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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported):
September 9, 2021

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)**	**(IRS Employer Identification No.)**

41 S Rio Grande Street
Salt Lake City, UT 84101
(Address of principal executive offices, including 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, $0.00001 par value 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 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On September 9, 2021, Recursion Pharmaceuticals, Inc. released an updated investor presentation. The investor presentation will be used from time to time in meetings with investors. A copy of the presentation is attached hereto as Exhibit 99.1.

The information furnished pursuant to Item 7.01 on this Form 8-K, including Exhibit 99.1 attached hereto, 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Investor presentation of Recursion Pharmaceuticals, Inc. dated September 9, 2021.
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.

RECURSION PHARMACEUTICALS, INC.

Date: September 9, 2021

By: /S/ Christopher Gibson
Name: Christopher Gibson
Title: Chief Executive Officer

Decoding Biology
To Radically Improve Lives

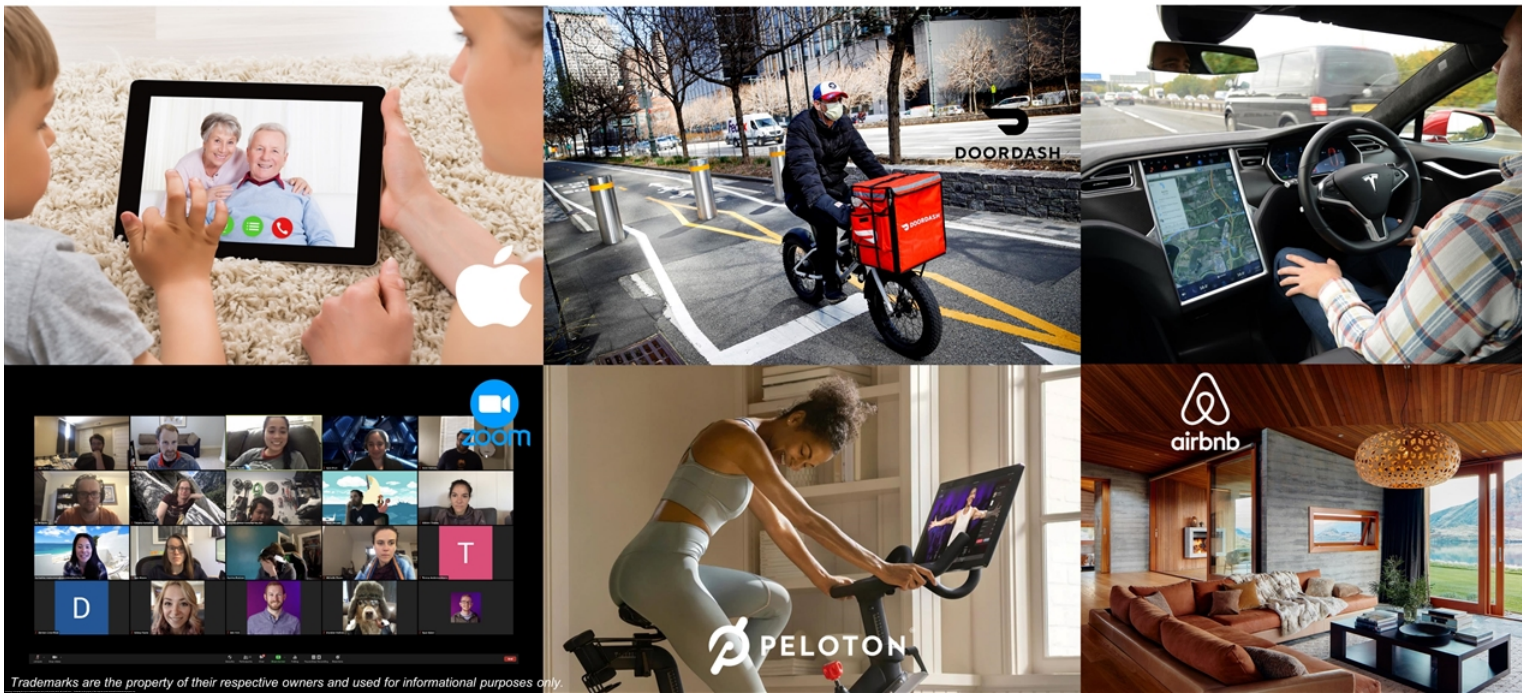
End of Q2 2021

Recursion

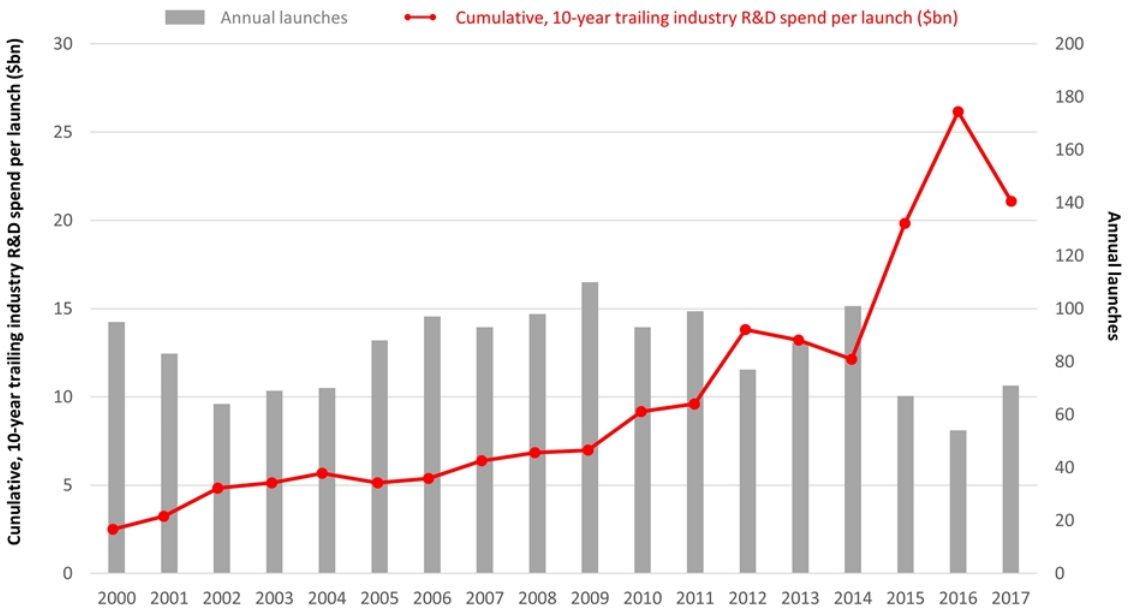
Forward-Looking Statements

This presentation and any accompanying discussion or documents may 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, management's beliefs and certain assumptions we have made. They are neither historical facts nor assurances of future performance, are subject to significant risks and uncertainties, and may turn out to be wrong. For a discussion of factors that could affect our business, please refer to the "Risk Factors" sections in our Prospectus filed with the SEC on April 16, 2021 and in our periodic filings with the SEC. 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.

Technology is disrupting the way we communicate, eat, move, work, exercise, travel, and so much more …



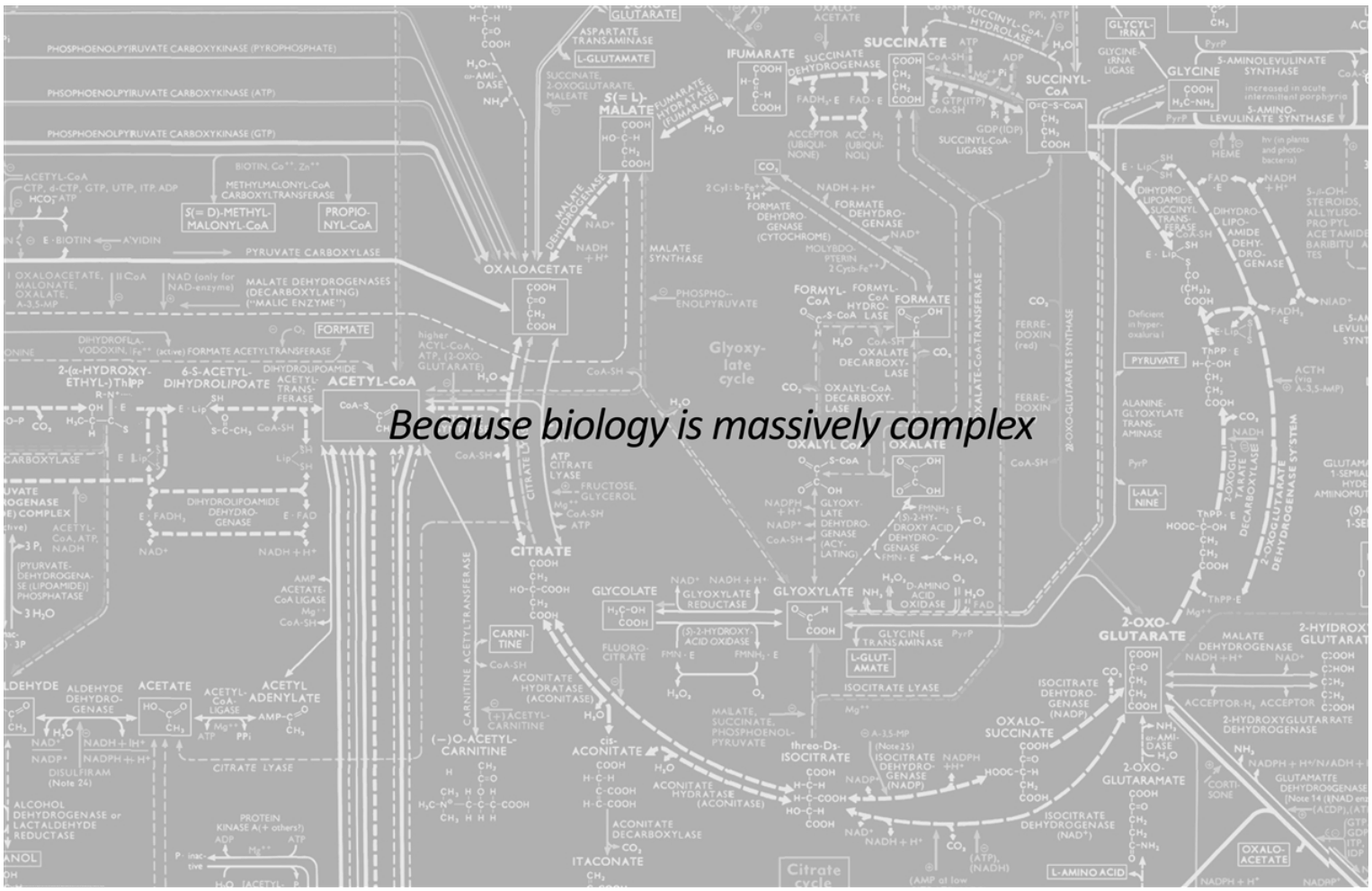
… but in biopharma, a decades long trend of increasing costs



About 90% of clinical trials fail and it takes about 14 years and $2B of R&D for each new drug approval

Source: based on *EvaluatePharma. Analysis is not inflation-adjusted. Analysis is not restricted to novel molecules, though it does exclude generics.*

Why have we not seen the same scale of improvements in drug discovery and development efficiency?


Because biology is massively complex


Exponential improvements in technology are converging to enable a less biased systems biology approach to industrialize drug discovery
Bio Tools
Tools like CRISPR allow CONTROL of Biology
Automation
Automation tools enable massive scale
Storage
1M-Fold Decrease In Costs over 40 years
Compute
1M-Fold Increase in Compute over 40 years
AI
Expert Systems given way to Modern AI

82M+

Proprietary experiments in human cells conducted in our own laboratories

37

Human cell types onboarded to our high throughput phenomics platform and hundreds of cell types/lines in-house for validation assays

9PB

At 9 petabytes, one of the largest proprietary biological and chemical datasets

179B+

Inferred relationships between human genes, chemical compounds and more using our Map of biology

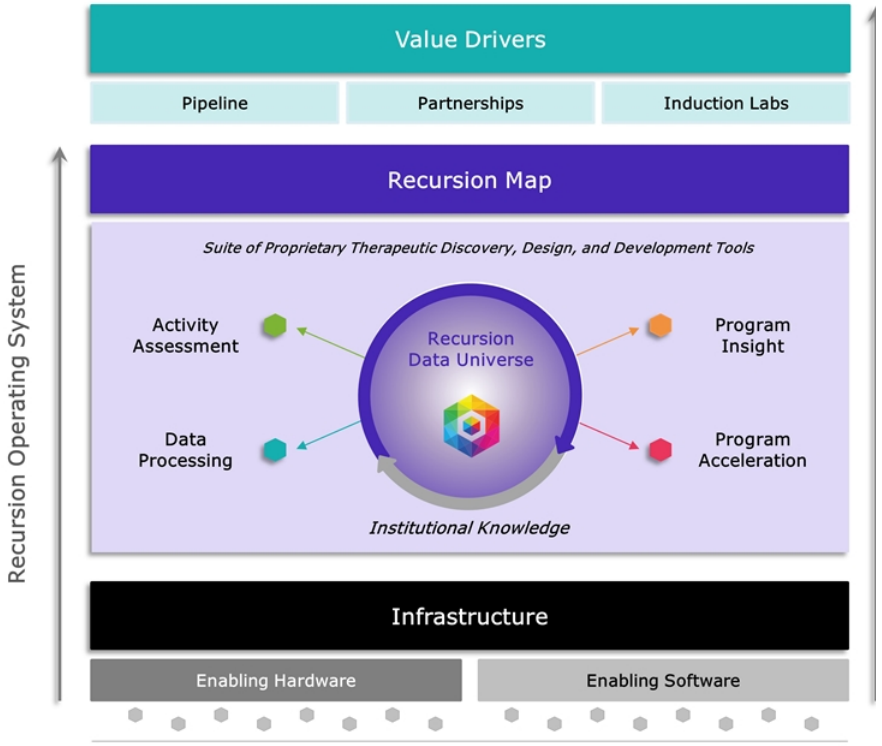
The Recursion Operating System for industrializing drug discovery

An integrated, multi-faceted system for generating, analyzing, and deriving insight from massive biological and chemical datasets to industrialize drug discovery.

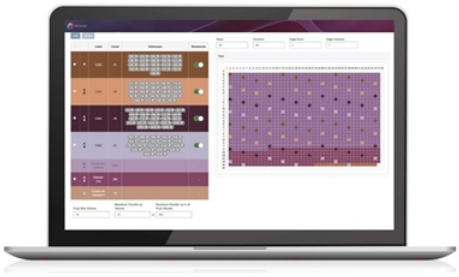
It is composed of:

- **Infrastructure Layer**
- **Recursion Data Universe**
- **Recursion Map**

…and held together by our ***People and Culture***

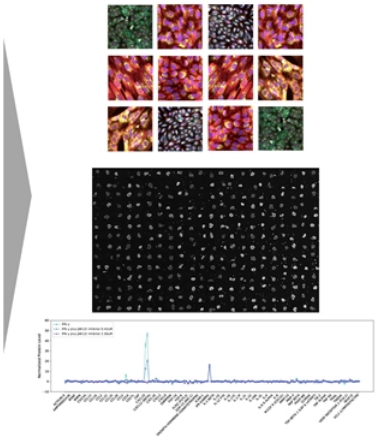


Our OS enables highly scalable, unbiased exploration of biology across multi-omics technologies, with phenomics (images) as a foundation…



Recursion in-house software to design, manage and execute experiments

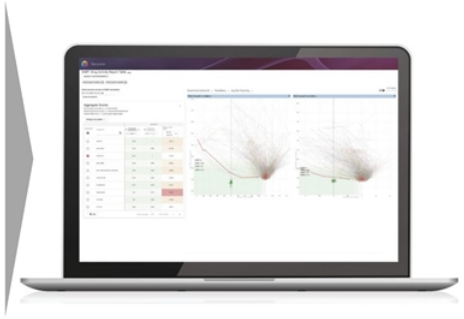
Execute up to 1.7 million experiments each week in highly automated laboratories



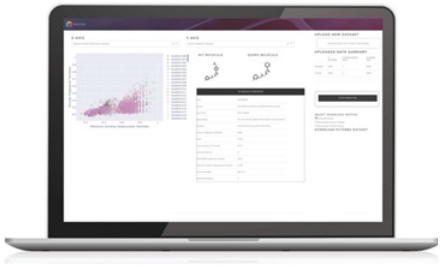
Generate high-dimensional data including *phenomics, proteomics, transcriptomics,* and more at scale

...and new investments in computational infrastructure and digital chemistry demonstrate we are scaling our technology stack

We have more data flux to the cloud than the firehose

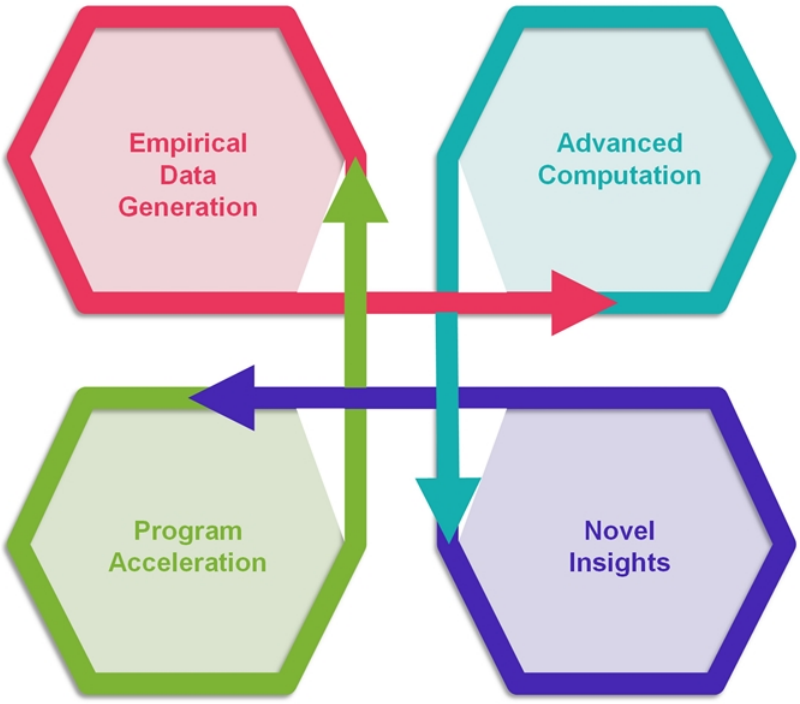


9 PB of data served to scientists using Recursion software to generate insights



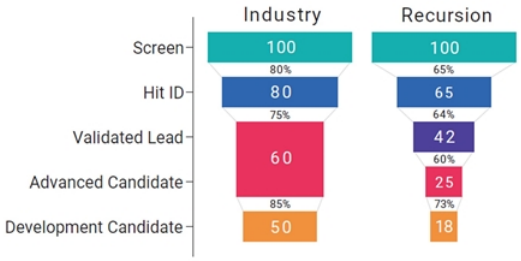
In-house digital chemistry tools to *in silico* screen 12 billion molecules

Our OS learns and grows thanks to a virtuous cycle of wet-lab and dry-lab side by side

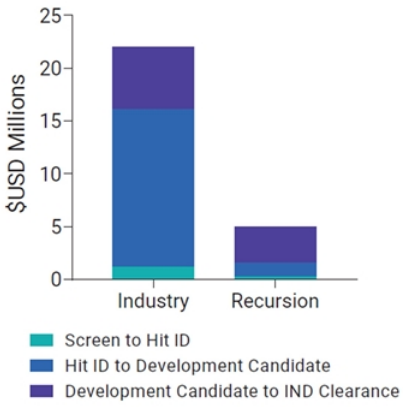


We are demonstrating meaningful leading indicators of industrializing drug discovery and development

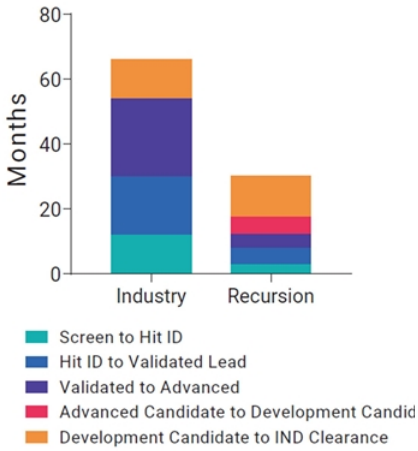
Failing faster and earlier to …



… spend less …

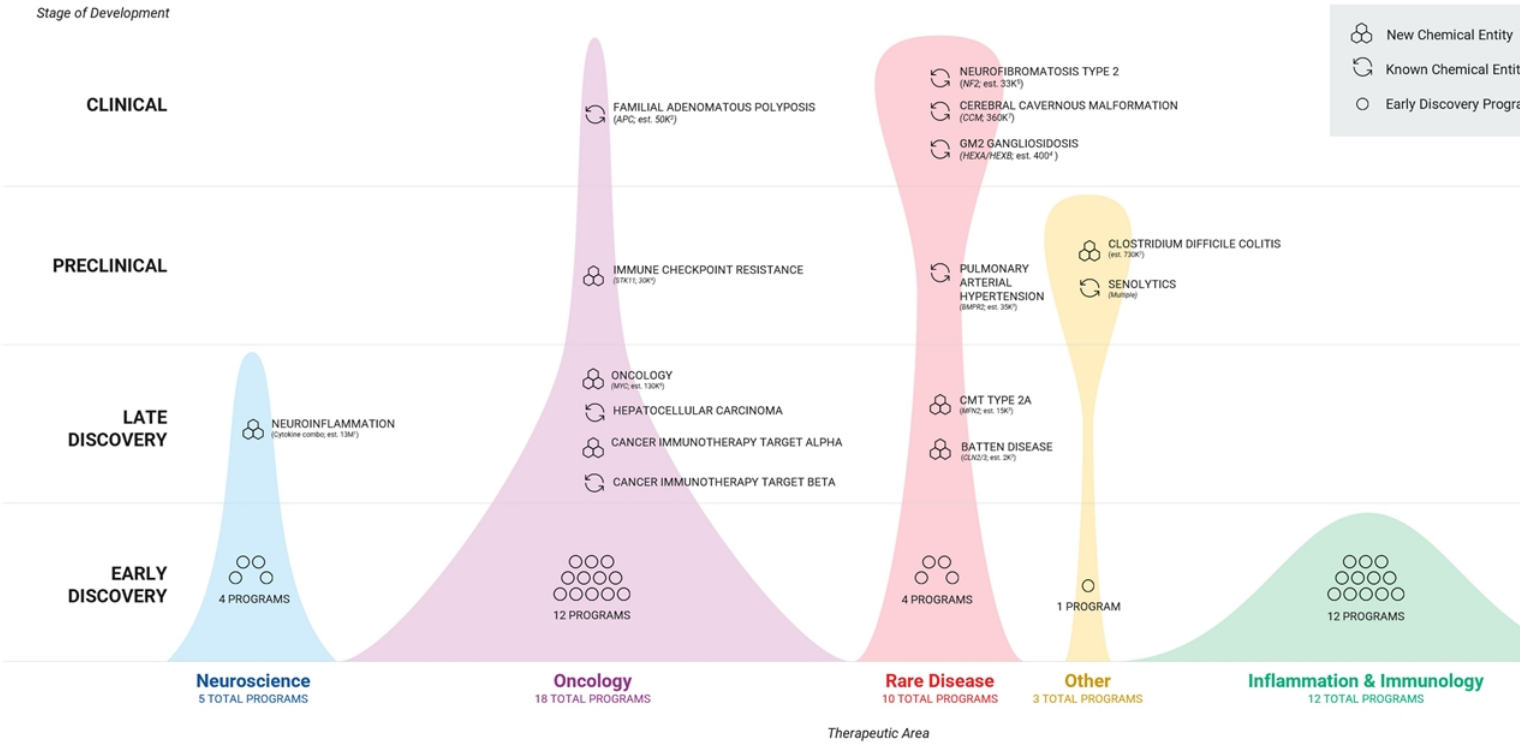


… and go faster



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

The power of the Recursion OS is demonstrated by the scale and breadth of active research and development programs



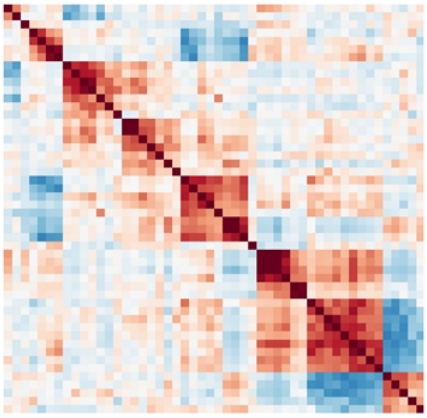
EU5 is defined as France, Germany, Italy, Spain and the UK. (1) Our program has the potential to address a number of indications within neuroinflammation, including multiple neurodegenerative diseases totalling at least 13 million patients in the US (2) 730,000 annual incidence in US and EU5. (3) Annual US and EU5 prevalence (4) Worldwide prevalence (5) Annual US and EU5 incidence for all *NF2*-driven meningiomas. (6) Our program has the potential to address a number of indications driven b alterations, totalling 120,000 patients in the US and EU5 annually. We have not finalized a target product profile for a specific indication. (7) Hereditary and sporadic symptomatic population.

Choose Your Own Adventure:

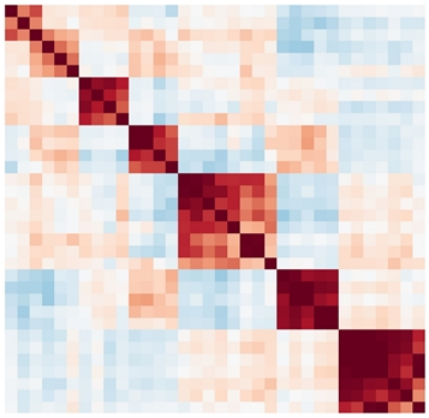
We are transforming drug discovery into a search problem

Using **82M+ proprietary experiments**, we can algorithmically infer **179B+ biological relationships** across the human genome, 100s of thousands of compounds and soluble factors to explore many therapeutic areas for novel targets, compounds and mechanisms:

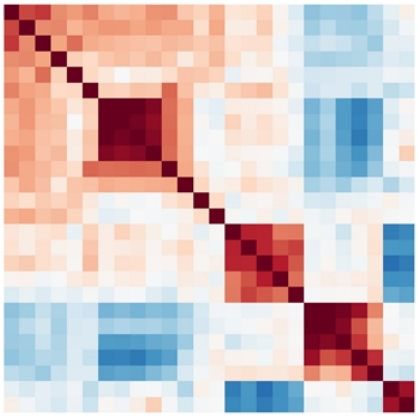
Oncology

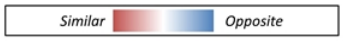


Neuroscience



Immunology



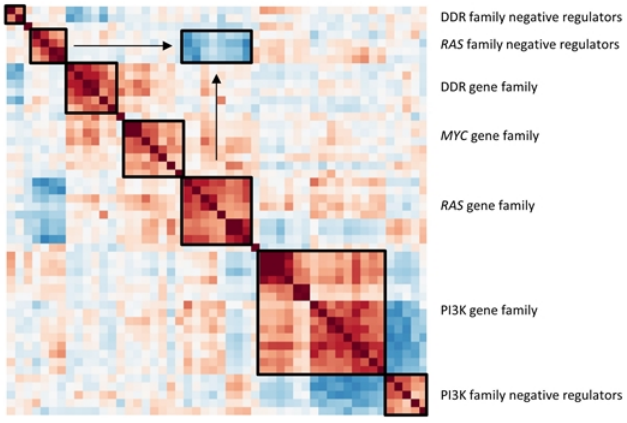


Oncology:

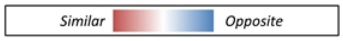
Known oncology pathways cluster together as expected

Shown below are therapeutic area specific subsets of the thousands of genetic knockouts, compounds, and soluble factors profiled by the Recursion OS

Oncology



Multiple oncology pathways cluster independently demonstrating ability to identify known biology, including negative regulators in the same pathway

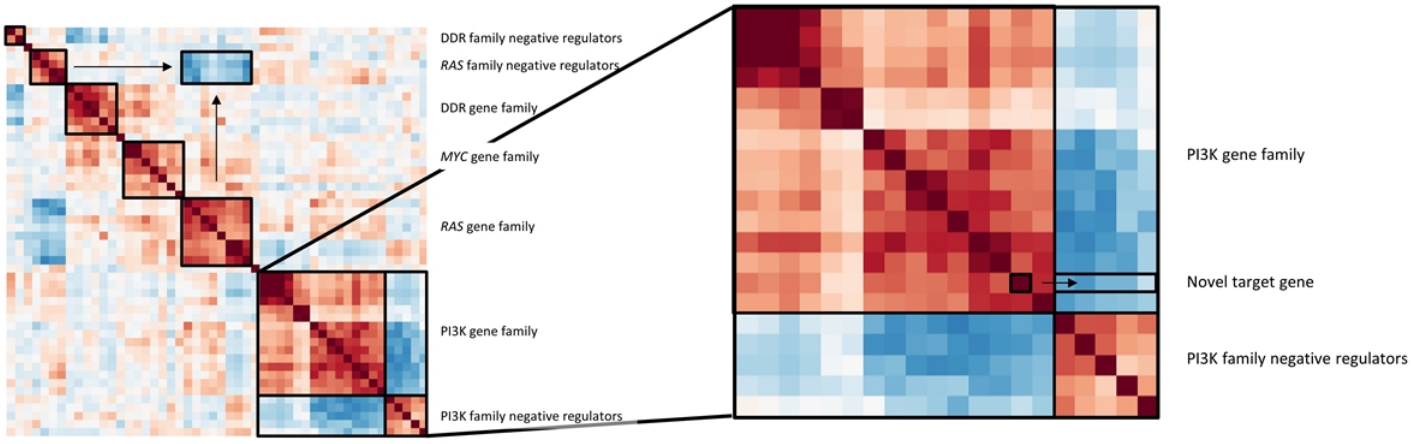


Oncology:

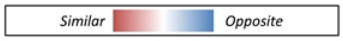
Novel targets can be identified as they cluster with known biology

Shown below are therapeutic area specific subsets of the thousands of genetic knockouts, compounds, and soluble factors profiled by the Recursion OS

Oncology



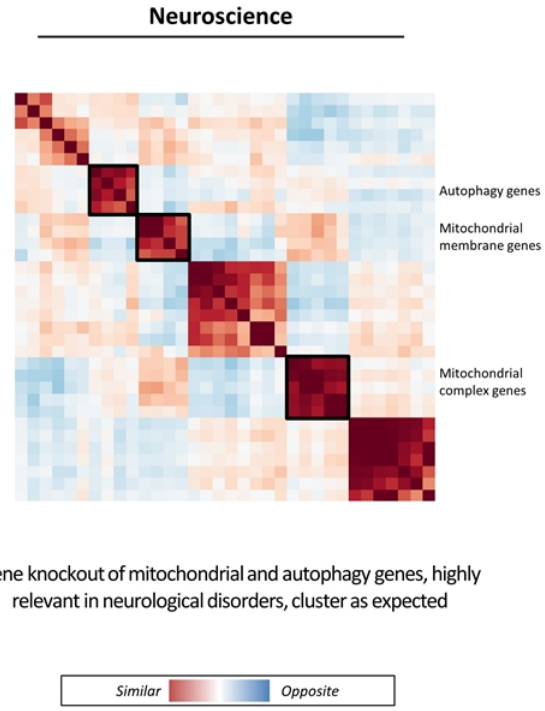
Knockout of novel gene is inferred to be similar to PI3K gene family, presenting a potential novel target gene



Neuroscience:

Neuro-relevant pathways cluster together as expected

Shown below are therapeutic area specific subsets of the thousands of genetic knockouts, compounds, and soluble factors profiled by the Recursion OS

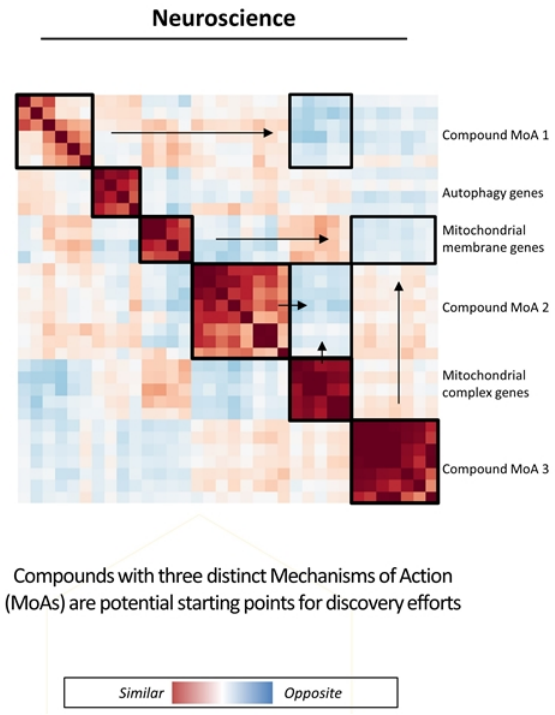


Gene knockout of mitochondrial and autophagy genes, highly relevant in neurological disorders, cluster as expected

Neuroscience:

Novel chemical insight provides fodder for discovery programs

Shown below are therapeutic area specific subsets of the thousands of genetic knockouts, compounds, and soluble factors profiled by the Recursion OS

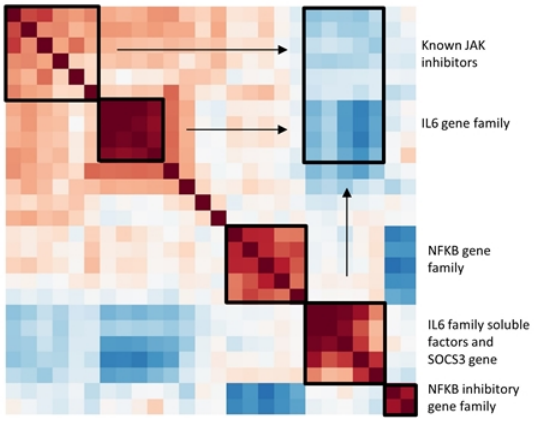


Immunology:

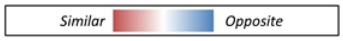
IL6/JAK biology recapitulates across gene knockouts and chemical subst

Shown below are therapeutic area specific subsets of the thousands of genetic knockouts, compounds, and soluble factors profiled by the Recursion OS

Immunology



Knockout of IL6 gene family and dosing of cells with IL6 show expected opposite relationship



Immunology:

Novel chemical insight provides fodder for discovery programs

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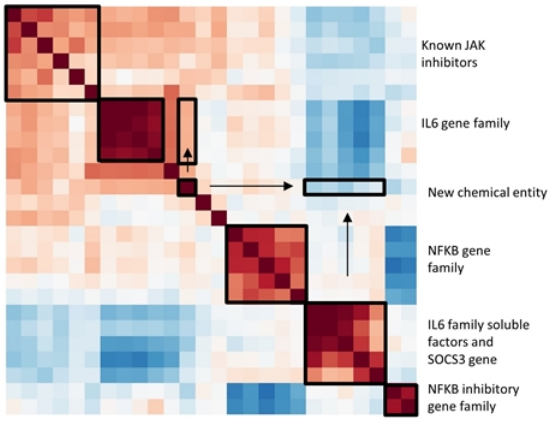
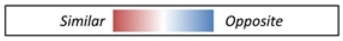
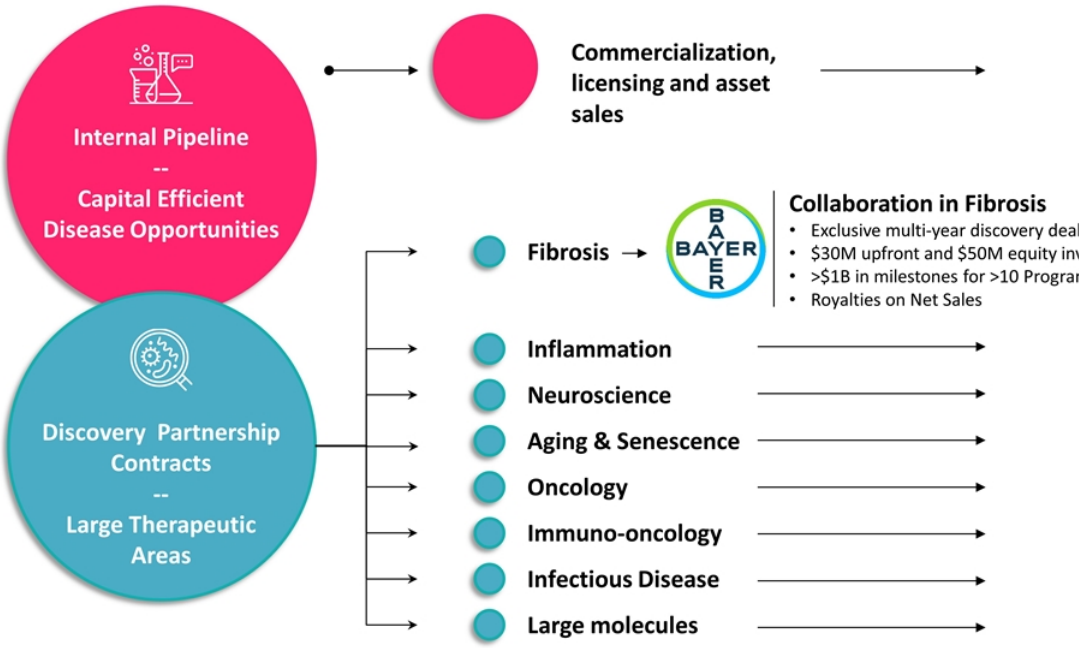
Immunology



A novel chemical series similar to IL6 gene knockout and opposite to IL6 soluble factor dosing present a starting point for a discovery effort



We leverage a capital efficient business strategy with broad ambition for the future



Partnership strategy

- Enterprise scale contracts
- Add knowledge to growing map of biology

A biotechnology company scaling more like a technology company

Forward program growth

Significant program growth
- Growing economic opportunity
- Reduction of binary risks

Year	2017	2018	2019	2020
Total Phenomic Experiments (Millions)	2.2	7.6	23.9	55.6
Data (PB)	0.5	1.8	4.3	6.8
Cell Types	7	12	25	36
Unique Perturbations[1] (Millions)	0.02	0.1	0.5	1.3
Total Chemical Library[2] (Thousands)	3	24	106	706
In Silico Chemistry Library (Billions)	0	0	0.015	3
Inferential Relationships[3] (Billions)	NA	NA	NA	13
Clinical Assets	0	1	2	4
Cost Per Experiment[4] ($)	0.63	0.45	0.36	0.33

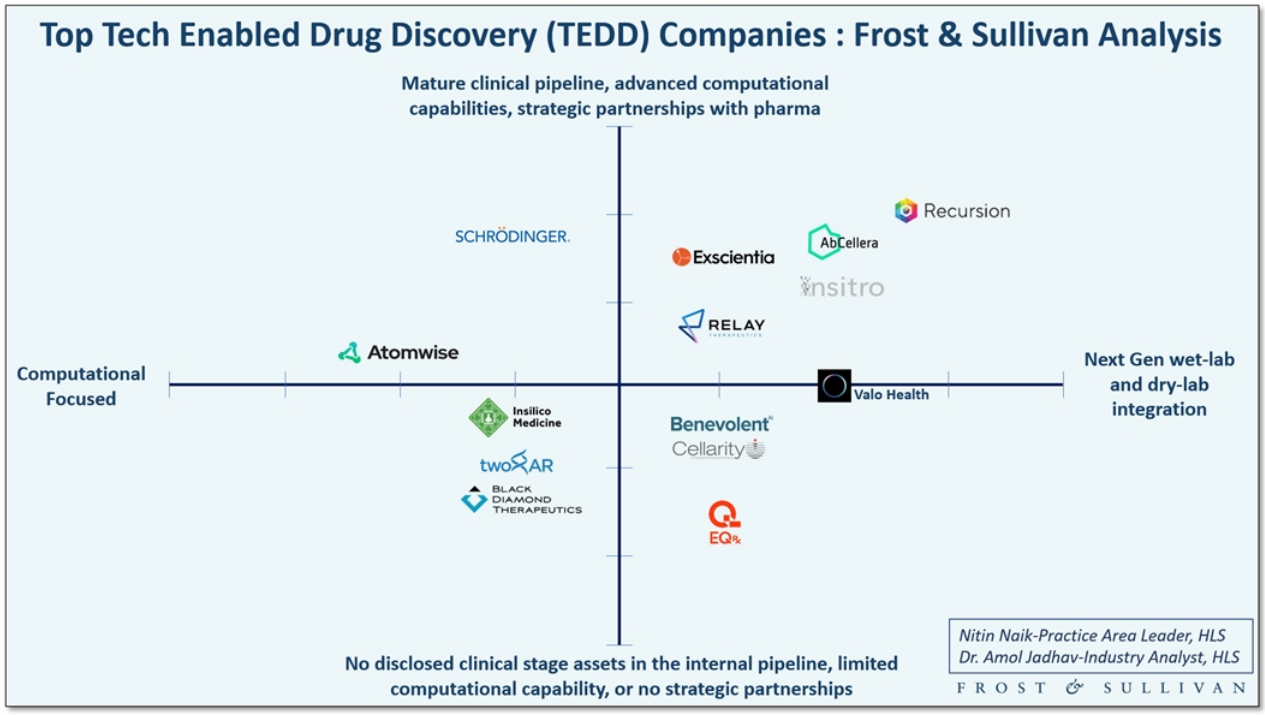
(1) 'Unique Perturbations' refers to the number of gene, soluble factor, cell and/or compound combinations physically explored. (2) Includes approximately 500,000 compounds from Bayer's proprietary library. (3) 'Inferential Relationships' refers to the number of Unique Perturbations that been predicted using our Recursion Map. (4) 'Cost Per Experiment' refers to the average adjusted direct cost to perform one phenomic experiment (defined as one well per perturbation) and is inclusive of consumable, compound and labor costs.

Comparison to relevant platform companies

Company	Early Discovery – Preclinical	Clinical / commercial assets
moderna	8	15
BIONTECH	15	13
CUREVAC	11	3
bridgebio	8	10
SCHRÖDINGER	6	*(multiple through collaboration)*
RELAY THERAPEUTICS	1	2
Recursion	44	4

Pipeline data from company websites as of 8/26/2021. Trademarks are the property of their respective owners and used for informational and educational purposes only.

Recursion is leading technology-enabled drug discovery



Our diverse interdisciplinary team is one of our greatest strengths

Team Credentials

300+ Employees today

~25% Advanced degrees (Ph.D. or M.D.)

Gender: % Women

~40% Below VP

~45% VP and above

Full-time Employee Split

~40% Biology, Chemistry & Development

~35% Data Science, Software Engineering & Automation

~25% BD, Product, Administration, Legal, IP, etc.

Team Experience

Our leadership team brings together experience & innovation to build the operating system for scaling biopharma discovery

Board of Directors

CHRIS GIBSON, PHD
Co-founder & CEO

DEAN LI, MD/PHD
Recursion Co-founder, President of Merck Research Labs

BLAKE BORGESON, PHD
Recursion Co-founder, Board member Machine Intelligence Research Institute

ZAVAIN DAR
Partner, Lux Capit

ZACHARY BOGUE, JD
Partner, Data Collective

ROBERT HERSHBERG, MD/PHD
Former EVP CSO & BD, Celgene

TERRY-ANN BURRELL, MBA
CFO & Treasurer
Beam Therapeutics

R. MARTIN CH
Vice-Chair of 6th Financial. Forme at GS

Executive Team

CHRIS GIBSON, PHD
Co-Founder & CEO

TINA LARSON
President & COO

SHAFIQUE VIRANI, MD FRCS
Chief Corp Dev Officer

MASON VICTORS
Chief Product Officer

RAMONA DOYLE, MD
Chief Medical Officer

HEATHER KIRKBY
Chief People Officer

BEN MABEY
Chief Technology Officer

RON ALFA, MD/PHD
SVP of Research

MICHAEL SECORA, PHD
Chief Financial Officer

LOUISA DANIELS, JD
Chief Legal Officer & Gene Counsel


Impact
RECURSION

Key Updates During Q2 2021

Infrastructure

- **Phenomics experiments** executed during Q2 increased more than 30% QoQ
- Operating **BioHive-1 Supercomputer**

Data Universe

- **Proprietary biological data** increased by >1 PB, total biological data now 9 PB
- >2x orthogonal **transcriptomics and proteomics** datasets

Map/Inference

- Nearly doubled **inferred relationships** to 179B+ across the human genome and 100s of thousands of compounds in multiple human cell types

Partnerships

- Advancing **multiple simultaneous discovery programs** with Bayer in fibrosis
- **Exploring enterprise-scale partnerships** in additional large therapeutic areas

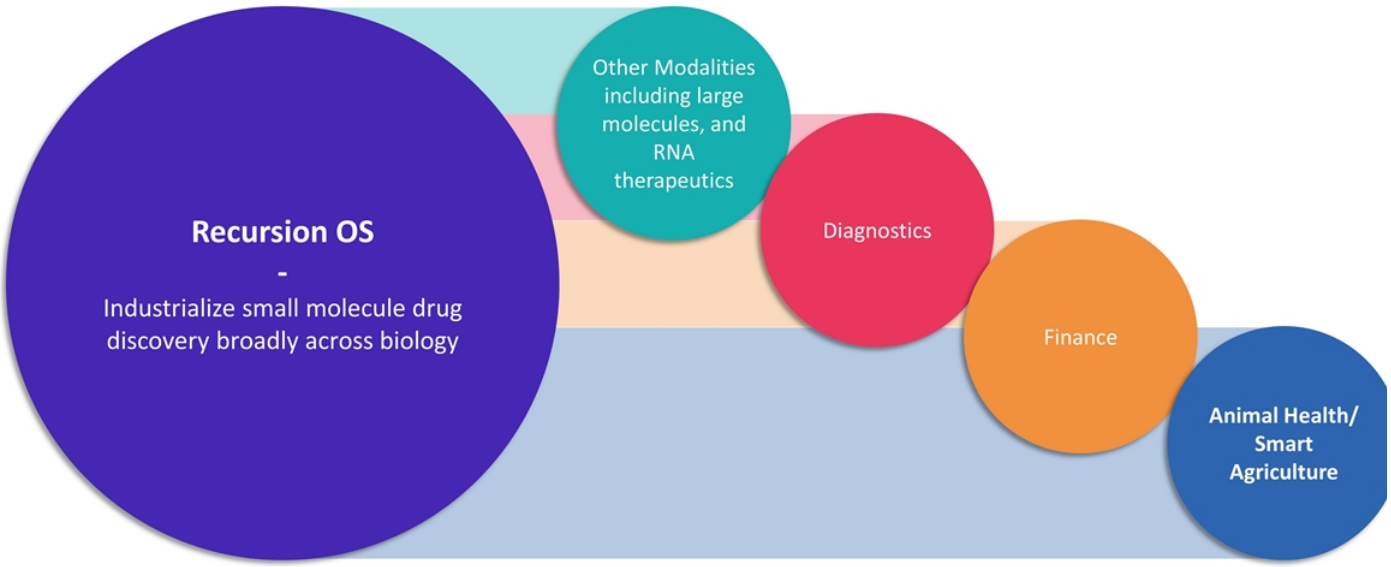
Programs

- **11 new research and development programs** added to pipeline across multiple therapeutic areas bringing **total programs to 48**
- Advancing **4 clinical-stage programs** to ph2 or ph2/3 studies in the next 3-4 quarters
- Advanced **first NCE program** (C diff) into IND-enabling studies
- Cancer immunotherapy target 'alpha' demonstrated **40% complete response** in CT26 model of immune checkpoint resistance

People

- Grew from 217 employees at IPO to **over 300 today**
- Formed **Therapeutics Advisory Board** chaired by Joseph Miletich MD, PhD
- Expanding operations into **Toronto and Montreal** with emphasis on software engineering and data science hires

Induction Labs is a growth engine for exploring additional market opportunities



REC-4881: Orally bioavailable MEK inhibitor for the potential treatment of Familial Adenomatous Polyposis (FAP)

Disease Overview:

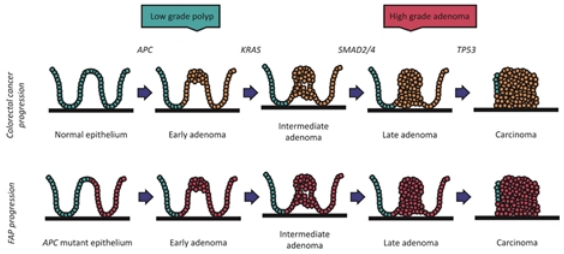
- Autosomal dominantly inherited rare tumor syndrome caused by mutations in *APC* gene affecting ~50,000 patients in US and EU5

Expected Milestone:

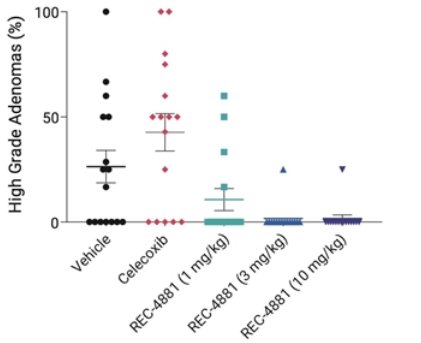
- First patient enrolled in a phase 2 randomized, double-blind, placebo-controlled trial within 3-4 quarters

Summary and differentiation:

- Orally bioavailable, gut-localized small molecule therapeutic being developed to reduce tumor size in FAP patients
- Phase 1 data with favorable ocular safety profile and confirmed pharmacodynamics on ERK signaling
- Projected Phase 2 dose at exposures with limited observed AEs in Phase 1

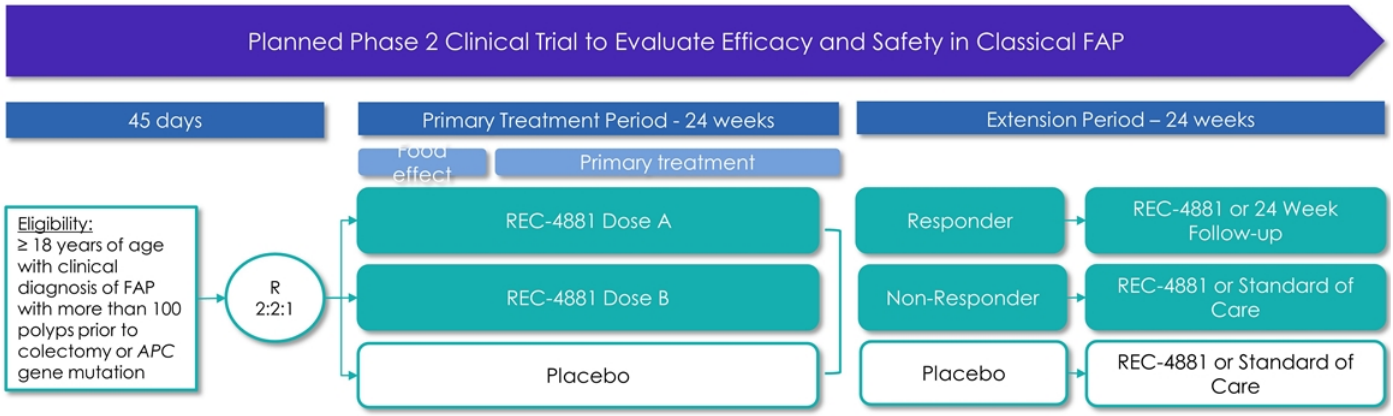


REC-4881 reduces high grade adenomas in *Apc^{min}* mouse model of FAP



EU5 is defined as France, Germany, Italy, Spain and the UK. Figure adapted from http://syscol-project.eu/about-syscol/

REC-4881: Planned Phase 2 clinical trial design to evaluate efficacy and safety in classical Familial Adenomatous Polyposis



REC-994: First-in-disease, orally bioavailable potential treatment for Cerebral Cavernous Malformation (CCM)

Disease Overview:

- Autosomal dominantly inherited neurovascular disease caused by mutations in CCM1, CCM2, or CCM3 genes affecting approximately 360,000 patients in US and EU5

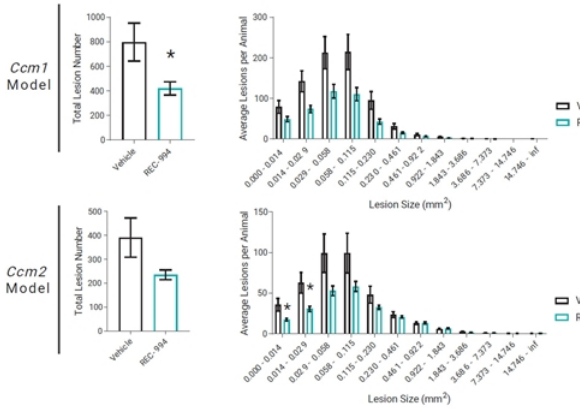
Expected Milestone:

- First patient enrolled in a Phase 2 double-blind, placebo-controlled trial within 3-4 quarters

Summary and differentiation:

- First-in-disease industry-sponsored oral small molecule therapeutic for treatment of Symptomatic CCM
- Well tolerated in healthy human volunteers with safety profile supporting proposed phase 2 doses
- To our knowledge, REC-994 is the only industry-sponsored therapeutic program in clinical trials for CCM targeting one of the largest unmet needs in the rare disease space

REC-994 reduces lesion number in chronic mouse models of



EU5 is defined as France, Germany, Italy, Spain and the UK

REC-994: Planned Phase 2 trial to evaluate efficacy and safety in Symptomatic Cerebral Cavernous Malformation patients

REC-2282: First-in-class CNS-penetrant, orally bioavailable HDAC inhibitor for the potential treatment of Neurofibromatosis Type 2 (NF2)

Disease Overview:

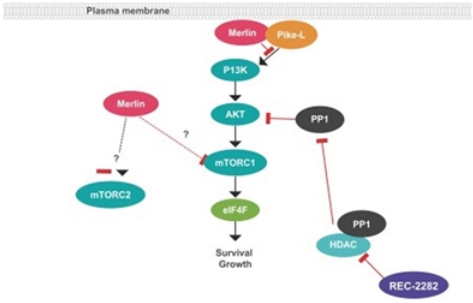
- Autosomal dominantly inherited rare tumor syndrome caused by mutations in *NF2* gene
- 33,000 patients per year in US and EU5 affected by both inherited and sporadic meningiomas with *NF2* mutations

Expected Milestone:

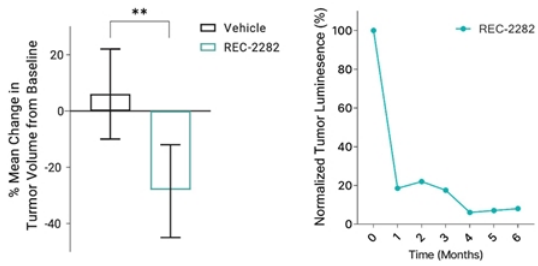
- Adaptive, parallel group, Phase 2/3 randomized, multicenter study with first patient enrolled within 3-4 quarters

Summary and differentiation:

- First-in-class, oral small molecule therapeutic for treatment of NF2-mutant meningiomas
- Oral bioavailability and CNS exposure together are unique among clinical-stage HDAC inhibitors
- Early Phase 1 data demonstrates intratumoral PK/PD in CNS tumors from NF2 patients
- Clinical precedent for long-term chronic dosing in a subset of patients from Phase 1 studies

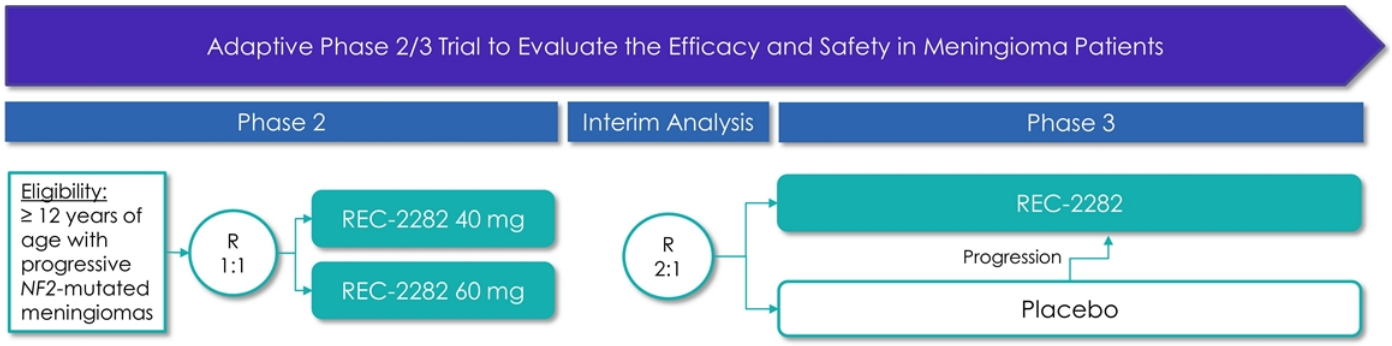


REC-2282 prevents growth of human vestibular schwannoma and meningioma tumor grafts in mouse studie



EU5 is defined as France, Germany, Italy, Spain and the UK. Figure adapted from Petrilli and Fernández-Valle. Oncogene 2016 35(5):537-48

REC-2282: Planned adaptive Phase 2/3 trial to evaluate efficacy and safety in Meningioma patients



REC-3599: First-in-class orally bioavailable, selective inhibitor of PKC and GSK3ß for the potential treatment of GM2 gangliosidosis (GM2)

Disease Overview:

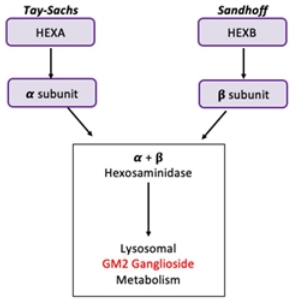
- Pediatric lysosomal storage disease caused by mutations in HEXA or HEXB genes affecting more than 400 patients worldwide resulting in neurological decline and death in the first few years of life

Expected Milestone:

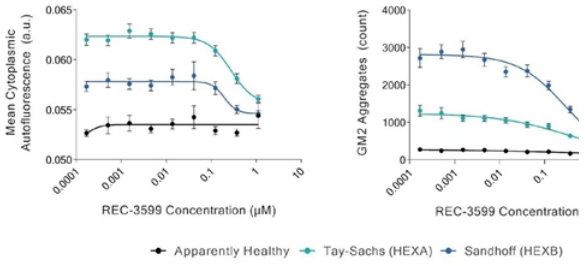
- First patient enrolled in open-label phase 2 study in patients with GM2 gangliosidosis within 3-4 quarters

Summary and differentiation:

- First-in-class orally bioavailable small molecule therapeutic for treatment of infantile GM2-gangliosidosis
- Human safety database with established chronic dosing
- Oral small molecule therapeutic with complementary MOA for potential combination with genetic therapies



REC-3599 reduces autofluorescence substrate accumulati and GM2 aggregates in GM2 patient-derived fibroblasts



Source: Solovyeva et al , Frontiers in Physiology DOI https://doi.org/10.3389/fphys.2018.01663, 2018

REC-3599: Planned Phase 2 clinical trial to evaluate efficacy and safety in infantile GM2 Gangliosidosis

Additional notable programs moving through our pipeline

C. difficile Colitis (REC-3964)

Current status: preclinical

- New chemical entity with potential to be orally active, gut-biased, *C. difficile* toxin inhibitors via glycosyl transferase inhibition.
- *C. difficile* affects up to 730k patients annually in the US and EU5
- IND-enabling studies underway

INFERENCE: Treatment of Immune Checkpoint Resistance in STK11-mutant NSCLC

Current status: preclinical

- Orally bioavailable small molecule to restore and improve sensitivity to immune checkpoint inhibitors in tumors harboring mutations in *STK11*
- Inference to Animal Model validation in ~6 months

Lead Molecules for the Treatment of Neuroinflammation

Current status: late discovery

- Multiple new chemical entities with potential to be first-in-disease, orally bioavailable, safe, CNS-penetrant small molecule inhibitors of microglial activation
- Neuroinflammation is a hallmark of many major neurodegenerative diseases
- Data suggests the target of these molecules may be novel and NF-κB independent

INFERENCE: Cancer Immunotherapy Target Alpha

Current status: late discovery

- Selected based on an inferential assessment of the strength of its relationship to known genes impacting immunotherapy response
- A small molecule inhibitor of target alpha demonstrated a 40% complete response in a CT26 model of immune checkpoint resistance

INFERENCE: MYC Inhibitors for Solid/Hematological Malignancies

Current status: late discovery

- Multiple scaffolds with confirmed MYC inhibitory effects in human cells
- Inference to in vitro validation in ~3 months

Lead Molecules for the Treatment of Charcot-Marie-Tooth 2A

Current status: late discovery

- Four new chemical entities (multiple scaffolds) with potential to be orally bioavailable, disease-modifying therapeutics to slow or reverse the progression of the mitochondrial disease CMT2A
- CMT2A is a rare, autosomal dominant peripheral nerve disease with no disease modifying therapies

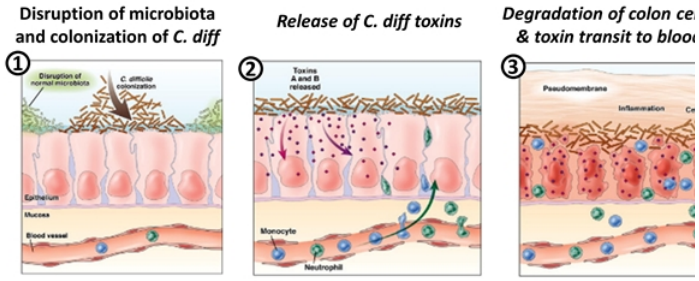
REC-3964: Orally active small molecule toxin inhibitor for prophylaxis and recurrent C. difficile infection

Disease Overview:

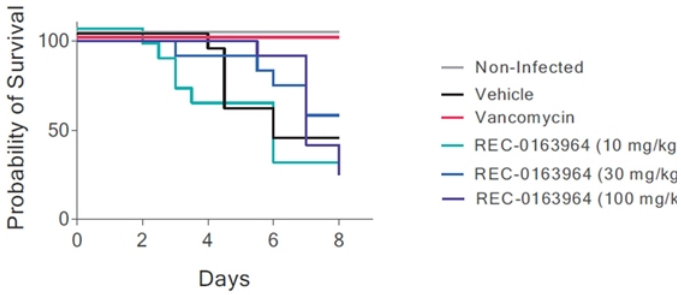
- Infectious disease caused by Clostridium difficile affecting more than 730,000 patients per year in the US and EU5 with hallmarks including severe diarrhea, colitis, and risk of toxic megacolon, sepsis, and death

Summary and differentiation:

- Orally active small molecule toxin inhibitor
- Glucosyl transferase inhibitor suppresses toxin-induced glycosylation of Rho-GTPases
- Gut-biased pharmacology to target infection at diseased locus after oral dosing
- Non-antibiotic approach with potential for combination with SOC and other therapies
- Lead candidates currently in IND-enabling studies



C. difficile-infected model hamsters treated with REC-163964 survive longer than vehicle-treated animals



EU5 is defined as France, Germany, Italy, Spain and the UK. Figure adapted from McCollum and Rodriguez, Clinical and Gastroenterology and Hepatology. DOI https://doi.org/10.1016/j.cgh.2012.03.008, 2012

STK11: Orally bioavailable, small molecule to enhance anti-PD-(L)1 response of *STK11* mutant cancers

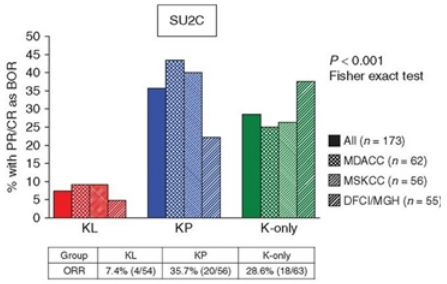
Disease Overview:

- *STK11* is a tumor suppressor mutated in a variety of cancers
- Mutations in *STK11* have been shown to underlie resistance of cancers to immune checkpoint inhibitors, especially in non-small cell lung cancer (NSCLC)
- *STK11* mutations characterize approximately 30,000 cases of metastatic NSCLC in the US and EU5
- There are currently no approved therapies to improve checkpoint sensitivity of tumors harboring mutations in *STK11*

Summary and differentiation:

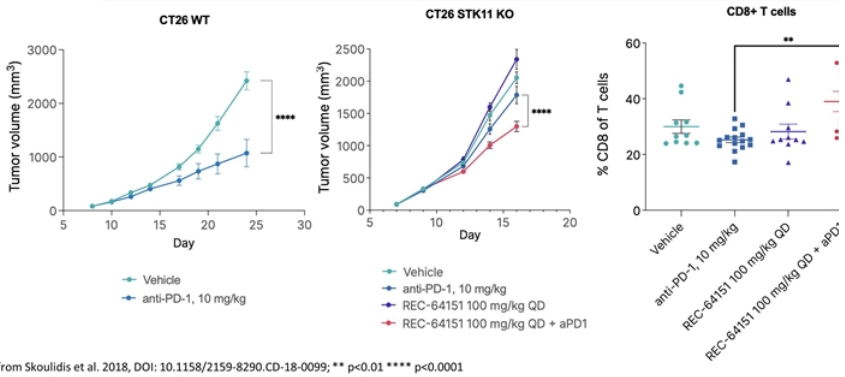
- Orally bioavailable, small molecule therapeutic to enhance immune responses of *STK11* mutant tumors
- For combination therapy with anti-PD(L)1 and targeted therapies in both checkpoint refractory and treatment naïve metastatic cancers

Anti-PD1 response in NSCLC patients harboring mutations in KRAS STK11 (KL), KRAS TP53 (KP), KRAS only (K-only)



Group	KL	KP	K-only
ORR	7.4% (4/54)	35.7% (20/56)	28.6% (18/63)

Relative to wild type, *STK11* KO show a diminished anti-PD1 response
REC-64151 restores anti-PD1 response of *STK11* mutant CT26 tumors
REC-64151 in combination with anti
demonstrates enrichment in CD8 T-



EU5 is defined as France, Germany, Italy, Spain and the UK. Figure demonstrating anti-PD1 response in NSCLC patients adapted from Skoulidis et al. 2018, DOI: 10.1158/2159-8290.CD-18-0099; ** p<0.01 **** p<0.0001

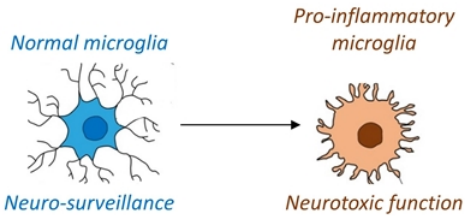
Neuroinflammation: Orally bioavailable, CNS-penetrant, small molecule modulators of microglial activation

Disease Overview:

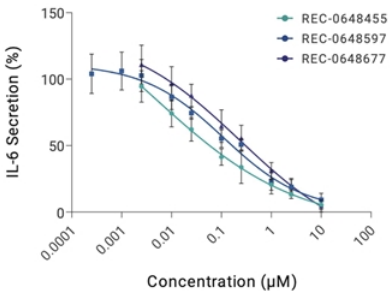
- Neuroinflammation is a hallmark of diseases of the CNS, including neurodegenerative diseases with hallmark of microglial activation and secretion of proinflammatory cytokines such as TNFα, IL-6, IL-1ß, MCP-1

Summary and differentiation:

- Orally bioavailable, CNS-penetrant small molecule modulators of microglial activation
- Modulation of proinflammatory pathways through NFkB- and JAK-independent mechanisms
- Additional potential therapeutic opportunities outside of CNS disease in systemic diseases of inflammation
- 3 NCE lead molecules (REC-648455, REC-648597, and REC-648677) in lead optimization phase



Rescue of TNFα-evoked IL6 secretion in human endothelial cells



Rescue of LPS-evoked *Iba1* expression in mouse microglial cells

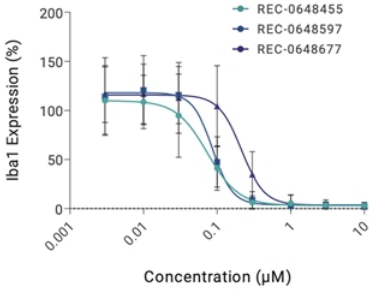


Figure adapted from Subramaniam and Federoff, Frontiers in Aging Neuroscience DOI https://doi.org/10.3389/fnagi.2017.00176, 2017

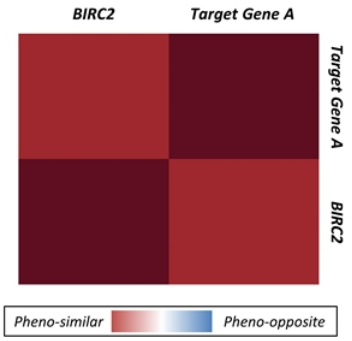
Cancer Immunotherapy Target Alpha: Inferential search identified targets and molecules active on checkpoint resistance pathways

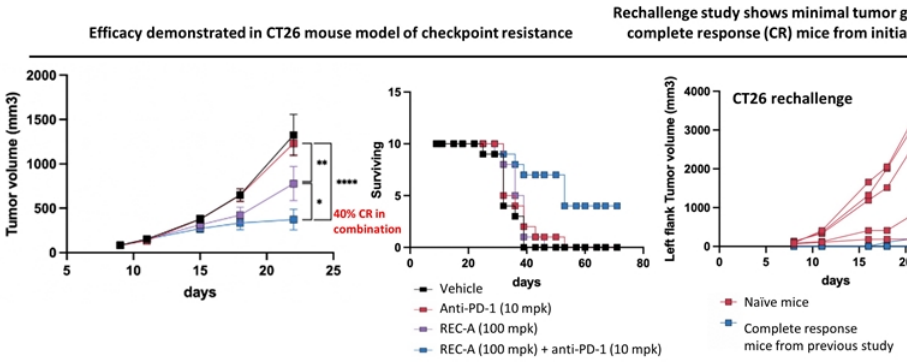
Disease Overview:

- Checkpoint therapy is rapidly becoming standard of care across a wide variety of oncology indications
- Resistance to checkpoint is a significant unmet need
- **Goal:** Identify novel targets and compounds capable of sensitizing tumors to checkpoint therapy

Summary and differentiation:

- PhenoMap clustering of known checkpoint sensitivity genes (e.g. *BIRC2*) reveals Target Gene A as a strong phenosimilar druggable target
- No known reported Target Gene A inhibitors in the clinic
- REC-A, a small molecule inhibitor of Target Gene A, alone or in combo with anti-PD-1, shows significant reduction in tumor growth vs. anti-PD-1 alone, including 40% complete response in combination with anti-PD-1
- Complete responders are robust to rechallenge





CT26: mouse colon carcinoma. REC-A was dosed PO, QD for 5 weeks. Anti-PD-1 was dosed IP, BIW for 5 weeks. 10 mice per group, dosing initiated when tumors reached ~ 80 mm3; * p<0.05 ** p<0.01 **** p<0.0001

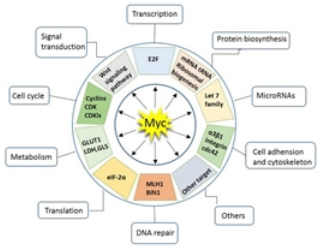
MYC: Small molecule inhibitors of *MYC* for the treatment of *MYC*-driven cancers

Disease Overview:

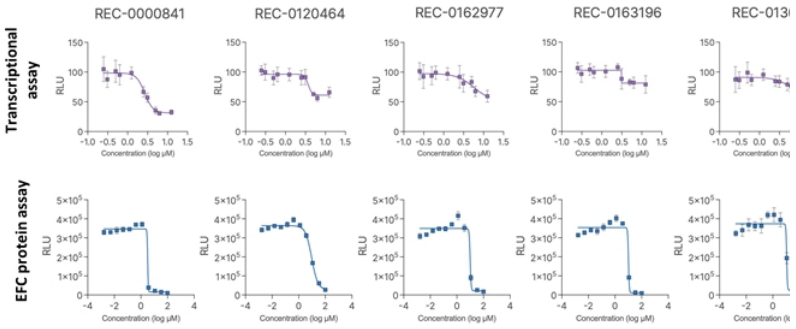
- *MYC* regulates diverse cellular processes involved in oncogenesis
- Gain-of-function alterations and amplifications in *MYC* have been identified in more than 50% of human cancers
- *MYC* pathway activation is observed in tumors harboring alterations in diverse oncogenic mutations, including WNT pathway activation
- *MYC* has remained an important undruggable target in oncology for decades

Summary and differentiation:

- Orally bioavailable, NCE small molecule inhibitors of *MYC* activation would be of broad utility in oncology
- Multiple structural and mechanistic classes have been identified and are being advanced through medicinal chemistry
- One mechanistic class represents a series of molecules that modulate *MYC* degradation (10 unique structural classes)



Subset of inference-based NCE hit molecules with verified activity in *MYC* transcriptional assay and c-Myc EFC[1] protein turnover assay



EU5 is defined as France, Germany, Italy, Spain and the UK. Figure adapted from Qing et al, Signal Transduction & Targeted Therapy, https://doi.org/10.1038/s41392-018-0008-7, 2018; 1. Enzyme fragment complementation

CMT2A: Potential first-in-disease, orally bioavailable disease modifying therapeutic for Charcot-Marie Tooth Disease, Type 2A

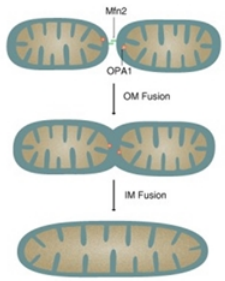
Disease Overview:

- Rare, autosomal dominant, peripheral nerve disease caused by mutations in *MFN2* estimated to affect approximately 15,000 patients in US & EU5 and leads to progressive muscle atrophy in the lower legs and hands

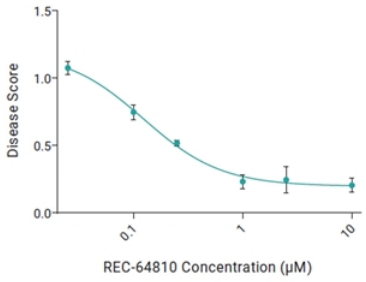
Summary and differentiation:

- Aim to discover and develop the first safe and efficacious, orally bioavailable small molecule disease-modifying therapy for CMT2A
- Multiple lead molecules identified and designed to be peripheral nervous system-penetrant to achieve activity on the affected tissues
- Target a mechanism novel to this disease but with established clinical precedent that supports the CMT2A target product profile

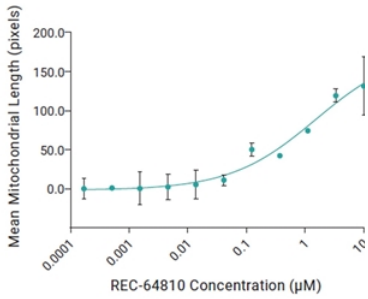
MFN2 activity in mitochondrial fusion



Rescue of *MFN2* cellular phenotype in human cells



Rescue of mitochondrial length in *MFN2*-deficient human cells



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