APC Mutant Cancers (REC-4881):** Our Phase 2 LILAC clinical trial is a biomarker enriched two part study of REC-4881 in participants with unresectable, locally advanced or metastatic cancer with AXIN1 or APC mutations. The study will initiate in late Q4 2023 or early Q1 2024 and will

explore the safety and efficacy of REC-4881 across three dose levels in 30-40 participants.
    - ***Clostridioides difficile* Infection (REC-3964):** In early September 2023, we announced completion of our Phase 1 clinical trial and reported that REC-3964 had been well tolerated in healthy volunteers with no serious adverse events. We expect to initiate a Phase 2 proof-of-concept study in patients with recurrent *Clostridioides difficile* infection in 2024.
    - **RBM39 HR-Proficient Ovarian Cancer:** RBM39 is a novel CDK12-adjacent target identified by the Recursion OS. We believe we can modulate this target to produce a therapeutic effect in HR-proficient ovarian cancer and potentially in other tumor types. This program is in the preclinical stage and IND-enabling studies are progressing.
- **Partnerships**
    - **Bayer:** Bayer and Recursion have signed an update to their collaboration around a select set of oncology programs. This decision allows Bayer to leverage Recursion's capabilities to identify novel targets and compounds applicable to traditionally undruggable oncology indications as well as Recursion's access to expansive oncology-focused, patient-centric data from Tempus for their closely partnered programs. Under the amended and restated agreement, Bayer will pay Recursion increased per program milestones which may be up to $1.5 billion for up to 7 oncology programs as well as royalties on net sales. In this oncology-focused collaboration, Recursion will use many of the new tools it has developed since the collaboration was first signed to potentially identify and nominate programs rapidly.
    - **Roche-Genentech:** In October 2023, Recursion announced that Roche-Genentech optioned its first partnership program in GI-oncology. This milestone represents a critical step in our joint efforts to initiate and advance new therapeutic programs using Recursion's approach to map and navigate biology and chemistry. In the near-term, there is the potential for option exercises associated with map building or data sharing initiatives as well as option exercises associated with additional partnership programs.

Third Quarter 2023 Financial Results

- **Cash Position:** Cash and cash equivalents were $387.3 million as of September 30, 2023. *This cash position excludes the $3 million to be paid by Roche-Genentech for optioning its first partnership program in GI-oncology.*
- **Revenue:** Total revenue was $10.5 million for the third quarter of 2023, compared to $13.2 million for the third quarter of 2022. The decrease was due to the timing of workflows from our strategic partnership with Roche-Genentech.
- **Research and Development Expenses:** Research and development expenses were $70.0 million for the third quarter of 2023, compared to $40.8 million for the third quarter of 2022. The increase in research and development expenses was due to increased platform costs as we have expanded and upgraded our capabilities.
- **General and Administrative Expenses:** General and administrative expenses were $29.2 million for the third quarter of 2023, compared to $19.5 million for the third quarter of 2022. The increase in general and administrative expenses was due to an increase in salaries and wages of $5.8 million and increases in software and depreciation expenses.

- **Net Loss:** Net loss was $93.0 million for the third quarter of 2023, compared to a net loss of $60.4 million for the third quarter of 2022.
- **Net Cash:** Net cash used in operating activities was $72.9 million for the third quarter of 2023, compared to net cash used in operating activities of $54.5 million for the third quarter of 2022.

About Recursion
Recursion 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

Recursion Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations (unaudited)
(in thousands, except share and per share amounts)

	Three months ended September 30,		Nine months ended September 30,	
	2023	**2022**	**2023**	**2022**
Revenue				
Operating revenue	$ 10,102	$ 13,053	$ 33,252	$ 26,005
Grant revenue	431	107	432	162
Total revenue	10,533	13,160	33,684	26,167
Operating costs and expenses				
Cost of revenue	10,877	15,409	32,706	37,435
Research and development	70,007	40,836	171,744	111,716
General and administrative	29,199	19,488	80,364	61,761
Total operating costs and expenses	110,083	75,733	284,814	210,912
Loss from operations	(99,550)	(62,573)	(251,130)	(184,745)
Other income, net	6,533	2,128	16,060	2,761
Net loss	$ (93,017)	$ (60,445)	$ (235,070)	$ (181,984)
Per share data				
Net loss per share of Class A, B and Exchangeable common stock, basic and diluted	$ (0.43)	$ (0.35)	$ (1.16)	$ (1.06)
Weighted-average shares (Class A, B and Exchangeable) outstanding, basic and diluted	214,327,186	173,435,970	203,090,637	172,122,974

Recursion Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets (unaudited)
(in thousands)

	September 30, 2023	December 31, 2022
Assets		
Current assets		
Cash and cash equivalents	$ 387,322	$ 549,912
Restricted cash	2,256	1,280
Other receivables	3,164	2,753
Other current assets	17,780	15,869
Total current assets	410,522	569,814
Restricted cash, non-current	7,629	7,920
Property and equipment, net	86,248	88,192
Operating lease right-of-use assets	34,062	33,255
Intangible assets, net	39,459	1,306
Goodwill	52,750	801
Other assets, non-current	155	—
Total assets	$ 630,825	$ 701,288
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 4,265	$ 4,586
Accrued expenses and other liabilities	39,806	32,904
Unearned revenue	43,997	56,726
Notes payable	695	97
Operating lease liabilities	5,355	5,952
Total current liabilities	94,118	100,265
Unearned revenue, non-current	51,383	70,261
Notes payable, non-current	1,126	536
Operating lease liabilities, non-current	44,300	44,420
Deferred tax liabilities	1,931	—
Total liabilities	192,858	215,482
Commitments and contingencies		
Stockholders' equity		
Common stock (Class A, B and Exchangeable)	2	2
Additional paid-in capital	1,312,591	1,125,360
Accumulated deficit	(874,626)	(639,556)
Total stockholders' equity	437,967	485,806
Total liabilities and stockholders' equity	$ 630,825	$ 701,288

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 the outcomes and benefits expected from access to the real-world multimodal data held at Tempus; outcomes and benefits of deriving therapeutic hypotheses by linking molecular data and outcomes data; outcomes and benefits of expanding our supercomputer; early and late stage discovery, preclinical, and clinical programs, including timelines for data readouts; licenses and collaborations, including option exercises by partners and additional partnerships; prospective products and their potential future indications and market opportunities; Recursion OS and other technologies; business and financial plans and performance, including cash runway; 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,” “could,” “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; inflation and other macroeconomic issues; 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.

Recursion Announces Data Collaboration Deal with Tempus, Top 50 Supercomputer Ambition Powered by NVIDIA and Updated Focus of Collaboration with Bayer to Precision Oncology

With additional patient centric data, compute power and an exciting new focus for its Bayer collaboration, the company is accelerating the shift of biotech to techbio.

SALT LAKE CITY, November 9, 2023 — Recursion (NASDAQ: RXRX), a leading clinical stage TechBio company decoding biology to industrialize drug discovery, today announced two significant updates with their collaborators NVIDIA and Bayer, and a new collaboration with Tempus Labs as it creates infrastructure and expands its ambitions and scope in the precision oncology space.

“Since our founding we have believed that the next generation of biopharma leaders would operate at the intersection of scaled datasets and accelerated computing,” said Chris Gibson, Ph.D., Co-founder and CEO of Recursion. “Today, we are thrilled to share three major initiatives that support this belief and our mission to bring better medicines to patients at speed and scale. With Tempus’s 20 petabytes of fit-for-purpose precision oncology data, NVIDIA’s support in quadrupling our supercomputing power to rapidly and reliably advance the exploration and construction of large AI models, and updating our collaboration with Bayer to rapidly pursue a set of precision oncology programs, we will continue to drive the transformation from BioTech to TechBio together.”

Tempus Collaboration Provides Recursion with Access to Data Containing More Than 20 Petabytes of Proprietary Patient-Centric Oncology Data

Recursion has come to an agreement with Tempus for preferred access to one of the world’s largest proprietary, de-identified, patient-centric oncology datasets, spanning DNA, RNA, health records and more to support the discovery of potential biomarker-enriched therapeutics at scale through the training of causal AI models. By combining the forward genetics approach of Tempus with the reverse genetics approach at Recursion, the company believes it has an opportunity to improve the speed, precision and scale of therapeutic development in oncology. As part of the agreement, Recursion will pay Tempus up to $160M in cash or equity over the next five years in exchange for continued and updated data access and use rights for therapeutic development purposes.

“We share Recursion’s commitment to a data-first approach to precision medicine,” said Eric Lefkofsky, Founder and CEO of Tempus. “We look forward to working in tandem to leverage our multi-modal data to uncover insights that have the potential to advance personalized therapeutics for patients around the world.”

In aggregate, Recursion will now have access to approximately 50 petabytes of proprietary data across biology and chemistry as well as real-world, patient-centric data that is relatable and fit for the purpose of training large-scale AI/ML models, which it plans to use to drive novel therapeutic hypotheses, biomarker strategies, and patient cohort selection.

Top 50 Supercomputer Powered by NVIDIA

To accelerate the impact of the proprietary data Recursion has accumulated, the company has committed to substantially expanding BioHive-1, its on-premise NVIDIA DGX SuperPOD-based supercomputer, adding over 500 NVIDIA H100 Tensor Core GPUs to the more than 300 NVIDIA A100 Tensor Core GPUs already in place to increase its computational capacity 4X. This greatly expanded compute power will support the company's pipeline, partnerships and the construction of one of the largest foundation models of its kind across multiple modalities of biology and chemistry.

Based on the June 2023 TOP500 list, Recursion projects that upon completion and benchmarking, BioHive-1 will likely be in the top 50 most powerful supercomputers in the world across any industry and would be the most powerful supercomputer owned and operated by any biopharma company. The company anticipates the enhancement of BioHive-1 to be operational in the first half of 2024.

"A new era in drug discovery is here, and life science and drug discovery companies are leading the way," said Jensen Huang, founder and CEO of NVIDIA. "Our ongoing collaboration with Recursion will bring scaled biological data together with one of the most powerful supercomputers to decode biology and get to better medicines faster."

Collaboration with Bayer in Precision Oncology Programs

Recursion announced an updated collaboration with its established partner, Bayer, for a select set of precision oncology programs. This decision allows Bayer to leverage Recursion's state-of-the-art capabilities to identify novel targets and chemistry applicable to oncology indications.Under the terms of the agreement, the companies may initiate up to seven oncology programs and Recursion is eligible to receive potential, success-based, future payments of up to $1.5 billion plus royalties on net sales.

"Our collaboration with Recursion is a testament to our commitment to shape the future of healthcare, using advancements in AI and drug discovery to push the boundaries of medicine with the aim of providing innovative cancer therapies for patients whose medical needs are not yet met by today's treatment options," said Stefan Oelrich, Member of the Board of Bayer AG and President, Pharmaceuticals.

About Recursion

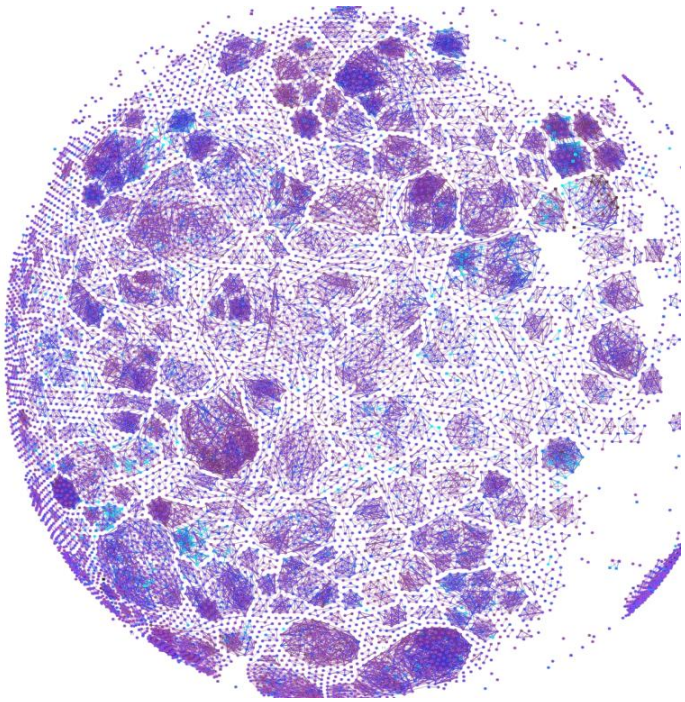
Recursion is a clinical stage TechBio company leading the space by decoding biology to industrialize drug discovery. Enabling its mission is the Recursion OS, a platform built across diverse technologies that continuously expands one of the world's largest proprietary biological and chemical datasets. 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.

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 the outcomes and benefits expected from access to the real-world multimodal data held at Tempus; outcomes and benefits of deriving therapeutic hypotheses by linking molecular data and outcomes data; outcomes and benefits of expanding our supercomputer; early and late stage discovery, preclinical, and clinical programs, including timelines for data readouts; licenses and collaborations, including option exercises by partners and additional partnerships; prospective products and their potential future indications and market opportunities; Recursion OS and other technologies; business and financial plans and performance, including cash runway; 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,” “could,” “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; inflation and other macroeconomic issues; 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



End of Q3 2023

Recursion

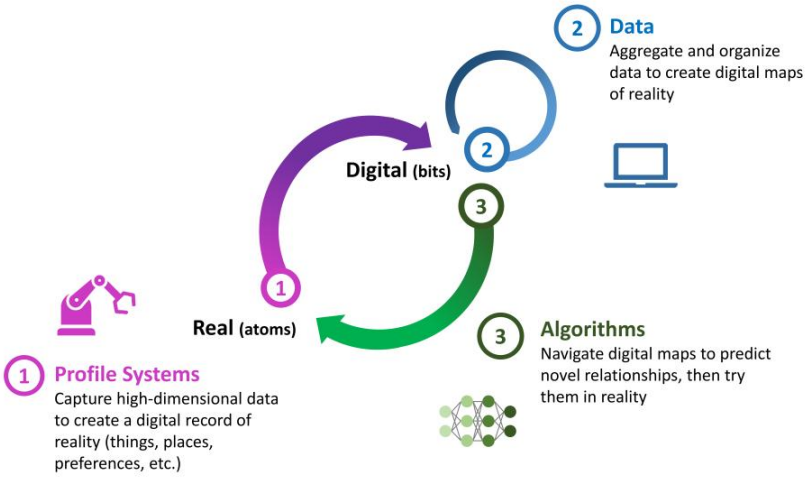
Disclaimers

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 Tempus partnership, including our ability to leverage the datasets acquired through the license agreement into increased machine learning capabilities and accelerate clinical trial enrollment; our planned expansion of the BioHive supercomputer capabilities; outcomes and benefits from licenses, partnerships and collaborations, including option exercises by partners and additional partnerships and ability to house tools on the BioNeMo Marketplace; 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 Annual Report for the Fiscal Year ended December 31, 2022, on Form 10-K and 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.

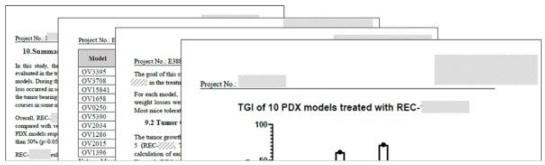
Since our founding, we have been building virtuous cycles of atoms & bits to accelerate & improve drug discovery



Our approach breaks down the data roadblocks that challenge the traditional Biopharma industry

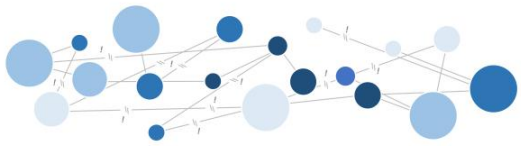
Analog Standard

The fax machine is alive and well in medicine, while in biopharma, study results from CROs are still often reported as PDFs or scanned printouts



Siloed Data in Pharma

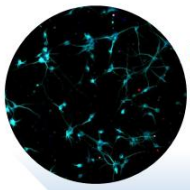
The culture of biopharma has led to 100s of petabytes of scientific data being stored on a project-by-project basis without the meta-data or annotation needed to relate it to other projects or questions in biology



Reproducibility Crisis

Multiple studies have shown that the vast majority of published academic literature cannot be recapitulated

To truly unlock the enormous promise of TechBio, an integrated approach combining wet-lab, the *right* data & powerful computation is imperative



Data: Each week we digitize millions of our own experiments across multiple layers of biology from cell to animal

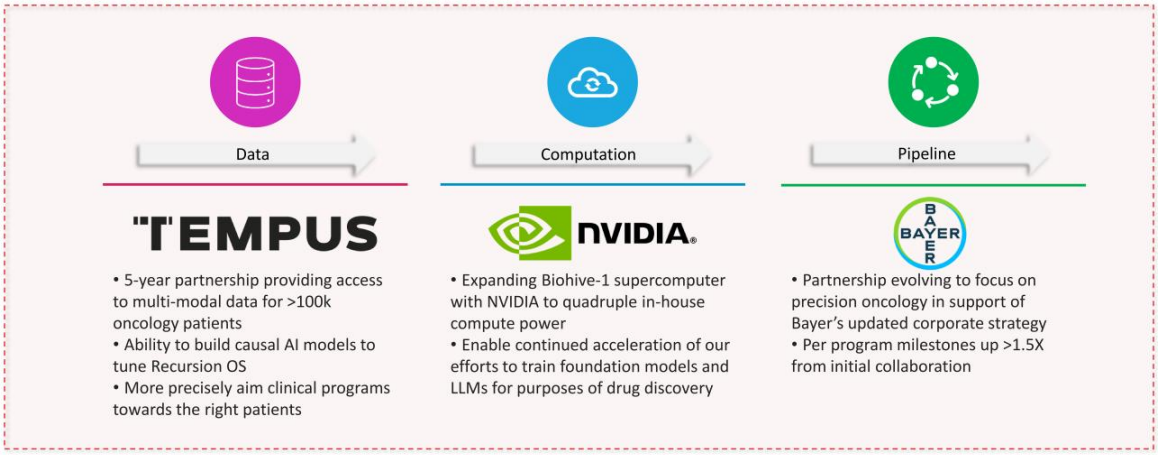
Profile Systems: We have built and continue to scale among the world's most prolific automated wet labs

ALGORITHMS: We own and operate one of the fastest supercomputers on earth, allowing us to train LLMs & FMs fit for the purpose of drug discovery

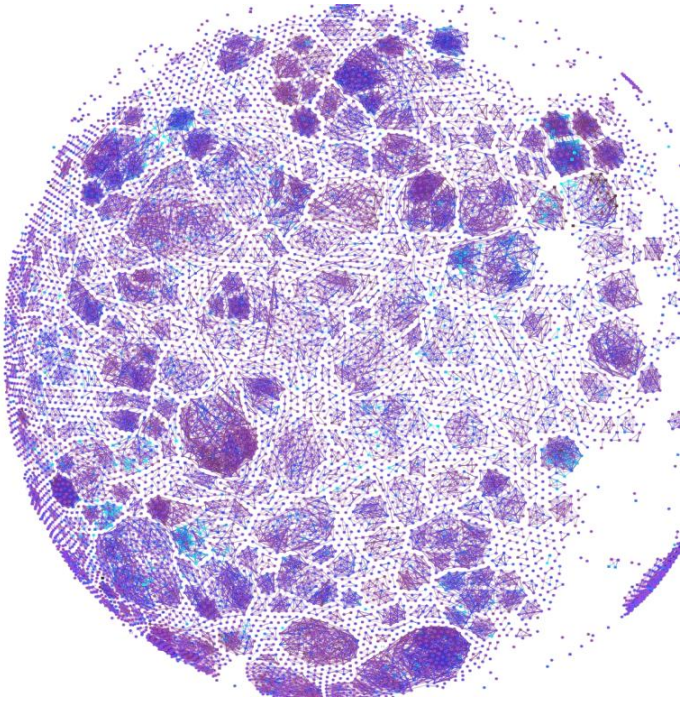
Improved and scaled clinical pipeline

A leap forward in our vision

Updates reinforce Recursion's position as a leader at the intersection of scaled biology and compute



Update 1:
Tempus Partnership



Recursion

Recursion to partner with Tempus

Proposed partnership accelerates clinical platform capabilities with ~50 PB of proprietary biology, chemistry, and translational precision medicine data purpose-built for AI / ML

Recursion + TEMPUS

- $160M paid by Recursion to Tempus in cash or equity, at our election, in increasing annual increments over five years, beginning with $22M of equity to be issued later this year

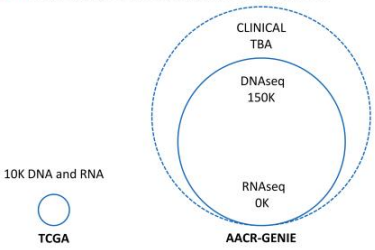
- Provides preferential access to DNA / RNA sequencing datasets tied to clinical records for >100,000 patients for the purpose of training causal AI models for therapeutic development

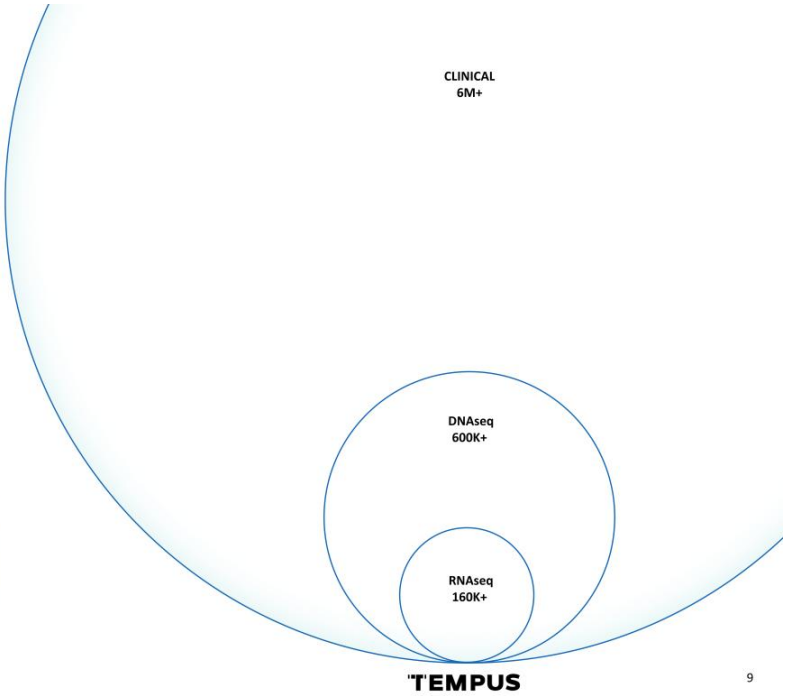
- Expected to accelerate model deployment, linking molecular data with outcomes
- Expected to enhance program translation as well as identification and enrollment of patients with higher probability of clinical response

Partnership provides preferential access to one of the world's largest and fastest growing libraries of real-world multimodal oncology data

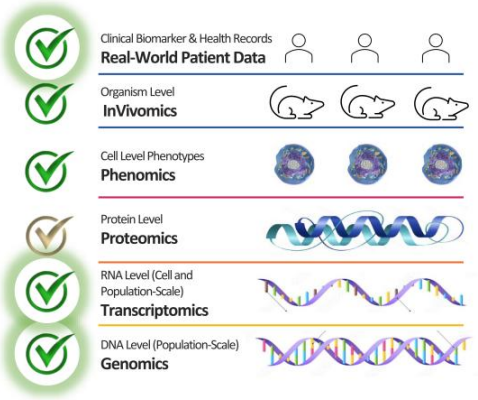
Creating another potential virtuous cycle: Recursion will direct biological exploration by the Recursion OS based on scaled patient data as well as drive programs into the clinic with biomarker and patient stratification insights at an unparalleled pace

20PB+ of data immediately available to Recursion





Partnership will create among the most comprehensive set of biological data layers in the industry

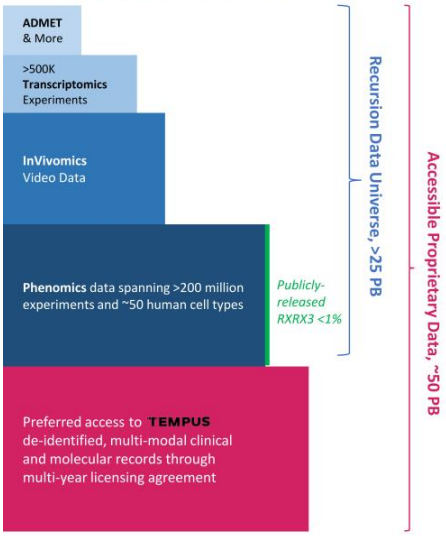


Built, scaled or partnered **Exploratory** **Aspirational**

Like digital maps of Earth, **connections within and between layers add useful context**. Similarly, Recursion is **mapping multi-omic layers of biology** and identifying connections within and between layers to **decode biology at scale**.

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

New capabilities accelerate scale & enhance Recursion's relatable data differentiation



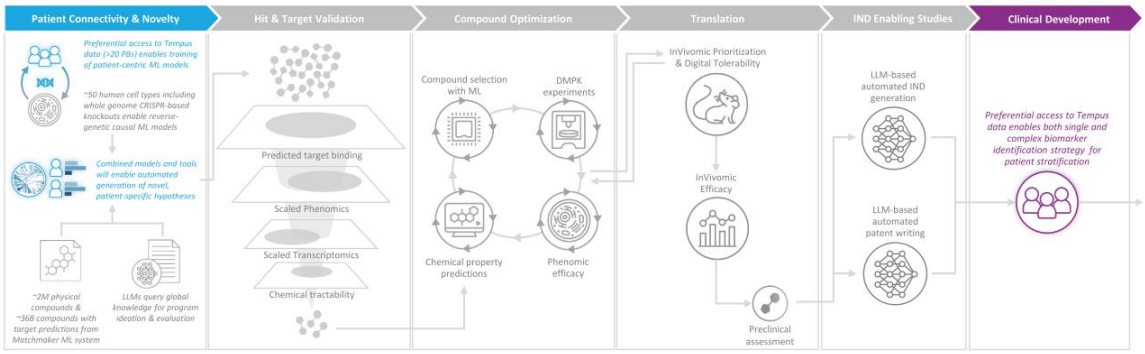
Recursion Data Universe: >25 PB of proprietary biological and chemical data, spanning phenomics, transcriptomics, inVivomics, and more

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

Preferential access to >20 PB of real-world patient data

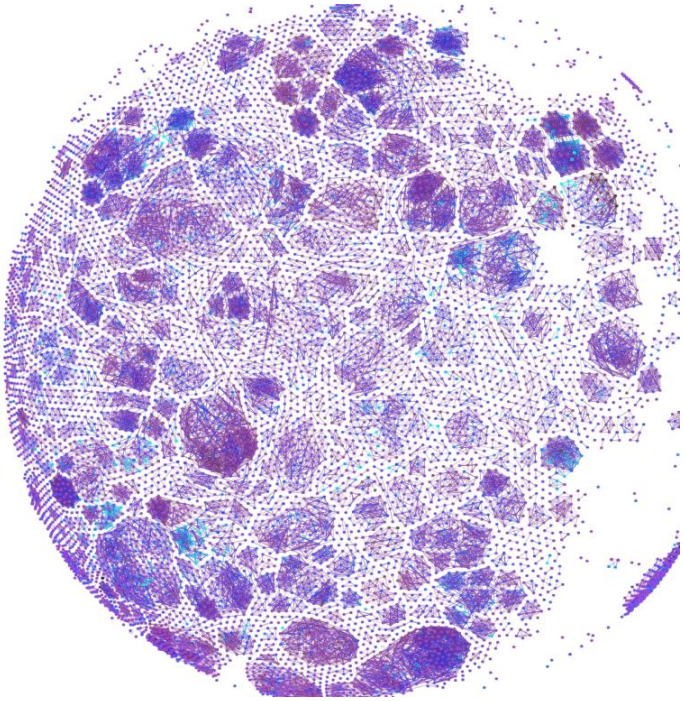
- Includes access to more than 100,000 oncology patient's de-identified records, DNA sequencing, RNA sequencing, and clinical outcomes on which we can train causal AI models to:
  - Tune our Recursion OS for increased translatability
  - Better target clinical programs to the right patients

Collaboration provides preferential access to TEMPUS multi-modal data to enhance precision medicine, translation and trial design



TEMPUS

Update 2: Supercomputer Expansion



Recursion

Recursion OS
Computational Tools

Expand BioHive-1 from:

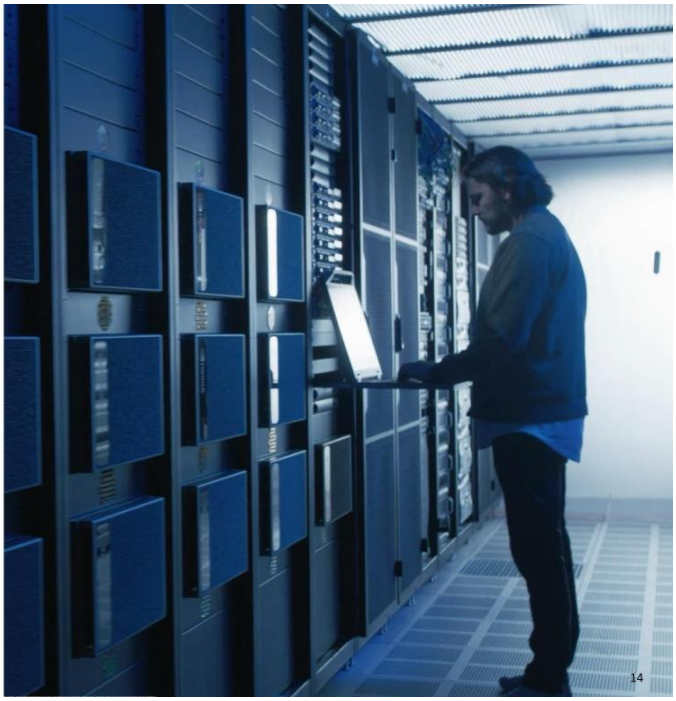
- 320 NVIDIA A100s…

…to include an additional

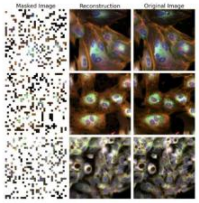
- 504 NVIDIA H100s

With operations beginning H1 2024

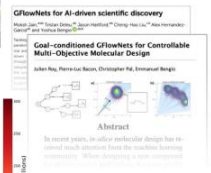
Likely to be the highest performing compute cluster owned and operated by any biopharma company on earth and among the top 50 compute clusters on the Top500 list



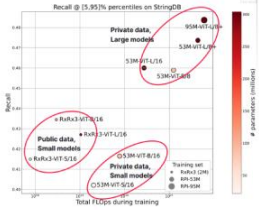
The combination of scaled data generation and accelerated computing is a key to advancing biological ML



World's largest phenomic foundation model for biology (PHENOM-1)



Increasingly powerful foundation models for chemistry

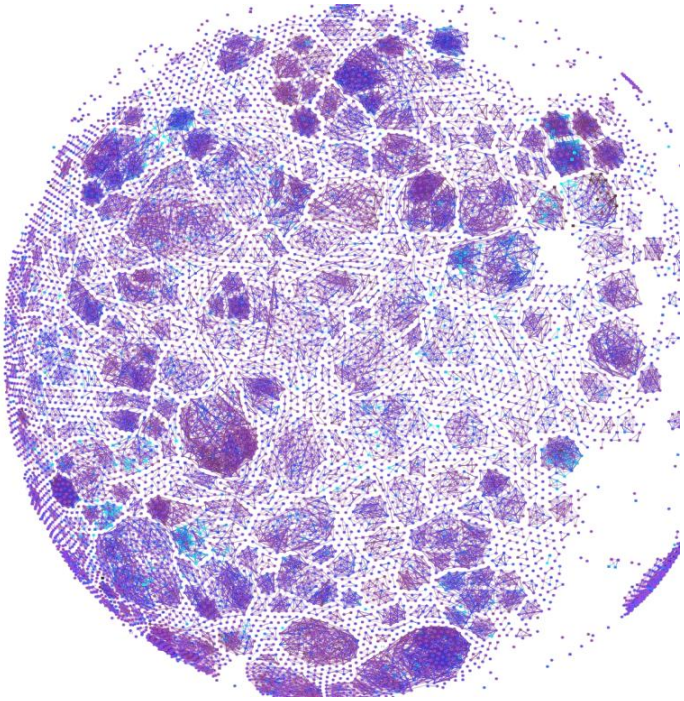


Vision:
Autonomous agents automatically explore, predict and execute our workflows to discover and develop medicines with hand-off to humans at later stages

Orchestration with custom LLMs to minimize toil and bias from discovery at scale

Advancements driven by ↑ increasingly scaled data generation and compute; leading to ↓ reductions in human bias at every step

Update 3:
Bayer Partnership Transformation



Recursion

Update of existing collaboration to exploit Recursion OS advancements and align with Bayer's strategic interest in precision oncology

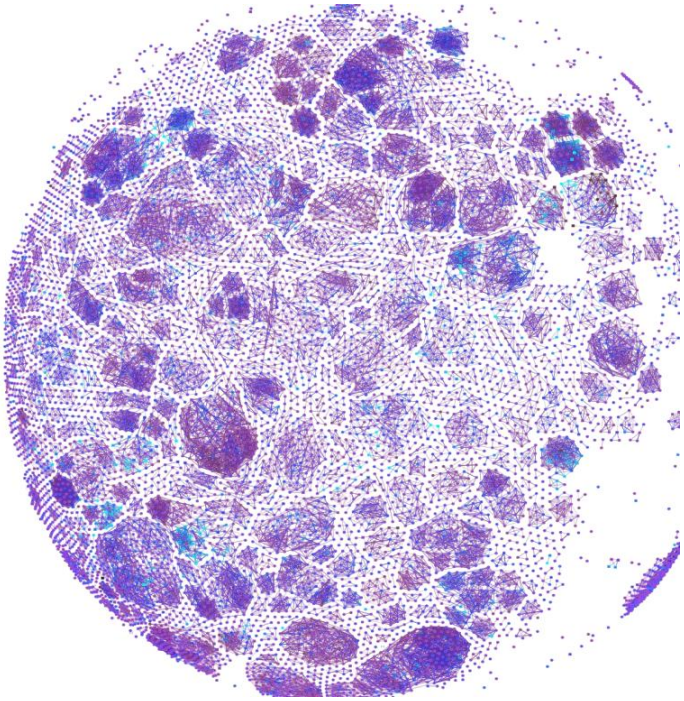
Original Collaboration
(announced Sept. 2020)

Focus: Fibrosis

Go-forward collaboration

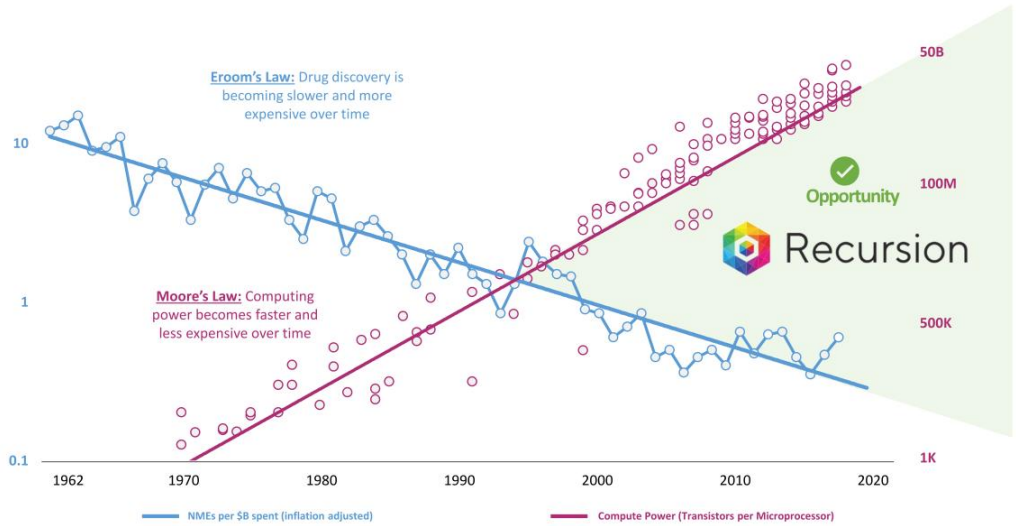
- **Re-aligned focus** to deliver on Bayer strategic objectives **in oncology**
- Up to **7 new Projects** anticipated
- **>1.5x increase** in per program economics
- Designed to **leverage advancements in Recursion OS platform since partnership inception**
  - **Foundation models** and **LLMs** deployed to identify novel targets of interest
  - **Industrialized workflows** prosecute programs with increasing likelihood of translation and minimal human bias
  - Application of **digital chemistry tooling** from acquisitions of Cyclica and Valence

In Brief: The Recursion Value Proposition



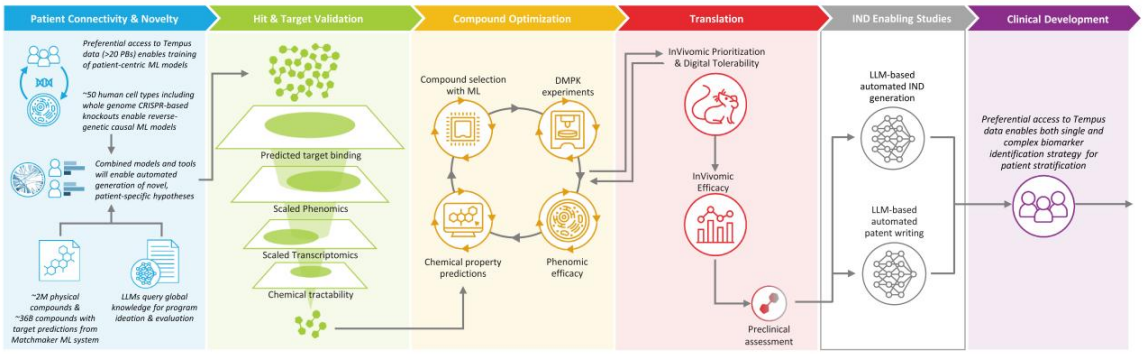
Recursion

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

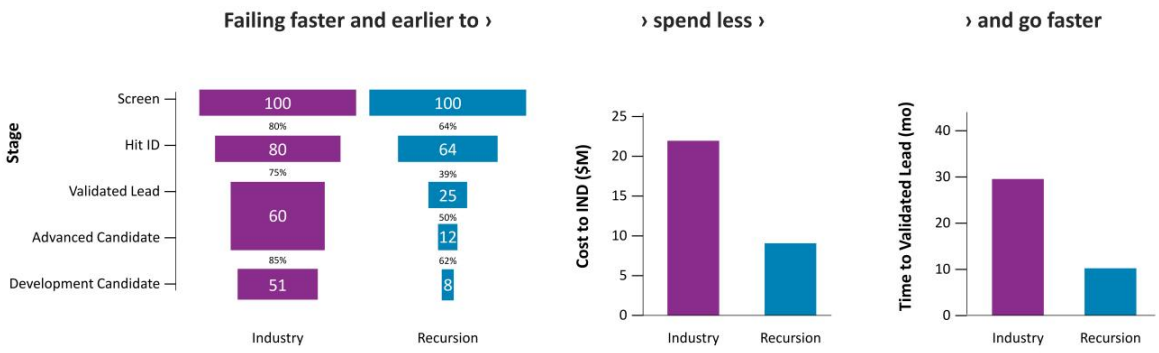


Adapted from Scannell, J et al (2012). Diagnosing the decline in pharmaceutical R&D efficiency. Nat Rev Drug Discov, 11, 191-200.

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

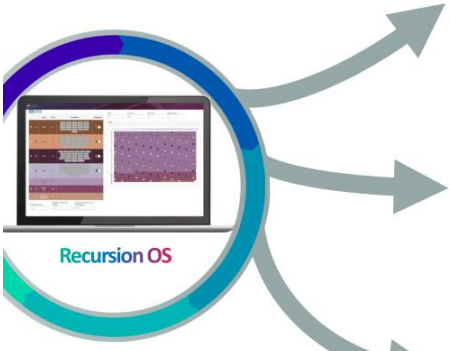


Mapping and navigating the complex systems of biology and chemistry has demonstrated leading indicators of efficiency



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 or competitive arbitrage

Leverage partner knowledge and clinical development capabilities

- **Neuroscience***
- **Undruggable Oncology**
- **Other large, intractable areas of biology (e.g. CV/Met)**

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 – first program already optioned by Roche-Genentech in GI-oncology

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) Prevalence for adult and pediatric population. (4) Our program has the potential to address several indications in this space. (5) 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 and recent partnerships represent some of the most significant scientific collaborations in TechBio across biopharma and tech

Therapeutic discovery collaborations

Roche / Genentech

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**
- **First program already optioned**
- **Mid to high single-digit tiered royalties** on net sales

BAYER

Announced Sept. 2020

Announced Nov. 2023

Undruggable oncology targets

- **$30M upfront** and **$50M equity investment**
- Increased per program milestones which may be **up to $1.5B for up to 7 oncology programs**
- **Mid single-digit royalties** on net sales
- **Recursion owns all algorithmic improvements**

Technology and data access collaborations

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**

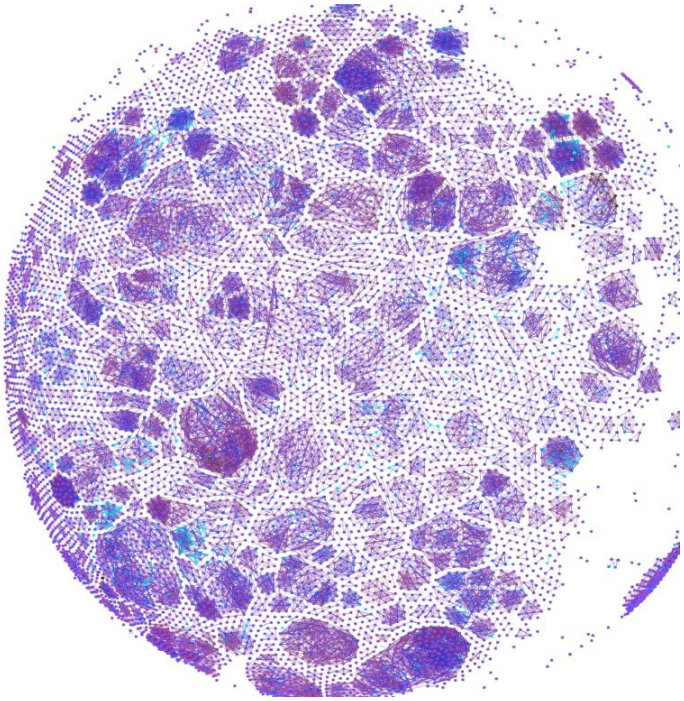
TEMPUS

Announced Nov. 2023

Real-world data access

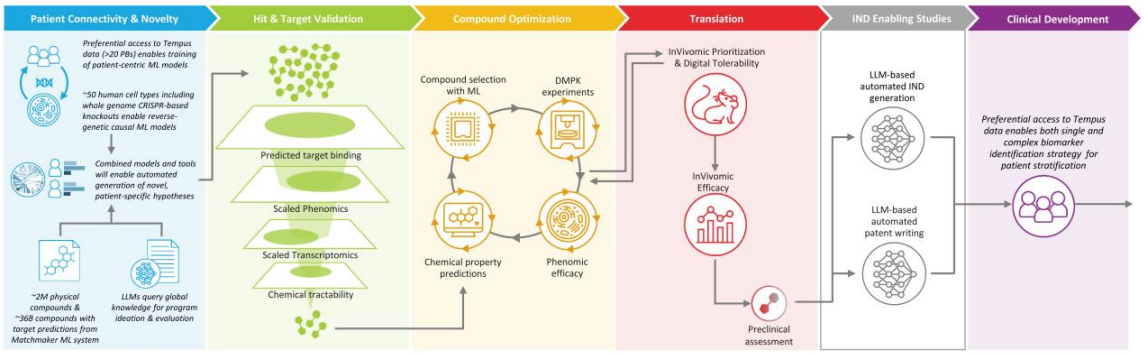
- **Preferential access to >20 PBs of Tempus real-world, multi-modal oncology data**, including DNA/RNA sequencing and clinical outcome data for more than 100,000 patients
- Ability to train **causal AI models** with utility in **target discovery, biomarker development & patient selection**
- **Opportunity to accelerate clinical trial enrolment** through potential access to broad clinical network

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

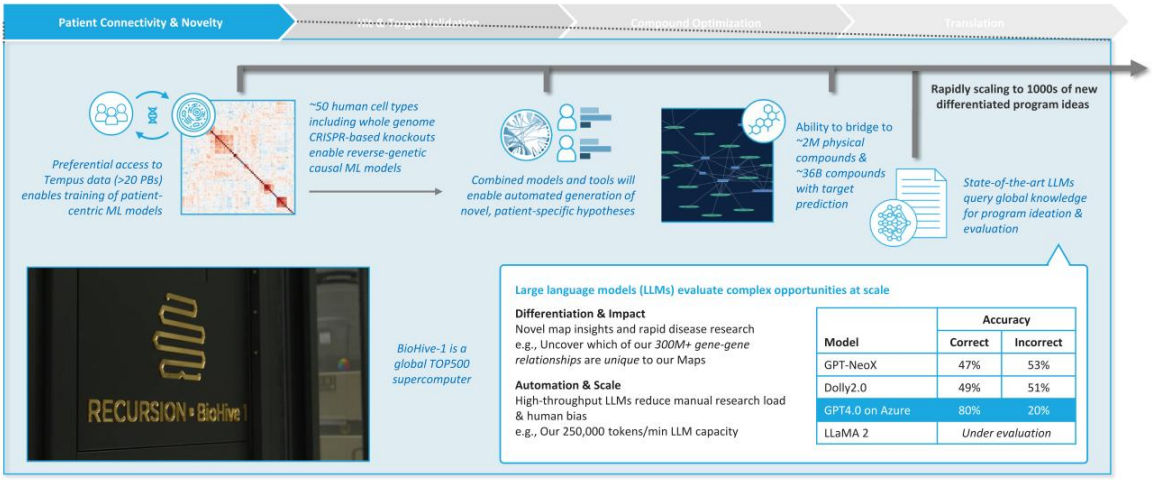


Recursion

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

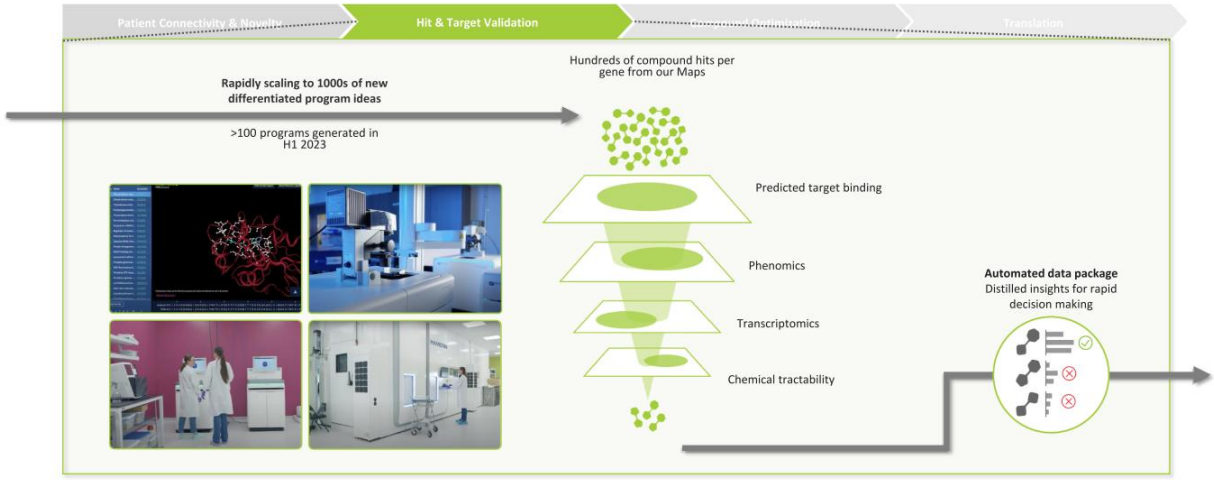


Our LLMs quickly distill the most promising novel ideas from >5 trillion relationship search space

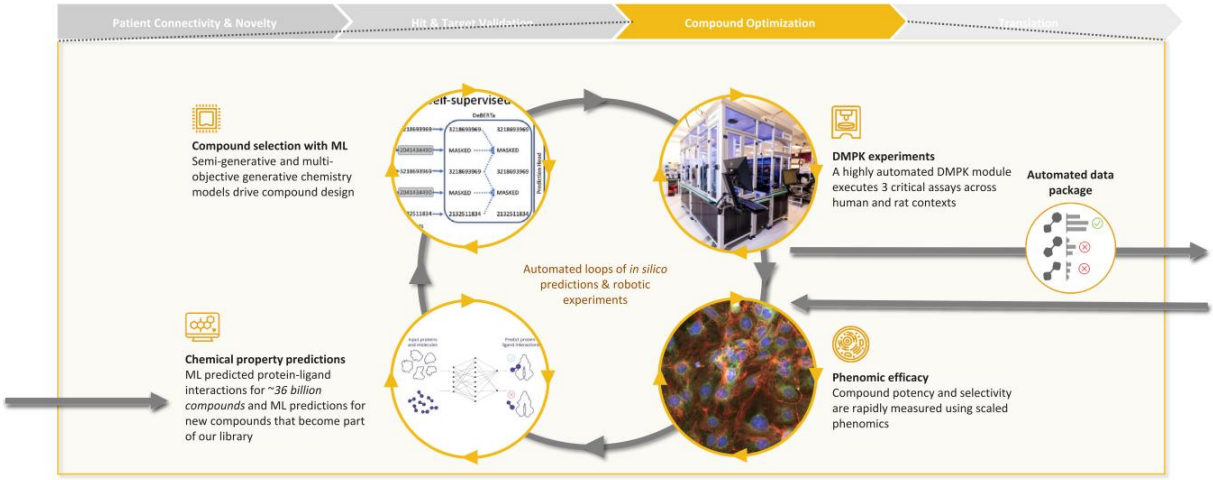


Model	Accuracy	
	Correct	Incorrect
GPT-NeoX	47%	53%
Dolly2.0	49%	51%
GPT4.0 on Azure	80%	20%
LLaMA 2	*Under evaluation*	

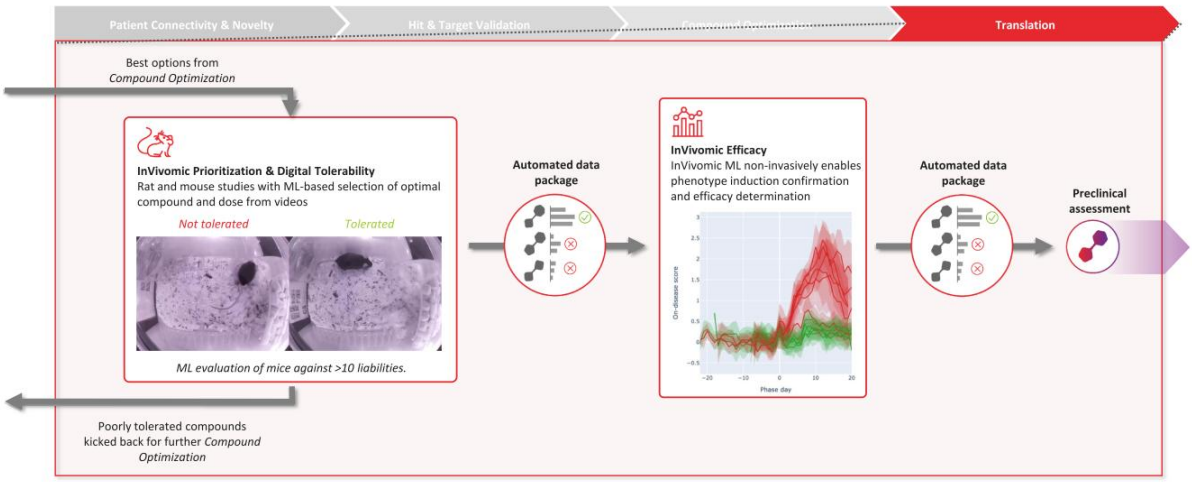
Automatic validation of map insights: we rapidly confirm novel predictions from our maps with automated, standardized, scaled -omics



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

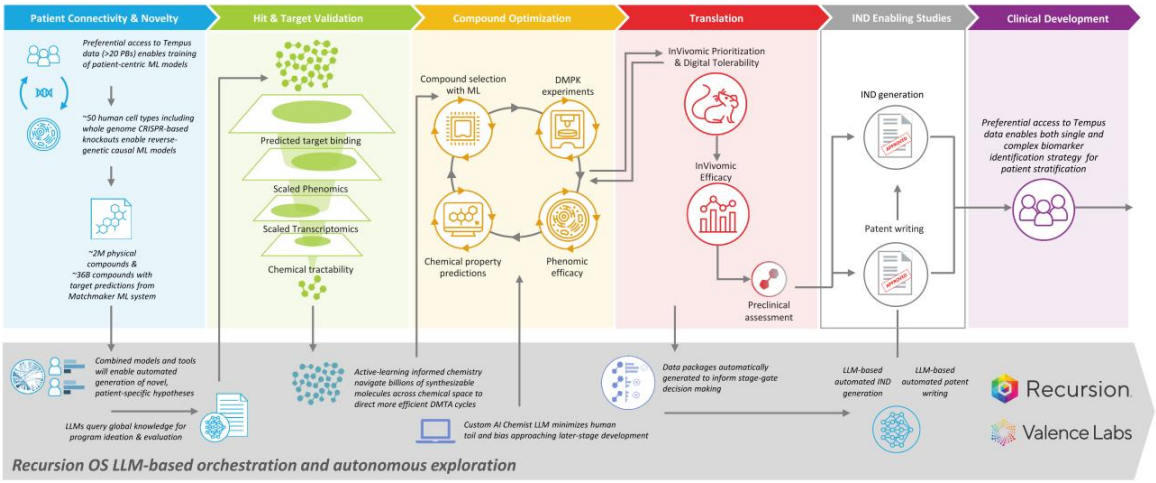


InVivomics improves whole organism understanding to rapidly translate programs towards the clinic



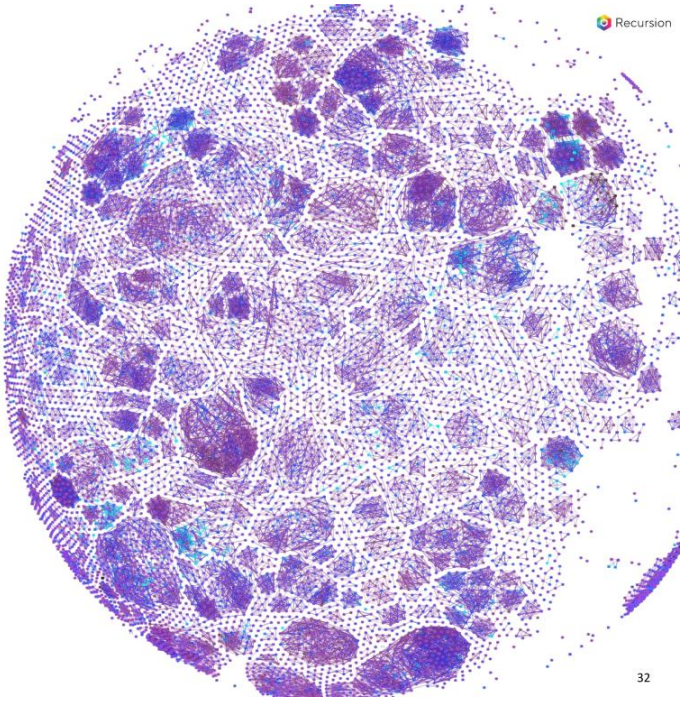
30

Roadmap: Integration and orchestration of tools with LLMs/API Calls to create super-empowered scientists & facilitate autonomous exploration



Our virtuous cycles of atoms and bits are already leading to first-in-disease development and beyond

Recursion



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

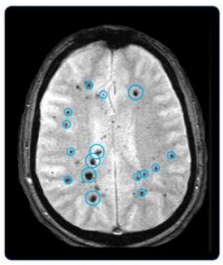
CAUSE

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

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

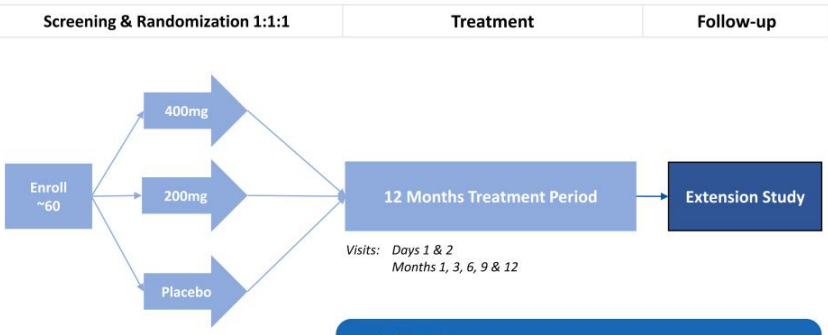
Phase 2 trial initiated in Q1 2022

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
- Vast majority of participants have completed 12 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/

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

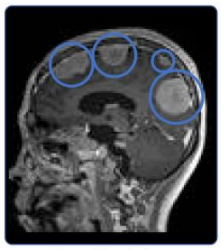
CAUSE

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

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

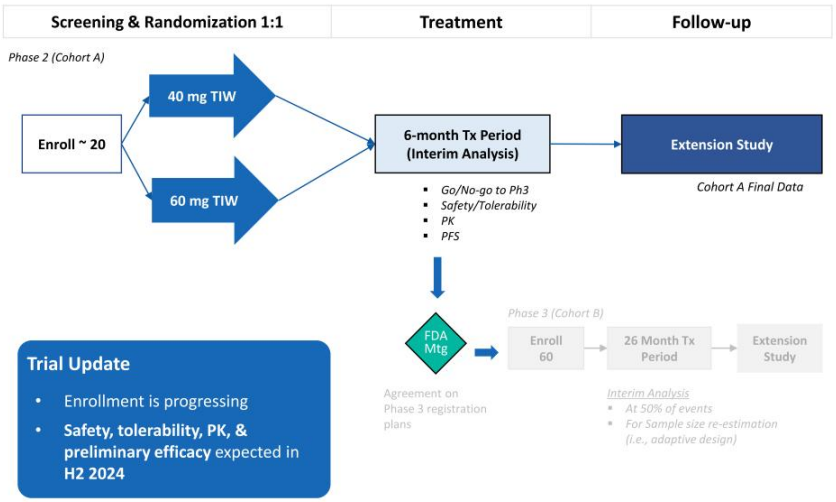
Phase 2/3 trial initiated in Q2 2022

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

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*

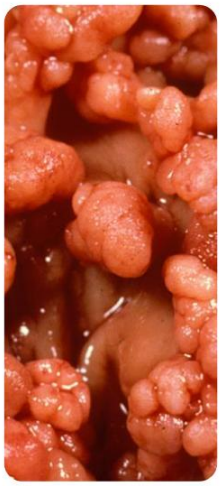
PATHOPHYSIOLOGY & REASON TO BELIEVE

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

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**



Polyps Found in Colon and Upper GI Tract

Clinical: FAP

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

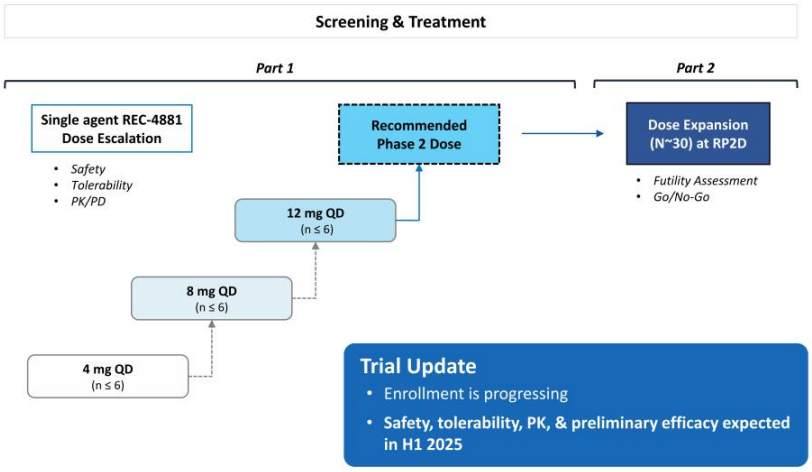
Phase 2 trial initiated in Q3 2022

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

- Enrollment is progressing
- **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

Clinical: AXIN1 or APC

LILAC Clinical Trial : 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 **late Q4 2023 or early Q1 2024**

Gross morphology of HCC

Clinical: AXIN1 or APC

LILAC Clinical Trial : REC-4881 PoC for *AXIN1* or *APC* mutant cancers

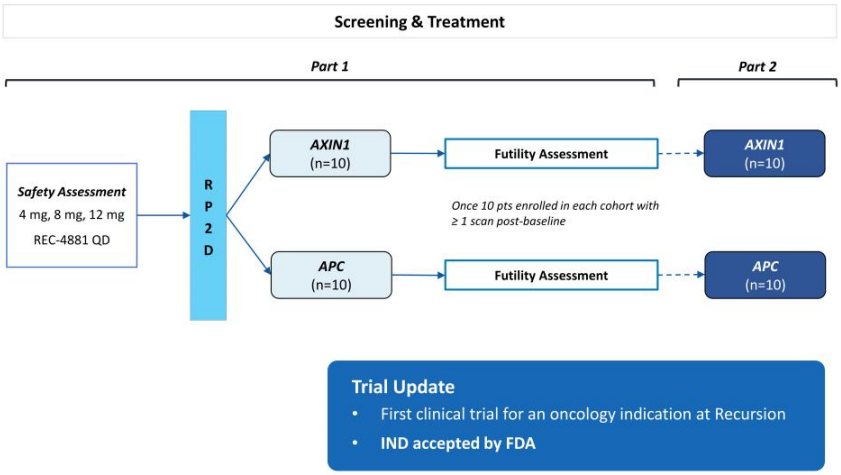
Expect Phase 2 initiation in late Q4 2023 or early Q1 2024

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



Trial Update

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

https://clinicaltrials.gov/ct2/show/NCT06005974, protocol amendments made to enhance quality and accelerate the pace of the trial

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

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

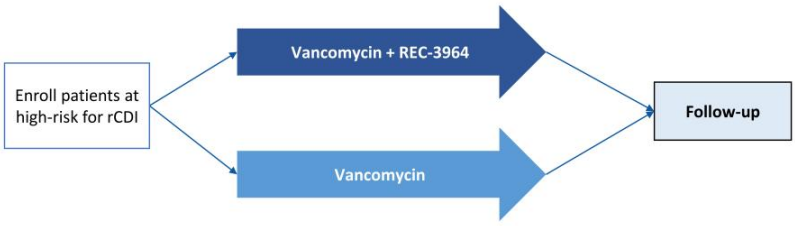
Clinical: C. Difficile

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



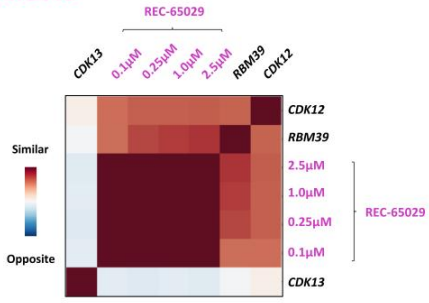
Trial Update

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

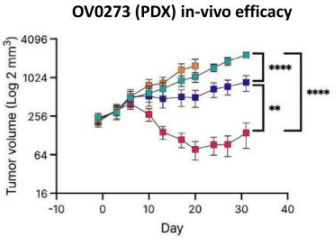
Recursion

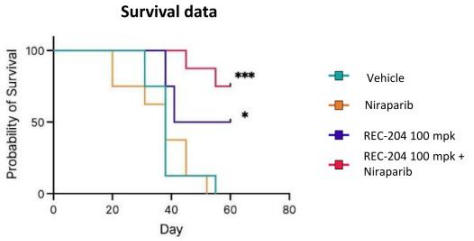
RBM39: Novel CDK12-Adjacent Target for HR-Proficient Ovarian Cancer

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



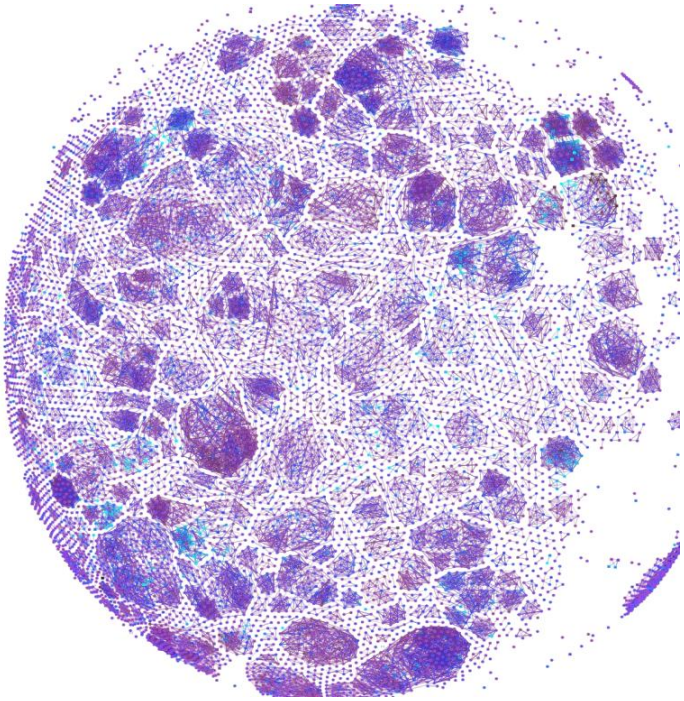
BRCA-proficient ovarian cancer PDX





*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*

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

Data shown reflective of Q3 2023, gender statistics include participating individuals

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

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

Chris Gibson, PHD
Co-Founder & CEO

Dean Li, MD PHD
Co-Founder of RXRX,
President of Merck Research Labs

Zavain Dar
Co-Founder & Partner of Dimension

Terry-Ann Burrell, MBA
CFO & Treasurer,
Beam Therapeutics

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

Blake Borgeson, PHD
Co-Founder of RXRX

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

Executive Team

Chris Gibson, PHD
Co-Founder & CEO

Tina Larson
President & COO

Michael Secora, PHD
Chief Financial Officer

Shafique Virani, MD FRCS
Chief Business Officer

David Mauro, MD PHD
Chief Medical Officer

Ben Mabey
Chief Technology Officer

Laura Schaevitz, PHD
SVP and Head of Research

Kristen Rushton, MBA
SVP of Business Operations

Nathan Hatfield, JD MBA
Chief Legal Officer

What to watch for at Recursion

Upcoming Potential Milestones

Near-Term

- Potential **option exercises** for **map building** initiatives
- Potential for **additional partnership(s)** in large, intractable areas of **biology such as CV/Met**
- Potential additional **option exercises** for **partnership programs**
- **Ph2 initiation** for **AXIN1 or APC mutant cancers** program expected in **late Q4 2023 or early Q1 2024**
- **Ph2 initiation** for **C. difficile Infection** program in **2024**
- Potential to **accelerate value creation** with additional **proprietary foundation models** for biology (including patient data) 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

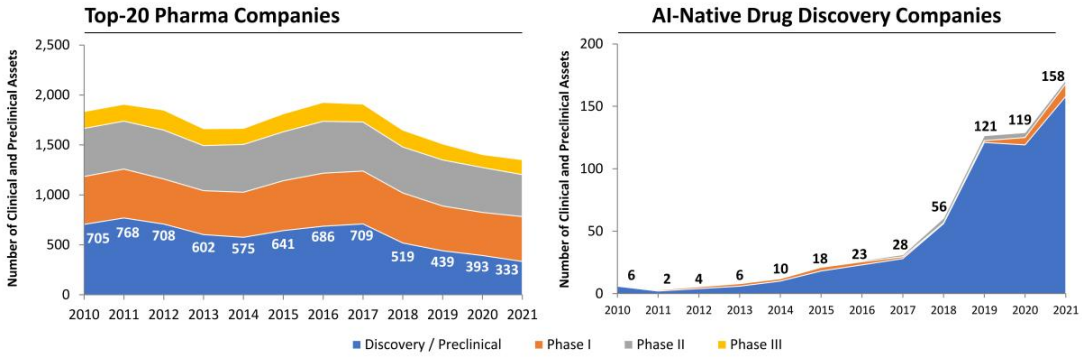
- Multiple **Ph2 readouts** for AI-discovered programs
  - **CCM** top-line data expected **H2 2024**
  - **NF2** & **FAP** safety & preliminary efficacy expected **H2 2024** & **H1 2025**, respectively
- Potential for **additional INDs and clinical starts**
- Potential **option exercises** for **partnership 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 Financial Position **~$387M in cash** at end of **Q3 2023**

Cash refers to cash and cash equivalents


Impact
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

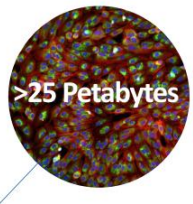
Images adapted from Jayatunga, M., et al. Nature Reviews Drug Discovery 2022.

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*

Robotic Automation at Scale

Up to 2.2 Million wet-lab experiments per week profiling genes and compounds, we believe we are one of the largest phenomics (human cellular image-based) data producers



Digitization of Biology and Chemistry

>25 Petabytes of proprietary high-dimensional data as of this filing, we believe this is one of the largest relatable *in vitro* biological and chemical datasets

Diverse Biological and Chemical Inputs

~50
different human **cell types**

~1.7 Million
small molecule library, we believe this scale is on par with some large pharma companies

~1 Trillion
hiPSC-derived cells produced since 2022, we believe that we are one of the largest hiPSC-derived cell producers

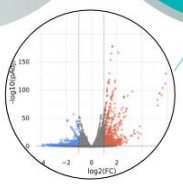
ML-Based Analysis

Top 500 supercomputer across any industry (TOP500 List, Jun 2023), we leverage vast neural networks and multiomics approaches to extract features and drive insights

Novel Insights at Scale

High-Dimensional Validation

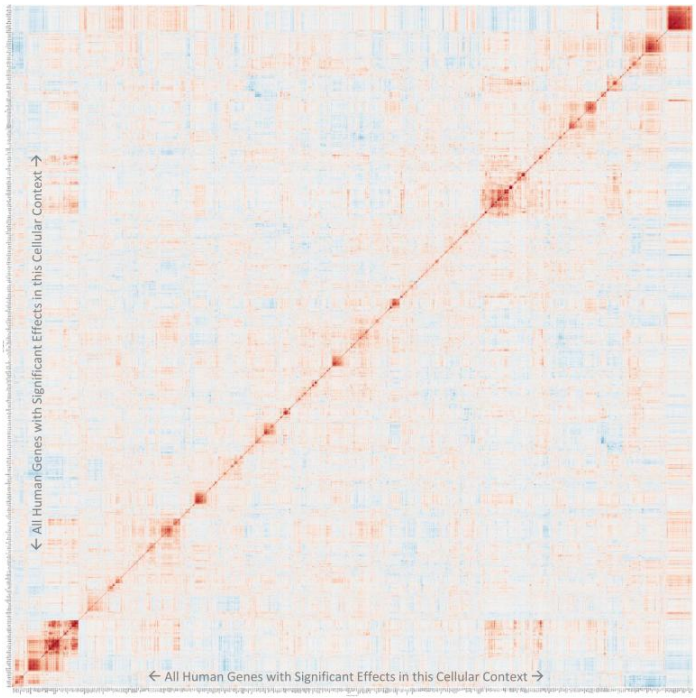
Up to
24K
near whole exomes per week, we believe we are one of the largest transcriptomics data producers



ML-Based Relationships

relatable hypotheses across multiple biological and chemical contexts

Metrics shown reflective of Q3 2023 unless otherwise indicated



Recursion

Genome-scale mapping

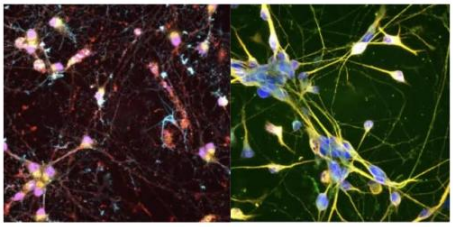
This is a **whole-genome arrayed CRISPR knock-out Map** generated in primary human endothelial cells

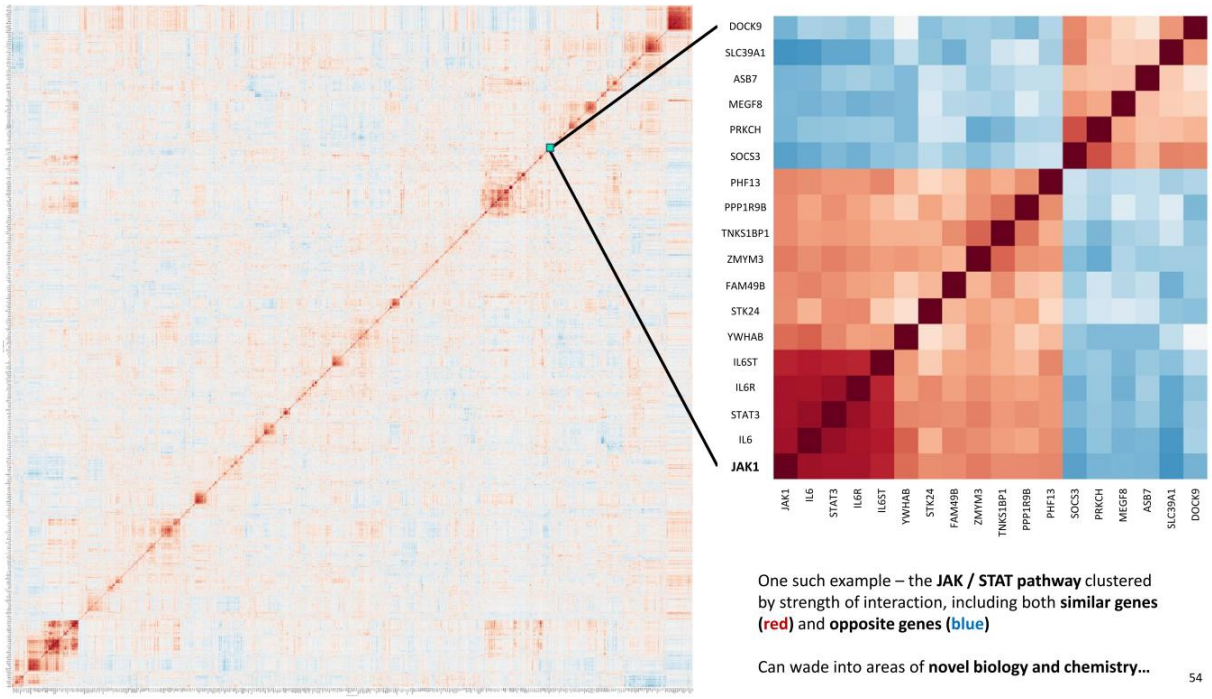
Every gene is represented in a pairwise way (each is present in columns and rows)

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

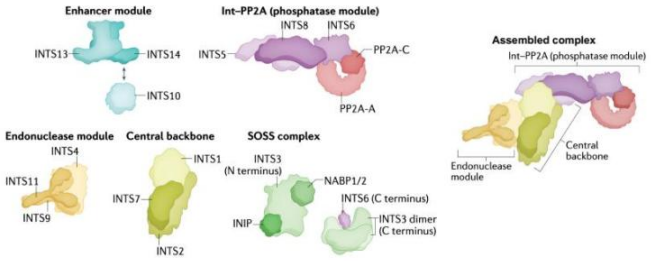
Thousands of examples of known biology and chemistry



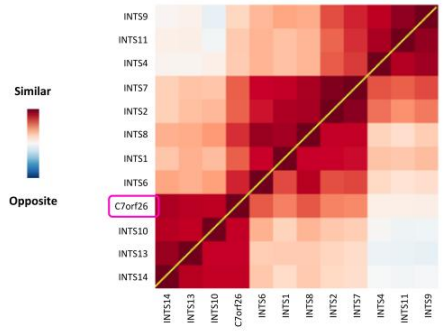


One such example – the **JAK / STAT pathway** clustered by strength of interaction, including both **similar genes (red)** and **opposite genes (blue)**

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



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



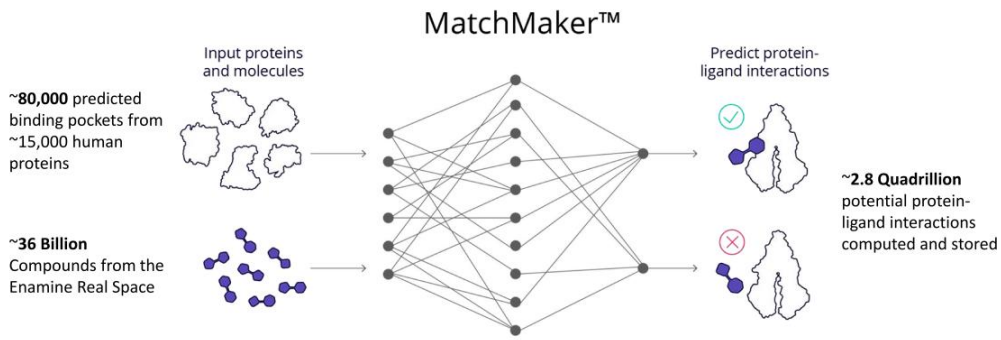
Maps reveal known and novel biology

- 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

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

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).

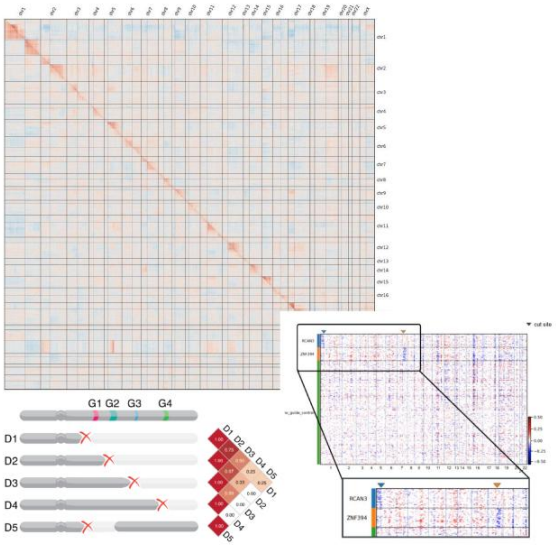
Source: Frost & Sullivan

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: Recursion OS correctly predicted 9 of 10 clinical trials

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

** Recursion did not screen ivermectin, but did screen the related compounds selamectin and doramectin. Both of these tested negative; consequently ivermectin was not expected to have efficacy. Fostamatinib recently read out positive Ph3 results in COVID but was discontinued in ACTIV-4.*

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

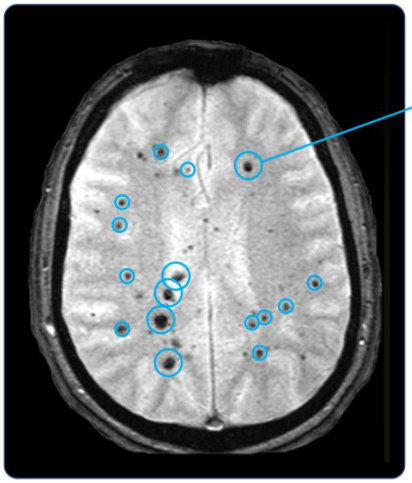
- Recursion conducted several AI-enabled experiments in **April 2020** to investigate therapeutic potential for COVID-19
  - Included FDA-approved drugs, EMA-approved drugs, and compounds in late-stage clinical trials for the modulation of the effect of SARS-CoV-2 on human cells
- Experiments were compiled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

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

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

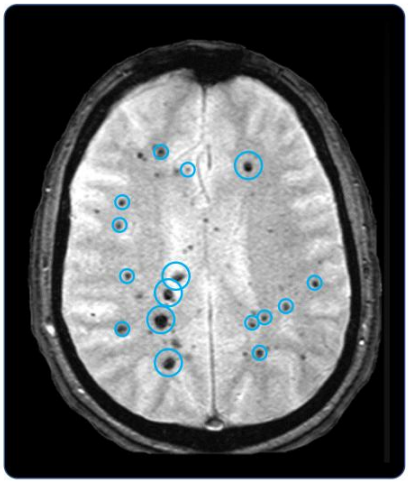
Disease Overview : CCM is an Under-Appreciated Orphan Disease

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)

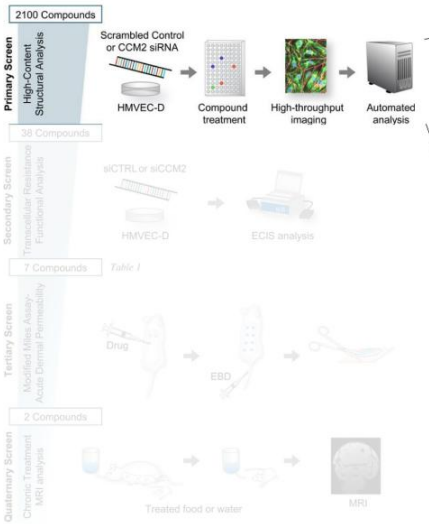


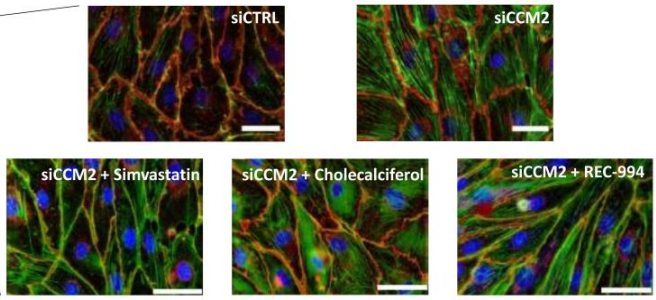
Novel therapeutic approach

- 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.

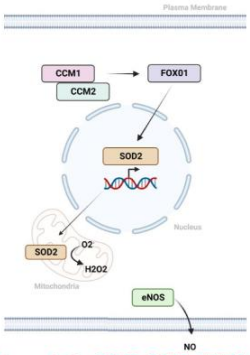
Through a set of follow-on confirmatory assays of increasing complexity, REC-994 stood out as one of two compounds we tested in a 5-month chronic CCM animal model where both compounds demonstrated significant benefit.

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

Clinical: CCM

REC-994 – Mechanism of Action

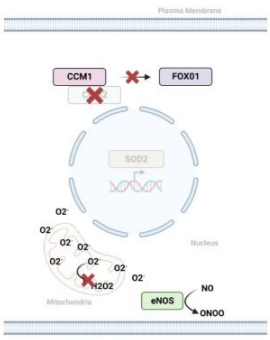
Healthy



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

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

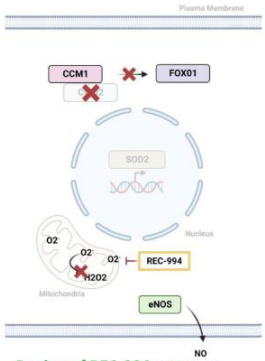
CCM



***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

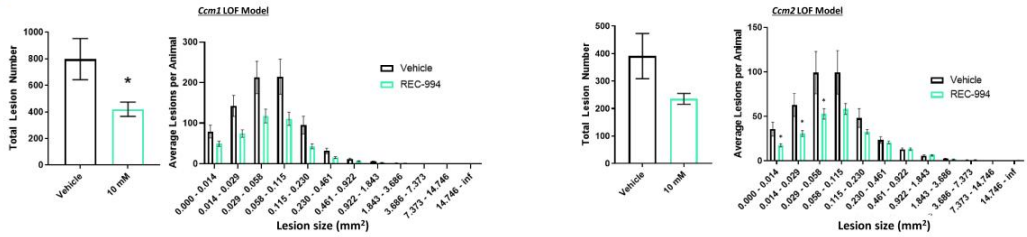
Adopted from REC-994 Investigator Brochure

Clinical: CCM

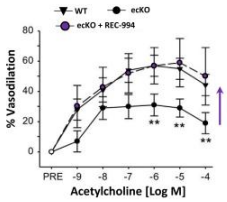
Further Confidence : Preclinical Studies Confirm Insight

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**

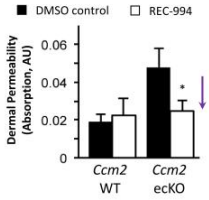


2 **Completely rescues acetylcholine-induced vasodilation defect**



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

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

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

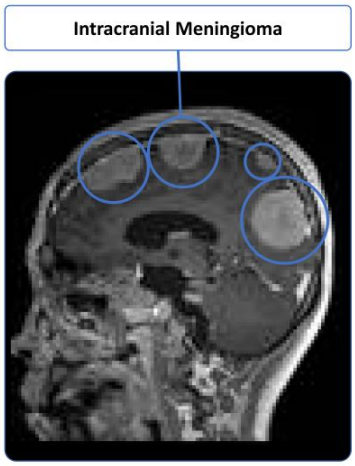
- **No approved drugs** for NF2
- **Surgery** is standard of care (when feasible)
- Location may make complete resection untenable, leading to hearing loss, facial paralysis, poor balance and visual difficulty

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

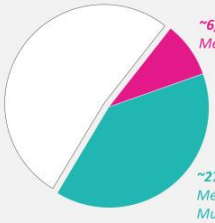
Clinical: NF2

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

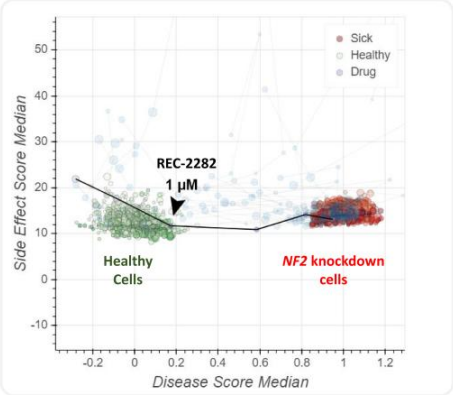
Treatable US + EU5 patients

- 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**

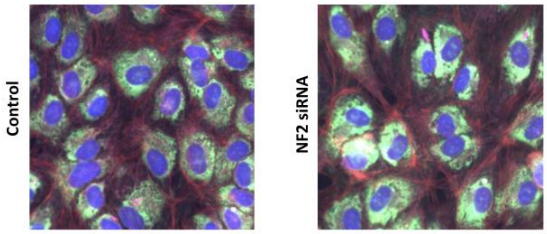
Source: Pemov, et al. Comparative clinical and genomic analysis of neurofibromatosis type 2-associated cranial and spinal meningiomas. Nature. 2020 Jul 28;10(12563). Doi: https://doi.org/10.1038/s41598-020-69074-z; NORD

Clinical: NF2

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



REC-2282 identified as rescuing HUVEC cells treated with NF2

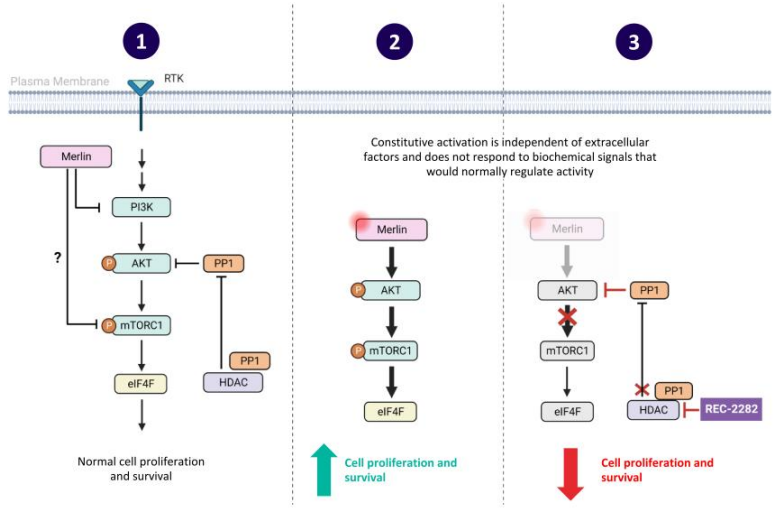


HUVEC, human umbilical vein endothelial cells; NF2, neurofibromatosis type 2; siRNA, small interfering RNA.

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

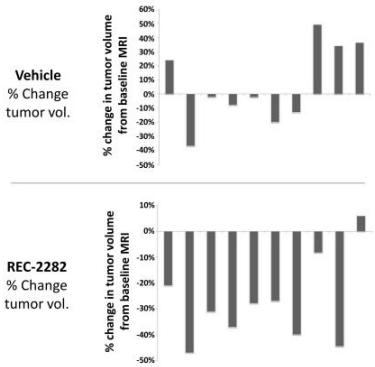
AKT, protein kinase B; eIF4F, eukaryotic initiation factor 4F; HDAC, histone deacetylase; mTor, mammalian target of rapamycin; mTORC1; mammalian target of rapamycin complex 1; NF2, neurofibromatosis type 2; PI3K, phosphoinositide 3-kinase; PP1, protein phosphate 1; Ras, reticular activating system.

Clinical: NF2

Further Confidence : Preclinical Studies Confirming Insight

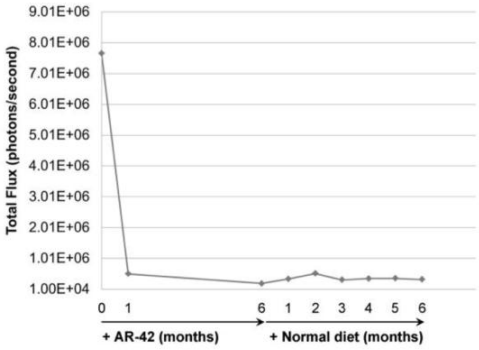
REC-2282 preclinical studies demonstrated clear in-vivo efficacy in multiple NF2 tumor types

1 **Shrinks vestibular schwannoma xenografts in nude mice**



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

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



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

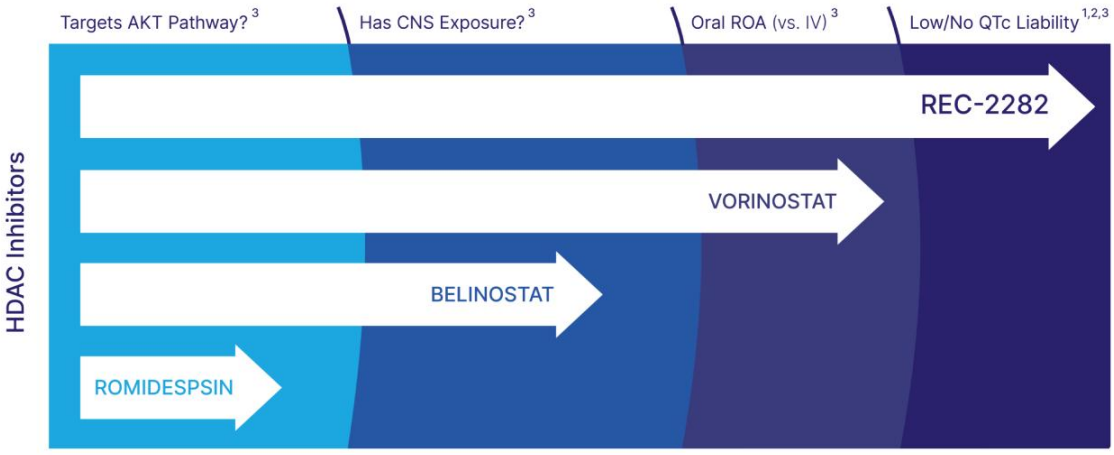
... with a drug-like profile

- 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



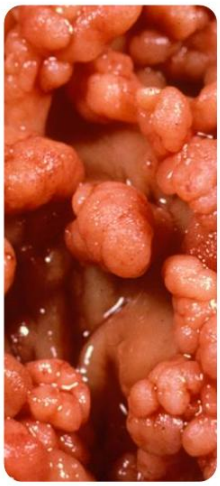
[1] Sborov DW, et al. A phase 1 trial of the HDAC inhibitor AR-42 in patients with multiple myeloma and T- and B-cell lymphomas. Leuk Lymphoma. 2017 Oct;58(10):2310-2318.
[2] Collier KA, et al. A phase 1 trial of the histone deacetylase inhibitor AR-42 in patients with neurofibromatosis type 2-associated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

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

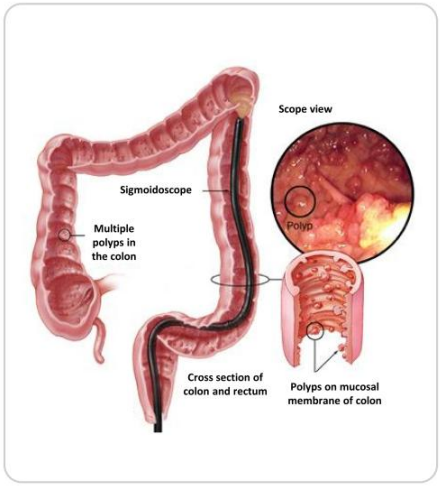
- Autosomal dominant tumor predisposition syndrome caused by a mutation in the APC gene
- Classic FAP (germline mutation) :
  - Hundreds to thousands of polyps in colon and upper GI tract
  - Extraintestinal manifestations (e.g., desmoid tumors)
  - 100% likelihood of developing colorectal cancer (CRC)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

~50,000 Diagnosed US + EU5 patients

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

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"

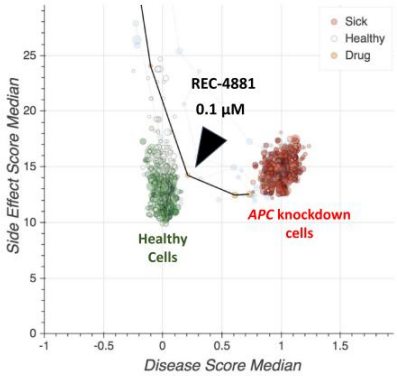
- **Niloy Jewel Samadder**, MD, Mayo Clinic

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



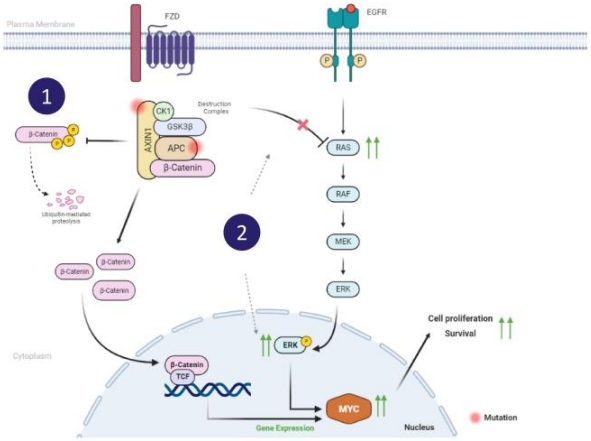
- Compared to thousands of other molecules tested, REC-4881 rescued phenotypic defects substantially better (including better rescue than other MEK inhibitors) for APC specific knockdown
- Findings validated in tumor cell lines and spheroids grown from human epithelial tumor cells with *APC* mutation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

Clinical: FAP

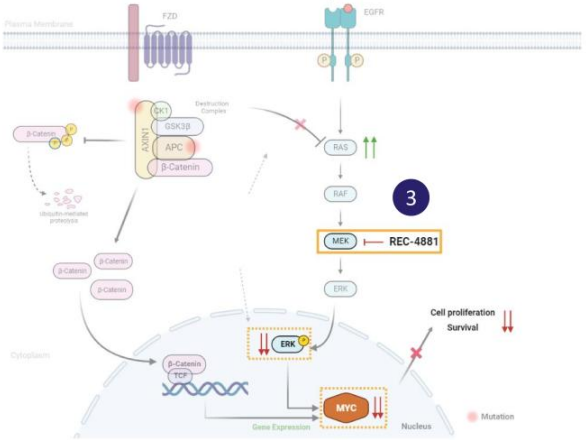
MoA : REC-4881 Blocks Wnt Mutation Induced MAPK Signaling

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).

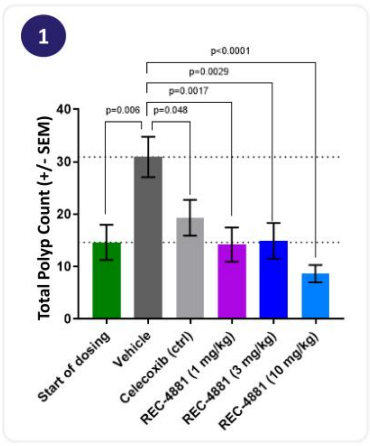
Clinical: FAP

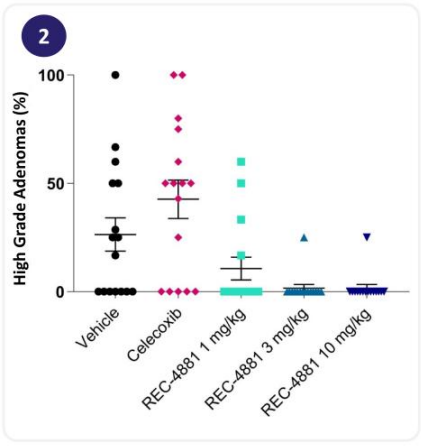
Further Confidence : Preclinical Studies Confirming Reduction in Polyp Count and High-Grade Dysplasia

- 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.

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

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

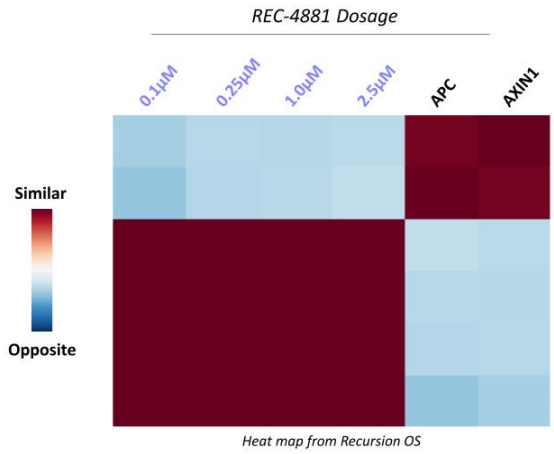
- *AXIN1* and *APC* genes covered by commercially available NGS panels and liquid biopsy detection assays
- FDA guidance supports utility of ctDNA as patient selection for the detection of alterations for eligibility criteria and as a stratification factor for trials enrolling marker-positive and marker-negative 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

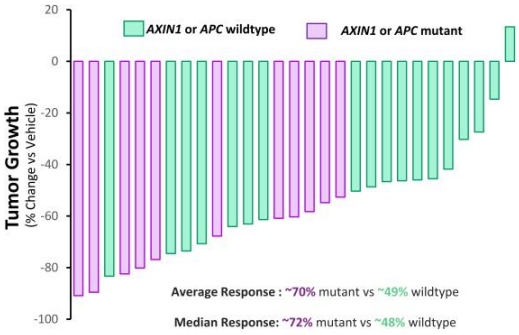
Recursion Differentiation: REC-4881 rescues tumor suppressor genes *APC* and *AXIN1*

- *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

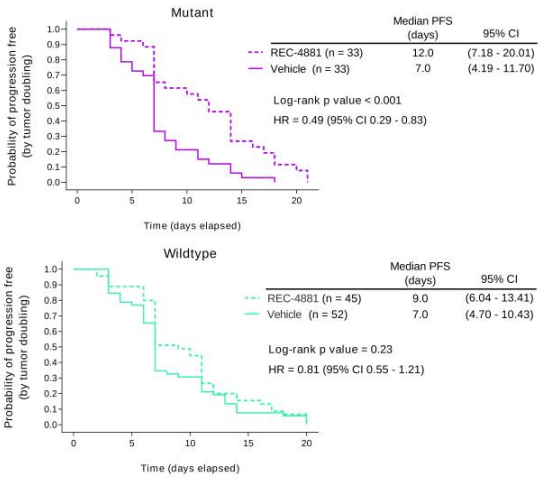
Further Confidence : Preclinical Studies Confirming Insight

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*

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

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**

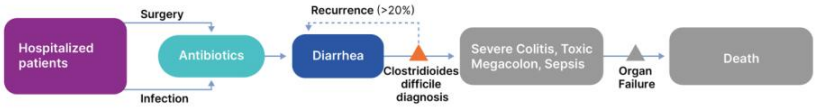
~730,000 **Diagnosed US + EU5 patients**

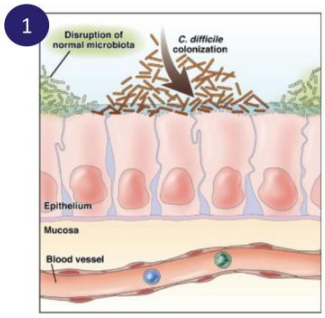
*Source, CDC *NAAT = Nucleic Acid Amplification Test; **rCDI = recurrent CDI*

Clinical: C. Difficile

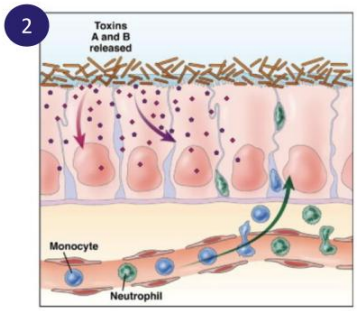
Disease Overview : C. Difficile Infection (CDI)

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

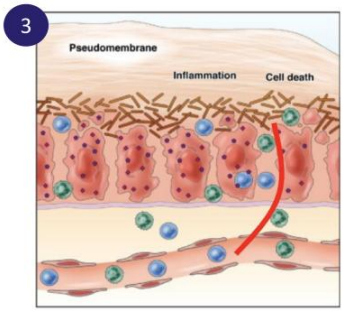




Disruption of microbiota and colonization of *C. diff*



Release of C. diff toxins

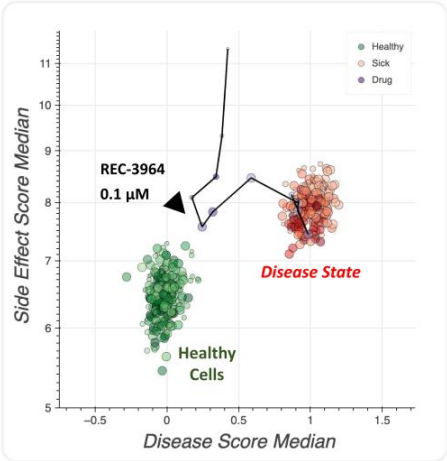


Degradation of colon cell junction & toxin transit to bloodstream

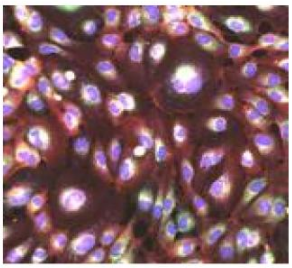
Source: McCollum, D., Rodriguez, JM . Detection, Treatment, and Prevention of Clostridium difficile Infection. Clinical Gastroenterology and Hepatology 2012 Mar 19. https://doi.org/10.1016/j.cgh.2012.03.008

Clinical: C. Difficile

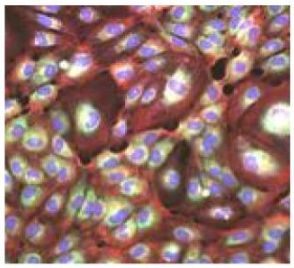
Insight from OS : REC-3964 Rescued Cells Treated with C. Difficile Toxins



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



C. diff toxin B phenotype

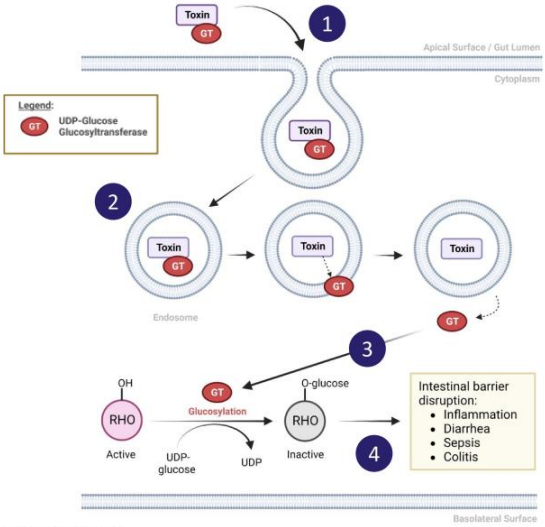


Healthy Control

Clinical: C. Difficile

REC-3964 : Selective Inhibitor of C. Difficile Toxins

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



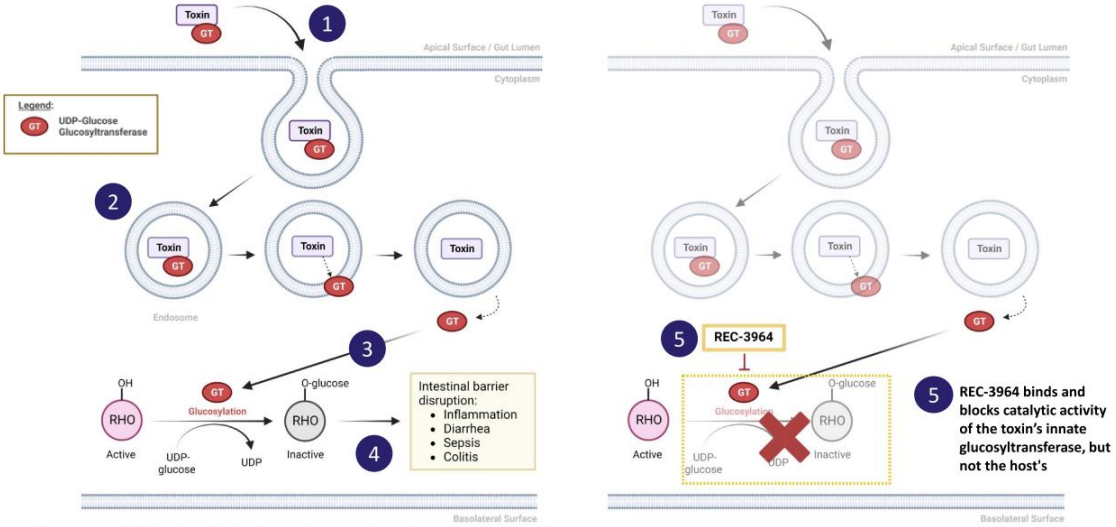
Adapted from Awad et al. 2014

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

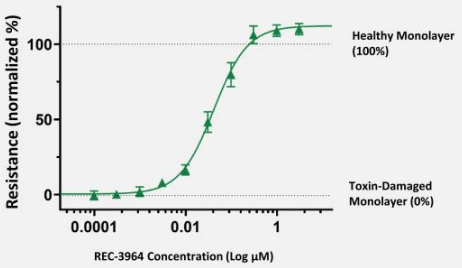


Adapted from Awad, MM. et al. (2014). Clostridium difficile virulence factors: Insights into an anaerobic spore-forming pathogen. Gut Microbes. 5(5), 579-593.

Clinical: C. Difficile

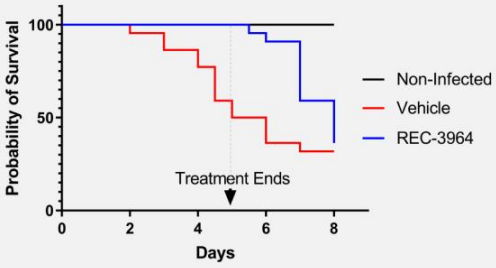
Further Confidence : Preclinical Studies Confirmed Recursion OS Insight

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

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