A Letter from Our Co-Founder and CEO

Dear Shareholders,

As we step into 2025, I want to take a moment to reflect on where Recursion stands today and where we are headed. The future of our company—and of the broader pharmaceutical industry—depends on our ability to maintain an unwavering commitment to a bold, audacious vision. This is even more true in challenging times where funding, both for biotech companies and the early research that drives our industry forward, are facing headwinds. At Recursion, we are driven by a singular mission: to decode biology to radically improve lives. We are harnessing the power of cutting-edge technology, vast datasets, and foundation models to transform the way drugs are discovered and developed. And while we've adjusted our sails to the winds of our industry, capital markets and more, we've never altered our destination. We won't settle for anything less than achieving this mission, and I'm proud to lead a company where we take that approach, from our employees, to our leadership, and to our Board of Directors. Our boldness in the face of stormy weather is one of the things that makes us the leader in TechBio.

Largest merger or acquisition

IN THE TECHBIO SPACE TO DATE WITH EXSCIENTIA

Recursion's commitment to revolutionizing drug development took a major leap forward last year with the announcement of the largest merger or acquisition in the TechBio space to date—our combination with Exscientia. This was not just a transaction; it was the formation of a first-of-its-kind, fully integrated, technology-first drug discovery platform, and it was a transaction that we've known could be transformative for years. By uniting Recursion's strength in scaling biological insights and clinical translation with Exscientia's precision chemistry and small-molecule expertise, we have created a seamless, AI-driven approach spanning from early discovery to clinical development.

Through this combination, we have built a unique full-stack platform. Way back in 2013, we started with a point-solution; leveraging computer vision to unlock all of the information in cell morphology. Our pioneering work in phenomics, which is now a part of nearly every large pharmaceutical company's discovery workstream, was just the beginning. While hundreds of TechBio startups today are optimizing their first point-solution, we've continued advancing our tech-enabled philosophy to build, buy and combine point solutions across virtually all major steps in drug discovery from target discovery to clinical development. We've continued investing, from scaling new high-dimensional -omics assays, to building BioHive-2, the most advanced supercomputer in the pharmaceutical industry, all because we believe more than ever that a technology-driven approach is what will finally unlock the much needed and anticipated shift in the way drugs are discovered and developed.

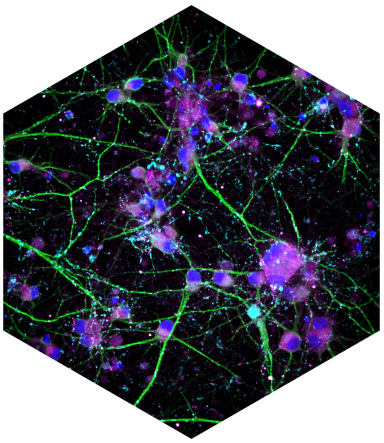
And while I'm proud that we have led the burgeoning TechBio space for more than a decade, I'm even happier to see hundreds of companies, big and small, following in our footsteps. For years we preached the potential of combining sophisticated computational techniques with large biological and chemical dataset creation to a skeptical (and sometimes hostile) audience. Today, the naysayers are part of a slimming minority and the progressive visionaries of the industry are all plotting their path to this inevitable future of drug discovery. The era of TechBio is truly here, and we are proud to be such a big part of it.

10 key clinical milestones

EXPECTED OVER THE NEXT 18 MONTHS

>$450 Million

IN COLLABORATION PAYMENTS TO DATE



A Look Back at 2024: Delivering on the Promise of AI and Data-Driven Drug Discovery

The strength of our approach is evident in our growing portfolio. We now have 10 clinical and preclinical programs, with approximately 10 key clinical milestones expected over the next 18 months. Beyond that, we have more than 10 advanced discovery programs advancing rapidly toward the clinic alongside some incredibly exciting programs and molecules that are a part of our discovery collaborations.

One compelling example is REC-1245, a potential first-in-class RBM39 degrader for biomarker-enriched solid tumors and lymphoma. This program, one of the first to result from our end-to-end AI-enabled platform, leveraged advanced maps of biology to identify RBM39 as a critical target and our early AI-enabled chemistry platform to advance the molecule to candidate. Through preclinical models, we validated that RBM39 degradation disrupts key DNA damage response (DDR) networks, potentially halting cancer growth. The journey from target identification to IND-enabling studies was completed in just 18 months—less than half of the industry average—leading to our first patient being dosed in the fourth quarter of 2024.

Another breakthrough is REC-617, our precision-designed CDK7 inhibitor, which has shown promising interim results in the Phase 1/2 ELUCIDATE trial. Early data demonstrates robust target engagement, a favorable pharmacokinetic and pharmacodynamic profile, and compelling initial clinical activity. Notably, a confirmed partial response was observed in a heavily pre-treated patient with platinum-resistant ovarian cancer, lasting more than six months, alongside four additional patients achieving stable disease. Designed entirely using our AI-led platform, REC-617 was synthesized from hit to candidate in just under 12 months, requiring only 136 novel molecules—an order of magnitude more efficient than conventional drug discovery.

Beyond our own programs, we continue to collaborate with leading biopharma partners like Roche and Genentech, Sanofi, Bayer, and Merck KGaA, Darmstadt, Germany. These partnerships validate our platform and amplify our impact. For example, our collaboration with Roche and Genentech achieved a groundbreaking milestone: the world's first genome-scale Neuromap, a comprehensive AI-powered model of neurobiology built from human-induced pluripotent stem cell (hiPSC)-derived neurons. This effort, which required generating over a trillion neurons, led to a first-of-its-kind neuroscience phenomap that Roche-Genentech optioned for $30 million.

Similarly, our work with Sanofi continues to drive value. In 2024, we received $15 million in milestone payments after advancing two discovery programs into lead optimization, each showing strong differentiation and best-in-class potential. To date, we have generated over $450 million in collaboration payments, not only through upfront payments, but by consistently delivering on milestones, a feat achieved by few other biotech companies in history. As we look ahead, we are well on our way toward unlocking up to $20 billion in potential milestone payments before royalties—fueling the next generation of AI-driven drug discovery and development.

2025 and Beyond: The Dawn of the Virtual Cell

For the small set of leaders in TechBio—spanning companies, institutes and academics - we are converging around a breakthrough in the coming years that has the potential to create a transformational shift. We are approaching a future where many biological processes can be accurately simulated—a concept we call the "virtual cell." Today, our wet labs primarily generate the data needed to train AI models. But in the near future, these labs will primarily validate AI-driven predictions, fundamentally flipping the paradigm of drug discovery.

Four interconnected layers of biology

- **Population-Scale Patient-Level Data**
- **Pathway-Level Data**
- **Protein-Level Insights**
- **Atomistic-Level Simulations**

We believe that achieving this vision will require excellence across four interconnected layers of biology:

1. **Population-Scale Patient-Level Data:** Thanks to the genomic revolution and the progressive thinking of a small number of governments around the world, we and many others have had access to population-scale -omics data from patients. In the last 18 months, we have dramatically expanded the power of our approach by signing deals with companies like Tempus and Helix to bring tens of petabytes of proprietary data to support our discovery and development.
2. **Pathway-Level Data:** We are far ahead in systematically mapping gene networks across multiple cellular contexts, using techniques like whole-genome CRISPR knockout and high-dimensional -omics analysis across hundreds of millions of proprietary experiments.
3. **Protein-Level Insights:** AlphaFold and similar tools have revolutionized protein modeling. By integrating state-of-the-art protein-protein interaction and ligand-binding predictions, we remain at the forefront of this rapidly evolving space.
4. **Atomistic-Level Simulations:** With Exscientia's quantum mechanics/molecular dynamics (QM/MD) expertise now part of Recursion, we are uniquely positioned to lead in simulating molecular interactions at atomic precision.

By integrating these layers, Recursion is building one of the most advanced predictive models of human biology ever created. This will allow us to explore the vast landscape of potential drugs and disease mechanisms in *silico* before ever stepping into the lab—dramatically accelerating drug development timelines and reducing costs.

Transforming Clinical Development with AI and Automation

In 2025, we are also doubling down on transforming clinical development through our ClinTech platform, powered by AI, automation, and real-world evidence. Our partnerships with Tempus, Helix and a growing cohort of other data sources provide us with access to critical patient data, allowing us to:

- Use AI-driven simulations to optimize trial design and enhance our probability of success.
- Automate critical processes like patient recruitment and site activation, dramatically reducing enrollment timelines.
- Leverage real-world evidence to inform regulatory strategies and increase the likelihood of clinical success.

And through partnerships with Faro Health and other industry leaders, we are industrializing clinical workflows, reducing trial costs, and streamlining operations—all while increasing the speed at which we bring new medicines to patients. We are in the early days of this work, but I am so excited at the potential I am already seeing. Coupling these advances with our discovery and translational platform will magnify all of our clintech work and continue to accelerate our lead in the TechBio space.

"This is not just about technology for the sake of technology. It is about ensuring that the boldest ideas in biotech are realized and that the future of medicine is shaped by those who are willing to embrace the extraordinary."

The Future of TechBio: A Call to Boldness

The path we are charting is not an easy one. It is filled with challenges, and it requires taking risks that others shy away from. But if we are to fulfill our promise—to revolutionize drug discovery and improve patient lives at scale—we must push forward with conviction.

This is not just about technology for the sake of technology. It is about ensuring that the boldest ideas in biotech are realized and that the future of medicine is shaped by those who are willing to embrace the extraordinary. As we step into 2025, I am more confident than ever that Recursion is leading the way. With a solid foundation, a world-class team, and a relentless commitment to innovation, we are poised to make this year our most transformative yet.

Thank you for your continued belief in our mission. Together, we are unlocking the future of medicine.

Chris Gibson, Ph.D.
Founder and CEO, Recursion

Item 1. Business.

Recursion At-a-Glance

The Problem

Discovering and developing effective new medicines is among the most challenging human pursuits due to the incredible complexity of biology, the vastness of chemical space, and both the ineffectiveness and inefficiencies in clinical development. Today more than 90% of clinical trials fail.

Our Mission and Philosophy

Recursion was founded in 2013 to decode biology to radically improve lives by building the next generation biopharma company from the ground-up, leveraging the latest technology tools to help map and navigate the incredible complexity of biology, vastness of chemical space, and the broken drug development process. We believe that rapid commoditization of artificial intelligence creates a once-in-a-generation market opportunity for companies with the ability to build the right datasets in biology and chemistry to win.

Our Competitive Advantage

That's why we have invested heavily in creating one of the most sophisticated automated wet-laboratories in the world where robots and sensors help us conduct and digitize millions of real-life experiments each week, spanning cellular systems, chemical systems, tissue systems, and animal models. We also partner with select companies to aggregate and relate data from patients and health systems at scale. In addition, we command industry-leading computational capabilities including BioHive-2 (the fastest supercomputer wholly owned and operated by any biopharma company), and employ hundreds of data scientists, software engineers, and AI researchers who build software to automate our work and foundational AI models that help us see patterns in our data at scale. Together our laboratories, data, software, compute, and team comprise what we believe is one of the most sophisticated operating systems for drug discovery on earth, The Recursion OS.

How we Create Value

We leverage the Recursion OS to deliver value in three ways: 1) our own pipeline of clinical and preclinical potential medicines focused in precision oncology, rare disease, and other niche areas of unmet need; 2) by discovering new medicines with large biopharmaceutical companies in some of the biggest areas of unmet need like neuroscience and inflammation; and 3) by leveraging our tools, technology, and data for the benefit of other partners in targeted and limited ways.

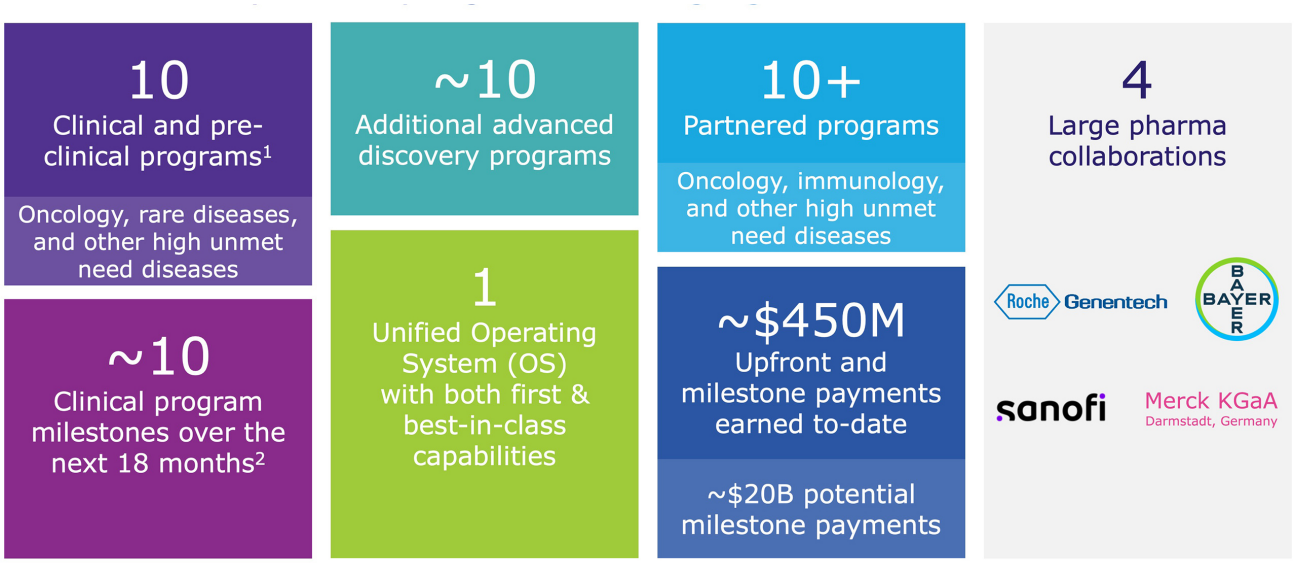


Figure 1. Portfolio poised for value creation from a unified operating system. [1]Includes preclinical programs (programs expected to enter the clinic within the next 18 months). [2]Program milestones include data readouts, preliminary data updates, regulatory submissions, trial initiation, etc.

2024 Highlights & Progress

In 2024, we accelerated the next wave of AI-driven drug discovery and development, delivering key milestones across multiple clinical programs, advancing our transformative partnerships, unveiling major breakthroughs in foundation models, and by consolidating some of the best tools, technologies, and talent into what we believe is the leading company in the burgeoning field of TechBio.

Advancements in the Pipeline:

- **REC-617:** A potential best-in-class CDK7 inhibitor optimized using our AI platform, delivered early Phase 1/2 results demonstrating promising safety and preliminary efficacy, including a durable partial response in a late-stage metastatic ovarian cancer patient and stable disease across four other patients with solid tumors (e.g. CRC, NSCLC)
- **REC-994:** A potential first-in-disease oral superoxide scavenger for symptomatic CCM, confirmed safety and tolerability of chronic dosing in a Phase 2 study, with exploratory analyses suggesting lesion volume reduction on MRI and symptom stabilization as evaluated by change in mRS scores
- **Clinical Advancements and Regulatory Milestones:** Initiated three clinical studies: DAHLIA (Phase 1/2, REC-1245 for solid tumors and lymphoma), TUPELO (Phase 1b/2, REC-4881 for FAP), and ALDER (Phase 2, REC-3964 for recurrent *C. difficile* infection), received IND clearance for REC-4539 (small cell lung cancer), CTA approval for REC-3565 (b-cell malignancies), and progressed REC-4209 (idiopathic pulmonary fibrosis) to IND-enabling studies

Advancements in Partnerships:

- **Roche and Genentech:** Generated whole-genome and chemical perturbation maps in a gastrointestinal oncology indication and a whole genome neuroscience phenomap. The neuro phenomap resulted in the exercise of a $30M milestone
- **Sanofi:** Achieved $15M in milestones, advancing multiple targets in immunology and oncology into lead optimization
- **Bayer:** Completed 25 multimodal oncology data packages and delivery of LOWE, our LLM-orchestrated workflow software, to enhance research capabilities
- **Merck KGaA (Darmstadt, Germany):** Advanced alliance to identify first-in-class or best-in-class targets across oncology and immunology

Advancements in Platform:

- **Full Stack AI Powered Platform:** Our constantly evolving Recursion OS spans target discovery through clinical development, enabling efficient molecule design and testing for both first-in-class and best-in-class opportunities
- **Breakthroughs in Foundation Models:** We've developed both unimodal and multimodal AI models like Phenom, MolPhenix, and MolGPS that accelerate our ability to make high-confidence predictions in our therapeutics programs
- **Advancement in Causal AI Models:** Through collaborations with Tempus and Helix, we integrate real-world, scaled patient datasets with our proprietary internal data to deepen biological insights and better match our therapeutic candidates with target populations
- **Emerging Focus on ClinTech:** We are using AI and machine learning to optimize clinical trial design, accelerate patient enrollment, and enhance evidence generation through data-driven methodologies

What's Next

In 2025, we plan to accelerate our pipeline with additional clinical readouts, deepen existing partnerships, and further expand our proprietary data suite. We anticipate up to 10 additional clinical program milestones over the next 18 months, exciting milestone achievements in our R&D collaborations, and continued breakthroughs in AI-driven discovery, advancing our mission to decode biology to radically improve lives. Significant milestones from our portfolio of pharma R&D partnerships and a focus on monetizing select assets in our pipeline will help to subsidize continued investment to expand our leading position in the TechBio space, which we view as a generational opportunity for value creation.

Business Overview

Recursion is a leading clinical stage TechBio company with a mission to decode biology to radically improve lives. We aim to achieve our mission by industrializing drug discovery using the Recursion Operating System (OS), a vertical platform of diverse technologies that enables us to map and navigate trillions of biological, chemical, and patient-centric relationships utilizing approximately 65 petabytes of proprietary data.

The Recursion OS integrates 'Real World' data generated in our own wet-laboratories or by select partners and a 'World Model' which is a collection of AI computational models we also build in-house. Today, our scaled 'wet-lab' biology, chemistry, and patient-centric experimental data feed our 'dry-lab' computational tools to identify, validate, and translate therapeutic insights, which we can then validate in our wet-lab to both advance drug discovery programs and to generate data to further refine our world model.

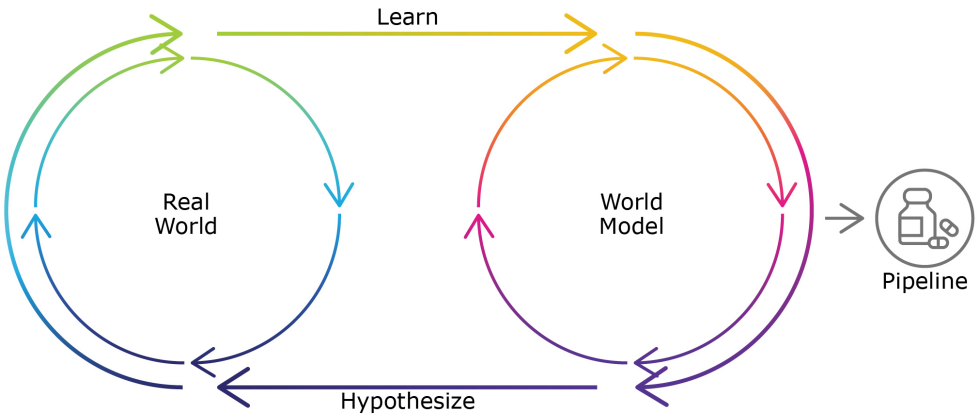


Figure 2. The Recursion OS. Recursion generates massive quantities of rich, high-dimensional real world –omics data (e.g., phenomics, transcriptomics and proteomics) and chemical data. We build and train ML and AI models that take the data and learning from the real world to understand and identify patterns and insights, using the fastest supercomputer wholly owned and operated by any pharmaceutical company globally (based on available data). This creates a virtuous cycle of learning and iteration based on real-world data and models that learn to simulate that real world. This virtuous cycle, i.e., the Recursion OS, generates value through our pipeline, in addition to building pipelines for our partners.

We have demonstrated that the Recursion OS already accelerates the timelines and scale of drug discovery, and we hope to prove in the coming years that we not only meet the industry average probability of success in clinical development but exceed it. If successful in achieving our mission, we may be able to build one of the most valuable businesses in our industry while also improving the lives of patients and pushing down the cost of healthcare.

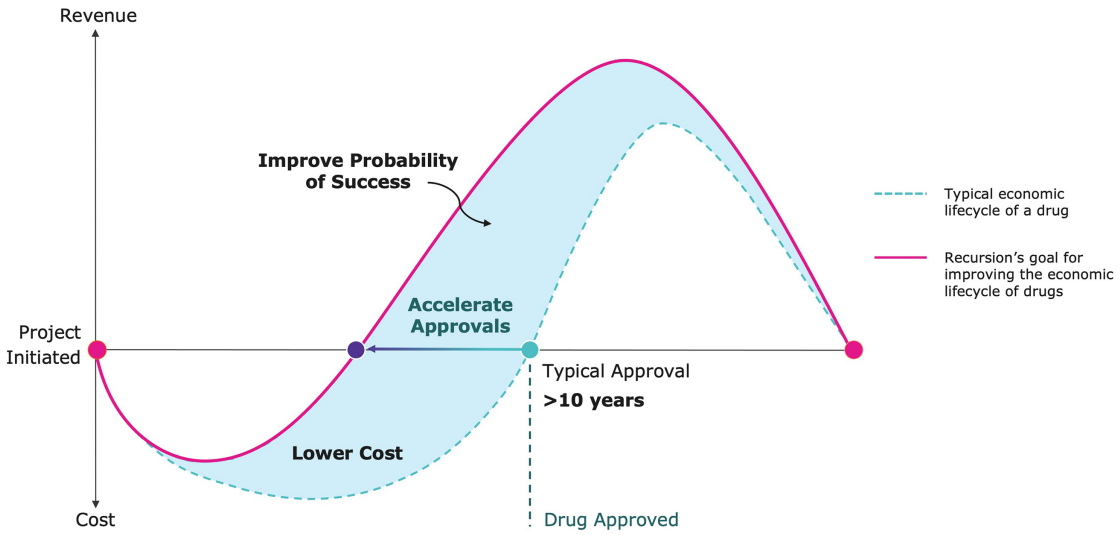


Figure 3. Over time, we believe our transformational way of designing and developing drugs can change the industry's underlying pharmacoeconomic model, what we call 'shifting the curve'. We aim to demonstrate that it is simultaneously possible to improve probability of success through designing better quality drugs while also reducing investment requirements through improved technologies and process. Recursion was created to take advantage of the discontinuity between these fields and harness the power of accelerating technological innovations to improve the efficiency of drug discovery and development.

The Recursion OS – A Platform that Powers a Portfolio

The Recursion OS is a full-stack solution delivering technology-enabled first-in-class and best-in-class molecules with speed, efficiency, and scale from target discovery through early clinical development. We generate and aggregate enormous quantities of high-quality, high-dimensional data spanning hundreds of millions of cellular perturbations across biology and chemistry, translational experiments, ADMET experiments, in vivo experiments, patient data, and from scaled automated chemical synthesis. In parallel, we have built foundation models that leverage those data to learn and understand the underlying biological and chemical interactions with broad predictive capabilities.

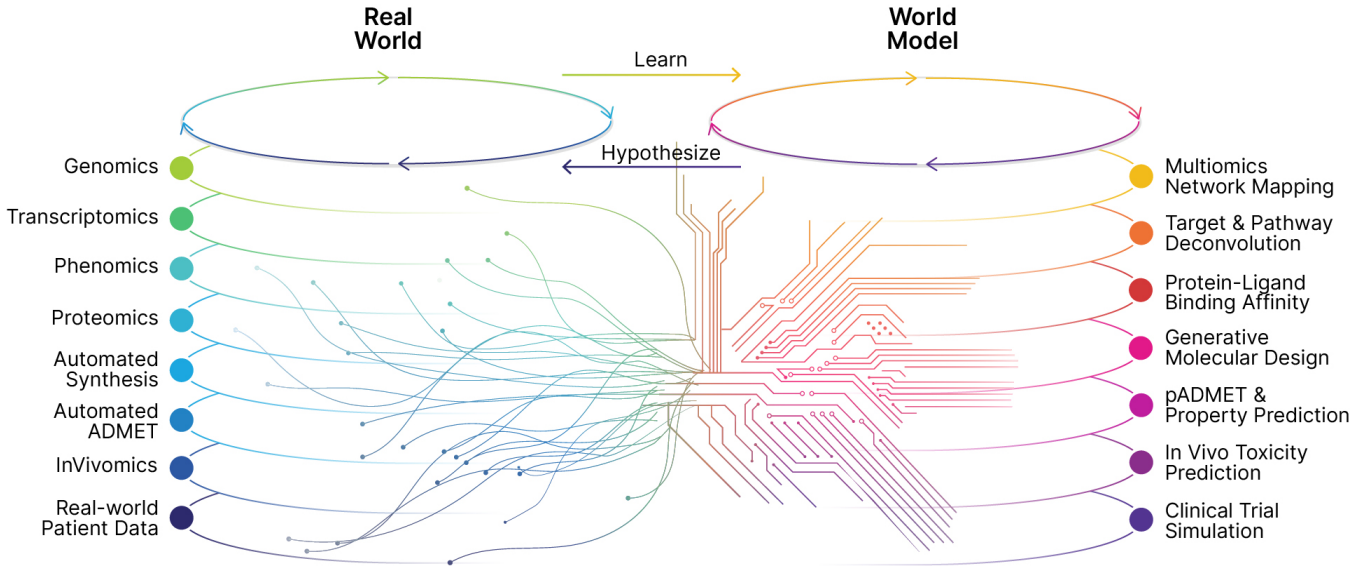


Figure 4. Recursion's World Model approach (1) Profile biological and chemical systems using automation to scale a small number of data-rich assays, including phenomics, transcriptomics, InVivomics, and ADME to generate massive, high quality empirical data; (2) aggregate and analyze the resultant data using a variety of machine learning models, in a process coordinated with in-house software systems and tools; and (3) map and navigate leveraging proprietary software tools to infer properties and relationships in biology and chemistry. These inferred properties and relationships serve as the basis of our ability to predict how to navigate between biological states using chemical or biological perturbations, which we can then validate in our automated laboratories, completing a virtuous cycle of learning and iteration.

Our competitive advantage compared to the hundreds of companies both large and small that seek to follow our path is the intense focus and early success in verticalizing this approach. The company began by pioneering a point solution to scaled target discovery and hit ID based on phenomics, the use of cell morphology and computer vision. Today, we are generating, aggregating, or simulating data from patients to cells, cells to pathways, pathways to proteins, proteins to atomistic interactions, cells to organoids, organoids to animals, and animals to people in the clinic. We're systematically capturing complex, high-dimensional datasets, training specialized machine learning and AI models, and building foundation models that synthesize insights across diverse data layers. As we combine and coalesce these foundation models, spanning target discovery through clinical development, we are increasingly building a 'world model' that contains within it a virtual representation of how biology and chemistry are working. Today, our world model is enabling us to make many high-confidence predictions about the result of previously untried or untested questions.

In the coming years we believe that our world model will attain a level of understanding of biology and chemistry of sufficient quality that our wet lab will move from data generation for model improvement as its primary use to 'scaled validation of simulated solutions.' In essence, our world model will become a 'virtual cell' where we can simulate an inexhaustible quantity of 'experiments,' identify those targets and chemistries that have the highest probability of success in modulating disease and achieving a desired (and automatically generated) Target Product Profile, and then our wet lab can validate those predictions at scale.

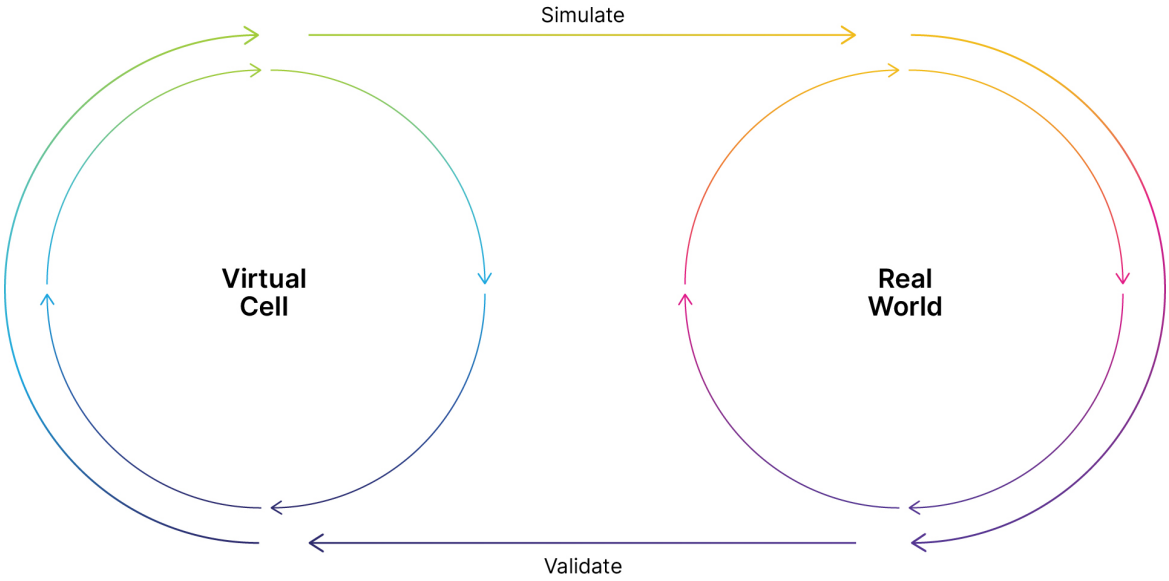


Figure 5. Over time, models can become broadly applicable and performant enough to be the first rather than last step in the process, that is "move to the left" in the diagram, with Real World Models serving to validate individual insights "on the right."

Building a Pipeline

Building on a first-in-class and best-in-class OS platform after the business combination with Exscientia, Recursion's pipeline now encompasses 10 clinical and preclinical programs and over 10 advanced discovery programs across oncology, rare diseases, and other areas of high unmet need. This broad and rapidly evolving portfolio reflects our commitment to advancing discovery and clinical development through unbiased, scaled scientific insights and AI-driven discovery. Programs in our internal pipeline are built on unique biological and chemical insights surfaced through the Recursion OS where:

- The etiology of the disease is well defined, but the subsequent impacts of the disease are generally obscure and/or the primary targets are typically considered undruggable,
- There is a high unmet medical need, no approved therapies, or significant limitations to existing treatments.

	Candidate	Target	Indication	Preclinical	IND-Enabling	Phase 1/2	Pivotal / Phase 3
ONCOLOGY	REC-617	**CDK7**	Advanced solid tumors[1]	ELUCIDATE			
	REC-1245	**RBM39**	Biomarker-enriched solid tumors & lymphoma	DAHLIA			
	REC-3565	**MALT1**	B-cell malignancies	EXCELERIZE			
	REC-4539	**LSD1**	Small-cell lung cancer (SCLC)	ENLYGHT			
RARE	REC-994	**Superoxide**	Cerebral cavernous malformations (CCM)	SYCAMORE			
	REC-4881	**MEK1/2**	Familial adenomatous polyposis (FAP)	TUPELO			
	REC-2282	**HDAC**	Neurofibromatosis type 2 (NF2)	POPLAR			
	REV102[2]	**ENPP1**	Hypophosphatasia (HPP)				
OTHER	REC-3964	**TcdB**	Prevention of recurrent *C. difficile* (rCDI)	ALDER			
	REC-4209	**Undisclosed**	Idiopathic pulmonary fibrosis (IPF)				
	~10 advanced discovery programs including a PI3Kα H1047Ri						

Figure 6. The power of our Recursion OS exemplified by our expansive therapeutic pipeline. [1]Includes non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer. [2]Joint venture with Rallybio.

Advancing our Pipeline

We are accelerating critical clinical milestones while delivering measurable progress against diseases with high unmet medical needs. At the same time, we continue to validate various components of the Recursion OS, which has played a role in advancing every program in our portfolio, reinforcing its potential to accelerate drug discovery and development.

We have already demonstrated promising safety and preliminary efficacy data for two of our programs. REC-994, a superoxide scavenger in development as a potential first-in-disease therapy for symptomatic CCM, was featured in a late-breaking oral presentation at the 2025 International Stroke Conference. Phase 2 data highlighted MRI-based lesion volume reduction and symptom stabilization trends. Next steps in this program will be informed by regulatory discussions and long-term extension data expected in 2025. REC-617, a potential best-in-class CDK7 inhibitor has demonstrated early clinical activity in advanced solid tumors, including a durable partial response in metastatic ovarian cancer and stable disease across patients with multiple tumor types. These findings support further clinical development as we continue to explore its potential in combination regimens.

In parallel, Recursion has recently initiated three other clinical studies: DAHLIA (Phase 1/2, REC-1245 for solid tumors and lymphoma), TUPELO (Phase 1b/2, REC-4881 for FAP), and ALDER (Phase 2, REC-3964 for prevention of recurrent *C. difficile* infection). Additionally, REC-3565 (B-cell malignancies) and REC-4539 (SCLC) are expected to enter dose escalation studies. REC-4209 (idiopathic pulmonary fibrosis) has progressed to IND-enabling studies and REV102 (HPP) IND-enabling studies have been initiated, further expanding our pipeline across oncology, rare diseases, and other areas of high unmet need.

Anticipated Near-term Catalysts. Recursion is poised for a catalyst-rich period, with multiple programs reaching critical milestones over the next 18 months. REC-3565 (MALT-1i) will enter Phase 1 for B-cell malignancies, with the first patient expected to be dosed in the first half of 2025. REC-617 (CDK7i) will initiate combination studies in advanced solid tumors in the first half of 2025. REC-4881 (MEK1/2i) will report Phase 1b/2 safety and early efficacy data for FAP during the same period. REC-2282 (HDACi) for NF2-related meningioma will undergo PFS6 futility analysis and REC-4539 (LSD-1i) will begin Phase 1 dose escalation in SCLC during the same period. Additional Phase 1 data from the ELUCIDATE trial for REC-617 (CDK7i) in advanced solid tumors is expected in the second half of 2025. Furthermore, we continue to rapidly advance development programs such as a PI3Kα H1047Ri and an ENPP1i towards the clinic.

Impact Through Partnerships

Through our business combination with Exscientia, we have doubled our partnership footprint with leading pharmaceutical companies including Roche and Genentech, Sanofi, Bayer and Merck KGaA (Darmstadt, Germany), securing $450M million in upfront milestone payments to date with the potential for over $20 billion in additional milestones before royalties. These global collaborations not only provide near-term cash flows but also combine our scaled biology, precision chemistry, and automated synthesis capabilities to pave the way for transformative therapies in oncology, neuroscience, immunology, and other therapeutic areas with high unmet need. By partnering with some of the best biopharmaceutical companies on earth in their respective areas, our platform and team have an opportunity to learn from some of the most experienced teams in the industry. By uniting our AI-driven platforms, vast proprietary data, and deep scientific expertise, we continue to unlock powerful innovations and expand patient impact. Below are some of the latest developments illustrating this momentum:

Roche and Genentech

- **Gastrointestinal-Oncology Advancements:** In partnership with Roche and Genentech, we generated multiple whole-genome phenomaps with chemical perturbations across various disease-relevant cell types, enabling deeper insights into how different cellular contexts respond to gene knockouts and chemicals.
- **Neuro-specific CRISPR KO Phenomap:** In partnership with Roche and Genentech, we have developed the first whole-genome CRISPR knockout map in neural iPSC cells, providing valuable data to identify potential new targets in neuroscience, an area with limited new discoveries.
- **Milestones and Collaboration:** The neuroscience phenomap work led to a $30M option from Roche and Genentech in August 2024, and we're moving forward with target validation projects.

Sanofi

- **Immunology & Oncology Achievements:** We reached milestones in three programs, generating $15M in aggregate payments from Sanofi for two of these programs in 2024.

Bayer

- **Oncology Achievements:** Completed 25 multimodal oncology data packages utilizing the Recursion OS platform. Multiple programs rapidly progressing to Lead Series nomination.
- **LOWE:** Additionally, Bayer was the first beta-user of our LOWE LLM-orchestrated workflow software to enhance their research capabilities.

Merck KGaA (Darmstadt, Germany)

- Our ongoing alliance with Merck KGaA, Darmstadt, Germany is focused on leveraging Recursion's discovery engine to identify first-in-class and best-in-class targets across oncology and immunology, driving innovation in these key therapeutic areas.

Leading indications of success in our business combination with Exscientia

We believe that to truly redefine the way drugs are discovered and developed, we need to build technology tools and data across the full-stack of drug discovery and development. Doing this well also requires the best talent from across many different fields. While Recursion has, in our view, achieved more than any other TechBio company, we constantly survey the market to find potential opportunities to augment and accelerate our business. The business combination with Exscientia was one such opportunity, bringing together the best biology-first TechBio platform in Recursion and one of the most comprehensive chemistry-first TechBio platforms in Exscientia, a compelling set of both first and best-in-class clinical programs, sector-leading partnerships and some of the best talent in the industry.

Given the compressed timeline between signing and close of the transaction (just over 3 months), prior to the close we prioritized in-depth assessments of each company's programs, partnerships, technology, capabilities, and ways of working. With this information in hand, we then conducted an organizational design process that allowed us to provide go-forward status and role clarity for each employee within 48 hours of close. We also outlined a set of goals to be accomplished in the first 90 days post close that will help us rapidly demonstrate the exponential value of the business combination and help employees to rapidly integrate across teams, portfolio, partnerships, and technologies. We are already seeing the benefits of this approach in terms of amplifying delivery, though much more work remains to be completed through 2025.

In the weeks post-close we focused on ensuring all employees understood where they were situated within the go-forward organization (role, manager, etc.) and connected them with new members of their teams. We wrapped 2024 with a 2-day Welcome Event in London, giving former Exscientians the opportunity to learn about Recursion, meet new colleagues across a variety of teams, celebrate their contributions to the deal close, and begin to shift their professional identity to that of a Recursionaut.

90 Day Goals

Before the transaction closed, we established a set of key goals to be achieved within approximately 90 days. These goals were designed to quickly demonstrate early indicators of the value of combining the companies. The goals largely focus on deploying relatively mature and unique elements of each company's technology to accelerate the other party's programs and processes. These goals also require key members of each legacy team to sprint together, accelerating the team forming and norming process. Key updates are as follows:

Pipeline

Using Recursion's causal AI to optimize Exscientia clinical programs - LSD1 Patient Stratification:

- Recursion is utilizing AI models and Tempus data to build a patient stratification framework in small cell lung cancer (SCLC). This work is informing clinical strategies for the planned REC-4539 Phase 1 study that originated at Exscientia and is commencing in the first half of 2025.
- We have expanded this work to explore indications for REC-4539 beyond SCLC and laboratory validation work is beginning imminently.
- This work will be used as a template to expand causal modeling for many programs beyond LSD1.

Use Exscientia's Centaur Platform to Accelerate Recursion's Internal Programs:

- Programs from legacy Recursion in early chemistry design cycles have already entered Exscientia's Centaur precision chemistry platform, where significant improvements in potency have been demonstrated.
- Advanced protein structure predictions are guiding compound optimization, aiming to enhance binding conformation and optimize key properties.
- In-progress synthesis and cryo-EM work are enhancing our understanding of binding interactions, informing the next design cycles and optimizing compound characteristics.

Partnerships

Use Recursion's Maps of Biology to Identify New Targets for Legacy Exscientia Partners:

- The Recursion OS has been used to identify hit compounds in 7 immune-relevant targets or dual target pairs and early validation work has commenced to prepare reports for our partners.

Accelerate Recursion's Partnered Programs Leveraging Exscientia's Centaur Chemistry Platform:

- We integrated Centaur into more than 10 design cycles for programs Recursion has previously partnered, with early validation work achieved and progress accelerating across multiple additional partnered programs.
- We have successfully delivered compounds for wet-lab testing on Recursion's platform using the legacy Exscientia automated synthesis platform for partnered programs.
- Applied a newly built pipeline using structural bioinformatics and molecular dynamics for more precise compound design, focused on addressing specific design challenges on partnered programs.

Platform

Incorporate Exscientia Tech into Recursion's Workflows:

- Reduced manual effort by 60% for evidence collection for hit nomination packages supporting entry into hit-to-lead, through knowledge graphs and LLM-based data aggregation with further reduction expected with additional data layers.
- Mapped 1.4 million active ligands to binding pockets for structure-based drug discovery and target deconvolution.
- Working to leverage Exscientia's tools to achieve a 75% reduction in time-to-program nomination by increasing alignment with portfolio strategy and bridge phenotypic- to target-based drug discovery and facilitating target-centric and structure-based drug discovery within Centaur Chemist.

Integrate Recursion models into Centaur:

- To augment Exscientia's chemical design platform with additional filters, experimental data for >950,000 compounds profiled in living cells were used to build two new models for (1) measurable cellular activity and (2) cytotoxicity. These large datasets provide highly generalizable models demonstrating a >2.5x increased efficiency in detecting new bioactive scaffolds with a >40% reduction in the flagging of likely cytotoxic compounds.
- 18 new combined ADMET data products and respective models representing the combined organization's datasets, and five program-specific phenomics response models have been added to Centaur, enabling use of legacy Exscientia's active learning based precision design technology with Recursion internal programs.

Corporate Updates

- In order to continue to streamline its operations and focus on its core geographic footprint, the Company's fully owned subsidiary, Exscientia AI Limited ("EXAI"), will carve out its Austrian operations. On February 27, 2025, the Company entered into an agreement to invest in and acquire 49% of the share capital of Alpha Biotechnology GmbH ("Alpha"), an Austrian startup that will leverage a patient-tissue platform for the development of precision therapeutics for the treatment of hematological and solid cancers, while focusing its efforts and moderating spend. Alpha will in turn acquire 100% of the share capital of Exscientia GmbH, a wholly-owned Austrian subsidiary of EXAI which holds certain intellectual property assets crucial to Alpha's operations and business activities. The closing of the transaction is expected in the first half of 2025, subject to customary closing conditions.

A clear vision, durable mission and a focus on people and culture drive success

Recursion was founded in 2013 with a vision to capitalize on the convergence of advancements in computation and machine learning to address the decreasing efficiency of drug discovery and development. We believe that this opportunity represents one of the most positively impactful applications of ML and AI. Our vision is to leverage technology to map and navigate biology, chemistry, and patient-centric outcomes to increasingly transition the process of developing medicines from discovery to design. We believe that advanced computational approaches, massive datasets or human intelligence alone cannot fundamentally shift the efficiency curve of drug discovery and development; instead, we believe that those companies that augment their teams with sophisticated computational tools and focus deeply on generating and aggregating the right datasets will have a significant advantage. Our success and the success of the burgeoning TechBio sector has the promise to drive more, new, and better medicines to patients at higher scale and lower prices in the coming decades. We are working to not only lead this space – but define it.

Our mission at Recursion, ***Decoding Biology to Radically Improve Lives,*** flows naturally from our vision. We interpret our mission expansively and believe it to be a durable direction and source of inspiration for our team. We seek not only to radically improve the lives of patients who could benefit from the medicines we help to deliver, but the lives of those who care for those patients, the lives of our employees and their families, as well as the communities in which we operate our company.

We've intentionally designed our culture to fuel the pursuit of our mission. Our Founding Principles are guideposts for scientific and technical decisions and our Values underpin how our employees engage day-to-day with colleagues inside and outside the company. The Recursion Mindset, a deep commitment to achieving impact at unprecedented scale through new industrialized approaches, is an essential component of building our TechBio ecosystem. Our employees bring all these to life, contributing their unique expertise and experiences from their incredible breadth of fields and industries. For all of our employees, Recursion is a unique company with a different way of working.

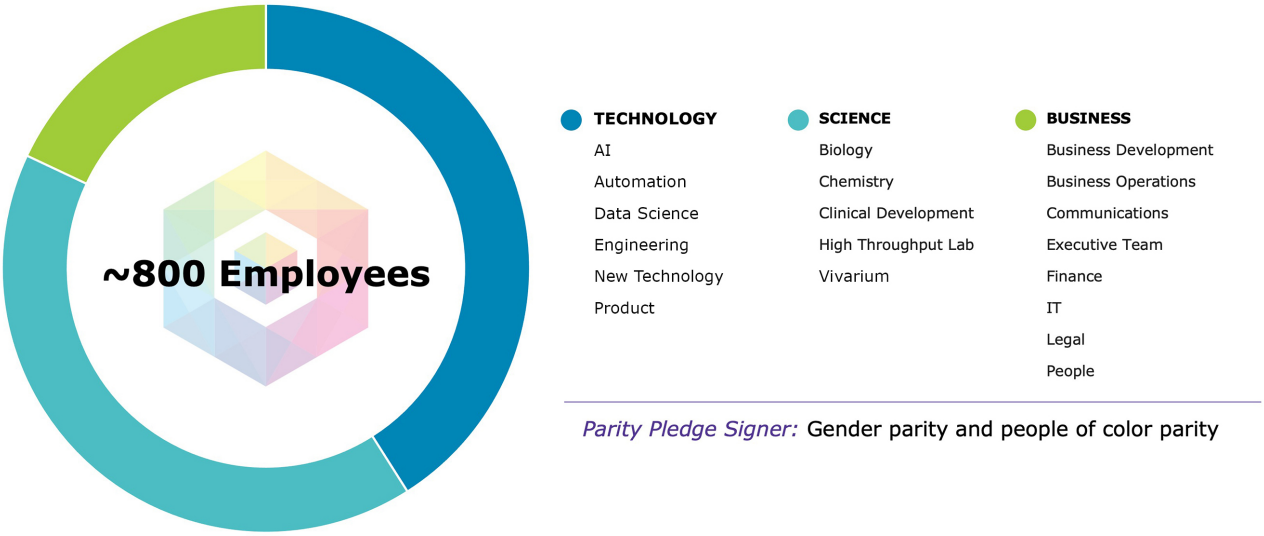


Figure 7. Recursion's team requires operating at the interface of many diverse fields. Building a TechBio company requires fluency in operating at the interface of many disciplines and fields not previously attuned to working as closely in traditional biopharma.

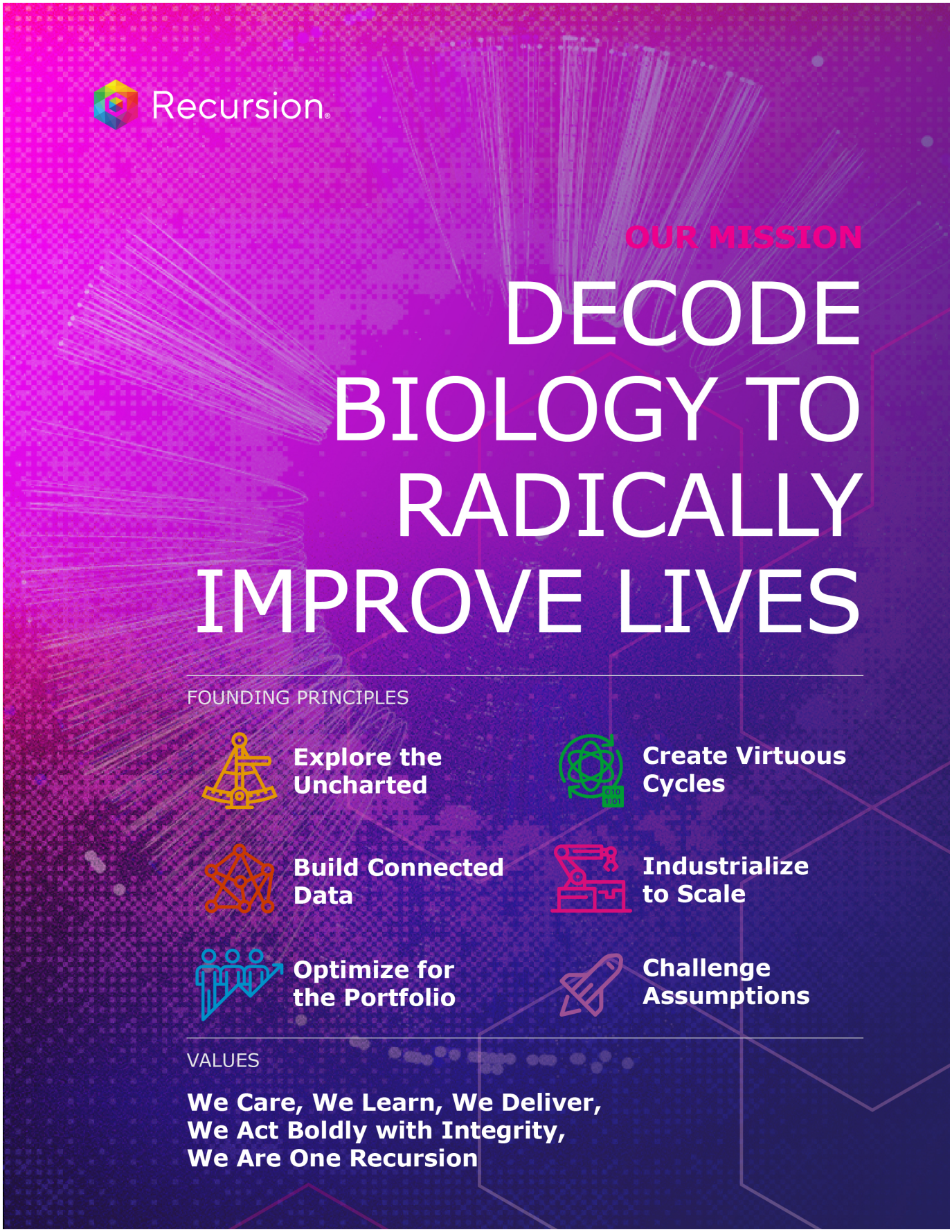


Figure 8. Recursion's Founding Principles and Values support our ambitious mission. Together, these elements shape Recursion's culture by guiding our people to high-impact decision-making and behaviors.

Recursion In-Depth

TechBio: The Industrialization of Drug Discovery and Development Problem

The traditional drug discovery and development process is characterized by substantial financial risks, with increasing and long-term capital outlays for development programs that often fail to reach patients as marketed products. Historically, it has taken over ten years and an average capitalized R&D cost of approximately $2 billion per approved medicine to move a drug discovery project from early discovery to an approved therapeutic. Such productivity outcomes have culminated in a rapidly declining internal rate of return for the biopharma industry.

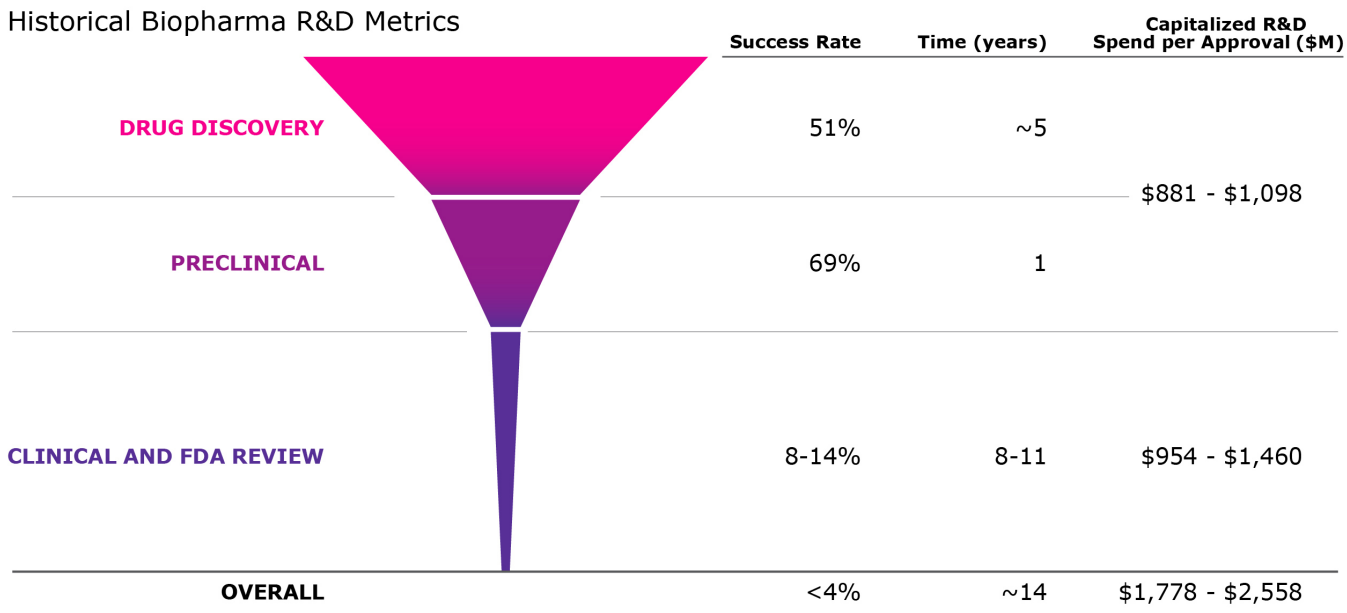


Figure 9. Historical biopharma industry R&D metrics. The primary driver of the cost to discover and develop a new medicine is clinical failure. Less than 4% of drug discovery programs that are initiated result in an approved therapeutic, resulting in a risk-adjusted cost of approximately $2.3 billion per new drug launched.[1,2,3,4,5]

Despite significant investment and brilliant scientists, these metrics point to the need to evolve a more efficient drug discovery process and explore new tools. Traditional drug discovery relies on basic research discoveries from the scientific community to elucidate disease-relevant pathways and targets to interrogate. Coupled with biology's incredible complexity, this approach has forced the industry to rely on reductionist hypotheses of the critical drivers of complex diseases, which can create a 'herd mentality' as multiple parties chase a limited number of therapeutic targets. The situation has been exacerbated by human bias (e.g., confirmation bias and sunk-cost fallacy). Accentuating this problem, the sequential nature of current drug discovery activities and the challenges with aggregation and interoperability of data across projects, teams and departments lead to frequent replication of work and long timelines to discharge the scientific risk of such hypotheses. Despite decades of accumulated knowledge, the result is that drug discovery has unintentionally created hurdles for innovation.

Simultaneously, exponential improvements in computational speed and reductions in data storage costs driven by the technology industry, coupled with the rapid rise of LLMs, generative AI and other ML tools, have transformed complex industries from media to transportation to e-commerce. Historically, the biopharma sector has been slow to embrace such innovations. Over the past 2-3 years, there have been remarkable shifts in perception among technology and biopharma companies as well as among regulators and policymakers, who highlight the utility of AI/ML for broad drug discovery and development from novel target discovery to automated chemistry synthesis and next-generation manufacturing. We believe this rapid acceleration and adoption of these technologies demonstrates the growing consensus that AI/ML is a catalyst for substantial leaps in drug discovery.

1 *Zhou, S. and Johnson, R. (2018). Pharmaceutical Probability of Success. Alacrita Consulting, 1-42*
2 *Steedman M, and Taylor K. (2024). Measuring the return from pharmaceutical innovation. Deloitte. 1-28.*
3 *DiMasi et al. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of Health Economics. 47, 20-33.*
4 *Paul, et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Reviews Drug Discovery. 9,203-214*
5 *Martin et al. (2017). Clinical trial cycle times continue to increase despite industry efforts. Nature Reviews Drug Discovery. 16, 157*

Opportunity

Late-stage clinical failures are the primary driver of reduced impact and IRR in today's pharmaceutical R&D model. Reducing the rate of costly, late-stage failures would be the most compelling way to achieve a more productive drug discovery and development process, though expanding the areas of biology that can be explored, accelerating the timeline from hit to a clinical candidate, decreasing the costs of discovery and creating more scalable systems would also create a more sustainable R&D model, all else held equal. To achieve this more sustainable model, we believe that in its ideal state, a drug discovery funnel would morph from the being shaped like the letter 'V' to being shaped like the letter 'T,' where a broad set of possible therapeutics could be narrowed rapidly to the best candidate in a scaled and efficient way. Subsequently, programs that advance through the remaining steps of the discovery and development process would proceed quickly and with no attrition. While such a path is impossible to fully achieve, rapidly improving technology tools across biology, chemistry and computation are creating the conditions where, in the right hands, progress towards this 'T'-shaped funnel is possible.

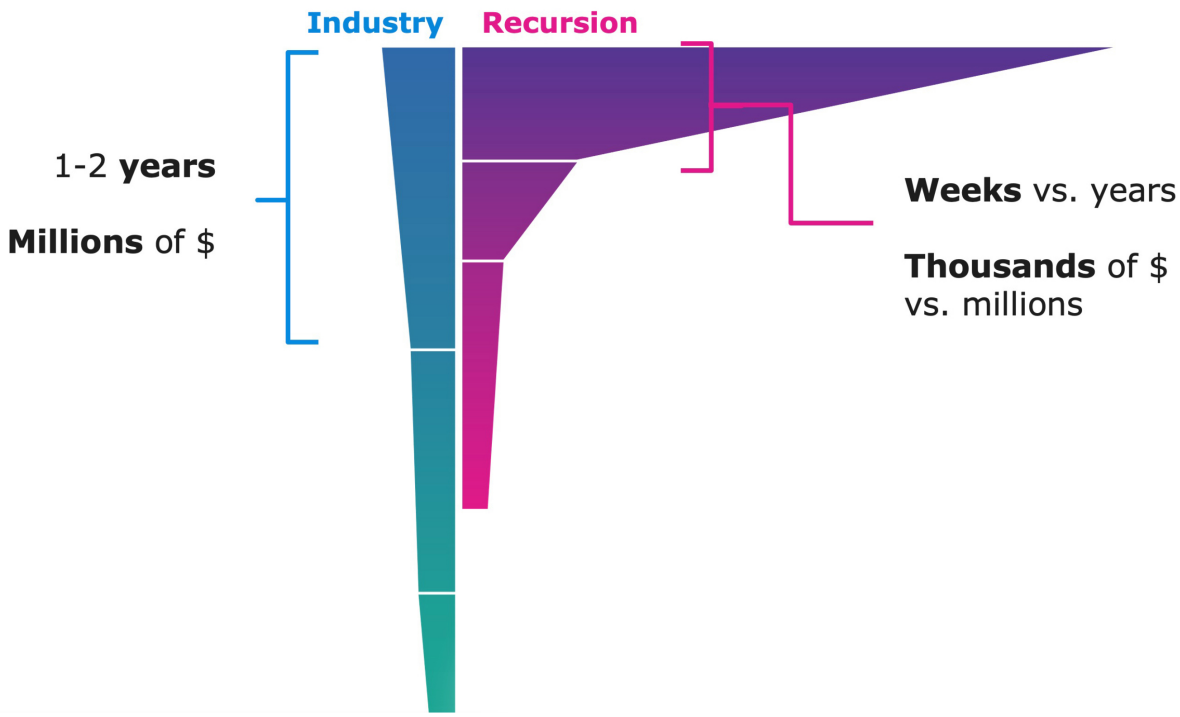


Figure 10. Reshaping the drug discovery funnel. Recursion's goal is to leverage technology to reshape the typical drug discovery funnel towards its ideal state by moving failure as early as possible to rapidly narrowing the funnel into programs with the highest probability of success.[6,7,8,9]

The Recursion OS provides an opportunity for mapping and navigating massive biological and chemical datasets that contain trillions of inferred relationships between disease-causative perturbations and potentially therapeutic compounds. Collectively, the components of the Recursion OS can be joined together in a modular way to identify, validate and advance a broad portfolio of novel therapeutic programs quickly, cost-effectively and with minimal human intervention and bias - industrializing drug discovery and development. We use standardized, automated workflows to identify programs and advance them through key stages of the drug discovery and development process which includes:

- Patient Connectivity and Novelty (i.e., program initiation)
- Hit and Target Validation
- Compound Optimization
- Translation
- IND-Enabling Studies
- Clinical Development

[6] *Steedman M, and Taylor K. (2020). Ten years on: Measuring the return from pharmaceutical innovation. Deloitte. 1-44.*
[7] *DiMasi et al. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of Health Economics. 47, 20-33.*
[8] *Paul, et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Reviews Drug Discovery. 9,203-214*
[9] *Martin et al. (2017). Clinical trial cycle times continue to increase despite industry efforts. Nature Reviews Drug Discovery. 16, 157*

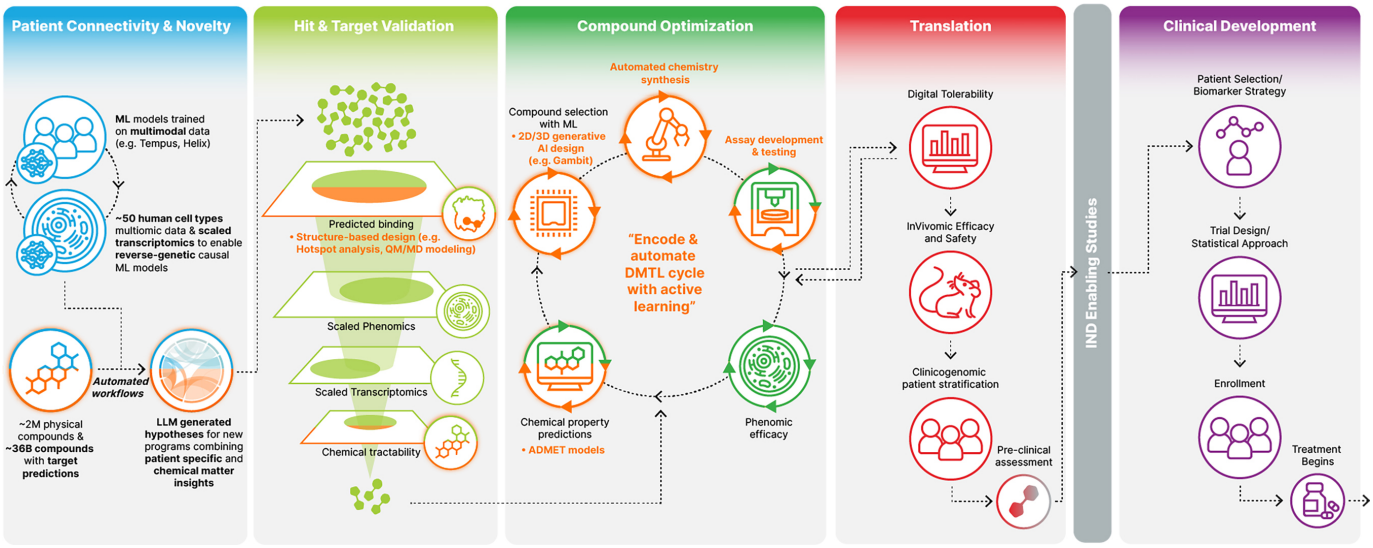


Figure 11. Multiple -omics modalities within Recursion OS form a full-stack platform that spans the drug development pathway, incorporating patient-centric scaled biology, target exploration, hit discovery, lead optimization, precision chemistry design, automated chemical synthesis, predictive ADMET (absorption, distribution, metabolism, excretion, and toxicity), biomarker selection, translational capabilities, and clinical development. Areas from legacy Exscientia platform indicated in orange.

We believe we have made progress in reshaping the traditional drug discovery funnel in the following ways:

- ***Broaden the funnel of therapeutic starting points.*** Our flexible and scalable mapping tools and infrastructure enable us to infer trillions of relationships between human cellular disease models and therapeutic candidates based on real empirical data from our own wet labs.
- ***Identify failures earlier when they are relatively inexpensive.*** Our proprietary navigation tools enable us to explore our massive biological, chemical, and patient-centric datasets to validate more and varied hypotheses rapidly. While this strategy results in an increase in early-stage attrition, the system is designed to rapidly prioritize programs with a higher likelihood of downstream success because they have been explored in the context of high-dimensional, systems-biology data. Over time, and as our OS improves, we expect that moving failure earlier in the pipeline will result in an overall lower cost of drug development.
- ***Optimize molecular design and synthesis through Centaur Chemist.*** Our Centaur Chemist platform integrates AI-driven generative design with automated synthesis, enabling rapid iteration and optimization of new chemical entities. By leveraging predictive modeling for potency, selectivity, and ADMET properties, we can efficiently generate high-quality, differentiated drug candidates while reducing synthesis timelines and experimental bottlenecks.
- ***Accelerate delivery of high-potential drug candidates to the clinic.*** The Recursion OS contains chemistry tools that enable highly efficient exploration of chemical space as well as translational tools that improve the robustness and utility of in vivo studies.
- ***Enhance clinical development efficiency through ClinTech.*** We are applying machine learning and AI to optimize clinical trial design, accelerate patient enrollment, and enhance evidence generation. By integrating scaled patient data with predictive analytics, we aim to improve patient stratification, match therapies with the right populations, and reduce trial failure rates—advancing high-potential medicines to patients faster and more efficiently.

By leveraging our Recursion OS to explore and advance our programs, we have shown leading indicators of improvement when compared to the traditional drug discovery process, particularly with respect to cost and time. We believe that combining Exscientia's state of the art chemical platform with Recursion's cutting edge OS will further enable us to (i) identify candidate compounds earlier in the research cycle, (ii) spend less per program, and (iii) expedite our drug discovery progress compared to industry. Across >280 Recursion programs from late 2017 through 2024 the average amount of time to reach the validated lead stage is less than 13 months. We also use AI/ML tools to better understand which molecules to make and test and ultimately design better quality molecules that can solve complex problems – on average, the industry synthesizes about 2,500 molecules to candidate, both legacy Recursion and legacy Exscientia synthesized 250, respectively.

Ultimately, we believe that future iterations of the Recursion OS will enable even greater improvements minimizing the total dollar-weighted failure and maximizing the likelihood of success allowing us to deliver better quality medicines to more patients in need.

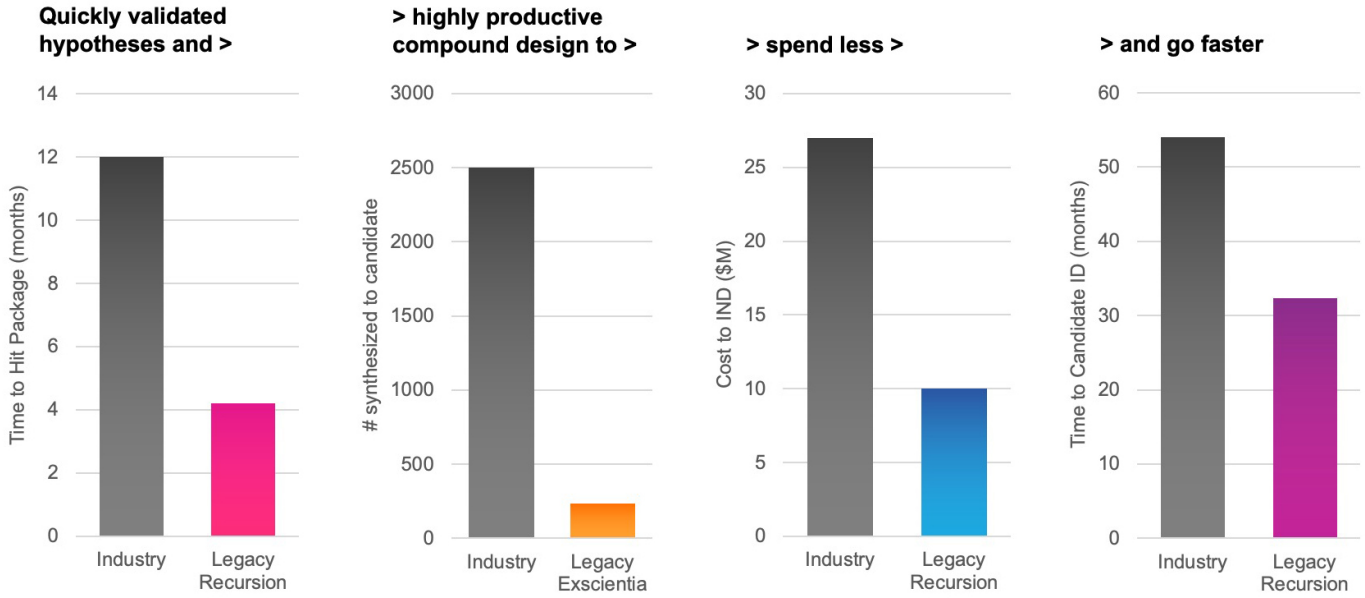


Figure 12. (Far Left): Time from hypothesis screening to validated hit package for legacy Recursion programs. (Center Left): Legacy Exscientia compounds synthesized from hit to candidate ID. (Center Right): Total spend from hypothesis screening to the completion of IND-enabling studies for legacy Recursion novel chemical entity (NCE) programs that advanced to clinical trials. The cost to IND has been inflation-adjusted using the US Consumer Price Index (CPI) (Far Right). Time to validated lead is the average of >280 legacy Recursion programs since late 2017 through 2024.[10]

The Recursion OS has not only improved speed and cost but also led us to explore novel targets which could give us a competitive advantage where multiple parties often simultaneously pursue a limited number of similar target hypotheses. Below one can see quantitative measures for how we prioritize programs characterized by (i) strong genetically driven biological evidence and (ii) differentiated novel biology.

[10] *Paul, et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Reviews Drug Discovery. 9,203-214*

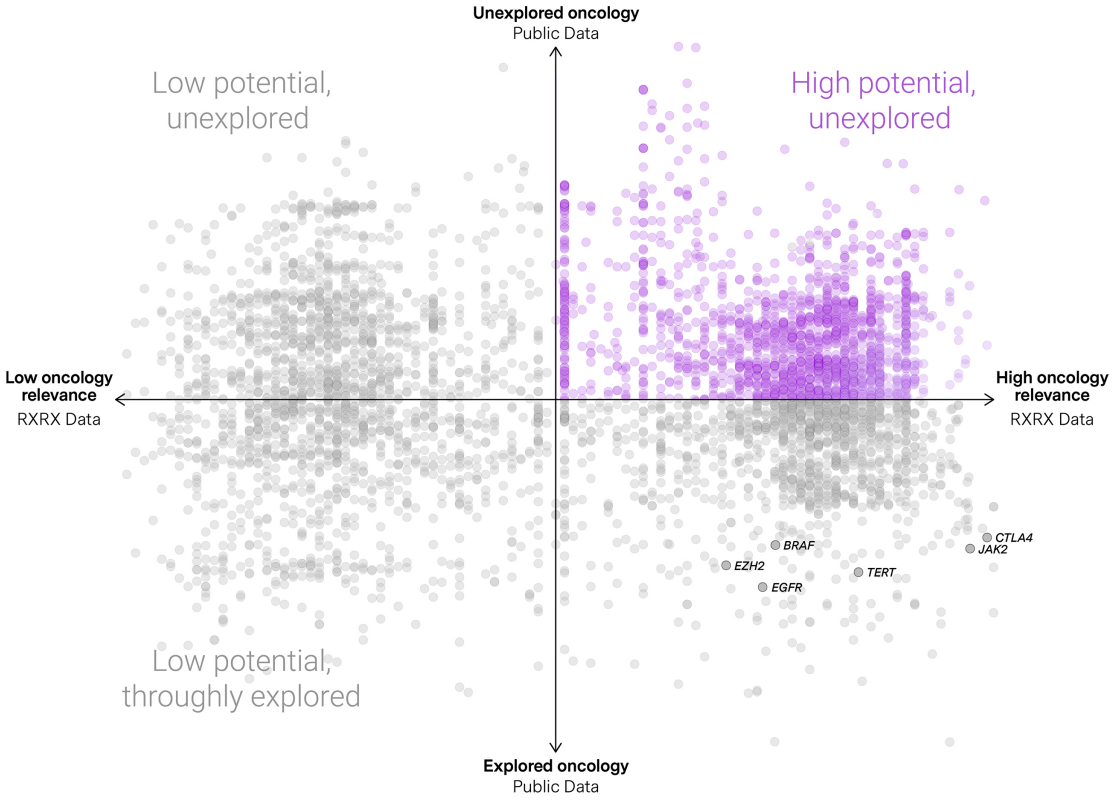


Figure 13. We use LLMs and software tools to organize and initiate internal programs using both proprietary and public data. We prioritize programs at scale by focusing on targets where our proprietary data provides a distinct arbitrage that suggests we can drive towards novel target identification and selection in oncology. Each circle represents a gene that can be searched by the Recursion OS across several biological and pharmacological factors. LLMs harness public datasets such as Cancer Dependency Map, Open Targets, TCGA, CCLE, and COSMIC and Recursion proprietary datasets such as phenomap inferences, Matchmaker assessments, InVivomics experiments, and ADME predictions.[11]

Approach

At Recursion, we are pioneering the integration of innovations across biology, chemistry, automation, data science and engineering to industrialize drug discovery in a full-stack solution across dozens of key workflows and processes critical in discovering and developing a drug. For example, by combining advances in high content microscopy with arrayed CRISPR genome editing techniques, we can rigorously profile massive, high-dimensional biological and chemical perturbation libraries in multiple human cellular contexts to create digital 'maps' of human biology. Leveraging advances in scaled computation, we can conduct massive virtual screens to predict the protein targets for billions of chemical compounds. Similarly, data generated from our automated DMPK module and InVivomics platform enables us to predict ADMET properties and identify toxicity signals, respectively, significantly faster than traditional methods. And now, with the business combination with Exscientia complete, we can drive many of our programs from hit to development candidate using an automated internal chemical synthesis platform.

[11] *Ochoa, et al. (2023). The next-generation Open Targets Platform: reimagined, redesigned, rebuilt. Nucleic acids research. 51(D1): D1353-D1359*

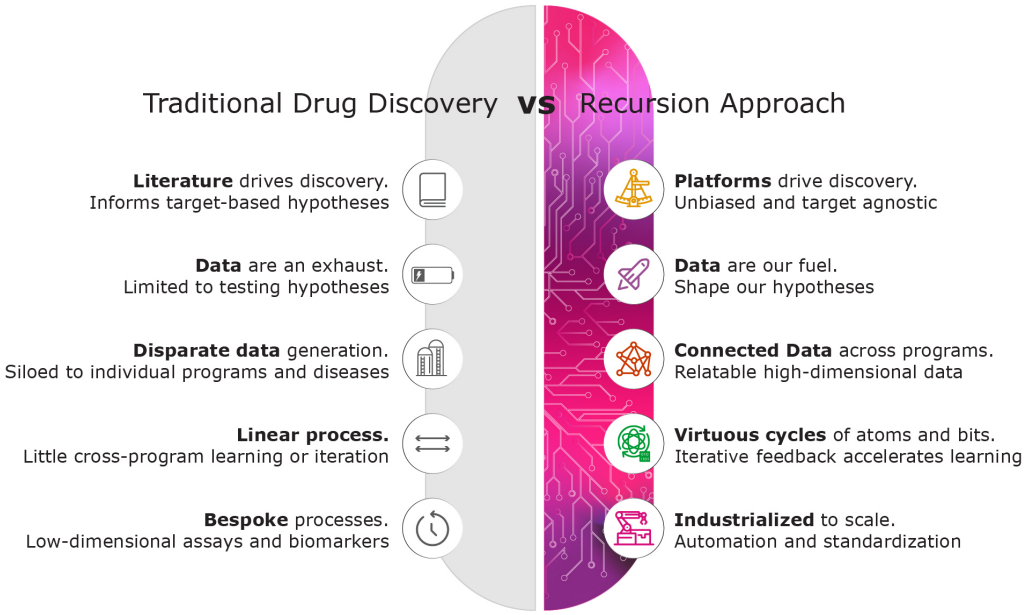


Figure 14. Recursion's approach to drug discovery. We utilize our Founding Principles on the right to build datasets which are scalable, reliable and relatable in order to elucidate novel biological and chemical insights and industrialize the drug discovery process.

We have used our approach to generate, aggregate, and integrate one of the largest proprietary biological, chemical, and patient-centric datasets in the world at approximately 65 petabytes at the end of 2024. This dataset includes proprietary phenomics, transcriptomics, predicted protein-ligand binding interactions, InVivomics, ADMET data, and more across many biological and chemical contexts as well as preferred access to over 20 petabytes of multimodal oncology patient data from Tempus. Additionally, we have built a proprietary suite of software applications within the Recursion OS which has identified over 7 trillion predicted biological and chemical relationships. With our approach, we endeavor to turn drug discovery into a search problem where we map and navigate biology in an unbiased manner to discover new insights and translate them into potential new medicines at scale.

Competitive Landscape and Differentiation

There are a few key factors that differentiate Recursion from other technology-enabled drug discovery companies.

1. Recursion has built a full-stack platform utilizing many biology, chemistry, and patient-centric proprietary datasets and modular tools to industrialize drug discovery, while most other competitor companies rely on a point solution to solve one important step in drug discovery. We recognize that drug discovery is made up of many steps, and a point solution is insufficient to generate efficiencies across the entire process. To decode biology, we must construct a full-stack technology platform capable of integrating and industrializing many complex workflows.
2. Recursion integrates wet-lab and dry-lab capabilities in-house to create a virtuous cycle of iteration. Fit-for-purpose wet-lab experimental data are translated by dry-lab digital tools into in silico hypotheses and testable predictions, which in turn generates more wet-lab data from which improved predictions can be made. Recursion is well positioned compared to companies of a similar stage either focused more specifically on the wet-lab only (traditional biotech or pharma companies) or dry-lab only (companies facing rapidly commoditized algorithms and a challenge differentiating on non-proprietary data).
3. Recursion has achieved a significant scale with respect to its scientific, technological, and business endeavors. With eight clinical-stage programs, an exciting preclinical pipeline, four of the largest discovery partnerships in the biopharma industry with Roche/Genentech, Sanofi, Bayer and Merck KGaA (Darmstadt, Germany), and four technology-focused partnerships, Recursion has achieved a scale, level of integration, and stage that few other TechBio companies have.

Value Drivers

While most small to medium-sized biopharma companies are focused on a narrow slice of biology or a single therapeutic area, the Recursion OS allows us to discover and translate at scale across biology. However, we are cognizant that building disease-area expertise, especially in clinical development, is essential. We have developed a multi-pronged, capital-efficient business model focused on key value-drivers that enable us to demonstrate our progress over time while continuing to invest in the development of the Recursion OS, which we believe is the engine of value creation in the long-term. While our mapping, navigating and designing tools have the plasticity to be applied across therapeutic areas and modalities, our business model is tailored to maximize value and advance programs cost-effectively based on the nature of market and regulatory dynamics associated with our three value drivers (internal pipeline, transformational partnerships, and fit-for-purpose proprietary biological, chemical, and patient-centric data).

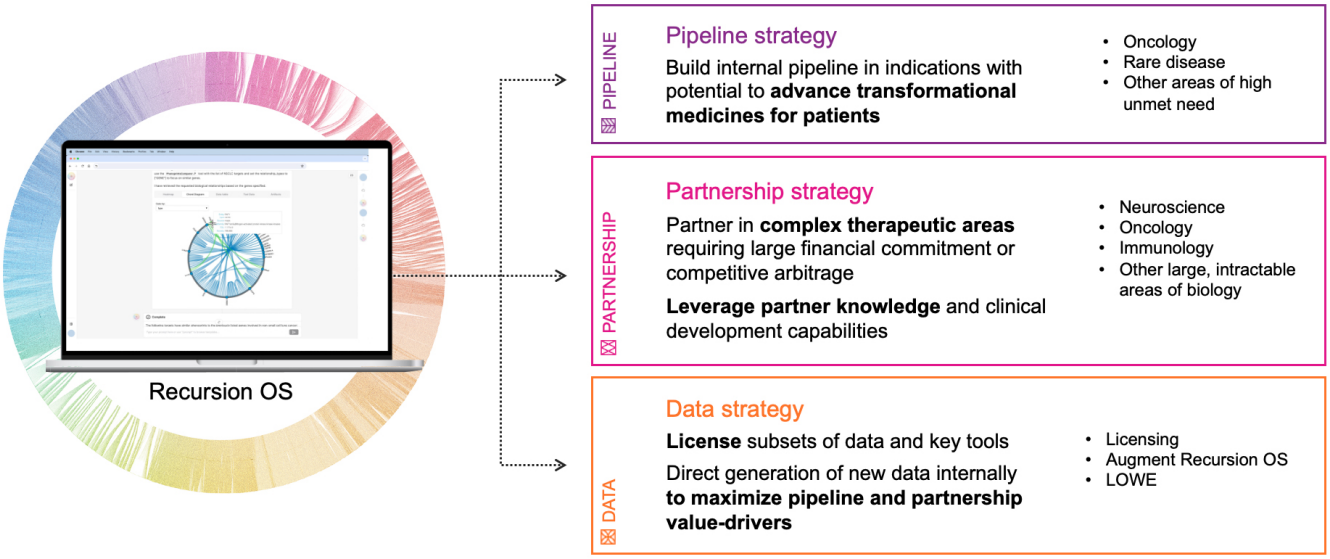


Figure 15. We harness the value and scale of our Recursion OS using a capital efficient business strategy. Our business strategy is segmented into our following value-drivers: (1) internally developed programs in capital-efficient therapeutic areas; (2) partnered programs in resource-intensive therapeutic areas; and (3) proprietary, fit-for-purpose data and models.

Value Driver 1 - Internally Developed Programs in Capital Efficient Therapeutic Areas

We believe that the primary currency of any biotechnology company today is clinical-stage assets. These programs can be valued using a variety of models by stakeholders in the biopharma ecosystem and most importantly, present the potential to meet critical patient needs. For Recursion, these assets have a variety of additional benefits, including: (i) validation of key elements of the Recursion OS, (ii) growing our expertise in clinical development and (iii) building in-house processes to facilitate smooth interaction with regulatory agencies and advance medicines towards the market. If the Recursion OS evolves as designed, then it will continuously improve with more iterations such that future programs could be more novel and potentially more valuable than today's programs. Operating as a vertically integrated TechBio company that leverages technology at every step from target discovery through clinical development (and even marketing and distribution) may be the long-term business model with the most upside for our stakeholders, including both investors and patients. We may be opportunistic about selling or licensing assets after they achieve key value-inflection milestones so that we can re-invest in our long-term strategy.

Value Driver 2 - Partnered Programs in Resource Intensive Therapeutic Areas

We believe that in its current form, our Recursion OS is already capable of delivering many more therapeutic insights than we would be able to shepherd alone today. As such, we have chosen to partner with experienced, top-tier biopharma companies like Roche and Genentech, Sanofi, Bayer, and Merck KGaA (Darmstadt, Germany) to explore intractable and resource-intensive areas of biology. The key advantages of these partnerships are that: (i) we are able to deploy the Recursion OS to turn latent value into tangible value in areas of biology where it would be challenging for us to do so alone; (ii) the clinical development paths for these large therapeutic areas are often resource-intensive and highly complex; and (iii) we are able to learn from our colleagues at these top-tier companies such that it could give us a competitive advantage in the industry over the longer term. This strategy also embeds us in the discovery process of large pharmaceutical companies and gives rise to an alternative long-term business model whereby we become a valued partner of many such companies. Based on how value is ascribed across our industry today, this model alone is not yet feasible to maximize our business impact. However, we feel that due to shifts within the biopharmaceutical industry there is some potential for this portion of our business model to accrete notable value over the long-term.

Value Driver 3 - Proprietary, Fit-for-Purpose Training Data and Models

As has been demonstrated in many other industries, a value driver and competitive advantage can be generated from the creation of a proprietary dataset. At Recursion, we have generated what we believe to be one of the largest fit-for-purpose, relatable biological, chemical, and patient-centric datasets on Earth. Spanning multiple omics technologies and more than 300 million unique experiments, the approximately 65 petabytes of data that Recursion generates, aggregates, and integrates has the fundamental purpose of being used to train machine learning models. Through intensive internal work, Recursion uses this data and our own models, algorithms, and software to advance our own internal pipeline of medicines (Value Driver 1) as well as in partnership with our collaborators to advance additional discovery programs (Value Driver 2). As our field increasingly recognizes the potential for a technology-driven revolution in drug discovery, our data has increasing potential to drive value directly. We increasingly see the potential to license select models and subsets of our data to a growing universe of collaborators for which internal efforts would be minimal, but value could be significant.

A Platform to Industrialize Drug Discovery

We have generated one of the largest relatable data sets in biopharma using our automated high throughput labs, which run over 2 million experiments per week. Our data includes cellular phenomics, captured using Brightfield microscopy, as well as chemical synthesis, transcriptomics, proteomics, ADMET, InVivomics, genomics and patient data. In total, we have approximately 65 petabytes of proprietary data which we use to train our algorithms and build our Maps of Biology.

In our relentless drive to continue building the most advanced full-stack AI-enabled discovery and development platform, we have now integrated Exscientia's Centaur Chemist platform for molecule design and automated synthesis capabilities with the Recursion OS, allowing us to rapidly move from target discovery to in silico design to physical compound testing.

And while we work daily to continue solidifying our data moat through wet-lab experimentation and simulation, our partnerships with Helix and Tempus give us access to hundreds of thousands of patient insights – including whole exome and whole genome sequencing – across a wide range of chronic diseases and in oncology. By integrating even limited patient data into the Recursion OS, we can derive powerful new insights that directly fuel our pipeline. We're also using patient data to match our drugs to the specific patient population most likely to benefit, to improve the probability of success of clinical trials – where 90% of drugs in development fail.

Our unique platform approach has continued to evolve over time and we continue to lead the industry in innovation and delivery of potential treatments through our pipeline and partnerships. When we first developed our phenomics-based biological map-making methods using HUVEC cells – creating over 100 billion cells per year for high throughput experiments, our work was dismissed by many. Now, the early success of our pipeline and partnerships, and the broad adoption of our phenomics approaches across nearly every large pharma company in the industry, suggests a much deeper impact. While others onboard technology we pioneered over a decade ago, we have moved to live-cell brightfield imaging and in partnership with Roche and Genentech, we built specific cell manufacturing technologies that derive neurons from hiPSCs at scale – ultimately producing over 1 trillion hiPSC-derived neuronal cells to build the world's first whole-genome neuronal phenotype or "Neuromap," triggering a $30 million payment.

Through our unique dataset and compute power, in the past year, we've launched a number of breakthroughs in foundation models – including powerful multimodal models like Phenom, MolPhenix and MolGPS. These models give Recursion deeper insights into underlying disease biology and how cells might respond to treatment with new drug candidates, and provide the company with a distinct advantage when driving decisions about which therapeutic programs to pursue.

The Recursion OS

The Recursion OS is the integrated technical and scientific vertical platform that underpins drug discovery and development at Recursion, from program initiation through our clinical trials. Collectively, the components of the Recursion OS can be joined together in a modular way to identify, validate, and advance a broad portfolio of novel therapeutic programs quickly, cost-effectively, and with minimal human intervention and bias. Connecting modules into a system allows us to quantitatively measure impact and make transformative improvements not just within local point solutions, but across the end-to-end drug pipeline, today and into the future.

To achieve this pipeline impact, the modules of the Recursion OS are connected by industrialized workflows that have been standardized, scaled, and automated. To drive greater efficiency, we approach the building of modules and workflows similar to modular programming, but for biology and chemistry, so that the same fundamental capabilities are transferable across drug discovery and development activities and reflected in a diverse portfolio for both our internal pipeline and large pharma partnerships.

In 2024, we:

- Increased the sophistication of modules that improve earlier parts of the pipeline by integrating chemistry-centric models from Exscientia, including our industrialized workflows for chemical optimization enabling both functional- and target-based discovery, biology- and chemistry-centric approaches, and first-in-class and best-in-class compound opportunities.
- Integrated causal models and other analytics based on real patient data into both program initiation phases, ensuring patient connectivity and novelty, as well as clinical development activities, including patient stratification.

A unique advantage of this modular approach is that assay and model outputs become a long-lasting data asset. This consistency, reliability and standardization allows us to build petabytes of data that can be connected across biological, chemical, and patient-centric sources, and across years of experiment execution, model insights, and data types.

Each type of data that Recursion generates in this manner becomes a vertical layer: a computable dataset that can be used to build increasingly ever more complete and generalizable machine learning models to infer biological and chemical states (properties) and relationships, iteratively mapping and navigating trillions of inferred relationships between disease-causative perturbations and potentially therapeutic compounds.

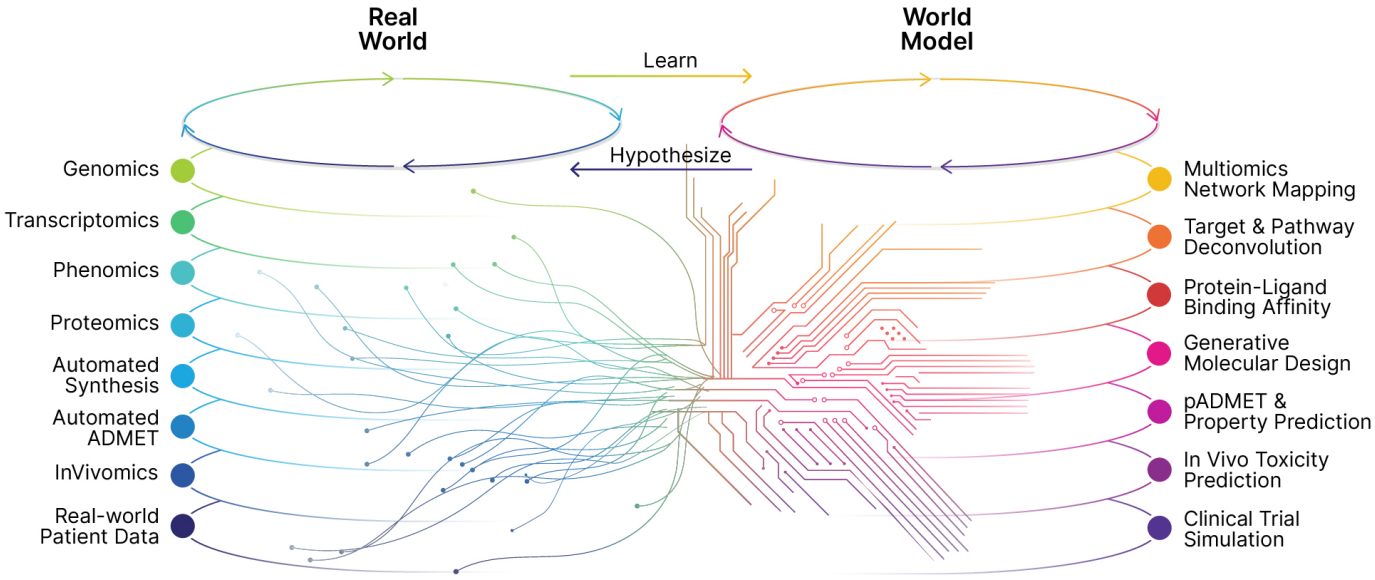


Figure 16. Recursion's World Model approach (1) Profile biological and chemical systems using automation to scale a small number of data-rich assays, including phenomics, transcriptomics, InVivomics, and ADMET to generate massive, high quality empirical data; (2) aggregate and analyze the resultant data using a variety of machine learning models, in a process coordinated with in-house software systems and tools; and (3) map and navigate leveraging proprietary software tools to infer properties and relationships in biology and chemistry. These inferred properties and relationships serve as the basis of our ability to predict how to navigate between biological states using chemical or biological perturbations, which we can then validate in our automated laboratories, completing a virtuous cycle of learning and iteration.

The creation of virtuous cycles of physical experiments and in silico models has been a competitive advantage for leaders in many industries outside of biopharma. In drug discovery, virtuous cycles of experimentation and machine learning predictions is an approach to efficiently map and navigate biology and chemistry at unparalleled scale and efficiency. Critically, at the scale Recursion operates, whole systems can be systematically and experimentally evaluated, such as the cellular level effect of individual gene knockouts not just for individual genes of interest, but across the whole genome. Such comprehensive Real World data sets can underpin new generation AI-enabled Model World predicted states, where rather than individual model predictions, we create model representations to reason about and prioritize opportunities across large swaths of biology or chemistry, such as the hundreds of thousands of protein-protein interactions across the human interactome.

Traversing across layers can allow us to extract more insights and higher confidence than any layer on its own. For example, patient data is the most relevant to human health and disease of all data modalities, but it suffers deeply from being intrinsically noisy, incomplete, expensive and difficult to collect. In comparison, cellular phenomics data can be collected cheaply, at scale, with extreme data reliability and completeness.

In 2024, we have demonstrated that by combining patient level data with cellular level data, we can extract genetic causal targets from small (24,000) patient data sets that had previously required patient data sets of over one million in some cases to overcome challenges with patient data quality. Similarly, we are exploring how protein-level data can add pathway interpretability and completeness to our cellular level data. We believe that by computationally combining data layers across the micro-meso-macro, we can unlock many new, powerful efficiencies and insights along the drug discovery pipeline.

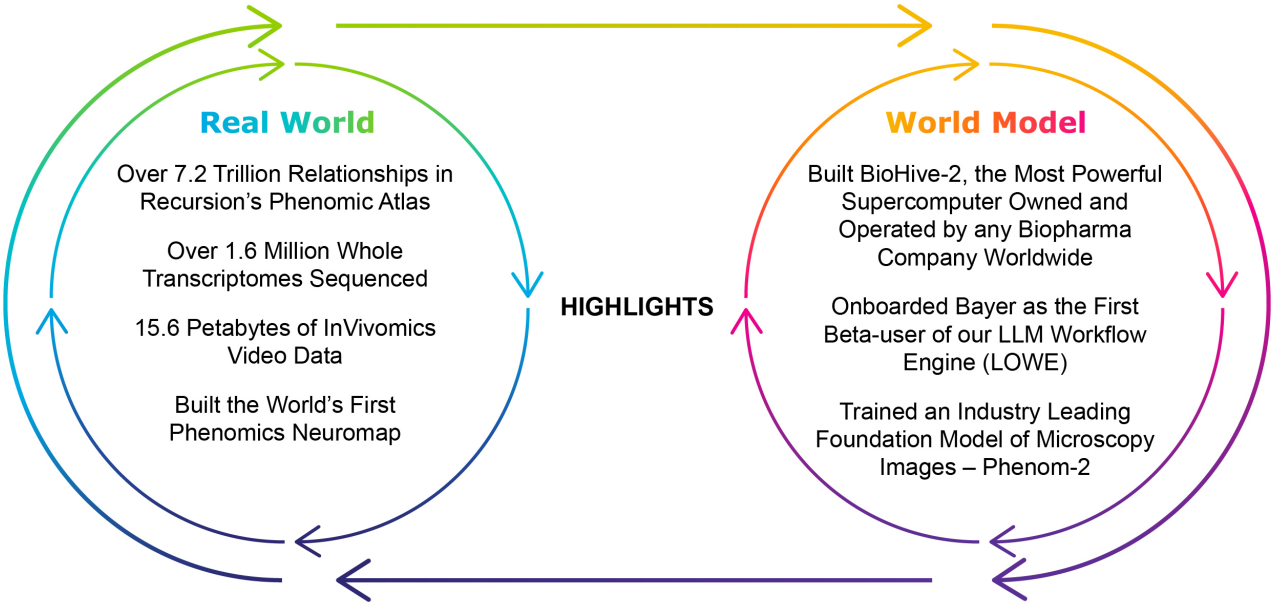


Figure 17. Highlights of Recursion's achievements to-date in generating real world data and building a world model demonstrate progress on our delivery of Recursion's mission to decode biology.[12,13]

Towards a Virtual Cell – How Recursion is combining data and compute across different scales

By closely integrating real world experimentation and AI in an iterative manner, and across multiple 'levels' of biology, one can create cycles of virtuous learning, where large fit-for-purpose wet-lab datasets support better in silico model generation and enable more focused future wet-lab experiments. Over time, this allows something powerful to emerge: rather than a data-first approach underpinning World Model creation, our drug discovery opportunities emerge from the World Model, and Real World physical experimentation serves to validate the most promising insights. The order of operations has swapped from experiments underpinning the creation of models, to a more scientifically comprehensive yet still more efficient approach: World Model predictions being selectively confirmed by Real World experiments. In essence, we will have created a Virtual Cell which we can test in nearly unlimited ways, selecting the most promising outcomes for validation in a Real World cellular system.

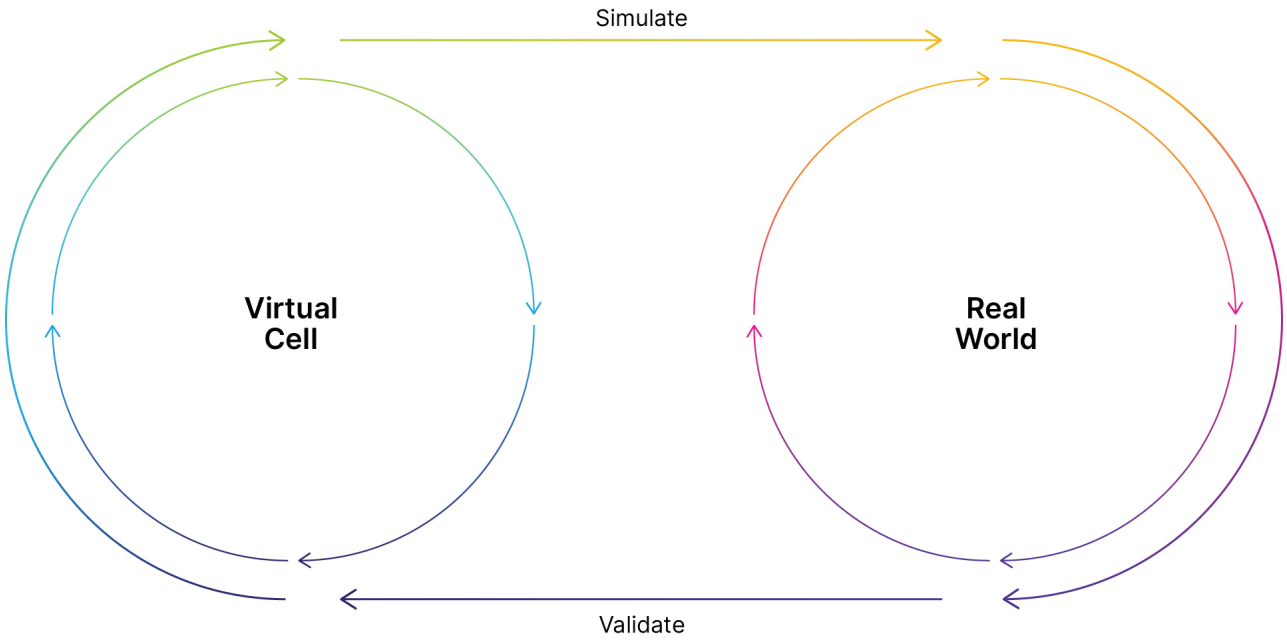


Figure 18. Over time, models can become broadly applicable and performant enough to be the first rather than a step in the process, that is "move to the left" in the diagram, with Real World Models serving to validate individual insights "on the right"

[12] *Internal data and analysis (2025).*
[13] *TOP500 List (2024). https://top500.org/lists/top500/list/2024/06/*

Because the utility and impact on drug discovery would be so profound if achieved, a handful of compelling organizations, spanning academics to institutions to companies, are competing to build a Virtual Cell. Success in this endeavor requires scaled hiqh-quality data, spanning multiple levels of biology alongside cutting-edge compute approaches. We believe Recursion is uniquely positioned to lead at the intersection of these needs.

Scale and Quality. Scale is achieved through three pillars:

- **Automation:** Automation powers our labs, ensuring we create high-quality data outputs at industry leading scale.
- **Relatability:** Output data is highly relatable allowing us to infer relationships and identify connections across many experiments.
- **In silico models:** Scaled relatable data is used to train in-silico models to infer and predict experimental outcomes at scale far exceeding what is possible in the real world, which can then be validated at scale in our automated labs.

Spanning multiple layers of biology

Our Real World data layer and World model are built to use data across three scales: macro, meso and micro. The following section provides examples of these models based on each scale.

- **Macro:** At the highest level, macroscale data informs on organism-level phenotypes and is typically deeply associative rather than causal – one can find associations between clinical outcomes and human observables, but the causal chain of how to go from variant to macro-scale phenotype is usually hidden. Different size scales and data generation formats tend to have differing levels of interpretability, data quality and noise, costs, and data completeness.
- **Meso:** In the middle, mesoscale data is measurements on cellular biological systems, such as phenomics and transcriptomics. Here, we built our first in silico maps of biology and have historically executed our largest laboratory experiments.
- **Micro:** At the smallest end, microscale data informs on molecular-level events like protein-small molecule binding and interactions and can enable insights at the level of target- and protein-interactions and properties. It is the realm of many of our physics- and chemistry-centric models, and our protein sciences and biochemical laboratory assays.

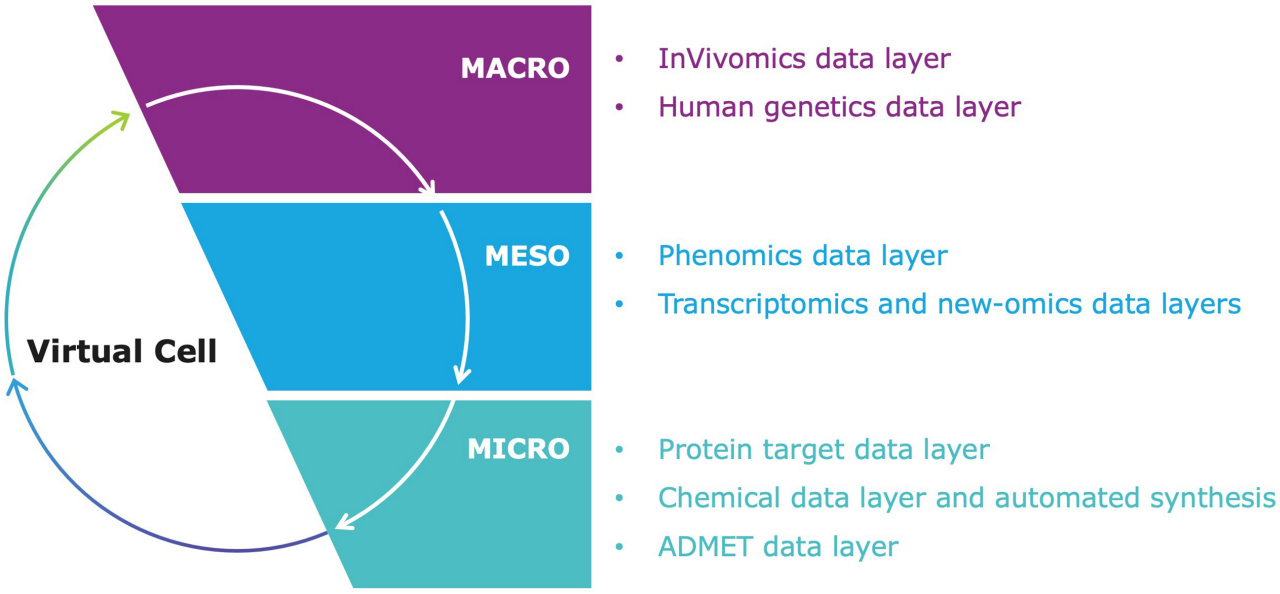


Figure 19. Formation of a highly predictive Virtual Cell from scales of data layers that form Real World data and World model. The macro data layer aims to find associations between clinical outcomes and human observables and determine causal chains of biology. The mesocale data uses measurements on cellular biological systems, such as phenomics and transcriptomics, to build in silico maps of biology. Microscale data uses molecular-level events, such as protein-small molecule binding and interactions using our protein sciences, biochemical assays, and physics- and chemistry-centric models, to enable insights at the level of target- and protein-interactions and properties.

Macro Scale Data Layers

Macroscale data informs on tissue-, organism-, and population-scale biology, enabling us to connect insights at the molecular (micro) and cellular (meso) levels to the behavior of drug candidates in patients, and to perform “reverse translation” of insights from patient populations to direct the initiation of programs at the beginning of discovery. In 2024, Recursion built investments in macroscale biology in both model organisms for in vivo testing (InVivomics) and human populations, spanning cancer –omic data, population genetics data for non-oncology indications, and real-world clinical data.

InVivomics Data Layer

Recursion's data layers combine to tell the story that our therapeutics will safely provide benefit to a patient. Currently, in vivo experimentation is necessary to confidently translate the initial insights from high throughput experimentation in biology and chemistry to applications in the real world. Our InVivomics platform removes human toil and bias from animal data collection. Leveraging this platform maximizes data collection while minimizing human effort in key in vivo experimentation areas, in vivo pharmacology and toxicology.

REAL WORLD	WORLD MODEL
Vivarium: Physical observations of animals including one million hours of video	IVP-1: InVivoPrints Foundation Model to detect organ toxicities as early as possible and prioritize new drug candidates
Physical measurements (body weight, blood work, etc.)	
Microchipping / collecting digital biomarkers for all animals	
149,000 environmental datapoints	

In 2024, InVivomics produced important data that drove decisions across disease models in fibrosis, neuroscience, and oncology. We integrated tolerability studies into our automated industrial workflows, streamlining the process from hit compound identification to animal model testing through a standardized set of experiments and decision criteria. Our in-house execution of a lung fibrosis model helped accelerate the delivery of a molecule now progressing to clinical trials. We also piloted studies in oncology and neuroscience. In neuroscience, we introduced new endpoint measurements like rotarod and CMAP. Developing this skill set and assessing how digital biomarkers can enhance and accelerate data not only supported an internal project decision but will also play a key role in advancing our partnership projects.

In total in 2024, we ran 62 InVivomic-informed studies at our Milpitas, CA facility. Of those, 27 were mouse tolerability studies, delivering richer data to project teams as they design downstream in vivo pharmacology studies. Across our internal portfolio, 7 projects leveraged this technology to inform dose selection as well as to evaluate impacts on specific tissues of interest. We are also exploring the use of our digital system in rat toxicology studies, evaluating the advantage gained both with the richer constant-monitoring data as well as better connection to our other data layers. We expect a data-driven evaluation in early 2025.

To extract maximum insights from this data, we also built a deep learning model called InVivoPrint V1 (IVP-1) that increases our ability to decode signals coming from these smart cages – detecting liabilities such as inflammation or toxicity earlier than our previous digital biomarker approach. IVP-1 allows us to detect organ toxicities linked to a compound or dose candidate as early as possible during in vivo tolerability studies – and to prioritize new drug candidates for the efficacy phase. Our current InVivomics dataset includes 1 million hours of video; 1 million hours of digital biomarkers such as locomotion, body temperature, wheel speed, and cage humidity levels; 149,000 environment data points, including cage slottings, rack used, rack room, sex, and birth time, as well as a number of other categories.

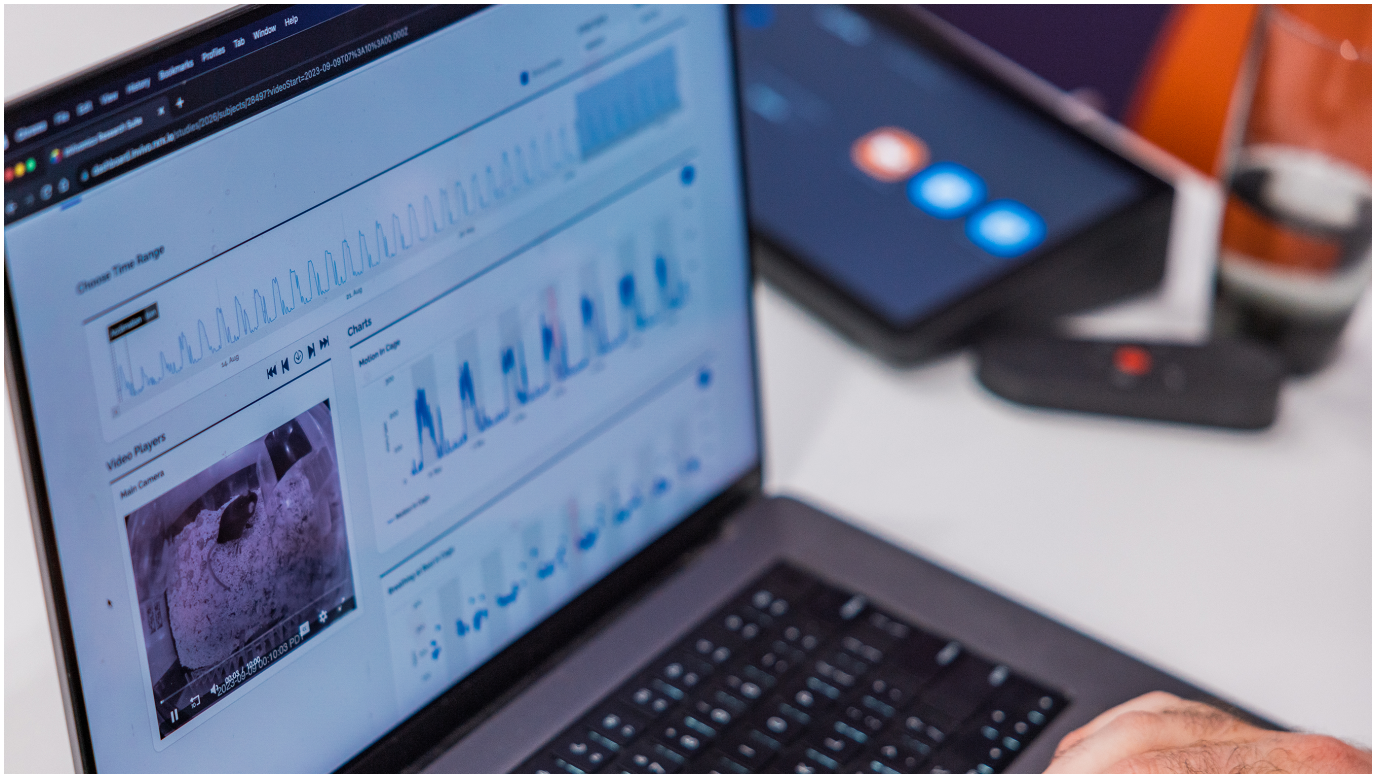


Figure 20. A Recursion scientist uses our in house dashboard to monitor digital readouts and live video of an ongoing animal experiment.

Human genetics data layer.

At the macroscale, patient omics and observational Real World Evidence (RWE) informs organism-level phenotypes, which is critical for discovering the underlying genetic associations of a particular disease. As an independent data layer, human genetics has proven to be undeniably important for increasing the probability of clinical success. Yet the full value of these patient datasets is limited by the fact that these data are inherently noisy, incomplete, and difficult to collect at a scale that allows for recall of sufficiently rare variants and disease phenotypes. At Recursion, we have the capability to bridge our highly controllable, densely sampled perturbative map data (meso) together with observational patient data (macro) in a joint forward-reverse genetics approach. Using human genetics, we can connect the macroscale down to the mesoscale to inform phenotypic discovery and deliver stronger, more disease-relevant and patient-connected insights. While conversely, by integrating scaled meso data, we in turn increase the power and derive further value out of macro data above standard approaches.

REAL WORLD	WORLD MODEL
Publicly available datasets including TCGA	Bootstrapping clinical genomics with phenomics to increase effective power of genetic association tests
Helix – non-oncology	Causal discovery models integrating reverse and forward genetics for target identification and program initiation
Tempus - oncology	Causal inference models for patient biomarker identification and optimized selection strategies
EHRs	
Historical and Recursion trial data	
Non-patient trial data	

In 2024, we expanded our real-world macro data layer by partnering with various clinico-genomics companies and acquiring other sources of RWE. In addition to retaining access to over 20PB of de-identified oncology patient data through our partnership with Tempus, we are now partnering with Helix and have scaled access to hundreds of thousands of de-identified non-oncology patient records consisting of longitudinal clinical records paired with Helix's Exome+® genomic data. We are working with real world data (RWD) providers and continue to augment the foundational macro layer with non-patient trial data such as fit-for-purpose natural history, and both historical and Recursion trial data.

With the integration of these real-world macro and meso data, we built critical components of the Recursion world model to increase the effective power of genetic association tests, inform on patient causality, and enable the precise selection of patient populations based on causal insights. In 2024, we demonstrated that we could extract genetic causal targets from small (24,000) patient data sets that had previously, depending on the target, required patient data sets of hundreds of thousands up to over

one million (3-67x increase in effective power). Recursion believes this to be a new and plausible capital-efficient approach to rare variant discovery.

We also developed a generalizable causal discovery workflow combining macro-meso data features and applied these models for target identification and program initiation purposes. This has led to over 60 genes identified through these causal models that are currently in testing on our validation platform. Beyond discovery, these causal AI models are deployed to identify potential population expansions on current development programs. We have also started testing causal inference models for predicting responsive patient populations to aid in biomarker identification and design optimized patient selection strategies.

Our diversification and expansion of our access to large-scale real-world data, has strengthened our foundation for building world models. This included the integration of electronic health records, claims data, non-patient clinical trial data, and historical trial data. These data sources are being leveraged to advance development through **intelligent trial design**—optimizing patient selection, trial protocols, and biomarker strategies based on predictive insights; **AI-powered clinical trial execution**—accelerating patient enrollment via data-driven site selection, automated outreach, and dynamic recruitment optimization; and **multi-modal RWE application at scale**—combining genomic, clinical, and claims data to inform decision-making across discovery, development, and validation.

Finally, we also accelerated patient enrollment with data-driven site selection and automated site outreach. Looking ahead, we will expand and develop these components, and the industrialized workflows that integrate these into the Recursion OS to drive industrialized clinical development and increase probability of success for our clinical programs.

Meso Scale Data Layers

Mesoscale data at Recursion informs us about cellular biology and serves a unique role: data on cellular systems integrates over biological pathways, revealing information about the multiple effects that individual molecules and targets may mediate to enhance translatability (polypharmacology), while simultaneously offering orders of magnitudes greater sample scale and interventional capability than macro-scale systems. Recursion has built and applied two high-throughput mesoscale assays and data layers, phenomics and transcriptomics.

Phenomics Data Layer

Phenomics measures the morphology of cultured cells grown in laboratory plates. Morphology is a holistic measure of cellular state that integrates changes from underlying layers of cell biology, including gene expression, protein production and modification, and cell signaling, into a single, powerful readout. Image-based -omics can be two to four orders of magnitude more data-dense per dollar than other -omics datasets that focus on these more proximal readouts, enabling us to generate far more data per dollar spent to inform our drug discovery efforts. Phenomics data on genetic and small molecule perturbations forms the backbone of Recursion's Maps of Biology.

REAL WORLD	WORLD MODEL
Phenomics: morphology provides a holistic measure of cellular biology integrating changes in gene expression and protein function. Recursion can run up to 2.2M phenomics experiments per week. Majority of Recursion phenomics capacity is now dedicated to multi-timepoint brightfield imaging, enabling measurement of cellular dynamics, beyond single endpoints.	BioHive-2 enabled continued scaling of Phenom models, with Phenom-2 demonstrating a 25.7% increase in expressed gene knockouts detected. Phenom models demonstrate potential path to direct relatability between historical fluorescent phenomics data and new brightfield data.

Our real-world experimental phenomics data has historically been captured using multi-channel fluorescence microscopy; through 2024, we transitioned the platform to acquire live-cell brightfield images, an imaging modality bringing the capability to measure dynamic cellular state across time, rather than at a single timepoint as is typical for fluorescence-based phenomics or sequencing. In 2024, Recursion's real-world phenomics experimental capabilities scaled to be able to generate up to 13.2 million cell paint images (110 terabytes) or up to 16.2 (135 terabytes) million multi-timepoint brightfield images across up to 2.2 million experiments per week.

Our state-of-the-art machine learning work in phenomics contributes deeply to the Recursion world model. In 2024, Recursion demonstrated the power of scaling laws in machine learning with the training and deployment of Phenom-2, a larger version of the Phenom-1 phenomics model from 2023, making use of the increased computational power of BioHive-2 to improve the detection rate of expressed gene knockouts by 25.7%. We further demonstrated the power of Phenom models on our data by training a Phenom-2-derived model to reconstruct fluorescent Cell Painting images from brightfield data alone, potentially enabling us to directly relate historical Cell Painting data to the brightfield data being collected today and in the future.

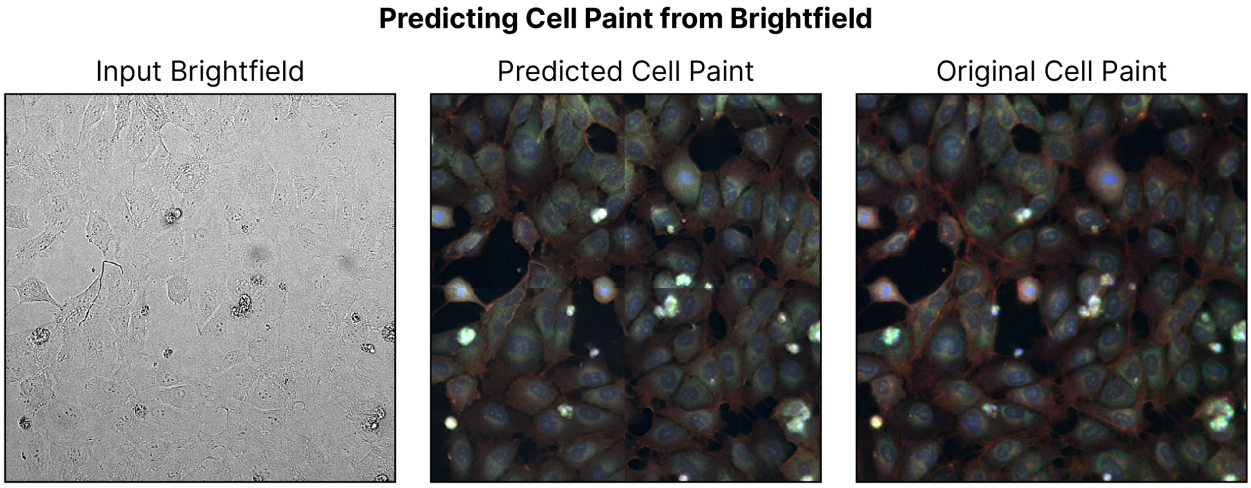


Figure 21. Predicting Cell Paint from Brightfield. Phenom-derived models are able to accurately impute fluorescent stains from brightfield-only images. Using paired brightfield and fluorescent phenomics ("Cell Paint") data, Recursion scientists trained a Phenom-derived model to reconstruct fluorescent images from brightfield data.

Transcriptomics and new –omics data layers

Transcriptomics is a high-dimensional measure of cellular biology distinct from phenomics that assesses gene expression by measuring RNA levels in the cell. Transcriptomics augments our mesoscale data acquisition in three key ways. First, it enables independent replication, at scale, of effects detected in phenomics to verify that they are not morphology-specific artifacts. Second, it offers a route to greater potential interpretability of high-dimensional biological effects by mapping perturbations onto identifiable genetic pathways. Finally, it potentially enables the acquisition of new kinds of biological information, including both effects specific to the transcriptome and new perturbations inaccessible on our phenomics platform.

REAL WORLD

Generated >1.6M individual transcriptomes since its launch in 2023, with just under 1M generated in 2024

Built world's first genome-scale CRISPR knockout map in primary human cells

WORLD MODEL

Developed algorithms to orthogonally confirm phenomics results using arrayed transcriptomics replacing disease-specific confirmatory assays, with 90% ability to filter out compounds that would have failed such bespoke assays

Initiated work on scaled representation learning in transcriptomics

We acquire transcriptomics data in the real world using both an internally developed high-density bulk arrayed transcriptomics platform as well as a newly developed pooled single-cell transcriptomics capability. In 2024, we have expanded our arrayed transcriptomics platform capability to enable the sequencing up to 62,000 wells per week and in 2024, generated just under 1 million individual transcriptomes of data. This year, we augmented our platform with the capability to read out pooled perturbations by single-cell RNA sequencing and demonstrated this capability with what we believe to be the world's first genome-scale CRISPR knockout map in primary human cells. We continue to explore investments in –omics technologies beyond transcriptomics, including but not limited to proteomics and metabolomics.

Transcriptomics represents the first extension beyond phenomics in the Recursion world model. In 2024, we applied Recursion algorithms operating on transcriptomic experiments confirming phenomics to replace time-consuming, disease-specific validation assays with a portfolio-wide multimodal analysis. This analysis demonstrated a 90% ability to predict compounds that failed later disease-relevant assays in internal tests and 60% ability to predict compounds that passed later disease-relevant assays in internal tests. The results of our whole-genome transcriptomic knockout map are now available for internal analysis in the Recursion Data Universe, and in 2025 we anticipate further development of scaled machine learning capabilities on transcriptomic data paralleling our historical development in phenomics.

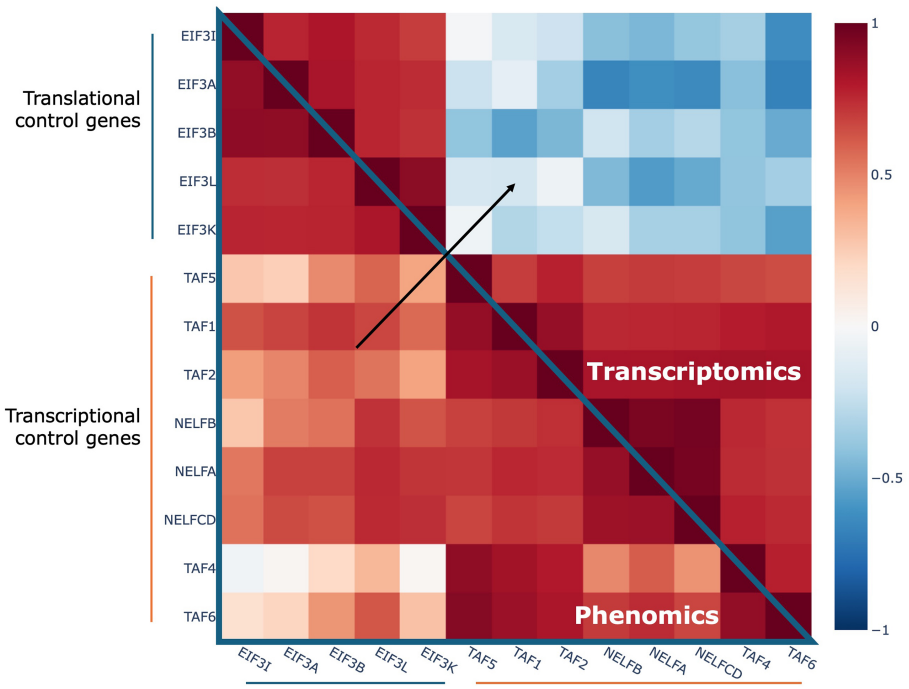


Figure 22. Phenomics and transcriptomics can provide complementary views of biology. In this figure, relationships between knockouts of genes involved in control of RNA transcription and protein translation are visualized, with relationships from phenomics in the lower triangle and those from our internal genome-scale transcriptomic knockout map in the upper triangle. As a distal readout, phenomics sees similar effects on cellular biology from the loss of either transcription or translation. By contrast, transcriptomics identifies opposite directionality of effect between knockouts of these two classes of genes, potentially offering higher resolution in certain areas of biology.

Micro Scale Data Layers

At the smallest end, microscale data informs on the key chemical and biophysical measurements needed to succeed in drug discovery. This scale covers the molecular-level events, such as the binding events between compounds and their target proteins, as well as the chemical reactions involved in synthesizing and metabolizing these compounds. Three data layers encompass this micro scale. *(1) Protein Target, (2) Chemical Data & Automated Synthesis, and (3) ADMET,* each encompassing scaled data generation and state-of-the-art AI models to accelerate our design initiatives.

Protein Target Data Layer

Our protein target data layer measures the protein-ligand binding interactions that drive drug discovery. Engaging protein targets with new compounds is a key driver in the development of effective medicines. This data layer encompasses the development of new target-centric functional assays, the automated platform conducting these real-world experiments, as well as our suite of advanced physics-based simulations that yield accurate synthetic data. These insights are captured by our *state-of-the-art* predictive chemistry models, using this data to guide automated design decisions.

REAL WORLD	WORLD MODEL
In-house support for over 250 unique assay types	Co-folding & ABFE simulations
Over 50% fully unattended assay ready plate production	MolGPS Foundation Model

In 2024, we scaled and automated our experimental bioassay platform, which drives the *testing* phase of our precision Design-Make-Test-Analyze (DMTA) active learning loop. The platform's key features include assay type diversity, speed of execution, and close integration with software tools to enable autonomous operation. The platform currently supports over 250 diverse biochemical and functional assay types, allowing us to drive diverse, high-quality target-enabled programs. All assay plates are prepared autonomously, without human intervention, with over 50% of assay plate preparations taking place overnight in unattended facilities.

Recursion enhances its automated bioassay platform with absolute and relative binding free energy simulations (ABFE/RBFE) of protein-ligand interactions and protein folding predictions, each serving a different purpose toward enhancing molecule design. ABFE and RBFE are accurate molecular dynamics (MD) simulations of protein-ligand binding interactions, which evaluate new chemical design on structurally enabled targets by computationally determining their affinities to the target. Our RBFE calculations have demonstrated an average accuracy of 1.3 kCal/mol. These evaluations prioritize which designed compounds are made and tested.

From there, protein folding and co-folding predictions are used to locate the ligand binding and mechanistic targets responsible for observed biology activities detected by our meso data layers (phenomics and transcriptomics). In 2024, we connected 1.4 million known active ligands mapped to specific pockets across a synthetic data layer of 3D human protein structures. These relationships are used to identify tentative off-target interactions, binding site (and their key active residues), and to initiate subsequent structure-based modeling, including ABFE and RBFE simulations. Bioactivity assays measured through the bioassay platform and sourced across the *Recursion Data Universe* are further modelled through a suite of state-of-the-art machine learning models. Notably, activity models are built with our MolGPS foundation model pretrained on thousands of chemical properties and biological activities. Together, each virtual model enhances the “Design” capability of the iterative Design Make Test Learning loop.

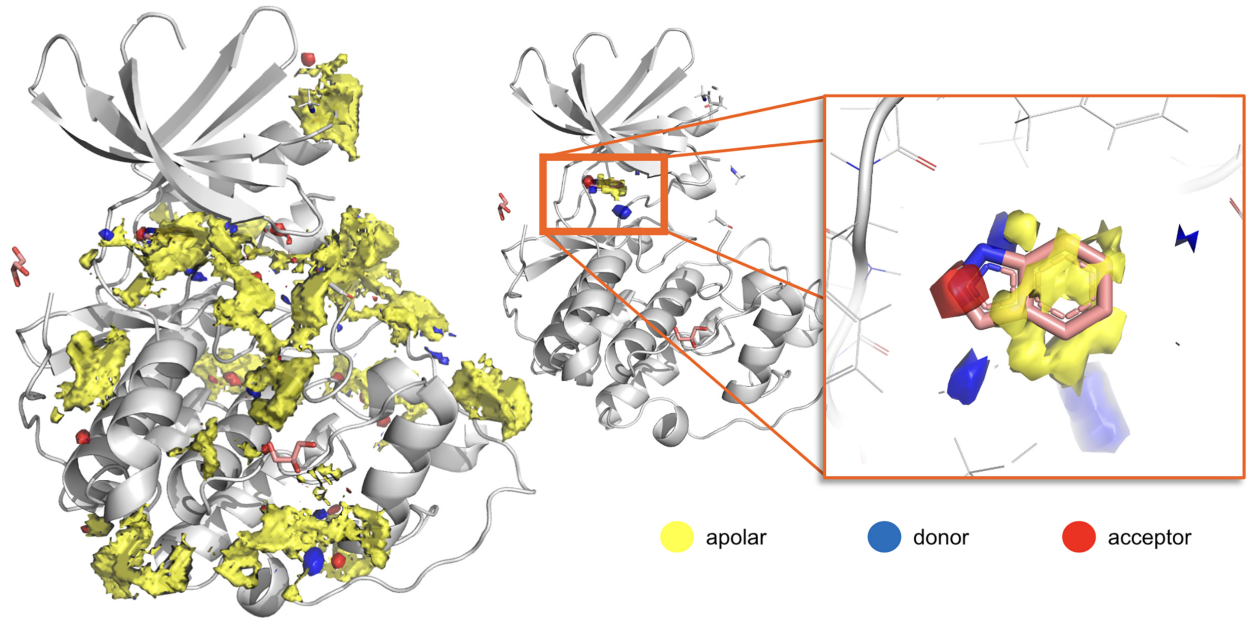


Figure 23. Interaction surfaces of a molecule as determined by fragment hotspot analysis. Fragment hotspot maps are used to identify druggable sites on protein surfaces, and to map target similarity across a synthetic data layer of 3D protein structures.

Chemical Data Layer & Automated Synthesis

Our chemical data layer integrates precision design, state-of-the-art molecular property prediction, and fully automated chemical synthesis, with the goal of designing and producing high-quality, differentiated medicines for patients. The precision design element transforms the drug discovery and development process. It replaces the current conventional/conservative approach with an AI-first learning system that is well-suited to the complexities of drug discovery in each step of the process. Our proprietary AI excels at generative molecular design, molecular property prediction and multi-parameter optimization - powering our platform to multiplex design against addressing more complex, desired profiles than conventional approaches, with synthetic accessibility at its core.

REAL WORLD	**WORLD MODEL**
Automated chemistry platform	Generative design
Reaction data generation	ADMET/potency prediction
Automated purification platform	Retrosynthesis prediction
	Reaction outcome prediction

The synthesis-first, generative design approach addresses a significant challenge posed by early generative methods, which frequently yield undesirable molecules that are difficult to synthesize. Our approach represents a substantial advancement in generative design and can be considered a next-generation solution. As we design molecules with AI-driven algorithms, our

platform, informed by our performant property prediction models, guides the design process towards compounds that are not only biologically and physiologically optimized, but also amenable to efficient synthesis on a unique, fully automated platform, suggesting the most cost and time-effective way to make the molecule with sophisticated retrosynthesis that is vendor-logistics-aware.

We capture reaction data, alongside bioassay data, and leverage active learning to ensure that our molecular property and synthesis prediction models continue to learn in step with the evolution of our pipeline, continuously refining our ability to identify the most promising molecules and predict the feasibility and success of future synthetic routes. Recursion's AI synthesis planning capability shows a 25% improved tractability assessment of AI-generated compounds over competitors and integrates with the Recursion OS. Incorporation of our platform into our discovery processes has resulted in a 35% improvement in design cycle productivity, enabling our design platform to support a broad pipeline.

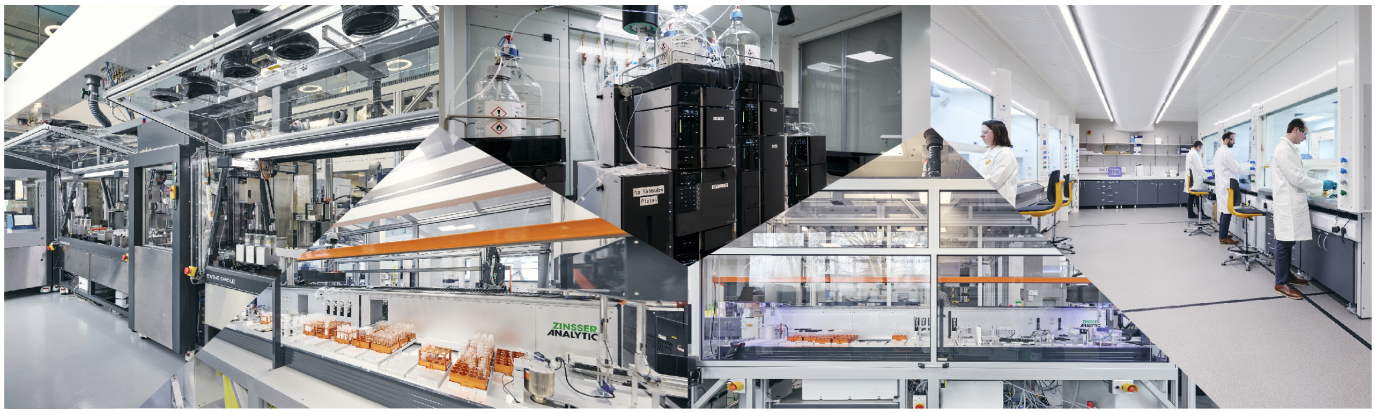


Figure 24. Recursion's automated chemistry wet lab, a modular system for chemical synthesis preparation, execution, analysis, work-up, and purification.

ADMET Data Layer

A durable truth in drug discovery is the requirement that we have confidence in our prediction of how our drugs will behave in patients. We must enter clinical experimentation assured that we have a reasonable expectation that we will safely deliver benefit to patients. A key part of building that confidence is early testing of a candidate molecule's pharmacokinetic (PK) properties, which informs the likelihood that the drug will stay in a patient's body for the right amount of time to be effective. At Recursion we strive to generate critical decision-making data as early as possible. Focusing our testing resources on compounds with higher likelihood to advance accelerates our mission to radically improve lives.

REAL WORLD	WORLD MODEL
High throughput experimentation on RADME-01	Prediction of compound properties to inform probability of clinical success
Experimentation at CRO's to add to our dataset and inform project decisions	Prediction of properties to inform the best compounds to advance
Publicly available datasets	Prediction of properties to inform the best compounds to make

In 2024, we leveraged our high throughput ADME platform, RADME-01, to generate a bolus of data informing a compound's likelihood to be viable. The RADME-01 platform semi-autonomously runs a suite of ADME experiments including passive permeability, metabolic stability in liver microsomes, and non-specific protein binding. Our platform has been operational since late 2023 and can evaluate two 384-well plates in all available assays each week. In 2024, we tested 12,209 novel compounds through this system, supporting both Recursion's internal pipeline and partnered projects. Throughout the year the automation system evolved and refined, allowing for continually less human intervention. A sophisticated in-house built software system intelligently prioritizes compounds and designs experiments to deliver highest value data while avoiding pitfalls related to compound analysis at scale. Drug discovery project teams can use this data to prioritize higher quality compounds for subsequent evaluation, and we've also installed pre-set criteria for compound evaluation in our earlier (hit to lead) stage. In this semi-autonomous loop, data is generated and compounds are nominated for in vivo PK testing without human effort or bias. We are evaluating these criteria on a regular basis to ensure we are giving our projects the best chance at advancing high quality projects and compounds.

Another primary use of data generated on our RADME-01 platform is to train predictive models, capable of evaluating designs before synthesizing new molecules. In 2024, we developed an automated machine learning framework that retrains and deploys new RADME-01 assay endpoint models weekly upon availability of new data, as well as several curated ADME property

datasets. These models included a broad set of properties such as intrinsic clearance, non-specific binding, solubility, efflux, drug-drug interactions, and several human PK parameters. Our teams used these models for both internal pipeline and partnership projects both for prioritization of experimentation and prioritization of new molecule synthesis targets. Recently, automated models derived from the RADME model were combined with their counterparts in the Centaur Chemist platform, further enabling rapid design compounds across both internal and partnership projects. Our combined datasets revealed very little direct overlap and have expanded the chemical space our models are trained on.

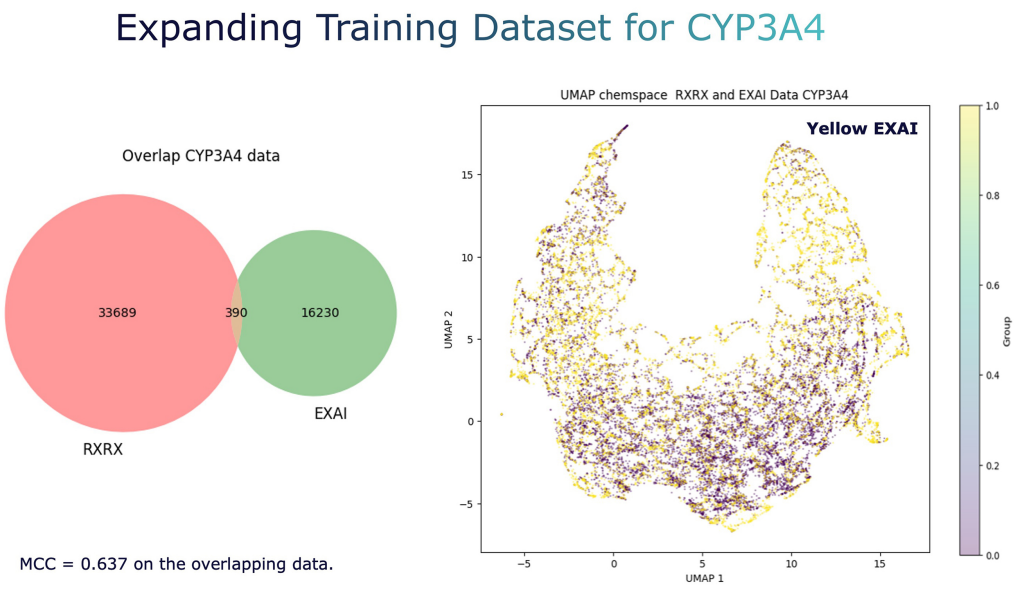


Figure 25. The Exscientia and Recursion ADME datasets had few overlapping compound matches but were sufficiently representative to train ADME models with equivalent or improved performances across all endpoints.

Scientific agents and industrialized workflows

Agentic systems are artificial intelligence systems, typically large language model-based, that can pursue complex goals with limited human intervention. They make decisions in a context-dependent manner and can learn and adapt through interaction with the world around them. They are perfectly suited to workflow design leveraging the data layer and model inference-based modules of the Recursion OS, automating the design of workflows to meet a human or machine-stated objective.

Our goal at Recursion is to industrialize drug discovery and development through standardization and automation. The early stages of our drug discovery process, filling the T-shaped funnel, benefits from standardization and exploitation of the program-agnostic data universe that Recursion has generated this past decade. Industrializing later stages of drug discovery, where the focus is on molecular design, make and test in a program-specific assay cascade, requires context-dependent automation and exploitation of program-specific data. Agentic systems, with their adaptability and flexibility, provide Recursion with the opportunity to industrialize the drug discovery and development process in its entirety.

The industrialization of drug discovery and development at Recursion is implemented via a series of Industrialized Workflows, each exploiting the Recursion OS to serve both the mission of decoding biology to radically save lives and the pipeline. The first of these workflows, Initiation Workflow, offers a standardized approach to program initiation, the filling of the T-shaped funnel. Its role is to generate and assess disease-gene hypotheses. It succeeds by querying the patient data and maps of biology that reside in the data universe and, with help from a suite of Recursion OS models, hypothesizes which genes are associated with which diseases. Large language model-based approaches are used to annotate these hypotheses with strategic insights collated from external, unstructured sources. Such insights inform the biological relevance, novelty, commercial opportunity, competitor landscape, and the opportunity to differentiate. LLMs are also responsible for assigning a score related to the strength of the hypothesized relationship between each disease-gene pair.

The industrialization of lead optimization requires a different approach. At this stage, a program's needs can be unique to that program. The assay cascade may be different and the chemical series undergoing optimization will be different. Recursion's AI precision design platform, Centaur Chemist, enables computational and medicinal chemists to build molecular design workflows that design molecules that are synthesizable on our automated chemical synthesis platform and meet a particular design cycle objective.

Our precision design approach represents a constant interplay of automated data generation from experimentation and intelligent learning systems, embodying virtuous cycles of improvement in chemistry optimization. Through our integrated platform, we can systematically encode the goals and strategy of each molecular design cycle, executing them through a sophisticated combination of scientific technology modules that form cohesive workflows. Compounds progress through synthesis and testing, generating valuable data that are automatically captured in our integrated platform, along with valuable annotations from our medicinal chemists, ready to inform and enhance our predictive modules. This closed-loop system helps translate design objectives into executable workflows, leveraging our 30+ scientific tech modules: from 2D and 3D synthesis-aware generative methods to property prediction models, reinforced with physics-based thinking, and active learning approaches for compound selection. As compounds are generated, synthesized, tested, and evaluated, the platform captures every decision point and experimental outcome, feeding this information back into our models to enhance future design choices. This recursive learning process ensures each iteration becomes more precise and informed than the last, driving the evolution of a more intelligent and efficient drug discovery engine that continuously learns and adapts.

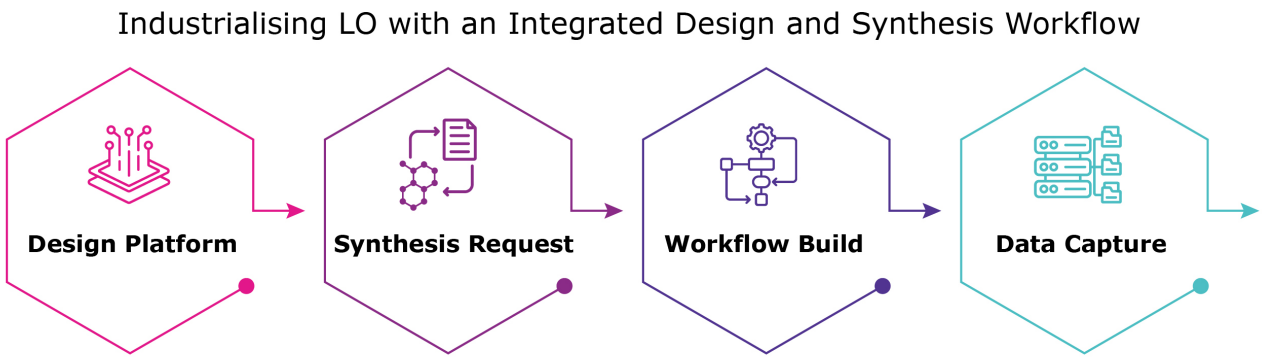


Figure 26. Industrializing lead optimization with an integrated design and synthesis workflow.

Processing and Data Storage Infrastructure

We believe modern drug discovery and development is a data and compute problem – the need to understand pathways, targets, compounds, and mechanisms of actions requires obtaining, synthesizing, or predicting large volumes of data. To store this data in an efficient and low-risk way, Recursion makes use of a combination of cloud storage, and on-premises storage. To process this data efficiently, we bring it close to where the compute will run – either in our HPC datacenter (BioHive) or to our cloud (partnering with Google Cloud). To make this more seamless for our scientists, we have invested in a hybrid storage and compute platform, which enables replication of data and locality of compute to allow us to use these resources as efficiently as possible.

This year we expanded our partnership with Google Cloud to explore generative AI capabilities, including Gemini models, supporting the Recursion OS, driving improved search and access with BigQuery, and helping scale compute resources.

We currently have over tens of petabytes of unique data replicated across our sites for redundancy and resiliency. We use this data to train state of the art (SOTA) foundation models of biology and chemistry and continue to push the limits of what is possible as we invest to scale up beyond Phenom-2 on the biology side, and bring unique Quantum Mechanics (QM) and Molecular Dynamics (MD) data to bear in our chemistry models like MolGPS. We largely train these models using our own supercomputer which consists of two generations of DGX SuperPod, with 504 H100s, and 320 A100s, and over 65 TB of VRAM.

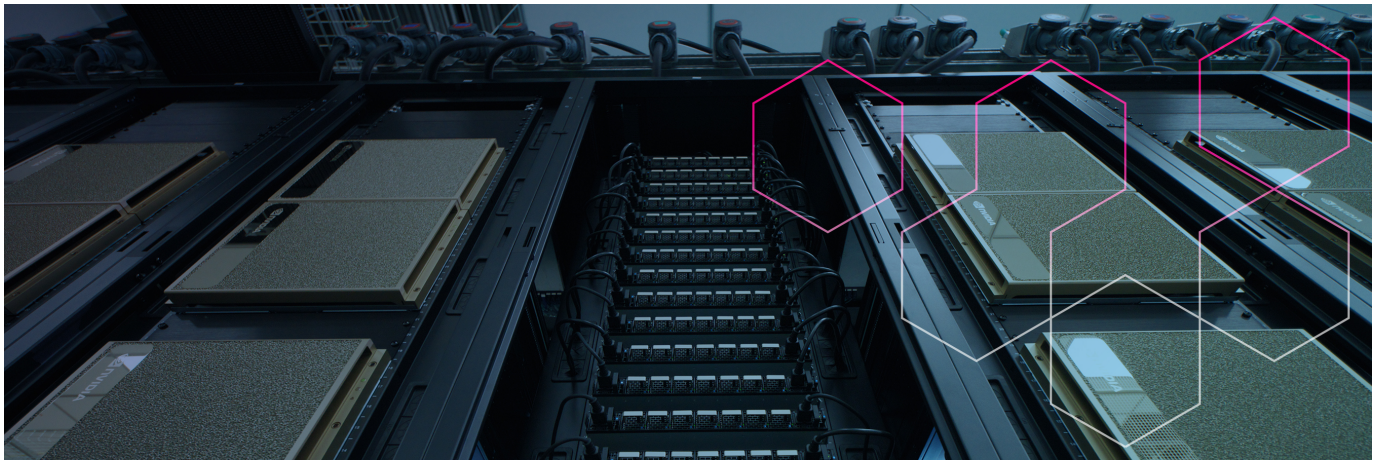


Figure 27. BioHive-2 is Recursion's new NVIDIA DGX SuperPOD AI supercomputer, powered by 63 DGX H100 systems with a total of 504 NVIDIA H100 Tensor Core GPUs interconnected by NVIDIA Quantum-2 InfiniBand networking. This NVIDIA-powered AI supercomputer results in over four times faster speeds than Recursion's original supercomputer, BioHive-1, in benchmark performance tests. Based on available data, BioHive-2 is the fastest supercomputer wholly owned and operated by any pharmaceutical company worldwide.

Bringing it together – Combining data scales to drive value

The vision of the Recursion OS is to integrate data and insights across biological scales to build a comprehensive and predictive World Model that deciphers biology with unprecedented efficiency. Our ability to generate and leverage real-world data at scale—across macro, meso, and micro levels—has already begun to reshape how we approach drug discovery. By combining these layers through the Recursion OS, we are moving toward an industrialized, AI-driven system that not only accelerates therapeutic discovery, but we also believe will help us to increase the probability of success in clinical development.

Our first demonstrations of this approach have successfully integrated macroscale patient data with mesoscale phenomics, allowing us to extract genetic causal targets from datasets previously considered too small for statistical power. This methodology enables a capital-efficient approach to rare variant discovery, increasing our ability to identify novel drug targets that are deeply connected to human disease, and it is just the beginning.

At the mesoscale, we have advanced our phenomics and transcriptomics capabilities to provide high-throughput, high-dimensional insights into cellular biology. By connecting these layers with microscale molecular interactions, such as protein-ligand binding and ADMET properties, we enhance the interpretability and mechanistic understanding of our drug candidates. We believe that bridging across all three scales—macro, meso, and micro—will unlock a deeper understanding of human biology and significantly improve the efficiency of drug discovery and development.

One of the most transformative outcomes of our integrated approach will be the ability to construct a Virtual Cell—an AI-powered system that simulates biological responses at scale. Traditionally, drug discovery has been an experiment-driven process where models are built from data collected in the lab. At Recursion, we are reversing this paradigm: our World Model is now driving the generation of new hypotheses, with real-world experimentation serving to validate the most promising insights. By iteratively refining these AI-driven predictions with physical experiments, we are creating a feedback loop that accelerates learning and reduces reliance on trial-and-error experimentation.

As this approach matures, we envision a future where the Virtual Cell serves as a comprehensive digital twin for human biology, enabling us to model drug interactions, disease progressions, and therapeutic interventions in silico before ever entering the lab. This shift—from experiment-first to model-first—has the potential to revolutionize how drugs are discovered, reducing both time and cost while significantly improving success rates.

Scaling Beyond What Was Previously Possible in 2024

In 2024, Recursion expanded its ability to industrialize drug discovery by enhancing the OS's automation, scalability, and machine learning capabilities. Key milestones included:

- The launch of BioHive-2, the most powerful supercomputer owned by any biopharma company, enabling the training of industry-leading foundation models like Phenom-2, MolPhenix, and MolGPS.
- The integration of Exscientia's automated chemistry platform, which has already generated over 500 custom molecules in under nine days per cycle.
- The successful completion of the world's first whole genome neuronal phenotype map (Neuromap) in partnership with Roche and Genentech, representing a significant leap forward in neuroscience drug discovery.

- The augmentation of our real-world data layer with hundreds of thousands of patient records through new partnerships with Helix and Tempus, dramatically improving our ability to connect patient-level insights with early-stage discovery.
- The rapid expansion of our transcriptomics capabilities, surpassing 1 million whole transcriptomes sequenced in a single year, reinforcing our ability to generate multimodal insights.
- The development of InVivoPrint V1 (IVP-1), an advanced deep learning model that enhances our ability to detect organ toxicities and prioritize drug candidates with greater precision.

The Road Ahead

Recursion is at the forefront of a new era in drug discovery, where data, AI, and automation converge to redefine the boundaries of what is possible. The continued evolution of the Recursion OS will focus on:

- **Further expansion of multimodal AI models** that integrate patient-level insights with cellular and molecular data to refine drug target selection.
- **Greater automation in preclinical validation** through advances in high-throughput biology and AI-driven chemistry.
- **Industrialized clinical development** leveraging AI-powered trial design and patient selection to increase the probability of success.
- **Scaling our Virtual Cell approach** to predict and validate therapeutic interventions with unparalleled accuracy.

As we move forward, we remain committed to the mission that has guided Recursion from the beginning: to decode biology to radically improve lives. With our unique combination of scaled experimentation, AI-driven insights, and industry-leading automation, we are not just advancing drug discovery—we are fundamentally redefining its future.

Our Pipeline

Programs in our internal pipeline are built on unique biological and chemical insights surfaced through the Recursion OS where:

I. The etiology of the disease is well defined, but the subsequent impacts of the disease are generally obscure and/or the primary targets are typically considered undruggable.

II. There is a high unmet medical need, no approved therapies, or significant limitations to existing treatments.

Following the combination with Exscientia, we have expanded our internal and partnered portfolio, adding multiple programs across oncology, immunology, rare diseases, neuroscience, and more. Beyond our 10 clinical and preclinical programs, we are advancing 10+ next-gen discovery programs for further development.

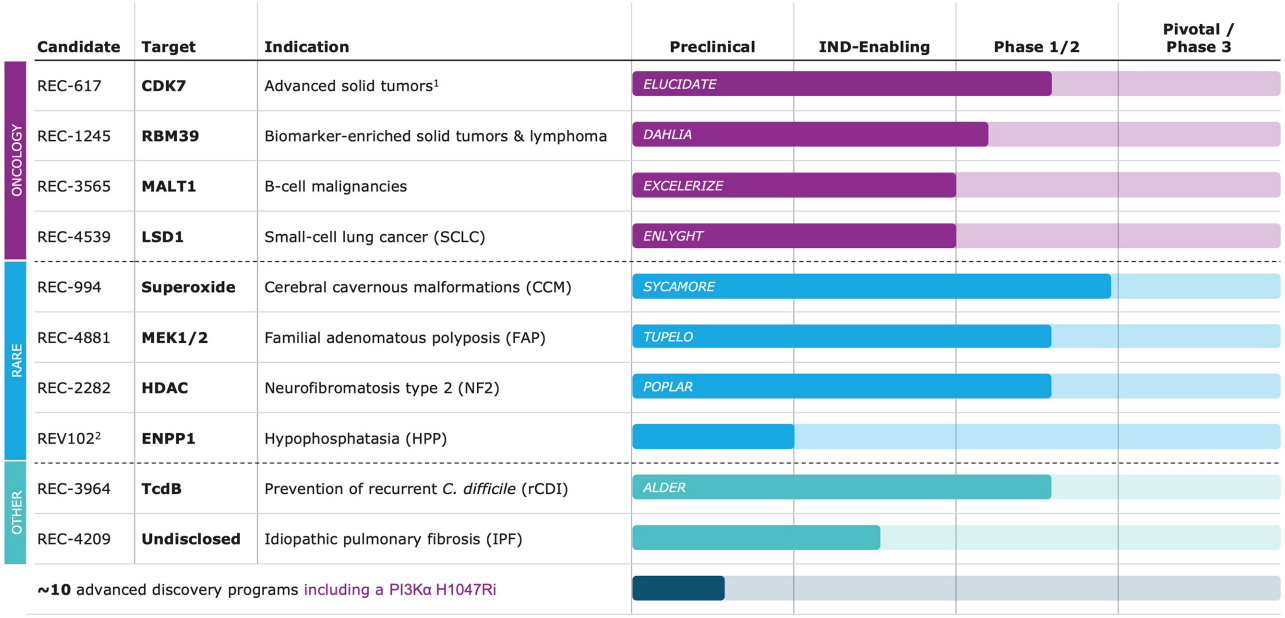


Figure 28. The power of our Recursion OS exemplified by our expansive therapeutic pipeline. [1]Includes non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer; [2]Joint venture with Rallybio.

Clinical Programs in Oncology

REC-617 – *Advanced Solid Tumors*

REC-617 is a potential best-in-class, potent and selective oral small molecule inhibitor of CDK7 with demonstrated activity in preclinical studies. CDK7 controls cell cycle progression and gene transcription, often overexpressed in advanced stage cancers reliant on transcriptional pathways. This program utilized our generative AI and active learning platform to optimize molecule design, including non-covalent binding and ADME/PK for rapid absorption. This rapid design cycle enabled us to synthesize 136 novel compounds and select REC-617 as our lead candidate in under 11 months.

A multicenter, open-label, Phase 1/2 *(ELUCIDATE)* monotherapy dose escalation (QD and BID) study is currently ongoing in advanced solid tumors. In December 2024, results from the initial 19 patients (18 response-evaluable at the time of cutoff) were presented at an AACR Special Conference in Cancer Research. REC-617 monotherapy demonstrated signs of preliminary efficacy. One heavily pre-treated ovarian cancer patient achieved a confirmed durable partial response (PR), which correlated with significant reductions in clinical tumor markers (CA125 and TK1). Four additional patients achieved durable stable disease (SD) as their best response. REC-617 was generally well-tolerated, with adverse events predominantly low grade, on-target, and reversible upon treatment cessation. The MTD was not reached and there were no treatment-related discontinuations.

Monotherapy dose escalation (QD and BID) remains ongoing, and we expect to initiate combination studies in the first half of 2025. We also expect to provide additional data updates from the Phase 1 in 2025.

REC-1245 – *Biomarker-enriched Solid Tumors and Lymphoma*

REC-1245 is a first-in-class, novel, potent, and selective molecular glue degrader of RBM39, a critical RNA-binding protein involved in alternative splicing and DNA damage repair (DDR) pathways. Leveraging the Recursion OS, we discovered that genetic knockout of RBM39 can phenotypically mimic CDK12 loss – a validated DDR target –without impacting CDK13. To our knowledge, we were the first to report this novel biological insight. Utilizing our phenomics based platform for SAR, we synthesized 204 candidates and advanced this program from target ID to IND-enabling studies in 18 months (vs. industry average of 42 months).

Preclinical data confirmed strong anti-tumor activity, including tumor regressions in a BRCA-proficient ovarian cancer model, minimal off-target effects, and no CDK12 kinase inhibition. With over 100,000 addressable patients in the US and EU5 each year, REC-1245 has the potential to be a novel therapy in a biomarker-enriched advanced solid tumors and lymphoma patient population – either as a monotherapy and/or in combination regimens.

Following IND clearance in September 2024, we initiated a Phase 1/2 *(DAHLIA)* study in December 2024 to evaluate the safety, tolerability, PK/PD, and preliminary efficacy of REC-1245 in unresectable, locally advanced, or metastatic cancers. The trial is currently enrolling at three US sites and includes a biomarker-enriched population that may benefit most from targeted RBM39 degradation. We expect to share an update on the Phase 1 dose-escalation portion of the study in the first half of 2026.

REC-3565 – *Relapsed / Refractory B-cell Malignancies*

We are advancing REC-3565, our reversible allosteric potential best-in-class MALT1 inhibitor, for the treatment of patients with relapsed or refractory B-cell malignancies. A variety of mutations seen in lymphomas induce constitutive MALT1 protease activation, leading to aberrant NF-κB signaling that drives survival and proliferation of B-cell tumors. Key preclinical data demonstrates sustained anti-tumor activity as a single-agent or in combination with BTK inhibitors.

We leveraged physics-based predictive modelling using our molecular dynamics toolkit and AI-powered hotspot analysis to deliver a candidate with lower predicted safety risk in the clinic. We synthesized 344 novel compounds and advanced this program from hit ID to lead candidate in 15 months.

The molecule's unique profile minimizes UGT1A1 inhibition risk, demonstrating superior target selectivity compared to oral competitors, both of which reported treatment-related hyperbilirubinemia in early Phase 1/2 studies. As a result, REC-3565's enhanced selectivity supports the potential for a more favorable therapeutic index not only as a monotherapy, but also in combinations with BTK and BCL2 inhibitors. A multicenter, open-label, dose escalation Phase 1 study *(EXCELERIZE)* cleared a CTA by the MHRA in December 2024. We expect to dose the first patient in the first half of 2025.

REC-4539 – *Small Cell Lung Cancer*

REC-4539 is reversible CNS penetrant, orally bioavailable, and potential best-in-class inhibitor of LSD1. LSD1 is an epigenetic enzyme that removes methyl groups from histones to control gene expression. SCLC is particularly dependent on LSD1 to maintain a neuroendocrine phenotype that drives tumor cell survival in this aggressive lung cancer subtype. Preclinical studies demonstrate that REC-4539 shows anti-tumor activity in SCLC human xenografts with limited impact on platelets.

Our program used multi-parameter optimization to design a unique candidate combining reversibility with CNS penetration. We synthesized 414 novel candidates to arrive at our lead candidate in 22 months. Following IND clearance in January 2025, we

expect to initiate a multicenter, open-label Phase 1/2 trial *(ENLYGHT)* in the first half of 2025. We plan to target an SCLC patient population as well as additional biomarker-selected cancers following the dose escalation portion.

Clinical Programs in Rare Diseases

REC-994 – *Cerebral Cavernous Malformation*

We are developing REC-994, an orally bioavailable small molecule superoxide scavenger, as a first-in-disease opportunity for symptomatic cerebral cavernous malformations (CCM). CCMs are rare vascular anomalies marked by abnormal capillary-venous structures, recurrent lesions, and stroke-like symptoms. REC-994 was discovered using the earliest version of Recursion's comprehensive drug discovery platform. In an unbiased CCM2 loss of function phenotypic screen, REC-994 demonstrated concentration dependent rescue and was advanced into preclinical studies. In animal models of CCM, REC-994 reduced the burden of CCM lesions by ~50%. In addition, REC-994 also reduced the vascular permeability defects in CCM2-deficient mice, which is critical in CCM pathology. This data supported the clinical development of REC-994, the first industry-sponsored trial for CCM.

In late 2020, initial results from the clinical program were reported and a randomized Phase 2 trial of REC-994 (SYCAMORE) was initiated in March 2022 in patients with symptomatic CCM. In April 2024, the Phase 1 SAD/MAD study was published. Initial results in September 2024 showed REC-994 met its primary endpoint of safety with encouraging trends in preliminary efficacy. The drug was well-tolerated, with no treatment-related discontinuations or Grade 3-4 adverse events reported. We presented the Phase 2 study data as a late-breaking oral presentation at the International Stroke Conference, or ISC, annual meeting in February 2025. The data presented showed signs of safety and efficacy as follows:

- REC-994 met the primary endpoint of safety and tolerability in CCM patients with no treatment-related discontinuations, SAEs or Grade ≥ 3 adverse events related to study drug
- No new safety signals observed, with the incidence of adverse events comparable across arms
- No treatment-related adverse events that led to discontinuations
- 50% of patients on REC-994 400 mg (n=20) achieved a reduction in total lesion volume versus 28% of patients in placebo (n=18) and 24% of patients on REC-994 200 mg (n=17)
- Trends towards improvement and/or stabilization of symptoms for patients treated with REC-994 400 mg (n=19) compared to placebo, which observed trends towards functional decline, based on changes in the Modified Rankin Scale (mRS) score from baseline to 12 months

Similar trends of exploratory efficacy (lesion volume reduction and functional outcome improvement) were seen in the cohort of patients with brainstem lesions treated with REC-994 400 mg

Most (80%) patients who completed at least 12 months of treatment in the Phase 2 study elected to continue into the long-term extension (LTE) portion of the trial. As of December 31, 2024, the LTE portion is ongoing. As there are no therapeutic options for patients with symptomatic CCM, we plan to seek regulatory guidance from the FDA and additional health authorities on a path forward for this potential first-in-disease program. We expect to share updates on next steps in 2025.

REC-4881 – *Familial Adenomatous Polyposis*

We are developing REC-4881, a highly potent and selective, potential best-in-class MEK1/2 inhibitor, for familial adenomatous polyposis (FAP). FAP is a genetic condition characterized by the development of adenomas throughout the GI tract. It is an orphan disease caused by inactivating mutations in APC, with most patients undergoing prophylactic colectomy due to nearly 100% likelihood of CRC by age 60.

During a collaboration with Takeda, we leveraged machine vision and automated analysis to quantify hundreds of cellular parameters linked to *APC* siRNA knockdown. We screened numerous compounds in this genetic background for 24 hours and identified REC-4881 as a potent molecule that rescued the phenotype in a concentration dependent manner. In preclinical studies, REC-4881 demonstrated over 1,000-fold selectivity in *APC*-mutant tumor cell lines and effectively inhibited spheroid growth and organization. In the APC^{min} mouse model of FAP, REC-4881 showed up to a 70% reduction in total polyps, surpassing celecoxib's 30% reduction, highlighting its potential as a highly selective and efficacious therapy for FAP.

In April 2022, the IND was reactivated and in September 2022, the Phase 1b/2 trial *(TUPELO)* of REC-4881 was initiated. As of December 31, 2024, Part 1 of the study is complete, and Part 2 remains ongoing. We expect to share safety and preliminary efficacy data in the first half of 2025.

REC-2282 – *Neurofibromatosis Type 2*

We are developing REC-2282, a CNS penetrant, potential best-in-class pan-HDAC inhibitor, for neurofibromatosis type 2 (NF2). NF2 is a rare genetic disease caused by loss of function mutations in the *NF2* gene which leads to deficiencies in the tumor suppressor protein merlin.

REC-2282 was identified as a potential therapeutic capable of rescuing HUVEC cells treated with *NF2* siRNA and subsequently in-licensed from Ohio State Innovation Foundation in December 2018. We initiated the POPLAR study, an adaptive, randomized, multicenter Phase 2/3 trial in June 2022, with the first patient dosed in October 2022. In November 2024, we announced that the trial was fully enrolled in the Phase 2 portion.

As of December 31, 2024, Phase 2 data is maturing, and we expect to share the results of the futility analysis (PFS6 rate) in the first half of 2025.

REC-3964 – *Prevention of Recurrent C. difficile infection*

We are developing REC-3964, a non-microbial, orally bioavailable, potential first-in-class *C. difficile (C. diff)* toxin B selective inhibitor for the prevention of recurrent *Clostridioides difficile infection (rCDI). C. diff* toxin B disrupts the tight junctions in colonic cells and increases vascular permeability, leading to a leaky gut. REC-3964 is Recursion's first new chemical entity to reach the clinic and binds and blocks the catalytic activity of the toxin's innate glucosyltransferase, while sparing the host. In a human disease relevant *C. diff*. hamster model, REC-3964 demonstrated a significant difference in the probability of survival versus bezlotoxumab alone.

Our program leveraged an ML-aided conditional phenotypic drug screen in human cells and identified novel mechanisms that mitigated the effect of C. diff. toxin B treatment. Through orthogonal validation screens, precursors to REC-3964 emerged as promising substrates for further advancement.

In June 2024, we presented Phase 1 data in healthy volunteers at the 6th Edition of World Congress on Infectious Diseases in Paris. In October 2024, we initiated a Phase 2 open-label, randomized, 3-arm study (ALDER) to evaluate the rate of recurrence in patients with a high-risk of CDI, who have achieved symptom resolution following treatment with oral vancomycin for 14 days. We expect to share initial results from the Phase 2 study in the first quarter of 2026.

Details on preclinical programs (e.g., ENPP1 inhibitor, Target Epsilon) will be shared in the next section.

Deep Dive into Clinical and Select Preclinical Programs

REC-617 for Advanced Solid Tumors – Phase 1/2

REC-617 is an orally bioavailable, cyclin-dependent kinase 7 (CDK7) inhibitor currently under development for the treatment of advanced solid tumors. Inhibiting CDK7 targets both cell cycle dysregulation and transcriptional "addiction", which are hallmarks of multiple aggressive cancers including, but not limited to, CDK4/6 resistant breast cancer, ovarian cancer, and other solid tumors. There are currently no CDK7 inhibitors approved by the FDA. ELUCIDATE, a Phase 1/2 open-label, multicenter, safety, PK, PD and preliminary efficacy study is currently underway. Interim Phase 1 safety, PK, PD, and efficacy data were shared in the fourth quarter of 2024. We expect to initiate combination studies in the first half of 2025.

Disease Overview

The importance of cell cycle inhibitors in oncology has been established with CDK4/6 inhibitors, which generated approximately $10.5 billion in sales in 2023. Aberrant CDK7 overexpression is common in many cancer indications and associated with poor prognosis. CDK7 presents an opportunity to improve treatment outcomes over CDK4/6 inhibitors due to CDK7's dual role in cell cycle and transcription. Potential specific indications include non-small cell lung cancer (NSCLC), colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer for which we estimate an addressable population of approximately 185,000 drug-treatable patients per year in the US and EU5.

Insight from Recursion OS

CDK7 inhibitor development has faced significant challenges, primarily due to off-target effects and suboptimal pharmacokinetics. Previous attempts often employed covalent binding mechanisms or exhibited poor oral bioavailability, leading to undesirable side effects in the clinic. Current candidates in development for CDK7 feature covalent binding or extended half-lives potentially resulting in substantial on-target toxicity. In addition, the reversible inhibitors under investigation are transporter substrates, likely compromising their absorption and exacerbating gastrointestinal adverse events. These limitations underscore the critical need for novel CDK7 inhibitor designs that optimize both safety and efficacy profiles.

Leveraging our AI-driven multi-parameter optimization approach, we identified critical design limitations in existing CDK7 inhibitors. This insight led to an improved target product profile and a novel molecule design. REC-617 is an orally bioavailable, potent and selective CDK7 inhibitor with enhanced oral bioavailability. It has a non-covalent, reversible mechanism of action, and a predicted shorter human half-life compared to other drugs in development. These characteristics potentially offer an improved therapeutic index, less off-target effects, and more consistent absorption.

Preclinical

REC-617 has demonstrated strong anti-tumor activities in preclinical studies and in vivo experiments showed potent tumor regression across multiple solid tumor types. Notably, in the OVCAR3 ovarian cancer xenograft model as shown below, complete tumor regression was observed in all 8 mice treated with 10 mg/kg by Day 27. Importantly, no significant body weight loss was observed across treatment arms. Mouse PK studies revealed that maintaining 8-10 hours of CDK7 IC_{80} coverage resulted in potent tumor regression with minimal side effects, while coverage beyond 10 hours led to significant body weight loss. This defined an optimal therapeutic window that guided target efficacious exposures in the clinic.

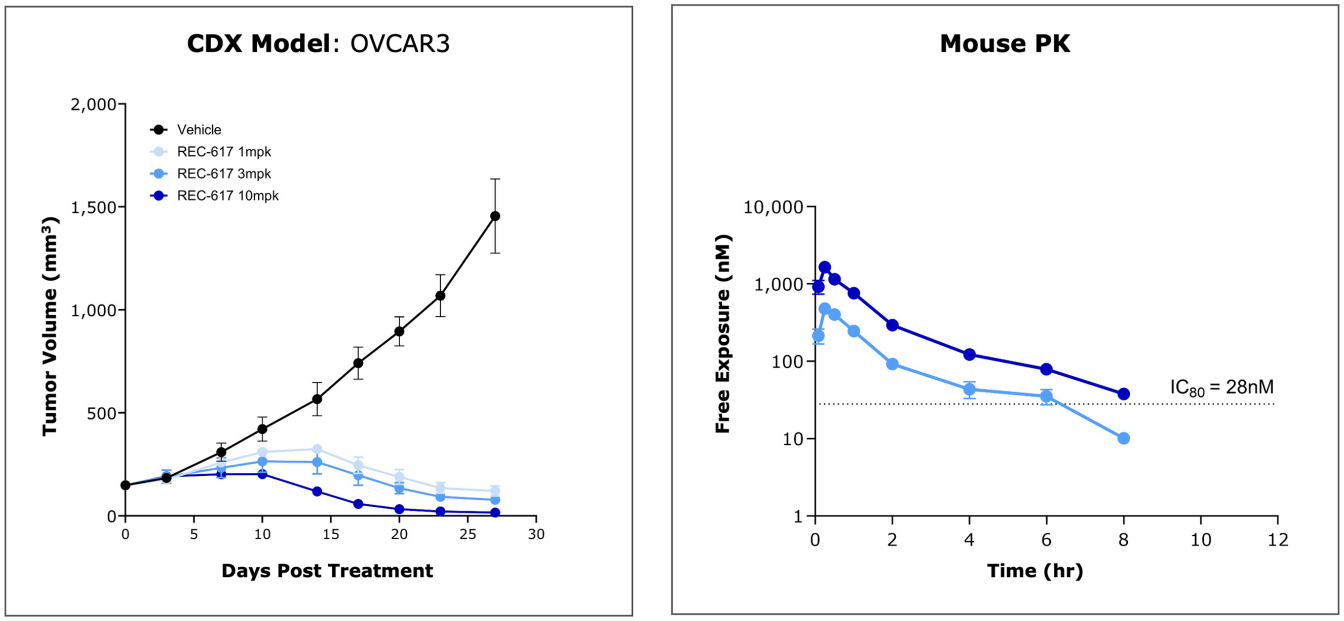


Figure 29. REC-1245 anti-tumor activity and PK in preclinical tumor models. (Left) REC-617 induces tumor regression in the OVCAR3 cell line derived xenograft mouse model. N=8, 28 days of treatment, REC-617 administered QD PO. (Right) REC-617 administration results in 8-10 hours of therapeutic coverage at IC_{80}. PK studies conducted in CD1 mice, single-dose administration. >10 hr IC_{80} results in significant body weight loss.[14,15]

Clinical

In the third quarter of 2023, we initiated a Phase 1/2 open-label, multicenter study *(ELUCIDATE)* in patients with advanced solid tumors, with the design shown in the figure below. Currently, monotherapy dose escalation (QD and BID) is ongoing, with combination study initiation expected in the first half of 2025.

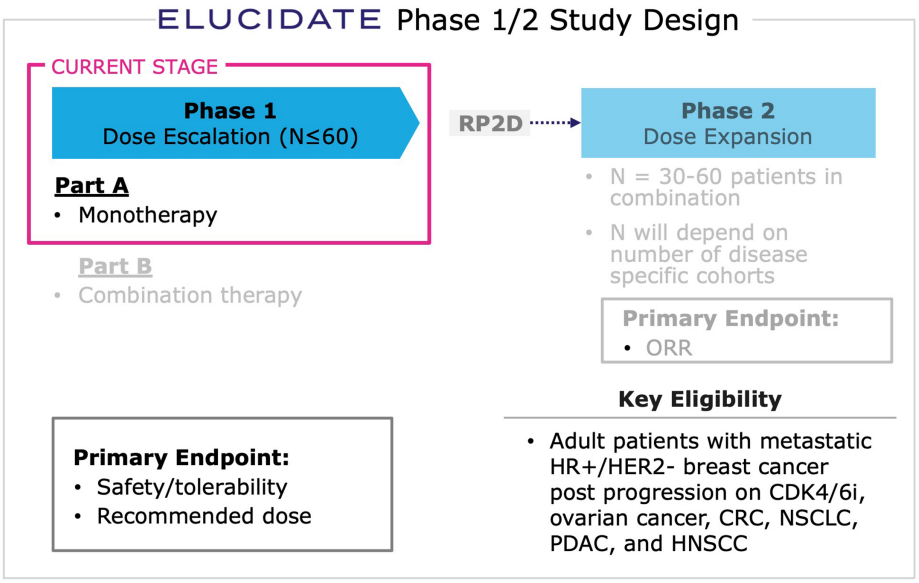


Figure 30. ELUDICATE study design. Phase 1/2 trial design to assess the safety, PK, exploratory PD, and efficacy of REC-617 in patients with advanced solid tumors.

[14] *Besnard, et al. (2022). AI-driven discovery and profiling of GTAEXS-617, a selective and highly potent inhibitor of CDK7 [abstract]. AACR; Cancer Res 2022;82(12_Supplement): 3930.*

[15] *Hallett, et al. (2024). Overcoming traditional design limitations with AI-based discovery. AACR Special Conference in Cancer Research: Optimizing Therapeutic Efficacy and Tolerability through Cancer Chemistry; Plenary Session 1*

In December 2024, we presented results from the initial 18 response evaluable patients at an AACR Special Conference in Cancer Research. REC-617 was well-tolerated with predominantly Grade 1-2 adverse events, no treatment-related discontinuations, and fewer GI side-effects than reported for other CDK7 inhibitors. Dose escalation (QD and BID) is ongoing, and the maximum tolerated dose (MTD) has not been reached. PK was dose linear and exceeded the CDK7 IC_{80} with rapid absorption (Tmax 0.5–2h) and short t½ (5–6h). Robust target engagement was also observed with rapid increases in POLR2A (3-4x), which normalized within 24 hours. These data are shown in the figure below.

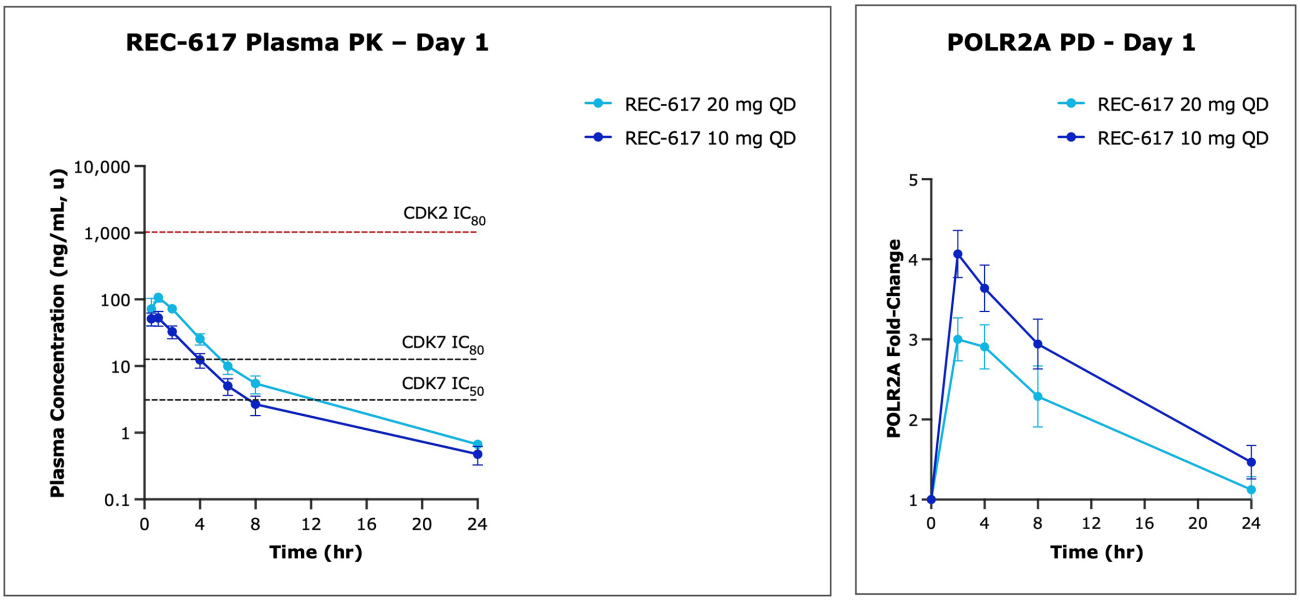


Figure 31. REC-617 clinical plasma pharmacokinetics and pharmacodynamics. (Left) REC-617 plasma concentration, in a dose-linear fashion, well above CDK7 IC_{80} at peak and well below CDK2 IC_{80}, indicating a broad therapeutic window for the study drug. (Right) POL2RA expression data (PD), which is associated with tumor regression, shows a rapid pharmacodynamic effect and short half-life.[16,17]

Encouraging antitumor activity included a confirmed partial response (PR), in a heavily pre-treated metastatic ovarian cancer patient, with a durable response that was maintained for more than 6 months of treatment. LDH levels were also normalized, and reductions were observed in CA125 (-44%) and TK1 (-68%). Four additional patients achieved the best response of stable disease (SD) lasting up to six months.

Competitors

We are aware of five active CDK7 inhibitor programs in clinical development:

- ***Samuraciclib (Carrick Therapeutics):*** In Phase 2 as a monotherapy and in a range of combination studies
- ***SY-5609 (Syros Pharmaceuticals):*** Completed Phase 1 monotherapy and in Phase 1/1b in combination with atezolizumab
- ***Q-901 (Qurient):*** In Phase 1/2 in monotherapy and combination with PD-1 inhibitors in solid tumors
- ***TY-2699a (TYK Medicines):*** In Phase 1 trial in China only
- ***EOC-237 (EOC Pharma):*** In Phase 1 trial in China only

REC-1245 for Solid Tumors and Lymphoma – Phase 1/2

REC-1245 is a novel, potent and selective molecular glue degrader of RNA-binding motif protein 39 (RBM39) currently under development for the treatment of biomarker-enriched solid tumors and lymphoma. There are currently no RBM39 degraders approved by the FDA. Following IND clearance in September 2024, we initiated a Phase 1/2 open-label, multicenter study (DAHLIA) to evaluate the safety, tolerability, PK, PD, RP2D, and preliminary efficacy of REC-1245. With the first patient dosed in December 2024, we expect to share an update on the program in the first half of 2026.

[16] *Papadopoulos, et al. (2020). EORTC-NCI-AACR (ENA) Symposium*
[17] *Hallett, et al. (2024). Overcoming traditional design limitations with AI-based discovery. AACR Special Conference in Cancer Research: Optimizing Therapeutic Efficacy and Tolerability through Cancer Chemistry; Plenary Session 1*

Disease Overview

Alternative splicing and RNA-binding proteins (RBPs) have recently emerged as attractive therapeutic targets for cancer due to their critical roles in the regulation of post-transcriptional modifications, impacts on DNA damage repair pathways, and modulation of cell cycle functions. Recent studies have revealed that RBM39 is an unexpected target of aryl sulfonamides, which can function as molecular glue degraders by forming a ternary complex with RBM39 and the E3 ubiquitin ligase receptor DDB1 and CUL4 associated factor 15 (DCAF15). Additionally, clinical trials have shown that aryl sulfonamides were well tolerated with modest anti-tumor activity seen across a variety of cancers. These findings suggest that RBM39 degraders may show promise as targeted cancer therapies, but the lack of predictive biomarkers and an inadequate understanding of RBM39 biology has limited their therapeutic potential. With over 100,000 addressable patients, with biomarker-enriched solid tumors and other select histologies in the US and EU5 each year, REC-1245 has the potential to be used as a single agent or in combination with chemotherapy and/or immunotherapy.

Insight from Recursion OS

Reports suggest that genetic or pharmacologic depletion of CDK12 can reduce the expression of several genes involved in the homologous recombination repair pathway such as BRCA1 and BRCA2, inducing a BRCA-like phenotype and DDR response. Thus, CDK12 has received considerable interest as a therapeutic target and tumor biomarker for HR-proficient cancers. Despite reports of functional redundancy, we observed that the genetic knockout of CDK12 could be clearly distinguished phenotypically from that of CDK13. Using map-based inference to characterize and relate cellular phenotypes, we identified RBM39 as an alternative target that selectively mimics CDK12 loss, but not CDK13, providing a novel approach for targeting CDK12 biology while circumventing any toxicities that may arise due to CDK13. We subsequently discovered REC-1245 as an RBM39 molecular glue degrader that closely mimics the phenotypic loss of CDK12 and RBM39, but not CDK13. Functionally, REC-1245 treatment globally impacts the expression of many DDR genes but does so in a CDK12 independent manner.

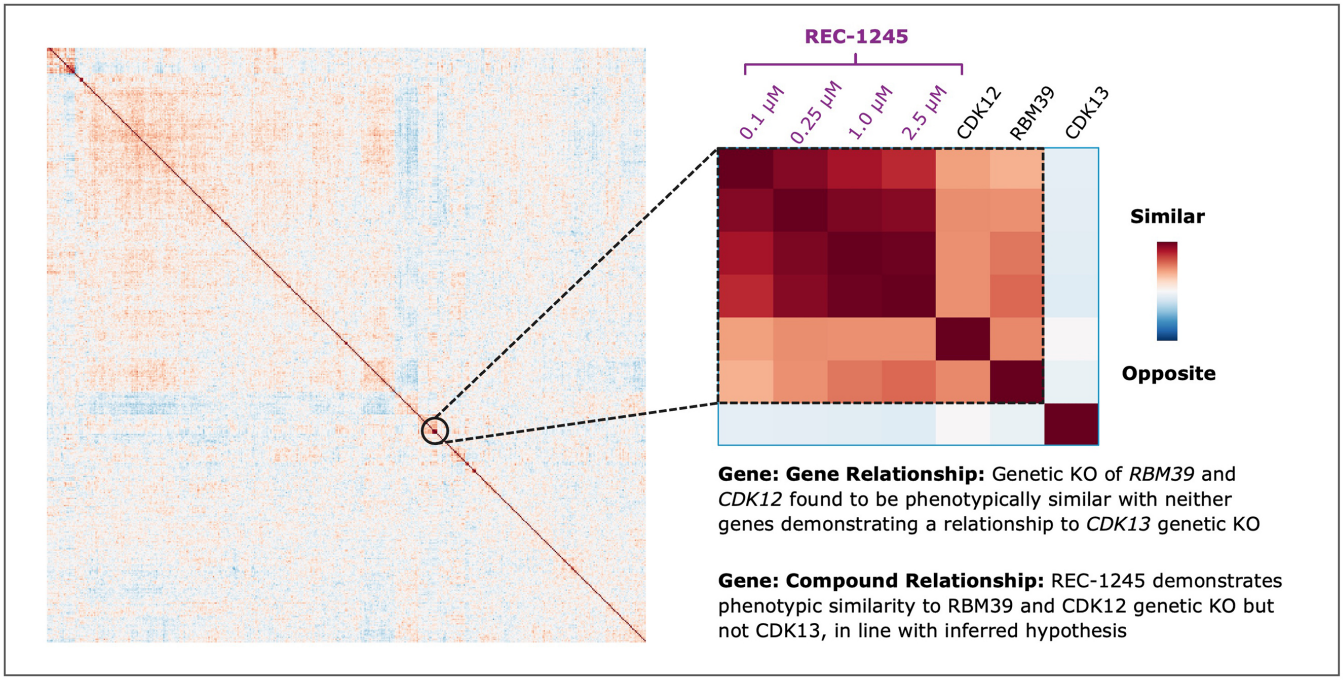


Figure 32. Inferred map relationships between CDK12, CDK13, RBM39 and REC-1245. Map representation demonstrates a high degree of phenotypic similarity between CDK12, RBM39, and multiple concentrations of REC-1245. CDK13 shows little or no functional similarity to CDK12, RBM39, or any concentration of REC-1245.

Preclinical

REC-1245 is a potent, potential first-in-class RBM39 molecular glue degrader with compelling preclinical activity. It showed no significant in vitro safety concerns (CEREP, hERG), no CDK12 kinase activity, and minimal ITGA2 liability – an off-target effect seen with prior RBM39 degraders. As shown in the figures below, REC-1245 demonstrated strong antitumor activities as a single-agent, including tumor regression in an ovarian cancer BRCA-proficient, p53 mutant, OVK18 *in vivo* cell line derived xenograft (CDX) model. In addition, dose-dependent anti-tumor activity correlated with increases in RBM39 degradation confirming target engagement and an exposure-response-efficacy relationship.

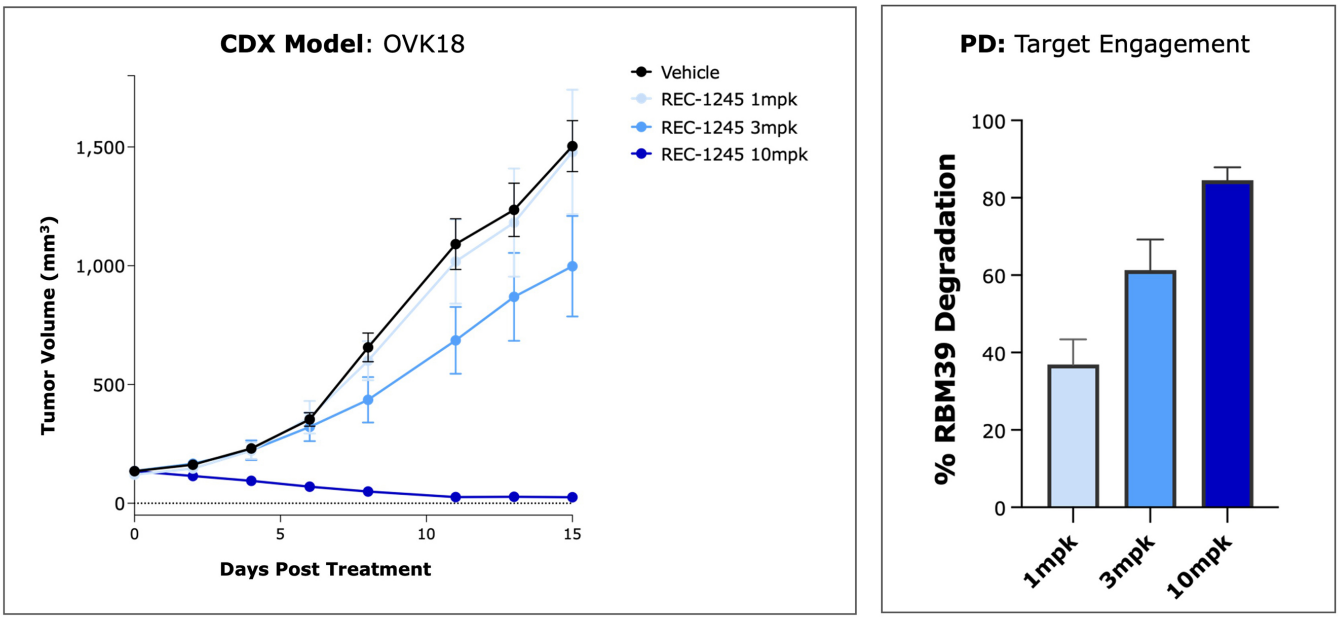


Figure 33. REC-1245 single-agent activity and target engagement. REC-1245 single-agent activity and target engagement. (Left) REC-1245 administered BID PO at doses noted for 15 days. N=8 mice per group. (Right) Percent RBM39 degradation (PD) evaluated at REC-1245 doses noted after 5 days BID oral administration of REC-1245. N=3 mice per group.[18]

Clinical

In December 2024, we initiated a Phase 1/2 open-label, multicenter study to characterize the safety, tolerability, PK, PD, and preliminary anti-tumor activity of REC-1245 in participants with unresectable locally advanced or metastatic cancer. As of December 31, 2024, the trial is currently active and enrolling at 5 US sites. We expect to share an update on the Phase 1 dose escalation portion in the first half of 2026.

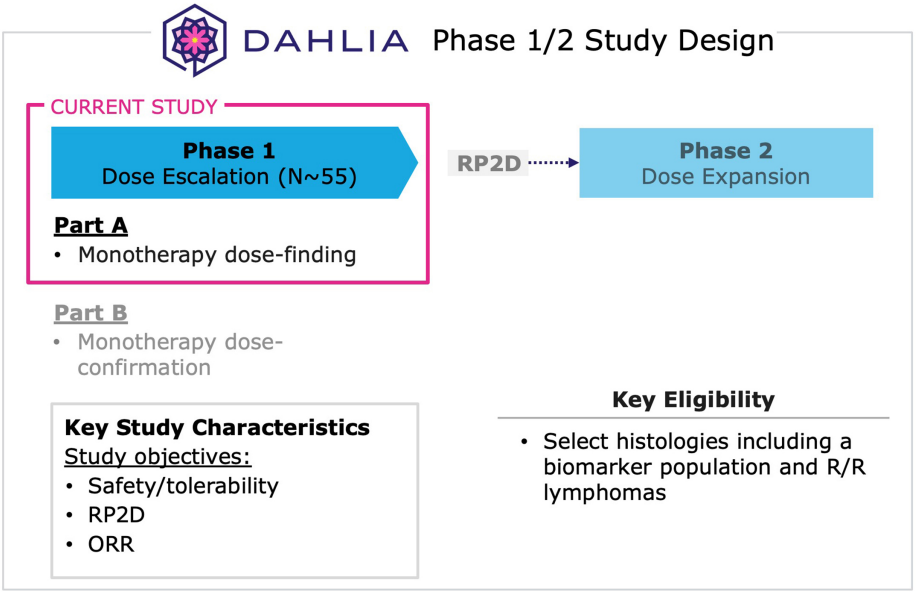


Figure 34. DAHLIA study design. Phase 1/2 trial design to assess the safety, tolerability, PK, PD, and preliminary anti-tumor activity of REC-1245 in participants with unresectable locally advanced or metastatic cancer, and who are refractory to, had a relapse on, or intolerant of, established standard of care treatment.

[18] *Data on file.*

Competitors

We are aware of only one other RBM39 development program, which is known to be active:

- ST-01156 (SEED Therapeutics): In IND-enabling studies

REC-3565 for B-Cell Malignancies – Phase 1

REC-3565 is an orally bioavailable, highly potent and selective, potential best-in-class MALT1 inhibitor currently under development for the treatment of B-cell malignancies, including chronic lymphocytic leukemia (CLL). MALT1 is a protease crucial for activation of the NF-κB pathway, which drives the proliferation of malignant B-cells in hematological cancers. There are currently no MALT1 inhibitors approved by the FDA. Following clearance of a CTA by the MHRA in December 2024, we plan to initiate EXCELERIZE, a Phase 1 open-label, multicenter, dose escalation study to evaluate the safety, tolerability, PK, PD, and preliminary anti-tumor activity of REC-3565. We expect the first patient to be dosed in the first half of 2025.

Disease Overview

B-cell malignancies encompass a range of hematological cancers, including lymphomas such as diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), and leukemias such as chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). These diseases are characterized by the dysregulated growth or function of B-cells and are often driven by chronic B-cell receptor (BCR) signaling, which leads to unchecked NF-κB activation. MALT1 functions downstream of the BCR and the widely targeted Bruton's tyrosine kinase (BTK), mediating pro-tumorigenic signals in malignant B-cells. Current therapies (e.g., BTK inhibitors) have transformed the treatment landscape, yet resistance remains a significant challenge. By inhibiting MALT1, REC-3565 may help overcome resistance and improve therapeutic outcomes, either as a monotherapy or in combination with BTK and/or BCL2 inhibitors. Notably, the total addressable population for MALT1 inhibitors spans multiple hematologic indications, with approximately 41,000 relapsed and/or refractory (R/R) patients with CLL and B-cell lymphomas in the U.S. and EU5 annually.

Insight from Recursion OS

BTK inhibitors and other therapies for B-cell malignancies can cause drug-induced liver injury (DILI), limiting combination treatment options. Current MALT1 inhibitor scaffolds significantly inhibit UGT1A1, leading to dose-limiting toxicities, potentially restricting their utility in combination. Leveraging our AI-driven, multi-parameter optimization approach, we focused on an allosteric mechanism to enhance potency, selectivity, and safety for REC-3565. Hotspot analyses and physics-based molecular dynamics guided our design strategy, helping us address the hydrophobic and highly mobile nature of the allosteric binding site. As a result, REC-3565 does not significantly inhibit UGT1A1, potentially mitigating liver toxicity risks and facilitating higher target engagement. This profile also supports combination strategies with agents known to affect liver function like BTK and BCL2 inhibitors, offering a path to potentially deeper and more durable responses.

Preclinical

REC-3565 demonstrated significant antitumor activity across multiple B-cell lymphoma models. As a monotherapy, it drove tumor regressions in ABC-DLBCL xenografts, and in combination with zanubrutinib – a next-generation BTK inhibitor – it produced durable responses, with 70% of mice displaying no palpable tumors 10 days after the last dose. Additional in vitro analyses revealed minimal UGT1A1 inhibitory effects relative to other MALT1 inhibitor scaffolds in clinical development, suggesting an improved safety and combination therapy profile.

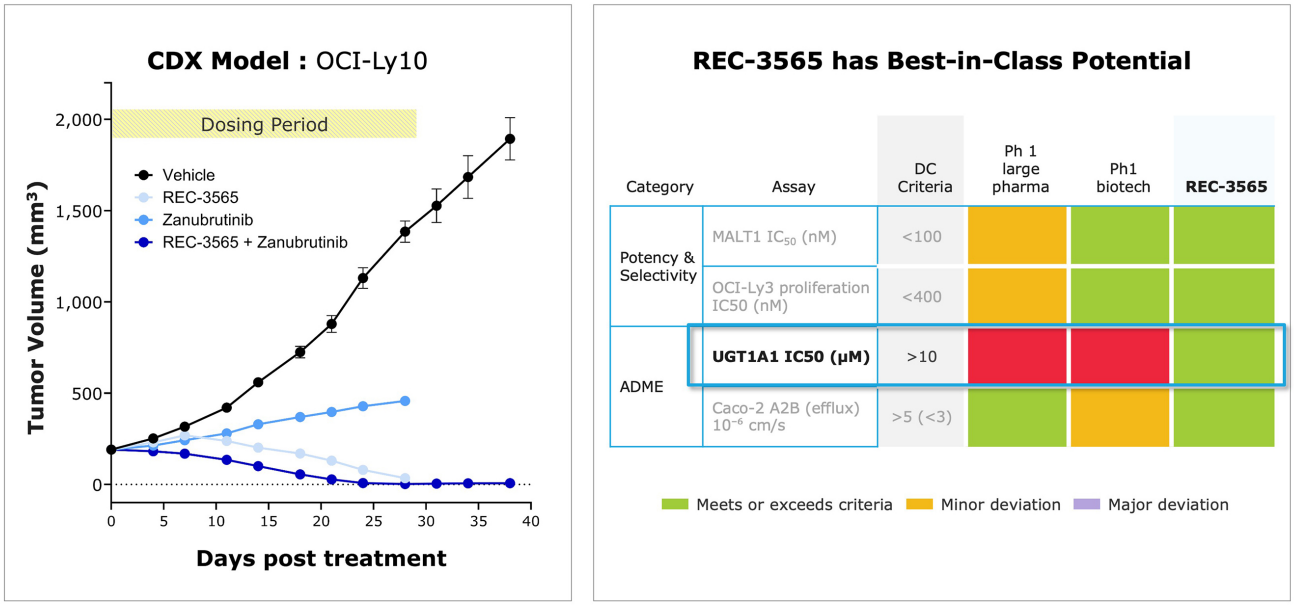


Figure 35. Preclinical data highlighting REC-3565 as a potential best-in-class MALT1 inhibitor. (Left) REC-3565 showed tumor growth regression as a single agent and when combined with zanubrutinib. N=10 per group mice per group, REC-3565 and zanubrutinib dosed BID. PD evaluated after 5 days BID oral administration of REC-1245 at doses noted. N=3 mice per group in PD portion. N=8 mice per group REC-3565 administered BID PO at doses noted. (Right) REC-3565 has best-in-class potential, especially given REC-3565 has >10 uM vs. <1 uM for other MALT1 inhibitors in clinical development. Development candidate criteria: MALT1 IC50 nM: green <100 nM; yellow >100-<300 nM; red>300 nM; OCI-Ly3 IC50 nM: green <400 nM; yellow >400-<1000 nM; red>1000 nM; UGT1A1 IC50 uM: green >10 uM; yellow <10->1 uM; red<1 uM; Caco-2 A2B (efflux): green >5(<3); yellow >1-<5(>3-<10); red <1(>10).[19,20]

Clinical

EXCELERIZE is a Phase 1 open-label, multicenter, dose escalation study designed to evaluate the safety, tolerability, PK, PD and preliminary anti-tumor activity of REC-3565 in patients with R/R B-cell malignancies. Part A will assess monotherapy dosing to identify a recommended dose for combination in Part B, which will evaluate combination regimens to inform future studies in B-cell cancers. Following CTA clearance by the MHRA in December 2024, we anticipate dosing the first patient in the first quarter of 2025.

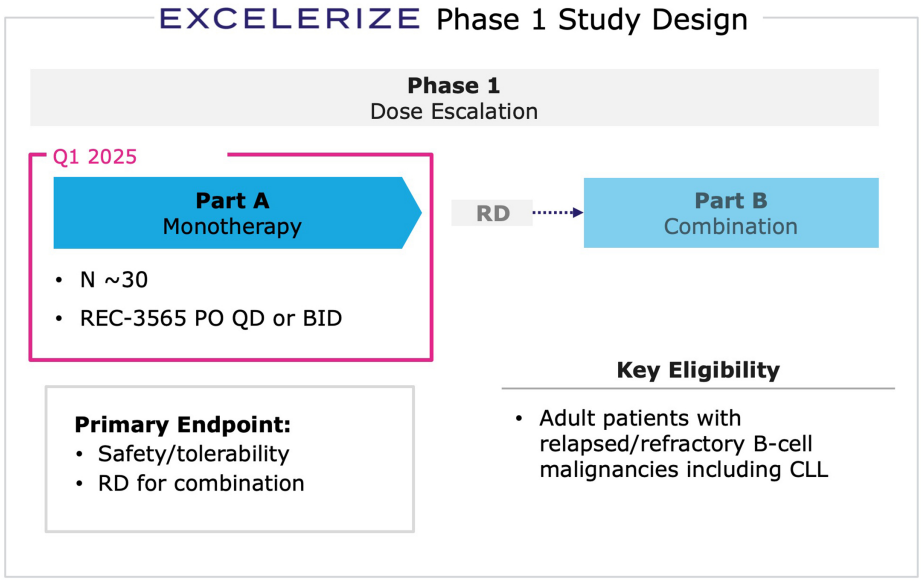


Figure 36. EXCELERIZE study design. Phase 1/2 trial to evaluate safety, tolerability, PK, PD and preliminary anti-tumor activity of REC-3565 in patients with R/R B-cell malignancies.

[19] *Payne, et al. (2024). Combining next-generation BTK and MALT1 inhibitors to enhance efficacy and therapeutic utility in B-cell malignancies [poster]. EORTC-NCI-AACR (ENA) Symposium: PB206.*

[20] *Data on file.*

Competitors

We are aware of five active MALT1 inhibitor programs currently in clinical development:

- ***ABBV-525 (AbbVie/Lupin):*** In Phase 1/2a trial in R/R B-cell malignancies
- ***JNJ-6786633 (Johnson & Johnson):*** Completed Phase 1/1b for NHL/CLL
- ***MPT-0118 (Monopteros):*** In Phase 1/1b in solid tumors with a planned Phase 1/2a in combination PD-L1
- ***SGR-1505 (Schrödinger):*** In Phase 1 in combination with BTK and BCL2 inhibitors for R/R B-cell lymphomas
- ***CTX-177/ONO-7018 (Chordia/ONO):*** In Phase 1 trial for patients with R/R NHL/CLL

REC-4539 for Small-Cell Lung Cancer – Phase 1/2

REC-4539 is an orally bioavailable, highly potent and selective, CNS penetrant, and potential best-in-class LSD1 inhibitor under development for the treatment of small-cell lung cancer (SCLC). LSD1 is an epigenetic regulator that removes methyl groups from histones, thereby controlling the expression of tumor suppressors and oncogenes. By inhibiting LSD1, REC-4539 promotes the reactivation of tumor suppressor pathways and may slow tumor growth or enhance sensitivity to cytotoxic agents. There are currently no LSD1 inhibitors approved by the FDA. In January 2025, the FDA cleared an IND application for *ENLYGHT,* a Phase 1/2 open-label, multicenter study evaluating REC-4539 patients with advanced SCLC. We expect the first patient to be dosed in the first half of 2025.

Disease Overview

Small-cell lung cancer (SCLC) is a poorly differentiated neuroendocrine tumor, representing roughly 15% of all lung cancer diagnoses. It is commonly categorized as limited stage (LS-SCLC) or extensive stage (ES-SCLC), with the majority of patients presenting with metastatic (extensive) or unresectable disease. SCLC is strongly linked to smoking, tends to grow rapidly, and frequently spreads early. Notably, over 50% of patients eventually develop brain metastases. Despite some improvements in frontline therapy such as chemotherapy plus immunotherapy, treatment options after progression remain limited. Median survival in ES-SCLC is poor, with a 5-year overall survival rate of approximately 3%. Across the US and EU5, more than 45,000 patients have a treatable Stage III/IV SCLC each year.

Within SCLC, LSD1 plays a key epigenetic role by demethylating histones that regulate critical tumor suppressor genes. Inhibiting LSD1 can reverse this epigenetic repression, upregulating pathways such as NOTCH, that promote differentiation of neuroendocrine tumor cells into a more quiescent state, potentially sensitizing them to cytotoxic therapies. However, effective LSD1 inhibition requires a reversible, brain-penetrant molecule with a short half-life to minimize risks such as thrombocytopenia. Many LSD1 inhibitors have failed to achieve these parameters, particularly brain penetration and controlled on-target effects, highlighting the unmet need that REC-4539 aims to address.

Insight from Recursion OS

Developing a selective LSD1 inhibitor for SCLC requires a reversible mechanism, a short half-life to minimize on-target toxicity (e.g., thrombocytopenia), and the ability to penetrate the blood-brain barrier to address frequent metastases. Many existing LSD1 agents fail to meet these criteria, resulting in dose-limiting toxicity and poor CNS exposure. Using our AI-driven, multi-parameter optimization approach, we generated and screened diverse chemical scaffolds for potency, selectivity, ADME properties, and CNS penetration. Active learning identified counterintuitive yet informative compounds, enabling a rapid design breakthrough. As a result, we created REC-4539 – a potent, selective, reversible, brain-penetrant, and potential best-in-class LSD1 inhibitor with a short predicted half-life. We believe these key attributes provide competitive differentiation for REC-4539 versus prior LSD1-targeted molecules.

Preclinical

REC-4539 demonstrated potent anti-tumor activity across multiple preclinical models, including the NCI-H1417 human SCLC xenograft. In this model, dose-dependent tumor regression correlated with a corresponding decrease in the neuroendocrine tumor biomarker progastrin-releasing peptide (proGRP). Additionally, REC-4539 treatment was well-tolerated, with minimal impact on platelet counts.

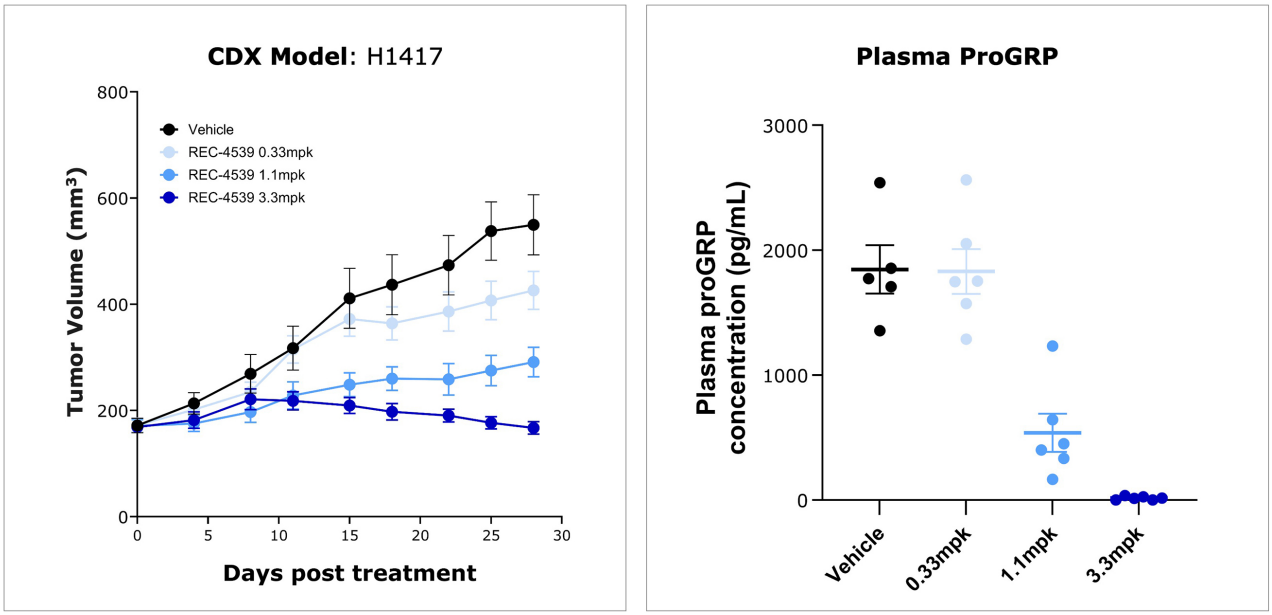


Figure 37. REC-4539 preclinical assessment in SCLC xenograft model. (Left) REC-4539 induces dose dependent tumor regression in the NCI-H1417 SCLC cell line derived xenograft mouse model. BALB/c mice, REC-4539 dosed BID, 28 day study. (Right) REC-4539 induces dose dependent tumor reductions in plasma proGRP. BALB/c mice, REC-4539 dosed BID, 28 day study.[21,22]

Clinical

ENLYGHT is a Phase 1/2, open-label, multicenter study designed to evaluate the safety, tolerability, and preliminary efficacy of REC-4539 in patients with SCLC. The FDA cleared an IND application in January 2025, and we expect the first patient to be dosed in the first half of 2025. Phase 1 will include both monotherapy dose escalation and REC-4539 combination with durvalumab, determining safety, tolerability, and a recommended dose. Phase 2 will focus on dose optimization for both monotherapy and combination arms, followed by expansion to further assess efficacy.

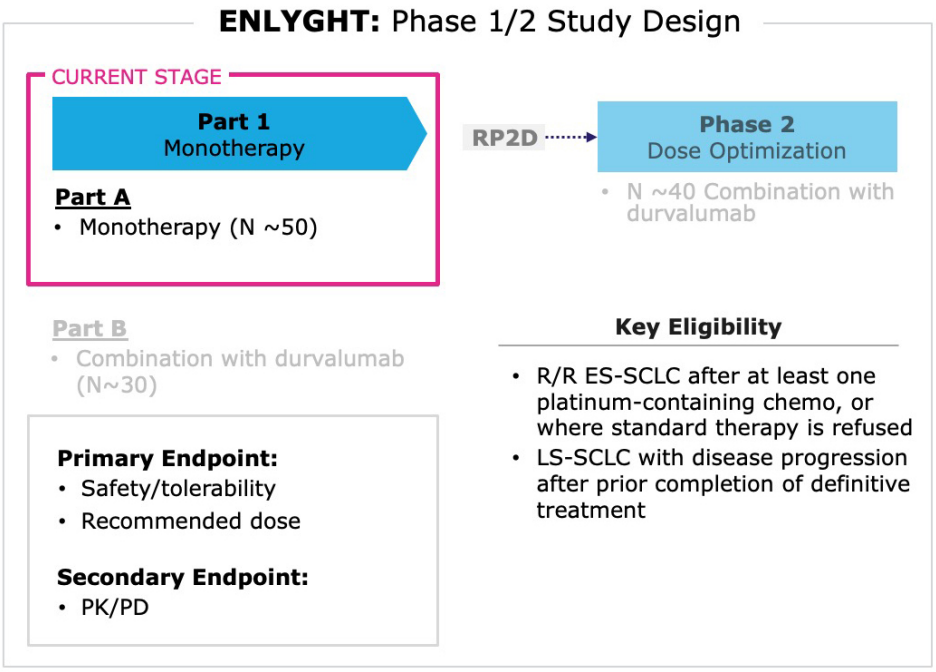


Figure 38. ENLYGHT study design. Phase 1/2 trial design to assess the safety, tolerability, and recommended dose of REC-4539 with dose escalation as monotherapy and in combination with durvalumab.

[21] *Payne, et al. (2023). Characterizing Antitumor Responses to EXS74539, a Novel, Reversible LSD1 Inhibitor with Potential in Small-cell Lung Cancer [poster]. American Association for Cancer Research (AACR) Annual Meeting: 6290.*

[22] *Data on file.*

Competitors

We are aware of three LSD1 inhibitor programs in various stages of clinical development:

- Bomedemstat (Merck): In Phase 3 trial in essential thrombocythemia (ET), a Phase 2 study in myelofibrosis (MF) and polycythemia vera (PV), and a Phase 1 study in AML (in combination with venetoclax); previously terminated Phase 1/2 SCLC trial in combination with PD-L1 maintenance
- Iadademstat (Oryzon): In Phase 2 for relapsed/refractory (R/R) SCLC and extrapulmonary high-grade NETs (in combination with paclitaxel), as well as a Phase 1b/2 trial in first-line extensive-stage SCLC (ES-SCLC) in combination with a checkpoint inhibitor; further trials are ongoing in AML
- JBI-802 (Jubilant Life Sciences): In Phase 1/2 basket study, with expansion cohorts planned in SCLC, neuroendocrine prostate cancer (NEPC), and other NETs

REC-994 for Cerebral Cavernous Malformation – Phase 2

REC-994 is an orally bioavailable superoxide scavenger under development as a potential first-in-disease therapy for symptomatic cerebral cavernous malformation (CCM). CCMs are rare neurovascular lesions characterized by abnormal capillary-venous structures, recurrent bleeding, and stroke-like symptoms. REC-994 emerged from an early version of Recursion's phenotypic platform, showing robust rescue in CCM2-deficient endothelial cells. In animal models, it reduced lesion burden by approximately 50% and improved vascular permeability. Phase 1 studies established its safety and tolerability, supporting the ongoing Phase 2 SYCAMORE trial, which to date has shown encouraging safety and preliminary efficacy signals. With no approved therapies for symptomatic CCM, we plan to consult with the FDA and other regulatory authorities on a path forward for this potential first-in-disease program and plan to share additional updates in 2025. REC-994 has received Orphan Drug Designation (ODD) in the United States and Europe.

Disease Overview

CCM is a neurovascular disorder affecting roughly 360,000 symptomatic individuals in the US and EU5, although actual prevalence may exceed one million due to underdiagnosis. CCM arises from mutations in any of three genes *(CCM1, CCM2, or CCM3)* that regulate endothelial function. These mutations result in enlarged capillary cavities with no intervening brain parenchyma, placing patients at high risk for seizures, progressive neurological deficits, and life-threatening hemorrhagic strokes. Up to 20% of cases are familial and inherited in an autosomal dominant pattern; sporadic disease makes up the remainder. Surgical resection and stereotactic radiosurgery are the primary interventions, yet many lesions – especially in the brainstem – are not amenable to resection. For approximately 25% of symptomatic cavernomas that occur in the brainstem, such invasive approaches carry substantial risks. Currently, there is no pharmacologic agent that reduces CCM lesion growth or bleeding propensity, highlighting a critical unmet need.

Insight from Recursion OS

Using a *CCM2* loss-of-function screen in human endothelial cells, our early phenotypic platform rapidly identified drug candidates capable of reversing disease-relevant phenotypes. REC-994 emerged from this unbiased approach as a potent molecule that modulated CCM pathology in vitro. These discoveries laid the groundwork for preclinical validation and subsequent clinical development, exemplifying how our platform can accelerate therapeutic innovation.

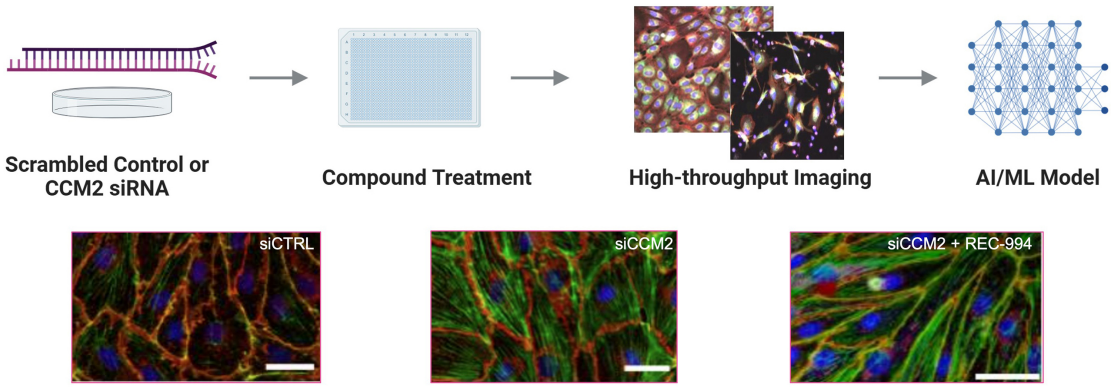


Figure 39: Rescue of structural phenotypes associated with loss of CCM2. Immunofluorescence images of endothelial cells modified with siCTRL, siCCM2, or siCCM2 and treated with REC-994. Cells stained for DNA (blue), actin (green) and VE-cadherin (red). REC-994 demonstrated image-based phenotypic rescue, as analyzed by a machine learning classifier trained on images.[23]

[23] *Gibson, et al. (2015). Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation. 131(3), 289-99.*

REC-994 is a therapeutic designed to alleviate neurological symptoms associated with CCM and potentially reduce the accumulation of new lesions with pharmacokinetics supporting once-daily dosing in humans. The putative mechanism of action of REC-994 is through reduction of reactive oxygen species and decreased oxidative stress that leads to stabilization of endothelial barrier function. In addition, REC-994 exhibits anti-inflammatory properties which could be beneficial in reducing disease-associated pathology.

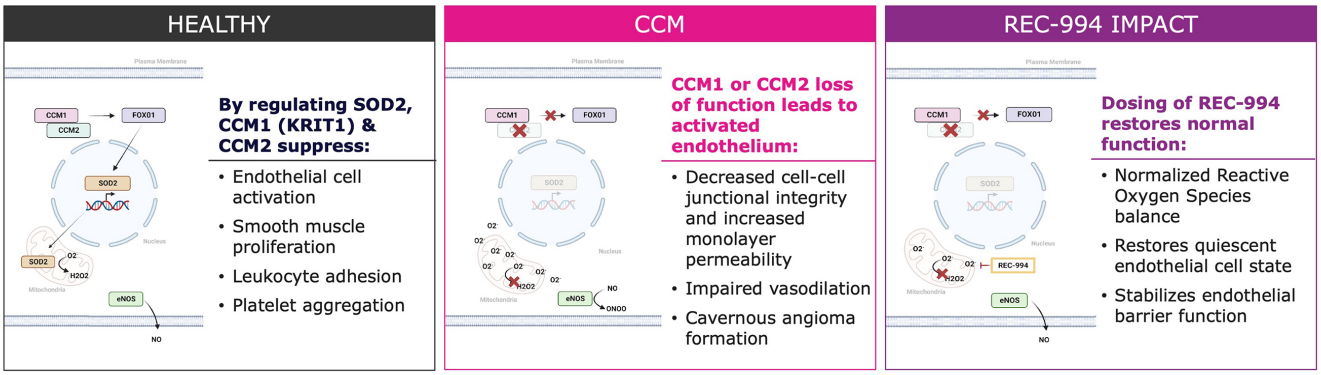


Figure 40. REC-994 mechanism of action and proposed potential therapeutic impact.[24]

Preclinical

In CCM mouse models (including *Ccm1*- and *Ccm2*-deficient strains), chronic REC-994 administration significantly reduced lesion number and size while improving vascular permeability parameters. These data supported further clinical evaluation of REC-994 investigation.

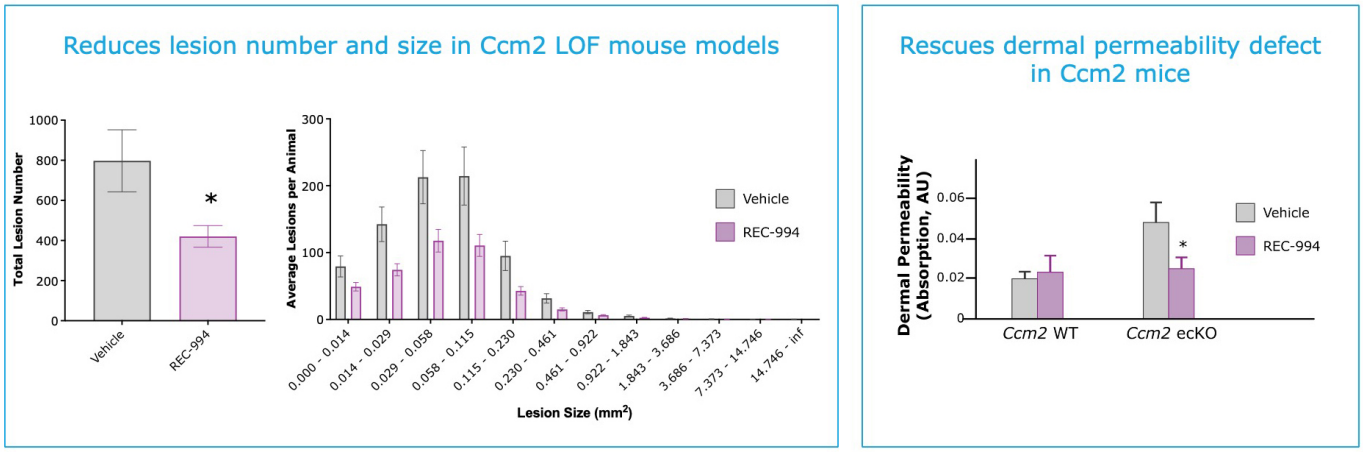


Figure 41. REC-994 reduces lesion severity and vascular permeability defects in CCM loss of function mouse models. (Left) Mice treated with REC-994 demonstrated a statistically significant decrease in the number of small-size lesions, with a trend towards a decrease in the number of mid-size lesions. (Right) REC-994 rescues the dermal permeability defects in Ccm2 endothelial specific knockout mice.[25,26]

Clinical

Phase 1

Single- and multiple-ascending dose (SAD/MAD) studies in healthy volunteers established the safety, tolerability, and pharmacokinetics of REC-994. The compound was well tolerated with no treatment-related discontinuations or serious adverse events, supporting once-daily dosing for chronic use.

[24] *Alfa R, et al. (2024). Clinical pharmacology and tolerability of REC-994, a redox-cycling nitroxide compound, in randomized phase 1 dose-finding studies. Pharmacology Research Perspectives. 12(3): e1200.*

[25] *Gibson, et al. (2015). Strategy for identifying repurposed drugs for the treatment of cerebral cavernous malformation. Circulation. 131(3), 289-99.*

[26] *Data on file.*

Phase 2 (SYCAMORE)

Initiated in March 2022, the *SYCAMORE* study is a two-part Phase 2 trial in patients with symptomatic CCM. Part 1 was a 12-month, randomized, double-blind, placebo-controlled comparison of 200 mg or 400 mg REC-994 vs. placebo daily and as of December 31, 2024, was completed. Part 2 is an optional long-term extension (LTE) for eligible participants and is currently ongoing. Approximately 80% of participants who completed 12 months of treatment opted to continue into the long-term extension portion of the study.

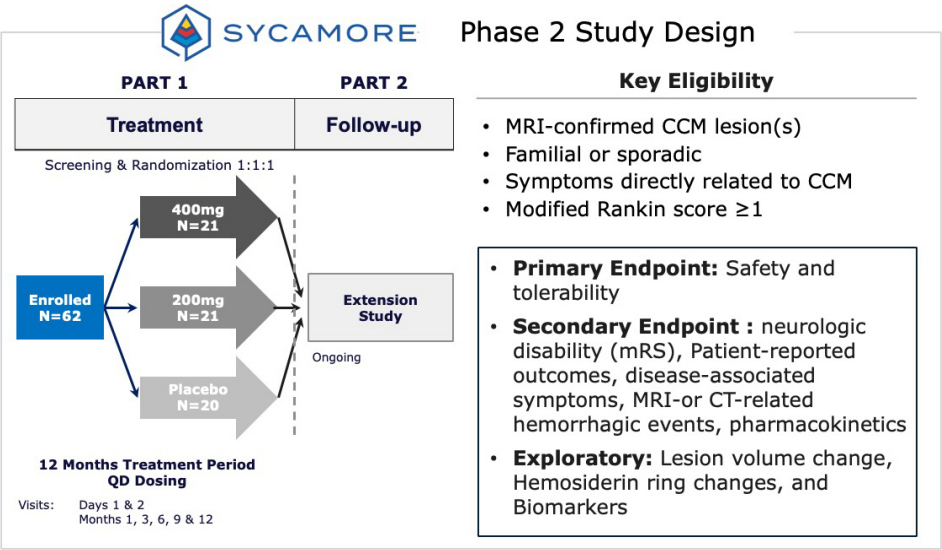


Figure 42. SYCAMORE Phase 2 study schema. Phase 2 trial design to assess the efficacy and safety of REC-994 in patients with symptomatic CCM. There was no patient enrichment by symptom, nor stratification. 13 US sites were enrolled in 18 months. Secondary and exploratory endpoints were not statistically powered.

Topline 12-month data from Part 1, shared in September 2024 and at the ISC annual meeting in February 2025, showed that REC-994 met its primary endpoints of safety and tolerability, in-line with Phase 1 results and with no new safety signals observed. Adverse events were similar between treatment and placebo groups. Common adverse events that occurred in ≥10% of patients included: dizziness, headache, back pain, constipation, COVID-19. There were no SAEs attributed to REC-994 or treatment-related adverse events leading to discontinuation. Data is highlighted in the table below.

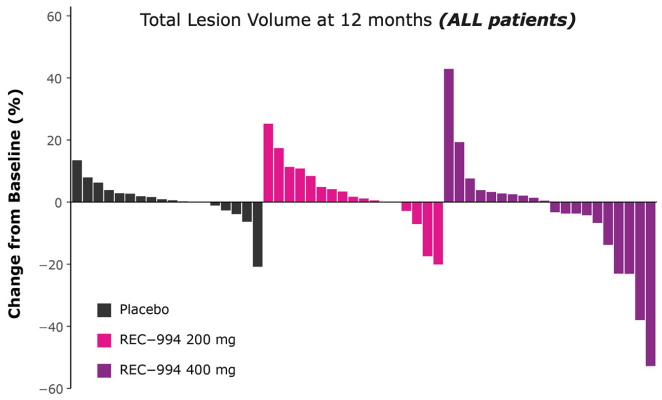
Event, n (%)	Placebo (N=20)	REC-994 200 mg (N=21)	REC-994 400 mg (N=21)	Total (N=62)
Any Treatment Emergent Adverse Event (TEAE)	**17 (85.0)**	**18 (85.7)**	**15 (71.4)**	**50 (80.6)**
TEAEs Grade ≥3	4 (20.0)	7 (33.3)	3 (14.3)	14 (22.6)
Any TEAE related to study drug[1]	**2 (10.0)**	**0**	**5 (23.8)**	**7 (11.3)**
Grade ≥3 TEAE	0	0	0	0
Discontinuation due to TEAE	0	0	0	0
Dose interruption due to TEAE	0	0	0	0

Figure 43: Summary of Treatment Emergent Adverse Events from 12-month data in Part 1 of Phase 2 Study. In the REC-994 400 mg arm these consisted of dizziness, rash, anemia, nausea and peripheral edema. In the placebo arm these consisted of dizziness and erythema multiforme. Across both arms, TEAEs related to study drug were Grade 1 or 2. TEAE=treatment-emergent adverse event.[27]

[27] *SYCAMORE data on file.*

Secondary and exploratory endpoints were centered around MRI assessments. These evaluations were performed by a single, blinded, central neuroradiologist according to a study specified protocol. Up to 10 of the most relevant CCM lesions were captured and evaluated longitudinally. Key aspects measured were lesions size, location, and acuteness of hemorrhage, if present.

An exploratory efficacy endpoint assessed lesion volume size and the changes from baseline to month 12. Patients receiving REC-994 400 mg showed an absolute mean decrease in total lesion volume of −457 mm^3 vs. 61 mm^3 increase and 53 mm^3 increase in the 200 mg and placebo arms, respectively. Notably, 50% of patients on 400 mg achieved a reduction in total lesion volume versus 28% observed in placebo. Patients treated with 200 mg REC-994 had similar changes in lesion volume compared to placebo.



All Patients with Baseline and 12-month Scans	Placebo (N=18)	REC-994 200 mg (N=17)	REC-994 400 mg (N=20)
Absolute mean change in LV[1] per patient	53 mm^3	61 mm^3	**– 457 mm^3**
Percent change in LV from baseline per cohort	1%	1%	**– 10%**
Percent of patients with any reduction in LV	28%	24%	**50%**

Figure 44. Change in total lesion volume from baseline to 12 months across all patients. Analysis of change from baseline between treatment and placebo in lesion volume (LV) at month 12 for REC-994 200 mg (p=0.912) and REC-994 400 mg (p-0.089) assessed by mixed model for repeated measures (MMRM) analysis.[28]

Further exploratory analyses suggested functional improvement in patients who received REC-994 400 mg as evaluated by the Modified Rankin Scale (mRS) score from baseline to month 12. The mRS is widely recognized and approved by the FDA as a clinically meaningful endpoint for assessing functional outcomes in acute stroke trials. A single point change on the mRS is clinically relevant, with the agency previously utilizing the scale as an endpoint in Phase 3 studies. At baseline, patients who received 400 mg REC-994 had a greater proportion of mRS scores ≥ 3, including an mRS score of 4-5, indicating that at the start of study these patients had worse clinical function compared to the placebo arm. Following 12 months of treatment, patients who received 400 mg REC-994 demonstrated trends toward improvement and/or stabilization of symptoms compared with the placebo arm, which observed trends towards functional decline.

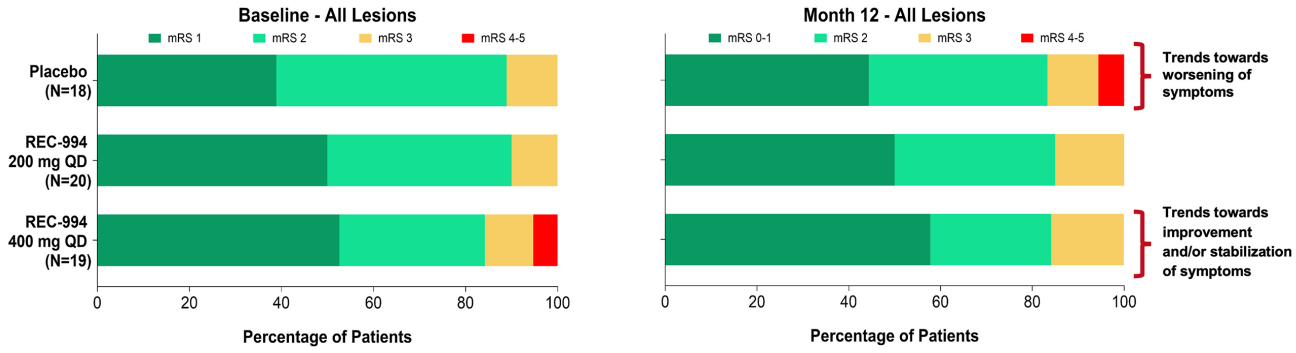


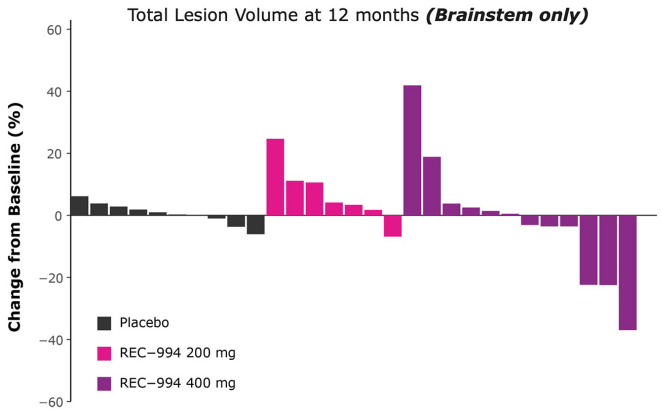
Figure 45. Summary of modified Rankin Scale Score at 12 Months for all lesions. All patients at baseline were required to have mRS >1. These observations are exploratory in nature and while not powered for statistical significance, we observed patterns that merit further investigation, and also observed a few patients transitioning down to mRS scores of 0. A single point change on the mRS is clinically relevant.[29,30]

[28] *Burkhardt, et al. (2025). The SYCAMORE Study Results: First Randomized, Placebo-Controlled Phase 2 Trial in Symptomatic Cerebral Cavernous Malformation (CCM) Evaluating REC-994 [late-breaking abstract]. International Stroke Conference (ISC); LB6*

[29] *Burkhardt, et al. (2025). The SYCAMORE Study Results: First Randomized, Placebo-Controlled Phase 2 Trial in Symptomatic Cerebral Cavernous Malformation (CCM) Evaluating REC-994 [late-breaking abstract]. International Stroke Conference (ISC); LB6*

[30] *Broderick, et al. (2017). Evolution of the Modified Rankin Scale and Its Use in Future Stroke Trials. Stroke. 48(7):2007-2012.*

Given the high unmet need in patients with brainstem lesions, where lesion volume can influence symptomatology, we evaluated lesion volume changes and mRS scores in this specific patient cohort. Patients on 400mg REC-994 had a −256mm^3 reduction in absolute mean change in lesion volume. In contrast, placebo patients had a 23mm^3 decrease in absolute mean change from baseline to month 12. Notably, 50% of patients on 400 mg also showed a reduction in total lesion volume versus 27% in the placebo arm. When evaluating the mRS score for this subgroup, a similar trend in improvement or stabilization in the REC-994 400mg arm was observed while patients in the placebo arm appeared to trend worse.



Brainstem only patients with Baseline and 12-month Scans	Placebo (N=10)	REC-994 200 mg (N=7)	REC-994 400 mg (N=12)
Absolute mean change in LV[1] per patient	-23 mm^3	123 mm^3	**– 256 mm^3**
Percent change in LV from baseline per cohort	-0.4%	7.5%	**-5.6%**
Percent of patients with any reduction in LV	27%	13%	**50%**

Figure 46. Summary of Total Lesion Volume at 12 months for Brainstem Only. Analysis of change from baseline between treatment and placebo for lesion volume (LV) at month 12 for REC-994 200 mg (p=0.987) and REC-994 400 mg (p-0.449) assessed by mixed model for repeated measures (MMRM) analysis.[31]

Additional secondary and exploratory analyses are summarized below:

- Time-dependent reductions in hemosiderin ring size observed in the 400 mg arm as compared to 200 mg and placebo
- Seizure frequency appeared to be reduced in the 400 mg arm as compared to 200 mg and placebo arms; however, there was imbalance with respect to seizure history and frequency across the arms
- Incidence of new symptomatic hemorrhage events were comparable across arms and in line with natural history studies
- Other PROs including PROMIS29, CCM-HI, NIHSS, SMSS, CGI, and PGI did not demonstrate differences between the treatment arms of the study nor placebo

All efficacy analyses were exploratory in nature and not powered for statistical significance. While we observed patterns that merit further investigation, these data require prospective validation. Approximately 80% of participants completing 12 months of therapy opted to continue in a long-term extension (LTE), which remains ongoing. Given the absence of approved therapies for CCM, we plan to discuss next steps with regulatory authorities and anticipate providing an update in 2025.

Competitors

To our knowledge, the REC-994 program is the first industry sponsored therapeutic program in clinical trials for CCM. If approved, REC-994 would be the first pharmacologic disease-modifying treatment for CCM, one of the largest areas of unmet need in the rare disease space.

We are aware of two other programs currently active in clinical development for CCM:

- ***NRL-1049 (Neurelis):*** In Phase 1 SAD study
- ***RLY-2608 (Relay Therapeutics):*** Expected to initiate FIH study Q1 2025

REC-2282 for Neurofibromatosis Type 2 - Phase 2/3

REC-2282 is a small molecule potential best-in-class HDAC inhibitor currently under development for the treatment of *NF2*-mutant meningiomas. In prior clinical trials, the molecule was well tolerated, including in patients who were dosed for multiple years. In contrast to approved HDAC inhibitors, REC-2282 is CNS-penetrant and orally bioavailable. An adaptive, Phase 2/3, randomized, multicenter study is ongoing with Phase 2 data continuing to mature. As of December 31, 2024, enrollment in Phase 2 is complete. Orphan Drug Designation in the US and EU as well as Fast Track Designation in the US were granted to REC-2282 for NF2. Results from the futility analysis (PFS6 rate) of the Phase 2 portion of the study expected in the first half of 2025.

[31] *SYCAMORE data on file.*

Disease Overview

Neurofibromatosis type 2 (NF2) is a rare, inherited tumor syndrome characterized by multiple nervous system tumors, primarily bilateral vestibular schwannomas and meningiomas. This autosomal dominant condition typically manifests in late teens or early 20s, with initial symptoms including unilateral hearing loss and focal neurological deficits. As the disease progresses, patients may experience bilateral hearing loss, facial paralysis, balance issues, and visual problems. Approximately 50% of NF2 patients develop meningiomas, often multiple, with a lifetime risk reaching 75%. Treatment is challenging due to tumor locations that often preclude complete resection, leading to significant morbidity and early mortality. With an estimated 33,000 *NF2*-driven meningioma patients annually in the US and EU5, there is an urgent need for new treatment approaches to reduce tumor burden and improve patient outcomes. There is currently no cure or approved treatment for *NF2*-driven meningioma.

Insight from Recursion OS

We selected REC-2282 as a candidate for our NF2 program using our brute-force phenotypic screening approach in *NF2*-deficent HUVEC cells. REC-2282 was uniquely identified as reversing the cellular and structural defects back to a wildtype like morphological state. The compound demonstrated concentration dependent rescue, showing no significant activity on other tumor suppressors or oncogene knockdown models. These data validated REC-2282's selective activity, supporting advancement into preclinical studies for *NF2* mutant tumors.

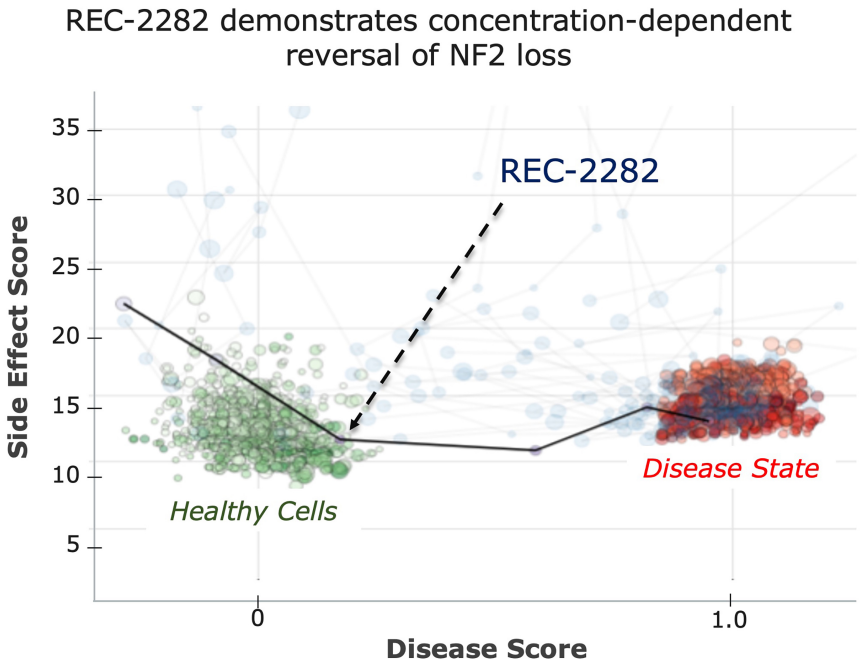


Figure 47. Discovery of REC-2282 in Recursion OS. REC-2282 rescued the high-dimensional disease phenotype as evidenced by a concentration dependent rescue from the disease state to the healthy state.

REC-2282 is an oral, CNS-penetrant pan-HDAC inhibitor with PI3K/AKT/mTOR pathway modulatory activity. With high oral bioavailability, CNS exposure, and no reported cardiovascular liabilities to date, REC-2282 is differentiated over existing HDAC inhibitors for treating NF2 and NF2-mutant CNS tumors. NF2 mutations disrupt merlin, a tumor suppressor that normally inhibits PI3K/AKT/mTOR signaling. REC-2282 targets this pathology by disrupting the PP1-HDAC interaction, suppressing PI3K/AKT signaling to induce cancer cell growth arrest and apoptosis. This mechanism addresses both HDAC-mediated epigenetic dysregulation and NF2-driven pathway hyperactivation.

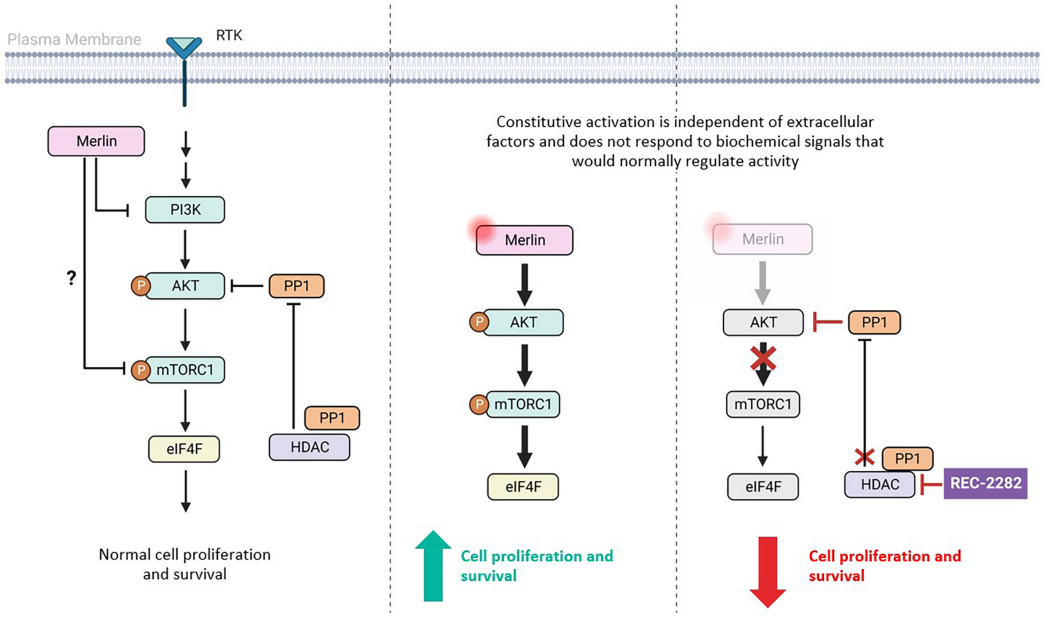


Figure 48. REC-2282 acts on an important pathway in tumor development to inhibit the growth of tumor cells. A potential mechanism of action of REC-2282 in NF2.[32]

Preclinical

REC-2282 demonstrated potent anti-tumor activity in NF2-relevant models, inhibiting proliferation of vestibular schwannoma (VS) and meningioma cells via AKT inactivation (cell cycle arrest/apoptosis). It suppressed tumor growth in NF2-deficient mouse VS allografts, human VS xenografts (25 mg/kg/day for 45 days), and orthotopic NF2-deficient meningioma models (Ben-Men-1 cells).

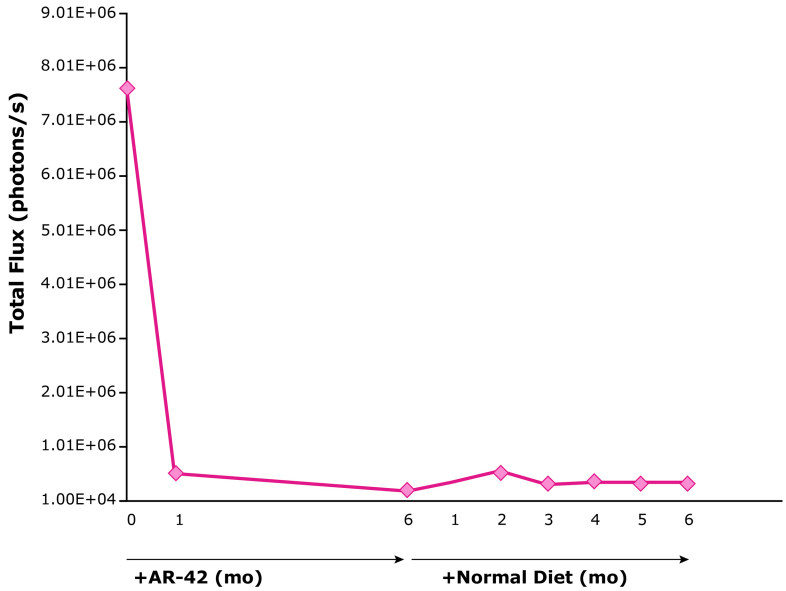


Figure 49. REC-2282 prevents growth & regrowth of tumors in the NF2-deficient meningioma mouse model. REC-2282 suppressed the growth of Ben-Men-1-LucB tumor xenografts as measured by tumor bioluminescence.[33]

[32] *Adapted from Petrilli and Fernández-Valle. (2016). Role of Merlin/NF2 inactivation in tumor biology. Oncogene, 35(5), 537-48.*
[33] *Burns SS, et al. (2013). Histone Deacetylase Inhibitor AR-42 Differentially Affects Cell-cycle Transit in Meningeal and Meningioma Cells, Potently Inhibiting NF2-Deficient Meningioma Growth. Cancer Res; 73(2), 792-803.*

Clinical

Four investigator-sponsored trials (ISTs) of REC-2282 established a 60 mg TIW MTD for solid tumors with manageable cytopenia. In an early Phase 1 pharmacodynamic IST, REC-2282 suppressed aberrant activation of ERK/AKT/S6 pathways in resected human, results which may be potentially difficult to achieve with single pathway inhibitors of ALK or MEK. An adaptive, Phase 2/3, randomized, multicenter study (POPLAR) to evaluate the efficacy and safety of REC-2282 in patients with progressive NF2-mutated meningiomas with underlying NF2 disease and sporadic meningiomas with documented NF2 mutations is currently ongoing. As of December 31, 2024, the Phase 2 portion is fully accrued with 25 adult participants enrolled. Once all 25 subjects complete six months of treatment, a futility analysis will be conducted to determine a go/no-go for the Phase 3 portion of the study. We expect to share this data in the first half of 2025.

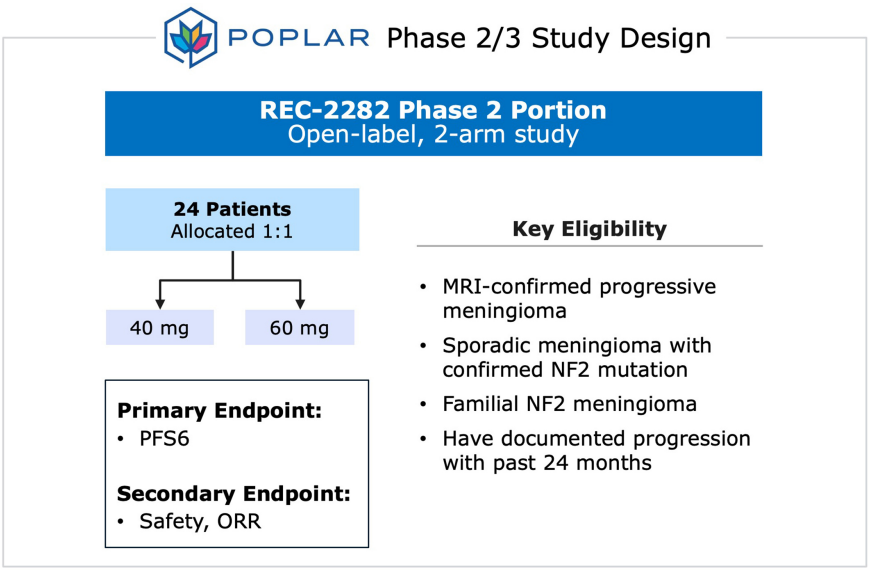


Figure 50. POPLAR Phase 2/3 study schema. Phase 2/3 study design to assess the safety, tolerability, and preliminary efficacy of REC-2282 in patients with progressive NF2-mutated meningiomas.

Competitors

We are aware of 4 programs currently in clinical development targeting NF2-driven meningiomas

- ***Selumetinib (AstraZeneca):*** Completed Phase 2 single-center study
- ***VT3989 (Vivace Therapeutics):*** In Phase 1/2 study
- ***Brigatinib and Neratinib (Takeda in collaboration with CTF and DFCI):*** Completed Phase 2 IST
- ***GSK225609 (Alliance for Clinical Trials in Oncology):*** Completed Phase 2 IST for meningiomas

REC-4881 for Familial Adenomatous Polyposis (FAP) - Phase 1b/2

REC-4881 is an orally bioavailable, non-ATP-competitive, allosteric small molecule inhibitor of MEK1 and MEK2 currently under development for familial adenomatous polyposis (FAP). REC-4881 was well tolerated in prior clinical studies, demonstrating dose-dependent increases in exposure and pharmacological activity. We are currently enrolling patients in TUPELO, a Phase 1b/2, open-label, multicenter study to evaluate the effect of REC-4881 on polyp burden reduction. Orphan Drug Designation in the US and EU as well as Fast Track Designation in the US were granted to REC-4881 for FAP. We expect to share Phase 2 safety and preliminary efficacy data in the first half of 2025.

Disease Overview

FAP is a rare, inherited tumor predisposition syndrome affecting approximately 50,000 patients in the US and EU5, resulting from heterogeneous mutations in the APC gene, a key negative regulator of the Wnt signaling pathway. FAP is characterized by the progressive development of hundreds to thousands of adenomas in the colon and rectum, with an almost 100% lifetime risk of colorectal cancer by early adulthood if untreated. While prophylactic colectomy during adolescence is the standard of care, many patients continue to develop adenomatous lesions in the rectum/pouch and duodenum sustain cancer risk, necessitating further endoscopic or surgical interventions. In advanced cases, larger adenomas and carcinoma may require localized surgeries, such as radical Whipple procedures, which carry significant morbidity and mortality. Despite this substantial disease burden, no approved therapies currently exist for FAP.

Insights from Recursion OS

REC-4881 was identified as a potential first-in-disease therapy for FAP using a high-content phenotypic screening approach targeting APC-deficient human cells. In this screen, REC-4881 emerged as a potent allosteric MEK1/2 inhibitor that rescued an APC siRNA genetic knockdown-associated morphological phenotype. Compared to other MEK inhibitors, REC-4881 demonstrated a highly selective and concentration-dependent response, suggesting best-in-class potential. As a result, REC-4881 was in-licensed from Takeda and subsequently advanced into preclinical studies.

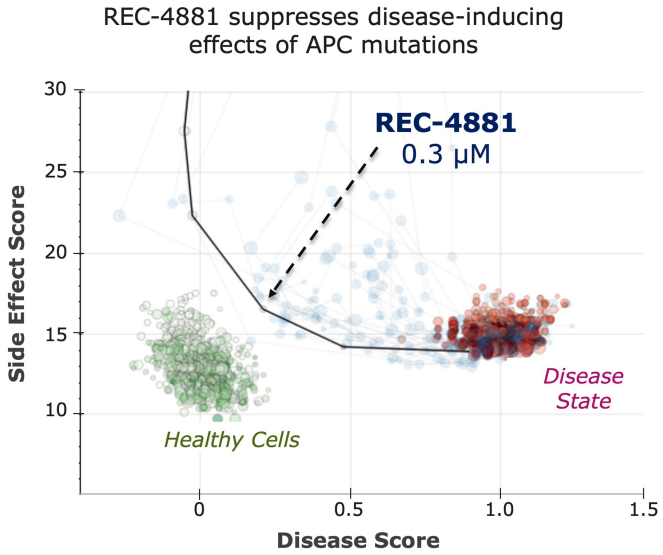


Figure 51. Discovery of REC-4881 in Recursion OS. Compared to thousands of other molecules tested, REC-4881 rescued phenotypic defects associated with APC siRNA genetic knockdown.

REC-4881 is an orally bioavailable, non-ATP-competitive allosteric inhibitor of MEK1 (IC_{50}: 2-3 nM) and MEK2 (IC_{50}: 3-5 nM) being developed as a potential first-in-disease therapy for FAP. Loss of APC disrupts β-catenin regulation, leading to uncontrolled Wnt signaling, RAS stabilization, and ERK pathway activation, which drives MYC-dependent proliferation. REC-4881 inhibits MEK1/2, and blocks ERK phosphorylation downstream. This reduces MYC expression levels in the cell and potentially restores Wnt pathway control. Given ERK signaling activity in both adenoma epithelium and tumor stroma, as well as frequent MAPK-activating mutations in FAP, MEK inhibition offers a targeted strategy to suppress disease progression.

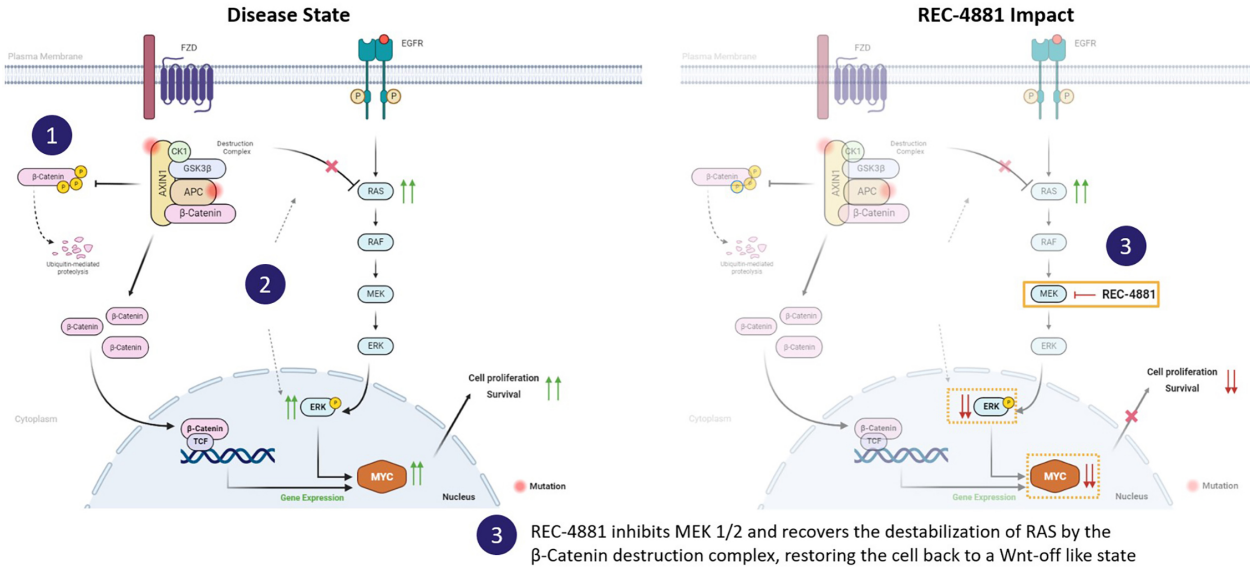


Figure 52. REC-4881 inhibits APC-mutation induced MAPK signaling to block cell proliferation in the context of FAP. A potential mechanism of action of REC-4881 in cells with loss of function mutations in APC.[34]

[34] *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).*

Preclinical

REC-4881's activity was validated in tumor cell lines and spheroid models derived from APC-mutant human epithelial tumor cells. In these systems, REC-4881 inhibited spheroid growth and disrupted cellular organization, demonstrating over 1,000-fold selectivity in APC-mutant cells. In a disease-relevant FAP model, $Apc^{Min/+}$ mice were treated with multiple oral doses of REC-4881 or celecoxib over eight weeks. While celecoxib reduced polyp formation by approximately 30% compared to vehicle, REC-4881 treatment led to a reduction of 50% (1-3 mg/kg), and 70% (10 mg/kg). Mice that were treated with 10 mg/kg REC-4881, the highest dose tested, exhibited an approximately 70% reduction in total polyps. Histological analysis of gastrointestinal tissues further revealed that, unlike celecoxib, which primarily affected benign polyps, REC-4881 significantly reduced both benign polyps and high-grade adenomas. These findings suggest that REC-4881 not only limits early polyp formation but may also inhibit progression to advanced adenomas, highlighting its potential to address both pre- and post-colectomy FAP populations.

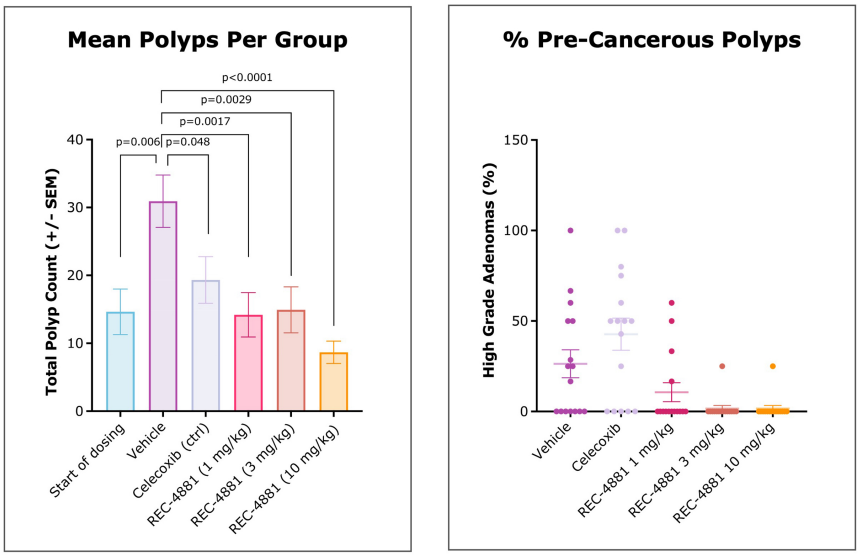


Figure 53. REC-4881 reduces GI polyp count and pre-cancerous, high-grade adenomas in the $Apc^{Min/+}$ mouse model of FAP. GI polyp count (left) and the percentage of high-grade adenomas (right) after oral administration of indicated dose of REC-4881, celecoxib, or vehicle control for 8 weeks. Polyp count at the start of dosing reflects animals sacrificed at the start of study (15 weeks of age). $P < 0.001$ for all REC-4881 treatment groups vs. vehicle control. Quantification of high-grade adenomas versus total polyps was based on blinded histological review by a pathologist. While celecoxib reduces benign polyps, most remaining lesions are high-grade adenomas. By contrast, REC-4881 reduces both polyps and high-grade adenomas.[35]

Clinical

REC-4881 has been evaluated in multiple clinical studies, demonstrating a well-tolerated safety profile and pharmacological activity.

Phase 1 Oncology Studies

In a prior dose-escalation study (C20001) conducted by Millennium Pharmaceuticals in 51 participants with non-hematologic malignancies, REC-4881 (formerly TAK-733) was administered at doses ranging from 0.2 mg to 22 mg once daily. The maximum tolerated dose (MTD) was determined to be 16 mg. The most common adverse events (AEs) were rash (67%), and treatment-related serious adverse events (SAEs) were infrequent. No unexpected safety concerns emerged, and pharmacokinetic analyses showed a less-than-dose proportional increase in exposure.

REC-4881-101 (Healthy Volunteers)

We conducted a Phase 1 study to evaluate the safety and pharmacokinetics of REC-4881 in 25 healthy participants receiving single doses of 4 mg, 8 mg, and 12 mg. REC-4881 was well tolerated, with no SAEs or dose-related safety concerns. The most common treatment-emergent adverse events (TEAEs) were mild and self-limiting, including transient blurred vision and vitreous floaters. No QTcF abnormalities were observed.

[35] *Data on file.*

TUPELO (Phase 1b/2 in FAP)

We are currently enrolling patients in TUPELO, a Phase 1b/2 open-label, multicenter study evaluating the efficacy, safety, pharmacokinetics, and pharmacodynamics of REC-4881 in FAP. Part 1 assessed safety, tolerability, and pharmacokinetics in FAP patients receiving 4 mg once daily for 14 days. REC-4881 was generally well-tolerated, with a safety profile consistent with other MEK inhibitors. Preliminary pharmacodynamic data suggests the 4 mg dose is pharmacologically active in FAP. Part 2 will evaluate efficacy, safety, and pharmacokinetics in post-colectomy FAP patients with confirmed germline APC mutations. Participants will receive once-daily REC-4881 for three months. Safety and preliminary efficacy data from Part 2 are expected in the first half of 2025.

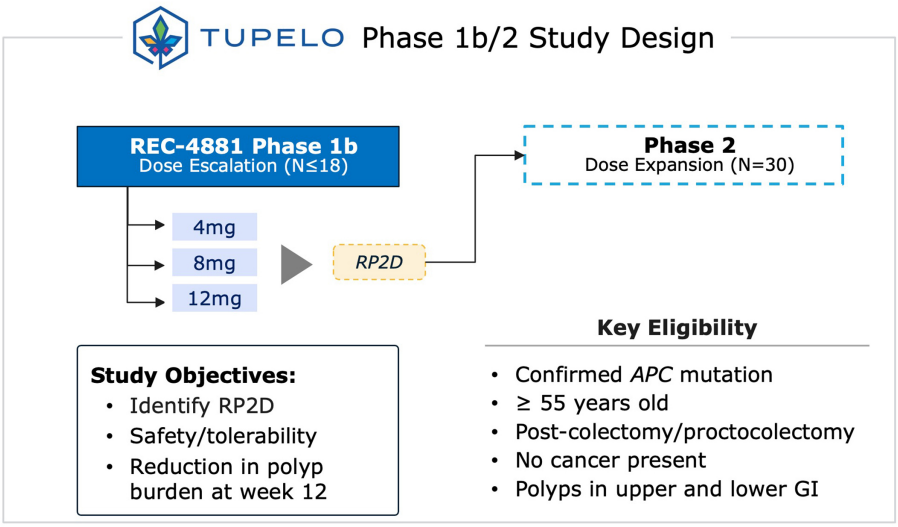


Figure 54. Phase 1b/2 study schema for REC-4881. Phase 1b/2 clinical study to assess the efficacy, safety, and pharmacokinetics of REC-4881 in patients with classical Familial Adenomatous Polyposis (FAP)

Competitors

We are aware of seven other currently active programs in clinical development for FAP:

- ***ALFA (SLA Pharma/KD Pharma):*** In Phase 3 trial in patients with confirmed APC mutations post-colectomy
- ***Flynpovi (Panbela Therapeutics):*** In Phase 3 combination therapy targeting lower GI disease in FAP
- ***eRapa (Biodexa Pharmaceuticals):*** Planned Phase 3 for FAP
- ***TPST-1495 (Tempest Therapeutics):*** Planned Phase 2 trial in FAP
- ***Lapatinib (Johnson & Johnson):*** Completed Phase 1 trial in FAP
- ***ST-316 (Sapience Therapeutics):*** In Phase 1/2 with dose expansion study ongoing in colorectal cancer
- ***ZKN-013 (Almirall/Eloxx Pharmaceuticals):*** In Phase 1 trial that includes an FAP cohort

REC-3964 for Prevention of Recurrent *Clostridioides Difficile* Infection - Phase 2

REC-3964 is an orally bioavailable, non-antimicrobial, small molecule designed to prevent recurrence of *Clostridioides difficile (C.diff)* infection (rCDI) and serve as a secondary prophylactic therapy in high-risk patients. Unlike antibiotics, which can further disrupt gut microbiota and contribute to relapse, REC-3964 selectively targets *C. difficile* toxin B without affecting the host. Identified using Recursion's AI-driven phenotypic screening platform, REC-3964 demonstrated potent toxin inhibition and barrier restoration in preclinical studies. A Phase 1 study established its safety, tolerability, and pharmacokinetics, supporting the initiation of the ALDER Phase 2 trial in Q3 2024. This trial is evaluating REC-3964's ability to reduce recurrence rates in patients recovering from a recent *C. diff* infection. We expect to share preliminary data in the first quarter of 2026.

Disease Overview

C. diff is a significant cause of antibiotic-associated diarrhea, leading to severe colitis and potentially fatal outcomes. Annually, over 730,000 cases are reported in the U.S. and EU5, with approximately 29,000 deaths in the U.S. alone. Standard antibiotic treatments can disrupt the gut microbiome, resulting in recurrence rates of 20 to 30% after initial infection, increasing to 40% after the first recurrence and 45–65% after multiple recurrences. This escalating pattern underscores the urgent need for novel therapeutic approaches that address rCDI.

Insight Recursion OS

Leveraging the Recursion OS, we identified REC-3964 as a new chemical entity that selectively inhibits the glucosyltransferase activity of *C. difficile* toxin B. This non-antibiotic approach was discovered through a high-content phenotypic screen, where REC-3964 demonstrated potent reversal of toxin-induced cellular damage in HUVEC. We drove SAR and optimization of REC-3964 directly on the platform and subsequently advanced the molecule into preclinical studies.

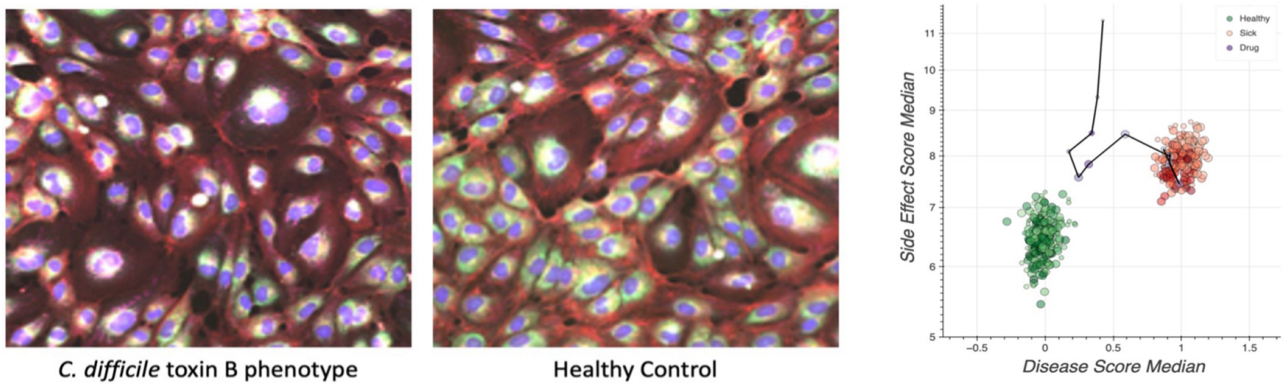


Figure 55. REC-3964 rescued the phenotype of human epithelial cells treated with *C. difficile* toxin. REC-3964 was identified as demonstrating concentration-responsive rescue in HUVEC cells treated with *C. difficile* toxin B on Recursion's phenomics platform.

Preclinical

REC-3964 was validated in orthogonal functional assays including the electrical cell-substrate impedance sensing (ECIS) assay where it demonstrated concentration-dependent activity in blocking toxin-mediated barrier disruption. In a hamster model of *C. diff*, REC-3964 treatment significantly prolonged survival compared to bezlotoxumab and control groups, indicating its potential to reduce both initial infection severity and recurrence rates.

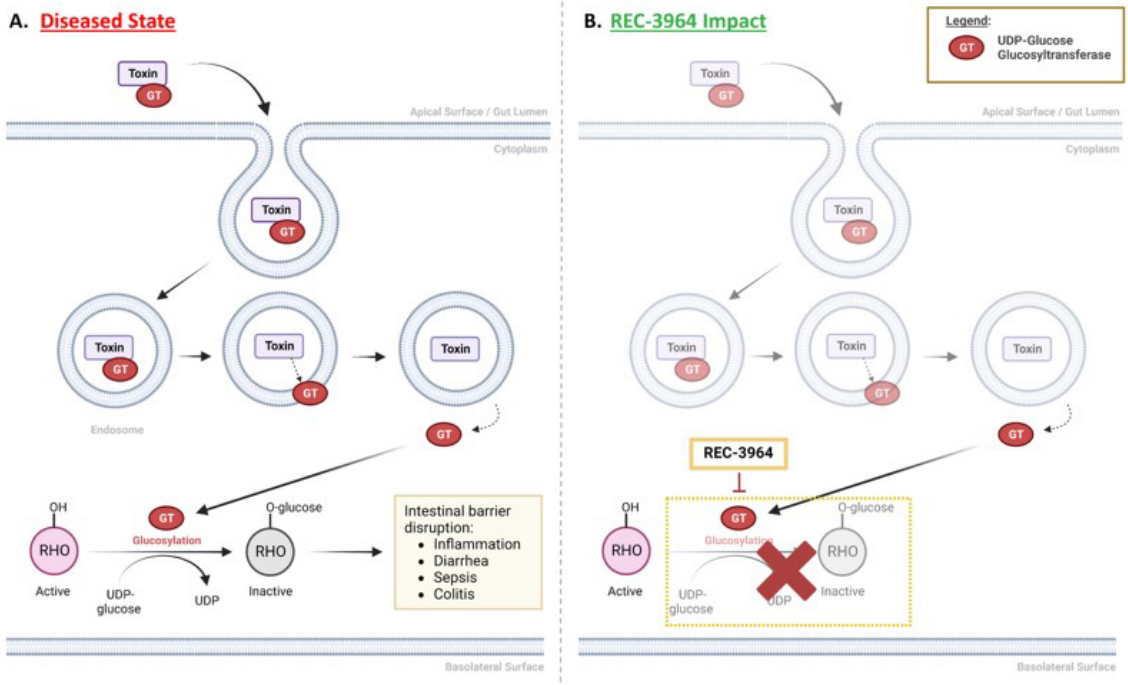


Figure 56. REC-3964 selectively inhibits the toxin's innate UDP-glucose glucosyltransferase. (Left) Autocatalytic event releases *C. difficile* toxin's glucosyltransferase enzymatic domain into the infected cell, which locks Rho family GTPases in the inactive state. Inactivation of Rho GTPases alters cytoskeletal dynamics, induces apoptosis and impairs barrier function which drives the pathological effects of *C. difficile* infection. (Right) REC-3964 binds and blocks catalytic activity of the toxin's innate glucosyltransferase with no effect on the host protein.[36]

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

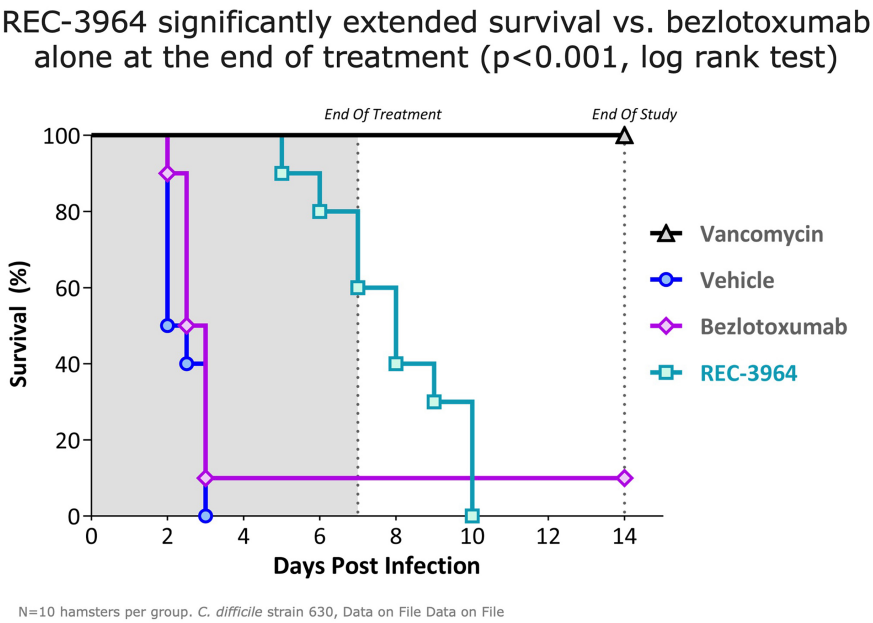


Figure 57. REC-3964 in vivo efficacy in a CDI hamster model. REC-3964 was administered at 200 mg/kg by oral gavage twice daily for 7 consecutive days along with groups for vehicle and vancomycin (50 mg/kg, QD). Bezlotoxumab was administered at 10 mg/kg BID 2 days prior to inoculation with C. difficile (strain 630). N=10 hamsters per group. Clinical observations were conducted from Day 0 to Day 7, with surviving animals monitored until Day 14. REC-3964 demonstrated a significant difference in the probability of survival vs. bezlotoxumab at the end of treatment (p<0.001, log-rank test).[37]

Clinical

REC-3964 has been evaluated in a Phase 1 study in healthy volunteers and is currently being investigated in the ALDER Phase 2 trial for rCDI.

Phase 1 (Healthy Volunteers)

A Phase 1 study assessed the safety, tolerability, and pharmacokinetics of REC-3964 in 90 healthy participants, including a cohort of elderly subjects (>65 years). REC-3964 was well tolerated at single doses up to 1,200 mg and multiple doses up to 900 mg, with no serious adverse events (SAEs), discontinuations, or deaths. The most common treatment-emergent adverse events (TEAEs) were mild and included fatigue, headache, and abdominal distension, with similar rates between REC-3964 and placebo groups. Pharmacokinetics demonstrated dose-proportional exposure with a 7 to10 hour half-life, supporting twice-daily (BID) dosing. No clinically significant effects on ECG parameters, vital signs, or laboratory markers were observed. Results were presented at the 6th Edition of the World Congress on Infectious Diseases in June 2024.

Phase 2 (ALDER – Ongoing, Initiated Q3 2024)

The ALDER study is a Phase 2 open-label, multicenter trial evaluating REC-3964 as secondary prophylaxis therapy in patients recovering from an initial *C. diff* infection. Participants will be randomized 2:1:1 to receive 500 mg or 250 mg BID for 28 days, compared to an observational cohort. The primary endpoints are safety, tolerability, and recurrence rates of rCDI. A Phase 2 data update is expected in the first quarter of 2026. To our knowledge, REC-3964 is the first orally bioavailable, non-antibiotic, *C. diff* toxin inhibitor that selectively targets bacterial toxin, while sparing the host.

[37] *Stiles, et al. (2024). REC-3964, a First-in-Class Molecule for the Prevention of Recurrent Clostridioides difficile Infection [poster]. World Congress on Infectious Diseases. 6th edition.*

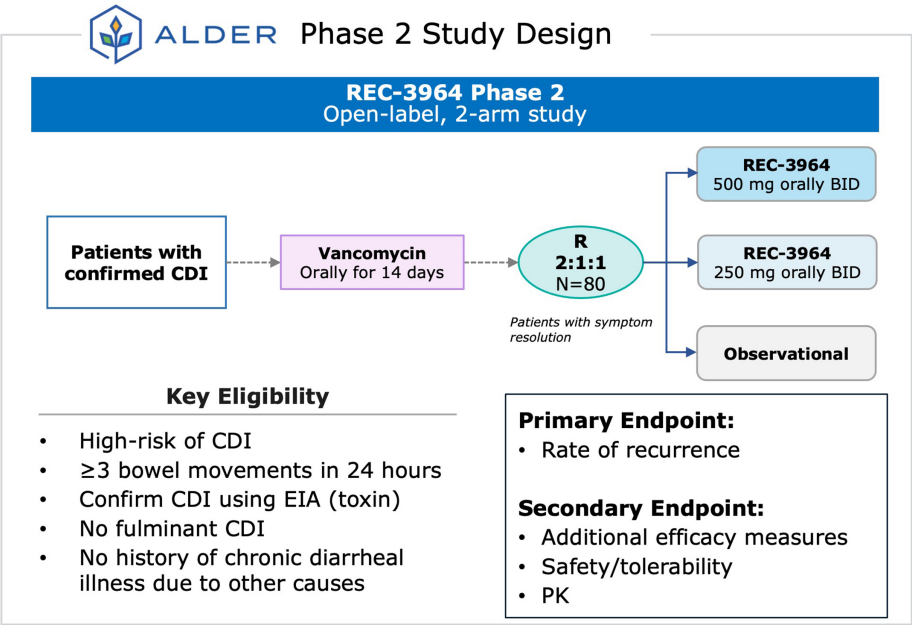


Figure 58. Planned Phase 2 study schema of REC-3964 for prevention of rCDI. Phase 2 open-label, multicenter clinical study to assess the safety, tolerability, PK, and efficacy of REC-3964 at two dose levels. Enrollment criteria include (1) High risk for rCDI; (2) C. difficile associated diarrhea with confirmation of toxin positivity (3) No fulminant CDI; (4) No history of chronic diarrheal illness due to other causes. The primary endpoints are safety, tolerability, and efficacy as determined by the rate of reduction of rCDI after initial clinical cure with vancomycin.

Competitors

There are a number of approved drugs for the treatment and prevention of C. difficile infection.

- ***Vancomycin, Fidaxomicin (Merck), and Metronidazole:*** Most commonly prescribed antibiotics; however, the efficacy of antibiotic therapy decreases with each recurrence
- ***Bezlotoxumab (Merck):*** Approved for reducing CDI recurrence in patients receiving antibiotics who are at high-risk for CDI recurrence
- ***RBX2660 (Ferring) and SER-109 (Seres Therapeutics):*** Approved stool derived microbiome products used for recurrent CDI prevention, following antibiotic treatment

We are aware of seven currently active programs in clinical development for the prevention of recurrent C. difficile infection:

- ***VE303 (Vedanta Biosciences):*** In Phase 3 study for 14-day course in patients with ≥ 1 prior occurrence of CDI, including a high-risk for recurrence population along with an open-label extension if recurrence of CDI occurs during study
- ***NTCD-M3 (Sebela Pharmaceuticals/Destiny Pharma):*** In Phase 3 planning stages for naturally occurring non-toxigenic strain of C. difficile
- ***LMN-201 (Lumen Bioscience):*** In Phase 2 study in patients newly diagnosed with CDI planning to receive antibiotic treatment
- ***CRS3123 (Crestone):*** In Phase 2 study assessing two different doses compared to vancomycin
- ***IMM-529 (Immuron):*** In Phase 2 study for primary and recurrent CDI
- ***OraCAb (MicroPharm):*** In Phase 2 planning stages to assess oral immunotherapeutic for primary and recurrent CDI
- ***AZD5148 (AstraZeneca):*** In Phase 1 study assessing the anti-toxin B neutralizing mAb injectable for the reduction of CDI recurrence

Selected Preclinical Programs:

- REV102 a potential first-in-class and best-in-class ENPP1 inhibitor for Hypophosphatasia (HPP)
- REC-4209, a potential first-in-class NCE for the treatment of Idiopathic Pulmonary Fibrosis (IPF)

REV102 for Hypophosphatasia – IND Enabling

In 2019, Recursion (formerly Exscientia) and Rallybio established a co-development and co-ownership joint venture to apply AI-driven drug discovery to rare diseases. Using Recursion's generative AI platform, Gambit, we identified ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) as a target for the treatment of Hypophosphatasia (HPP). ENPP1 catalyzes the production of inorganic pyrophosphate (PPi), exacerbating the mineralization imbalance in HPP patients. Inhibiting ENPP1 offers a novel therapeutic approach to restoring PPi balance, promoting proper bone formation. This led to the discovery and development of REV102, a selective, orally bioavailable ENPP1 inhibitor optimized for chronic dosing with high potency and a favorable safety profile. As of December 31, 2024, REV102 has advanced to development candidate status, with IND-enabling studies expected in 2025. If successful, REV102 could provide the first oral treatment for juvenile-onset and adult HPP, addressing the limitations of enzyme replacement therapy (ERT) and expanding treatment options for patients with unmet needs.

Disease Overview

HPP is a rare genetic disorder caused by ALPL mutations, leading to deficient tissue-nonspecific alkaline phosphatase (TNAP) activity and PPi, a potent inhibitor of bone mineralization. PPi accumulation disrupts hydroxyapatite formation, resulting in skeletal deformities, fractures, and premature tooth loss. HPP severity varies from severe early-onset cases, presenting in infancy with life-threatening complications, to juvenile-onset and adult forms, which cause progressive fractures, pain, and mobility issues. Current treatment is limited to enzyme replacement therapy (ERT), and is associated with frequent injections, immunogenicity, and costs exceeding $1 million per year. By selectively inhibiting ENPP1, REV102 aims to restore physiological mineralization by normalizing PPi levels, offering a non-immunogenic, oral alternative to ERT. With an estimated 7,800 diagnosed HPP patients at birth in the US and EU5, REV102 has the potential to expand treatment access to underserved patients.

Insight from Recursion OS

Using our GenAI platform, we designed REV102, a potential first-in-class and best-in-class orally bioavailable and highly selective ENPP1 inhibitor for HPP. Our proprietary generative AU design algorithm, Gambit, guided precision optimization, incorporating rigorous 3D and 2D constraints to ensure high potency and suitability for lifelong chronic dosing. This AI-driven approach allowed the discovery of a structurally distinct compound with strong target engagement, designed to restore PPi homeostasis and improve bone mineralization in juvenile-onset and adult HPP patients.

Preclinical

In preclinical studies, our first-generation tool compound, REV101, demonstrated improved bone mineralization in HPP mouse models. Bone morphometry analysis showed that L3 vertebrae in treated HPP mice reached mineralization levels comparable to wildtype mice, while trabecular regions of the distal femur exhibited slight improvement. Notably, REV101 significantly reduced plasma PPi levels by approximately 30%, restoring them to wildtype levels after 100 days of dosing. These findings validate ENPP1 inhibition as a viable therapeutic approach for HPP and informed the design and optimization of REV102 for clinical development.

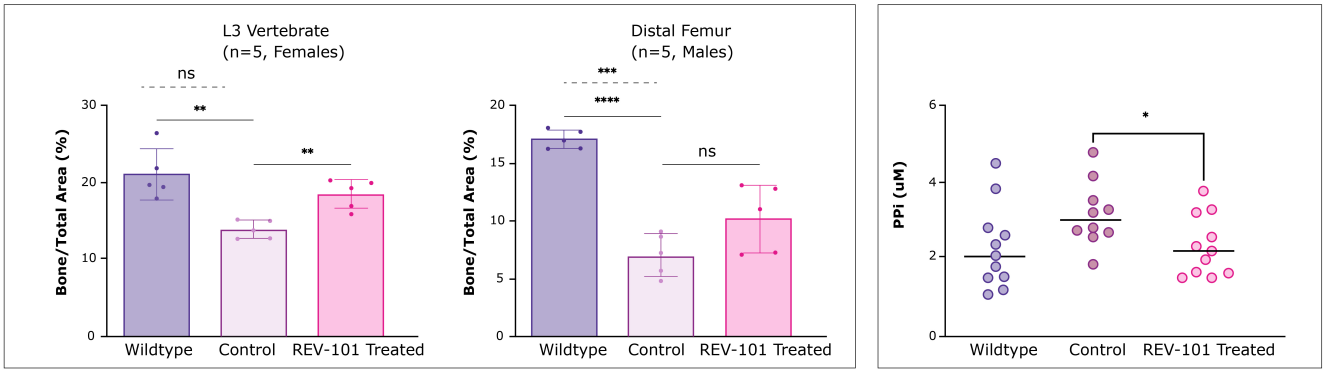


Figure 59. (Left) ENPP1 inhibition results in improved mineralization in mouse models of HPP. Alpl-/^{Prx1} mouse model. 2D Bone morphometric analysis of trabecular bones was performed on Von Kossa-stained sections using the Kawamoto's film method. (Right) ENPP1 inhibition reduces PPi levels to those of wild-type mice. Alpl-/^{Prx1} in an adult-onset HPP mouse model. Plasma levels of PPi following 100 days of dosing.[38]

[38] *Narisawa, et al. (2024). ENPP1 Inhibition as a Therapeutic Approach for Later-onset Hypophosphatasia [late breaking poster]. American Society for Bone and Mineral Research (ASBMR) Annual Meeting.*

REC-4209 for Idiopathic Pulmonary Fibrosis (IPF) – IND Enabling

Recursion identified REC-4209, a potential first-in-class, orally bioavailable immuno-mesenchymal modulator for idiopathic pulmonary fibrosis (IPF) using phenotypic screening of human PBMC-derived fibrocytes. This approach uncovered Target Epsilon, a novel regulator of fibrotic diseases. REC-4209 selectively modulates fibrocytes, fibrotic macrophages, and adaptive immune cells, offering a potential disease-modifying approach distinct from current therapies. REC-4209 is currently undergoing IND-enabling studies in preparation for clinical development.

Disease Overview

IPF is a chronic, progressive interstitial lung disease characterized by fibrotic remodeling of lung tissue, leading to irreversible respiratory decline. The disease affects approximately 3 million patients globally, with incidence rising significantly in individuals over 50 years old. Fibroblast accumulation, myofibroblast activation, and excessive extracellular matrix deposition contribute to progressive lung volume loss and impaired gas exchange. Repeated epithelial injury, coupled with immune dysregulation and fibroblast dysfunction, drives self-perpetuating fibrosis in IPF. Current antifibrotic therapies, nintedanib and pirfenidone, only slow disease progression, leaving an urgent unmet need for disease-modifying treatments that restore tissue integrity.

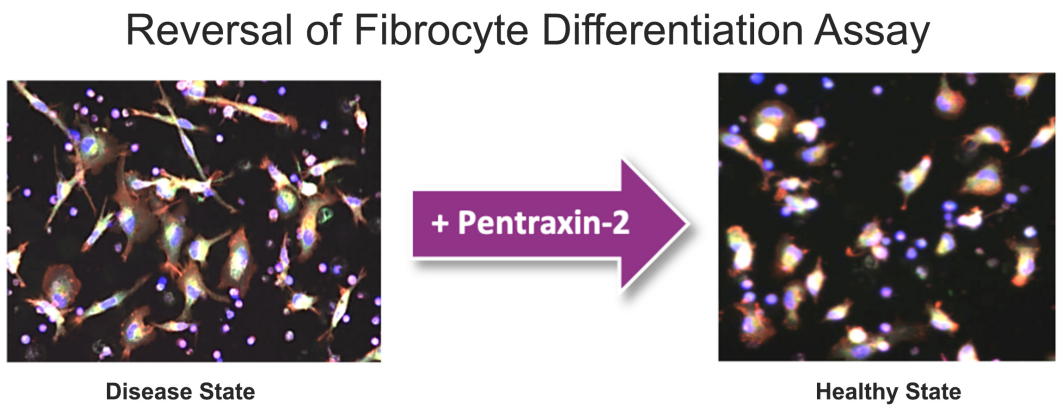


Figure 60. Phenotypic screening assay. Differentiation of human PBMCs into fibrocytes can be reversed by Pentraxin-2, a tissue repair protein, to mimic a healthy state. Small molecules are identified which rescue disease state to healthy state.

Insight from Recursion OS

We developed a PBMC-derived fibrocyte phenotypic screen to model fibrotic disease and identify novel therapeutic targets in an unbiased manner. This approach identified multiple small molecules capable of mimicking the effects of pentraxin-2 (PTX-2), an endogenous anti-fibrotic protein involved in monocyte differentiation and macrophage polarization. Combining our inferential search capabilities within the Recursion OS, we uncovered Target Epsilon, a novel regulator of immuno-mesenchymal cell function. Biochemical validation confirmed small molecule binding to Target Epsilon, leading to the identification and optimization of REC-4209, a potent and selective compound designed to reverse fibrosis by restoring immune-mesenchymal homeostasis.

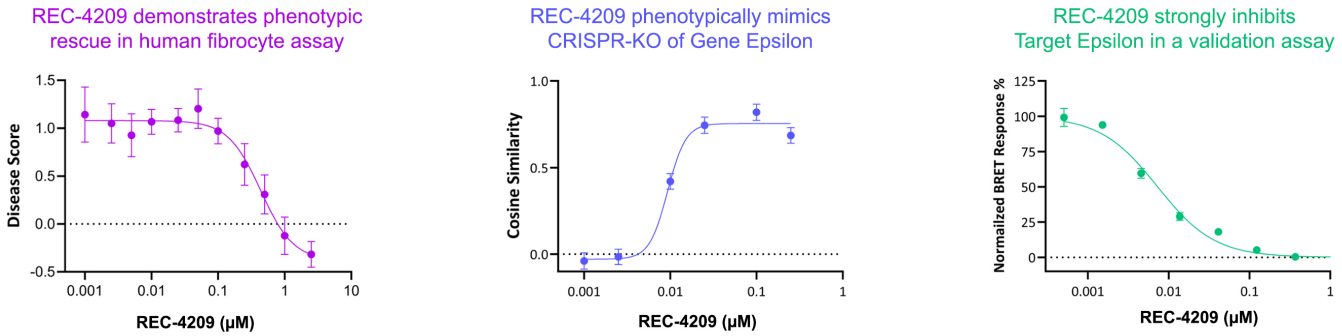


Figure 61. Target and compound identification and validation related to Target Epsilon. (1) Disease Score of 1.0 reflects "disease state" while disease score of 0.0 reflects "healthy state"; (2) cosine similarity between REC-1169575 and genetic knockout of Epsilon is the cosine of the angle between the two vectors in high-dimensional space. Values near 1.0 suggest the angle between perturbations is near 0° and is interpreted as directionally phenosimilar; and (3) Target Epsilon NanoBRET assay.[39]

[39] *Data on file.*

Preclinical

REC-4209 demonstrated potent activity in phenotypic reversal assays, with an EC_{50} of 0.40 µM in fibrocyte rescue and an IC_{50} of 12 nM to Target Epsilon. In digital tolerability studies, REC-4209 was well tolerated in C57BL/6 mice at doses up to 300 mg/kg/day (PO, 6 days), with no significant effects on body weight, breathing rate, motion, or body temperature. In a rodent fibrosis model, REC-4209 significantly reduced collagen deposition, a key histological marker of fibrosis. These findings support REC-4209's potential to halt fibrotic progression, positioning it as a novel disease-modifying therapy for IPF.

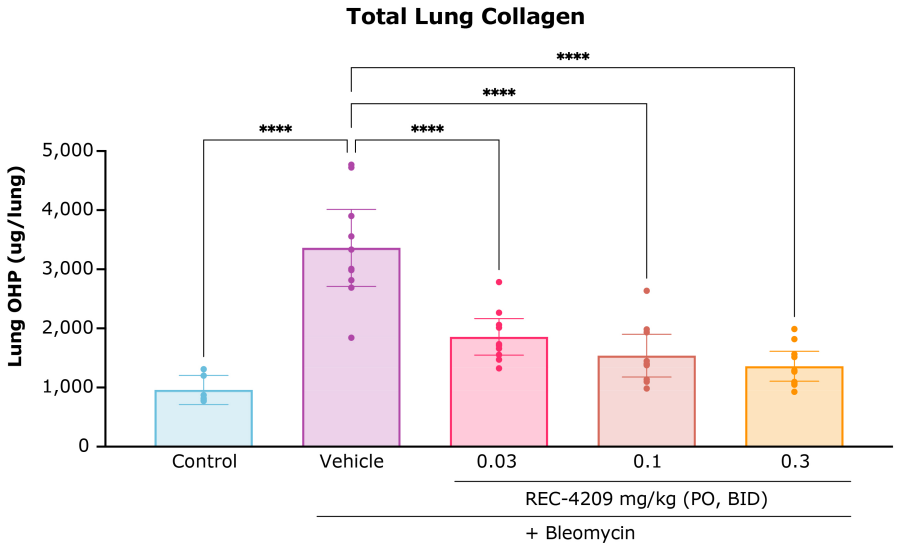


Figure 62. REC-4209 reduces collagen in a mouse model of fibrosis. REC-4209 at low doses reduces total lung collagen by 45% to 60% versus vehicle treated mice. Groups (n=10 per group; n=6 in control) compared to vehicle. ****p<0.0001; one-way ANOVA with Tukey's multiple comparison test. Data reflects mean ± 95% CI.[40]

Therapeutics Partnerships: Driving Innovation Across Multiple Diseases

At the core of Recursion's mission is the pursuit of breakthrough therapeutics for patients. Recursion collaborates with leading pharma partners to explore a wide range of disease areas—including fibrosis, neuroscience, oncology, immunology, and inflammation. Together, these partnerships aim to identify novel targets and therapeutic candidates spanning small molecules, large molecules, gene therapies, and cell therapies.

Each partnership is designed to advance therapeutic development, with multiple pathways to success:

- Novel Therapeutics: By leveraging Recursion's comprehensive maps of biology capabilities, large compound libraries are rapidly screened, uncovering differentiated therapeutics without preconceived target hypotheses. This approach allows Recursion to identify unique solutions that address significant medical needs. With our newly added precision chemistry capabilities, we can support our partners towards potential first-in-class and best-in-class therapies.
- Novel Targets: Recursion's platform's ability to profile diverse biological perturbations—including genetic factors—enables the discovery of novel druggable targets. Recursion then collaborates with partners to transform these insights into promising therapeutic candidates.

Recursion's strategic business combination with Exscientia has significantly expanded its partnership value, bringing leaders like Sanofi and Merck KGaA into the fold. **To date, Recursion has secured $450 million in upfront milestone payments, with the potential to unlock over $20 billion in additional milestones before royalties.** These high-impact collaborations not only generate near-term financial value but also leverage Recursion's combined capabilities in biology, precision chemistry, and automated synthesis to accelerate the development of transformative therapies.

By collaborating with top-tier biopharmaceutical companies, Recursion gains access to invaluable knowledge from some of the most experienced teams in the industry. Together, with Recursion's AI-driven platforms, proprietary data, and deep scientific expertise we continuously drive innovation, expand patient impact, and revolutionize the treatment of complex diseases. Below are some of the latest milestones reflecting this exciting momentum.

[40] *Data on file.*

Key Highlights

Roche and Genentech

In December 2021, we entered into a multi-year, strategic collaboration with Roche and Genentech in key areas of neuroscience and an oncology indication. Through the partnership, we are working with both Roche and Genentech's R&D units to leverage our Recursion OS and Maps of Biology, along with extensive single-cell perturbation screening data from Roche and Genentech, to rapidly identify novel biological relationships to initiate and advance therapeutic programs. Together we may initiate up to 40 programs over a decade or longer.

- Gastrointestinal-Oncology Advancements: In partnership with Roche and Genentech, we generated multiple whole-genome phenomaps with chemical perturbations across various disease-relevant cell types, enabling deeper insights into how different cellular contexts respond to gene knockouts and chemicals.
- Neuro-specific CRISPR KO Phenomap: In partnership with Roche and Genentech, we've developed the first whole-genome CRISPR knockout map in neural iPSC cells, providing valuable data to identify potential new targets in neuroscience, an area with limited new discoveries.
- Milestones and Collaboration: The neuroscience phenomap work led to the exercise of a $30M option from Roche and Genentech in August 2024, and we're moving forward with target validation projects.

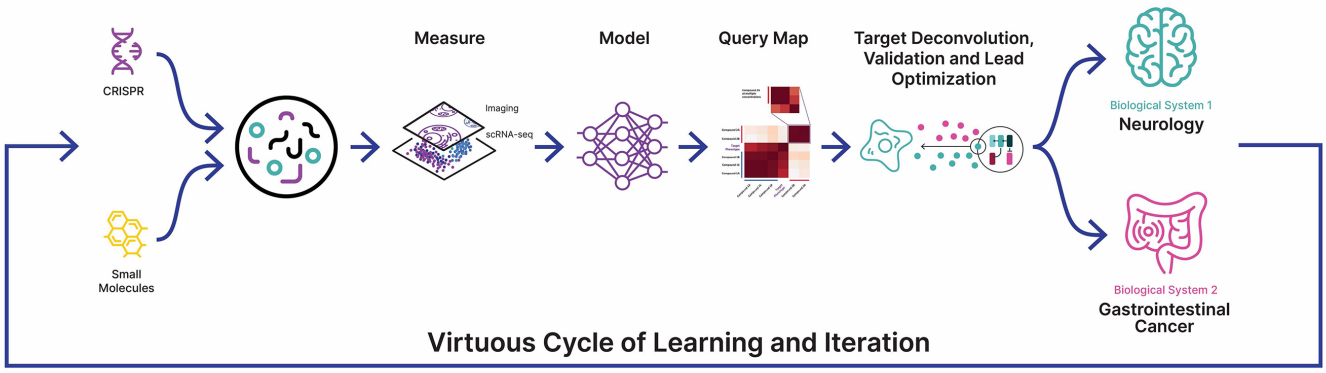


Figure 63. Under our collaboration with Roche & Genentech, we are creating multimodal maps of cellular biology to elucidate novel targets and starting points.

Sanofi

In January 2022, we entered into a strategic research collaboration with Sanofi to develop an AI-driven pipeline of precision-engineered, small molecule medicines. Through this collaboration, we are using our end-to-end integrated platform to discover and advance up to 15 novel targets in the oncology and immunology therapeutic areas. As part of this agreement, we received an upfront cash payment of $100 million, with the potential to receive up to $5.2 billion in total aggregate milestone payments plus tiered royalties.

- ***Immunology & Oncology Achievements:*** in 2024, we reached milestones in two programs, generating $15M in aggregate payments from Sanofi in 2024.

Bayer

In November 2023, we announced an updated collaboration with our established partner, Bayer, for a select set of precision oncology programs. The collaboration will leverage our state-of-the-art capabilities to initiate and advance the identification of novel therapeutic targets for challenging oncology indications with high unmet need. Under the terms of the agreement, we 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.

- ***Oncology Achievements:*** Completed 25 multimodal oncology data packages utilizing the Recursion OS platform, with programs rapidly progressing to Lead Series nomination.
- ***LOWE:*** Additionally, Bayer has adopted our LOWE LLM-orchestrated workflow software to enhance their research capabilities.

Merck KGaA (Darmstadt, Germany)

In September 2023, we entered into a collaboration with Merck KGaA, Darmstadt, Germany. This multi-year collaboration utilizes our AI-driven precision drug design and discovery capabilities while leveraging Merck KGaA, Darmstadt, Germany's disease expertise in oncology and immunology, clinical development capabilities, and global footprint.

- Recursion is continuing to focus on leveraging our discovery engine to identify first-in-class and best-in-class targets across oncology and immunology, driving innovation in these key therapeutic areas.

Case Study: Delivering the World's First Neuromap

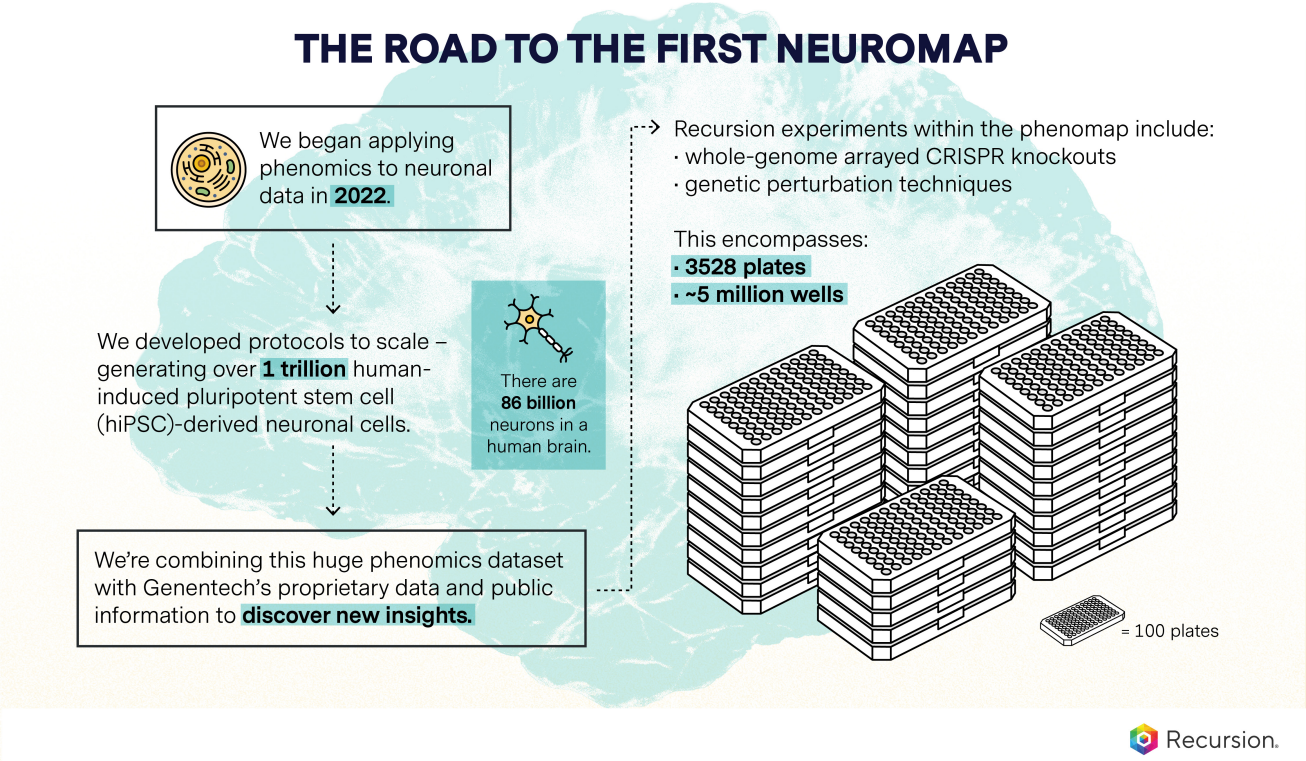


Figure 64: Recursion launched a transformational collaboration with Roche-Genentech, delivering the world's first whole-genome neuromap in 2024.

Overview

In 2021, Recursion launched a transformational collaboration with Roche-Genentech to create the world's first Neuromap—a comprehensive and scalable neuronal data model powered by machine learning. This effort aimed to uncover novel insights into neurodegenerative diseases, a category of illnesses that has long been difficult to tackle using traditional drug discovery methods. With a dedicated team of 50 people, Recursion set out to overcome numerous technical and biological challenges, all with the goal of driving innovation in neuroscience.

The Challenge

When the project began, the team faced significant uncertainty. The goal was ambitious: produce enough neurons, knock out genes, and generate a reliable signal from machine learning models to guide the development of potential drug programs. This challenge was particularly daunting given the complexity of neuronal cells, which do not divide or proliferate like other cell types. Unlike other cell types, such as human umbilical vein endothelial cells (HUVECs), which Recursion had previously worked with to create large-scale disease maps, neuronal cells posed a unique set of hurdles due to their limited ability to be produced at scale.

Neurodegenerative diseases had long been a difficult area for drug development. The traditional approaches has yielded limited breakthroughs, and the complexity of the biological system presented a higher bar for success. Recursion needed to develop new technologies and methodologies to produce and analyze neuronal data on a scale never before attempted in drug discovery.

Recursion had already proven its ability to create large-scale cell maps in other disease areas, notably in gastrointestinal oncology, as part of its partnership with Roche and Genentech. The success of this collaboration demonstrated the power of Recursion's phenotypic screening platform, which uses high-throughput technologies to produce vast amounts of biological data. However, creating a Neuromap would require more than just expanding on previous work—it required adapting the process to handle the unique challenges posed by neuronal biology.

Execution

To tackle this challenge, Recursion collaborated with Genentech to develop and refine a model using human-induced pluripotent stem cells (hiPSCs), which could be differentiated into neurons. This protocol enabled Recursion to produce large quantities of neurons, ultimately generating over 1 trillion hiPSC-derived neuronal cells. These neurons served as the foundation for the Neuromap, a data-rich resource that Recursion, Genentech and Roche could use to gain deeper insights into the genetic underpinnings of neurodegenerative diseases. In addition to the joint development of the neuronal cell context, Recursion's machine learning team played a pivotal role in developing algorithms capable of processing the massive amounts of data generated by the Neuromap. The combination of scalable cell production and cutting-edge computational models allowed Recursion to generate the first whole-genome neuronal phenomap that can be utilized by the partnership to uncover new relationships between genes and the phenotypes associated with neurodegeneration.

Outcome

Our work led to the exercise of a $30M option by Roche and Genentech in August 2024 with the Neuromap offering an unbiased view of the genetic relationships related to neurodegenerative diseases and providing insights that could pave the way for development of novel therapies in neuroscience. Unlike traditional approaches that are often guided by pre-existing hypotheses, researchers in the collaboration can now explore new biological pathways and identify potential therapeutic targets that may not have been considered before. Even as these avenues are being explored, the team is also pursuing the development of even more robust Neuromaps. This first map is a genetics-only map, with the whole genome knockout and many additional perturbations related to neurodegenerative diseases. Future maps could comprise additional cell types or large compound libraries.

Technology Partnerships

As Recursion continues to generate and leverage highly relatable and reliable datasets to support our internal pipeline and therapeutic partnerships, we continue to invest in advanced compute capabilities and data-centric solutions to strengthen our drug discovery and development efforts. Expanding on our previous release of select datasets and models, we are exploring additional opportunities to make more datasets and foundational models available to the broader scientific community. Our collaborations with NVIDIA. Google Cloud, Helix, and Faro Health underline our commitment to implementing AI and technology-enabled solutions to support our efforts to bring better medicines to patients faster.

NVIDIA

In July 2023, we entered a strategic collaboration with NVIDIA to accelerate the development of our groundbreaking AI foundation models for biology and chemistry using our supercomputer, BioHive-1, and priority access on NVIDIA DGX™ Cloud. In May 2024, we completed BioHive-2, Recursion's new NVIDIA DGX SuperPOD AI supercomputer, powered by 63 DGX H100 systems with a total of 504 NVIDIA H100 Tensor Core GPUs increasing the computational capacity by over 4X. The BioHive-2 supercomputer is believed to be the most powerful supercomputer wholly owned and operated by any pharmaceutical company and was ranked as number 54 in the top supercomputers globally by the Top500 list in 2024.

Helix

In May 2024, we entered into a multi-year agreement with Helix to access hundreds of thousands of de-identified clinic-genomic records consisting of longitudinal clinical records paired with Helix's Exome+® genomic data. The Helix dataset expands our efforts to use real-world patient data to train causal AI models and design biomarker and patient stratification strategies across broad disease areas.

Google Cloud

In October 2024, we announced an expanded collaboration with Google Cloud leveraging their technologies to accelerate drug discovery research and further enhance our ability to bring new medicines to patients faster. Through this collaboration, we will explore generative AI capabilities, including Gemini models, to support the RecursionOS. We will improve data search and access from our proprietary dataset with BigQuery and facilitate the scaling of compute resources to run large inference workflows effectively. Additionally, in November 2024, we announced the release of OpenPhenom-S/16 in Google Cloud's Vertex AI Model Garden. OpenPhenom, a non-commercial, publicly available foundation model built on microscopy data, sets a new "gold standard" for the industry, outperforming CellProfiler. This model offers the potential for researchers to replace their existing workflows with an off-the-shelf model that outperforms traditional microscopy analysis pipelines without requiring any additional tuning or training.

Faro Health

In December 2024, we entered into an agreement with Faro Health to leverage their AI-powered platform for clinical protocol design to reduce clinical trial costs and complexity while minimizing burden to trial participants and sites. We plan to use the Faro platform to optimize the protocol design for upcoming clinical trials. We also anticipate utilizing the structured study definitions created through Faro's software to automate traditionally labor-intensive and time-consuming historically downstream tasks, such as building the Electronic Data Capture system for each study.

People and Culture

Essential to leading and defining TechBio is our team of over 800 Recursionauts, comprising life scientists such as chemists and biologists (approximately 43% of employees) and computational and technical experts such as data scientists and software engineers (approximately 36% of employees). This kind of functional balance intentionally stands in contrast to traditional biotechnology companies. Together our team creates an environment where empirical data, statistical rigor and creative thinking is brought to bear on the problems we address. While we are united in a common mission, Decoding Biology to Radically Improve Lives, our strength lies in our differences: expertise, gender, race, disciplines, experience and perspectives. Deliberately building and cultivating this culture is critical to achieving our audacious goals.

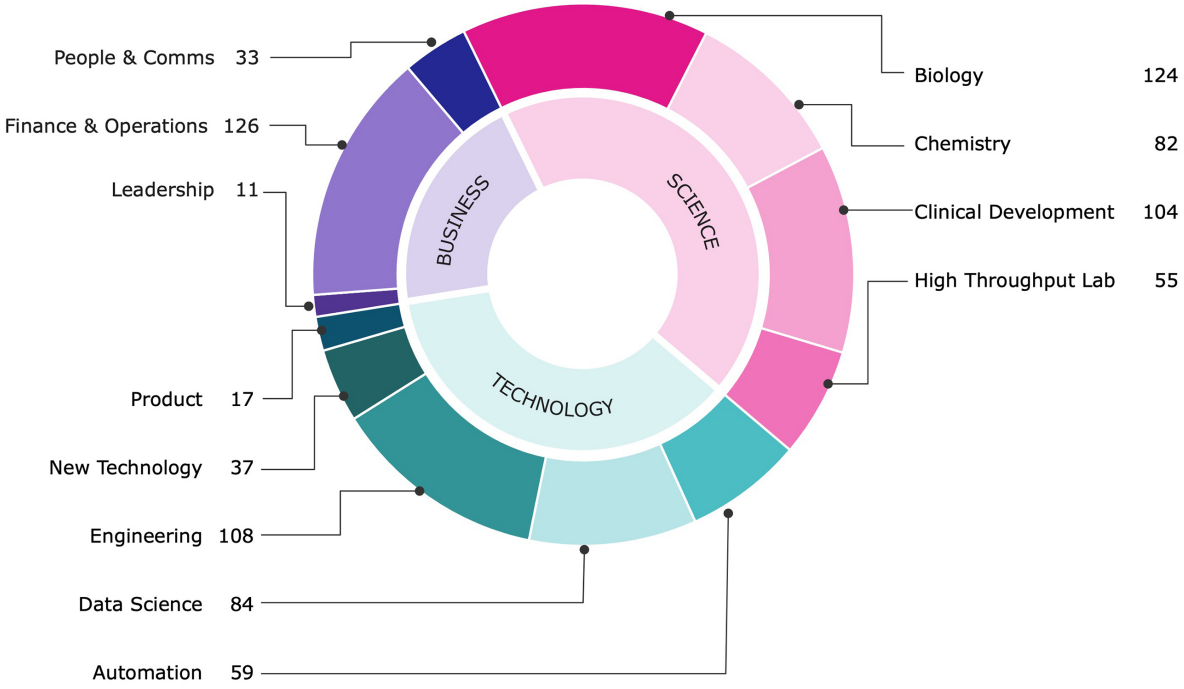


Figure 65. Breakdown of Recursion's over 800 employees across life sciences, technology and strategic operations.

One of the most critical elements supporting Recursion's leadership in TechBio is what we call the Recursion Mindset – a deep belief and commitment to industrialization through automation, systems-thinking, algorithms and data to deliver our mission. This mindset fuels our creative energy focused on Recursion's hardest problems. The Recursion Mindset is made manifest through our Founding Principles and supported by our culture and values. Our Founding Principles are the guideposts for our technical and scientific decision-making. Our values are the core standards and behaviors that define how we work together to achieve our mission. Combined they shape our culture and inspire us to reimagine how medicines are made.

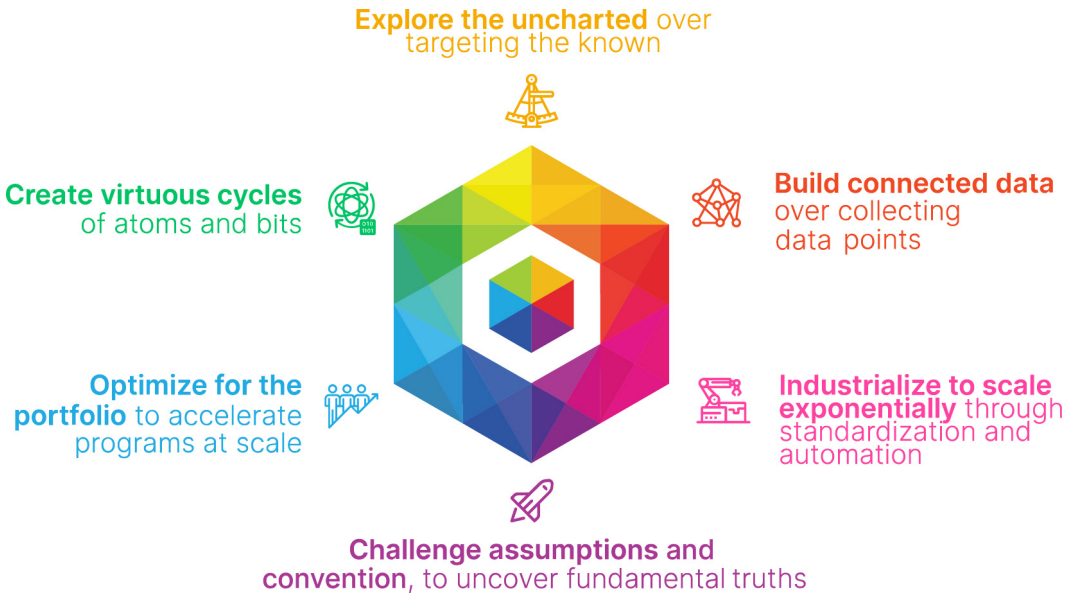


Figure 66. Recursion's Founding Principles. These six founding principles differentiate our approach from nearly every other biopharma company, enable us to lead TechBio and form the foundation for a mindset we teach and enrich for at Recursion.

Figure 67. Recursion's Values. These five values support our founding principles and guide our culture at Recursion.

Maximizing Delivery through Diversity

At Recursion we believe a diversity of experiences, backgrounds, ideas and expertise will create high performing teams. Varied and diverse perspectives support better complex decision-making, foster greater innovation and ultimately result in greater company performance and success. We seek the best talent by maximizing diversity at the top of the recruiting funnel and then mitigating bias through objective decision-making throughout the hiring process. We foster an environment of inclusion for candidates and employees to unleash the strength of our differences.

Employee Recruitment, Development and Training

We are intentional about the employee experience at Recursion, with a fit-for-purpose system that finds, grows and retains top talent to deliver our mission. Our people are mission-driven, humble, bright, generous of spirit and constructively dissatisfied with the status quo. We employ a targeted approach to identify, attract and hire diverse employees across highly technical scientific disciplines including: biology, chemistry, data science, machine learning, engineering, robotics, clinical development and more. We seek people that are aligned with – and emboldened by - our commitment to industrialization as defined by our Recursion Mindset.

We expect our employees to be constantly learning and adapting in order to evolve as quickly as Recursion. Learning and development happens through daily work and projects, as well as formal training and industry conferences and engagements. We offer a unique 2-day immersive experience to all employees called Decoding Recursion. It is an opportunity for close interaction with senior leaders who teach the Recursion Mindset through stories. Continual learning is reinforced throughout our performance system which creates accountability for our learning, delivery and impact on others.

People stay at Recursion because of the opportunity to impact the world and grow in a place where they feel challenged, supported and connected. Throughout the employee experience we create moments, rituals, programs and spaces that inspire ambition, reward contributions and growth and foster belonging.

Employee Health and Safety

We have dedicated Standard Operating Procedures to manage occupational health and safety, safety training and injury and illness and incident reporting. Every employee is responsible to ensure these procedures and policies are followed. We offer extensive training to ensure understanding and compliance. Compliance is mandatory for all laboratory employees per requirements of the Occupational Safety and Health Administration standard on Hazardous Chemicals in Laboratories. Our Co-Founder and CEO is the Director of Public Safety at the company and has the ultimate responsibility for chemical hygiene within the organization. Our Chemical Hygiene Officer and Lab Manager oversees the day-to-day management of institutional chemical hygiene.

Read more about how we invest in and motivate our people to achieve our mission in Recursion's latest Environmental, Social and Governance Report, available at our corporate website.

Facilities Headquarters

Our United States headquarters is in downtown Salt Lake City, Utah where we lease ~200,000 square feet of office and laboratory space. The lease for half of this space expires in May 2028 with the remainder expiring in May 2032. Our modern headquarters is a draw for local, national and international talent.

Our European headquarters is in London's Kings Cross neighborhood, where we lease 6,792 square feet of office through January 2029. We also have laboratory space in Milton Park, Oxfordshire for our automation laboratory with approximately 20,151 square feet.

Figure 68. Our US headquarters is centrally located in downtown Salt Lake City, Utah and our EU headquarters in London with laboratory space in Milton Park, Oxfordshire. Working with state and local government, we are helping to create a burgeoning life science ecosystem around a downtown cluster of companies centered around our headquarters.

Core Satellite Offices and Facilities

In addition to our two major headquarters in Salt Lake City, UT and London-Oxford, UK, we operate core satellite offices and a digital vivarium in key markets to attract top talent.

Toronto and Montréal

In Toronto, we operate a 28,110 square foot space in Toronto's Queen Street West Neighborhood. The lease for this space expires in November 2032. In addition to our Toronto office, we have a 8,367 square foot site in Montréal that houses our semi-autonomous artificial intelligence research engine, Valence Labs, which is located in the world-renowned artificial intelligence and machine learning hub MILA.

New York

In January 2025, we opened a new 11,655 square foot office in New York City's Hudson Yards neighborhood. This office serves as a key location for our clinical development team and executive functions.

Figure 69. Recursion's satellite offices and facilities in key markets to attract top talent.

Digital Vivarium

We lease a 25,557 square foot property that serves as a rodent vivarium. This lease expires in May 2028. We use this facility to conduct drug-discovery enabling pharmacokinetic, pharmacodynamic and exploratory safety studies. The facility is equipped with proprietary, digitally enabled cage technology.

Corporate Social Responsibility

We believe that to achieve our mission, we must act like the company we aim to be, which means we must be a good corporate citizen. In recognition of our commitment to excellence in environmental, social and governance stewardship, Recursion received a Prime Rating in 2024 for ESG performance from Institutional Shareholder Services (ISS). The ISS ESG Corporate Rating provides an assessment of a company's environmental, social and governance activity. A Prime Rating is awarded to companies with ESG performance above a sector-specific threshold and is defined by ISS as "absolute best in class." Additionally, as of January 2024, Recursion was ranked 6 out of 367 companies (approximately top 2%) in the Biotech category by Morningstar Sustainalytics.

To date, we have focused our community efforts in areas of impact that are aligned with our Values and our strengths, including: (i) diversity, equity and inclusion in technology and biotechnology (e.g., in 2020 the Recursion Foundation launched Altitude Lab, a life science incubator and accelerator for diverse health care entrepreneurs); (ii) the growth and sustainability of our local life science and technology ecosystems (e.g., Recursion is a founding member of BioHive, a Utah life science collective); and (iii) the promotion of sustainable environmental practices (e.g., Recursion aims to achieve net-zero greenhouse gas emissions across our operations by the year 2030). We believe that through these principles of community engagement, we can extend our mission of radically improving lives to those in our communities.

Read more about how we are delivering on that belief in Recursion's Environmental, Social and Governance Report.

Commercialization

We may retain significant development and commercial rights to some of our drug candidates. If marketing approval is obtained, we may commercialize our drug candidates on our own, or potentially with a partner, in the United States and other geographies. We currently have no sales, marketing, or commercial product distribution capabilities. Decisions to create this infrastructure and capability will be made following further advancement of our drug candidates and based on our assessment of our ability to build the necessary capabilities and infrastructure with competitive advantage. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure, manufacturing needs and major trends as to how value is accrued in the industry may all influence or alter our commercialization plans.

Manufacturing

We currently utilize contract development and manufacturing organizations to produce drug substance and investigational drug product in support of the assets within our pipeline. To date, we have obtained drug substance and drug product for our drug candidates from third party contract manufacturers. We are in the process of developing our supply chain for each of our drug candidates on a project-by-project basis based on our development needs.

Strategic Partnership and Collaboration Agreements

To achieve our mission, we may partner with leading biotechnology companies, pharmaceutical companies and academic research institutions to access datasets, molecules, or other intellectual property.

Roche & Genentech Collaboration and License Agreement

On December 5, 2021, we entered into a Collaboration and License Agreement with Genentech, Inc. and F. Hoffmann-La Roche Ltd, pursuant to which we will construct, using our imaging technology and proprietary machine learning algorithms, unique maps of the inferred relationships amongst perturbation phenotypes in a given cellular context (each a “Phenomap”) and together with Roche and Genentech will create multimodal models and maps to further expand and refine such inferred relationships, in both cases, with the goal to discover and develop therapeutic small molecule and target programs in a gastrointestinal cancer indication and neuroscience (each an “Exclusive Field”).

Upfront Payment. In January 2022, Roche paid us an upfront cash payment of $150.0 million.

Phenomap Creation, Acceptance and Access. Under the Collaboration Agreement, we are responsible for creating a certain number of phenomaps in each of the Exclusive Fields. We will also provide Roche results to requested queries, at Recursion’s discretion, of our pre-existing human umbilical vein endothelial cells (HUVEC) phenomap. Roche will have specified rights to request queries or have direct access to the Phenomaps to generate novel inferences that may lead to the discovery or development of therapeutic products.

Phenomap-Related Options in neuroscience. Each of the neuroscience phenomaps requested by Roche and created by Recursion may be subject to either an initiation fee, acceptance fee or both. Such fees could exceed $250.0 million for sixteen (16) accepted phenomaps. In addition, for a period of time after Roche’s acceptance of certain phenomaps, Roche will have the option to obtain, subject to payment of an exercise fee, rights to use outside the collaboration the raw images generated in the course of creating those phenomaps. If Roche exercises its External Use Option for all twelve (12) eligible phenomaps, Roche’s associated exercise fee payments to Recursion could exceed $250.0 million.

Collaboration Programs and Roche Options. Roche and Recursion will collaborate to select certain novel inferences with respect to small molecules or targets generated from the phenomaps for further validation and optimization as collaboration programs. There can be up to 40 programs initiated as part of this collaboration. Roche and Recursion may also combine sequencing datasets from Roche with Recursion’s phenomic imaging data and collaborate to generate new algorithms to produce multimodal maps from which additional collaboration programs may be initiated. For every collaboration program that successfully identifies potential therapeutic small molecules or validates a target, Roche will have an option to obtain an exclusive license to develop and commercialize such potential therapeutic small molecules or to exploit such target in the applicable Exclusive Field. In October 2023, Roche exercised its Small Molecule Validated Hit Option to further advance our first partnership program in GI-oncology. This program continues in the hit to lead series phase.

Payments if Roche Exercises Option for a Collaboration Program. Under the collaboration, Roche may initiate up to forty (40) small molecule programs. Each small molecule collaboration program, if optioned and successfully developed and commercialized by Roche, could yield more than $300.0 million in research, development, commercialization and net sales milestones for Recursion, as well as mid- to high-single digit tiered royalties on net sales. Recursion is also eligible for research, development, commercialization and net sales milestones for target collaboration programs optioned by Roche.

Recursion Programs. If Roche does not exercise its options in the Collaboration Agreement for certain collaboration programs, we may, with Roche's prior consent, choose to independently validate, develop and commercialize products in a limited number of such programs, subject to agreed milestones and royalties to Roche. Roche will have rights to obtain an exclusive license to exploit such products by providing notice and paying us an opt-in fee and economics exceeding those that would otherwise be applicable if Roche had exercised its option for such program.

Exclusivity. During an agreed period of time after the Collaboration Agreement's effective date, we are subject to certain exclusivities that limit our ability to conduct certain research and development activities with respect to compounds and targets in the Exclusive Fields, other than pursuant to the collaboration with Roche. However, we may continue pursuing products that we are researching and developing in the Exclusive Fields as of the effective date of the Collaboration Agreement.

Termination. The Collaboration Agreement includes standard termination provisions, including for material breach or insolvency and for Roche's convenience. Certain of these termination rights can be exercised with respect to a particular Exclusive Field or exclusive license, as well as with respect to the entire Collaboration Agreement.

Sanofi License Collaboration and License Agreement

In January 2022, we entered into a Collaboration and License Agreement, with Sanofi, or the CLA, and in July 2023 and December 2023, we amended the Collaboration and License Agreement, with such as amended CLA referred to as the Amended CLA. Pursuant to the Amended CLA, we will use our artificial intelligence-driven, end-to-end integrated platform to discover and validate novel targets in the oncology and immunology therapeutic areas. We will collaborate with Sanofi to advance certain of these targets into small molecule inhibitor drug research projects and accelerate the identification of certain small molecule development candidates.

Sanofi made an upfront cash payment of $100 million to us on signing the CLA and made an additional payment of $4 million in connection with the expansion of the collaboration pursuant to the December 2023 amendment. Under the Amended CLA, Recursion and Sanofi may initiate up to 15 novel small molecule programs. Each program, if successfully researched, developed and/or commercialized, will yield research, clinical development, regulatory, and commercial milestone payments of up to approximately $343 million including up to $193 million in the aggregate for certain specified research, development and regulatory milestones, and up to $150 million in the aggregate for certain specified commercial milestones. The Amended CLA could potentially provide us with up to approximately $5.2 billion in aggregate milestone payments across all 15 potential programs.

In the case that a therapeutic product resulting from the research collaboration is commercialized, we will also be eligible to receive tiered royalties on net sales ranging from high-single-digits to mid-teens. We also have an option for clinical co-investment which, if exercised, would increase the tiered royalty rates to up to 21% on net sales of co-funded products.

The collaboration may utilize Recursion's AI-based capabilities and precision medicine platform from target identification through patient selection. Once a target is identified, Recursion will be responsible for leading the design, translational and early preclinical studies to determine development candidates. Upon Sanofi's selection of a compound as a development candidate, Sanofi will be solely responsible for the IND-enabling studies and clinical development, manufacturing and commercialization of such development candidate at its own cost and expense. Under the Amended CLA, Sanofi has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one qualifying small molecule product in at least one agreed upon major market.

The research component of the collaboration will be overseen by a joint steering committee comprised of an equal number of representatives from each of Recursion and Sanofi. Recursion and Sanofi may agree to utilize our precision medicine platform for patient enrichment in Sanofi's non-small molecule programs.

Pursuant to the Amended CLA, Recursion granted to Sanofi an exclusive license (with the right to grant sublicences through multiple tiers) to the intellectual property that is the subject of each small molecule research program for all purposes, throughout the world. Sanofi has the right to control the prosecution and maintenance of any patent rights related to intellectual property that is the subject of each small molecule research program.

After the CLA's effective date, we are subject to varying exclusivity arrangements for specified periods of time which limit our ability to conduct research and development, manufacturing or commercialization activities (whether ourselves or in conjunction with a third party) with respect to compounds and targets which are within the scope of the Amended CLA and with respect to certain agreed pathways of interest.

The Amended CLA contains standard termination provisions, including for material breach or insolvency and for Sanofi's convenience. Certain of these termination rights can be exercised in respect of a given target, or in respect of the CLA as a whole. In certain circumstances, upon termination, we have the right to terminate the licenses granted to Sanofi and to pursue the development, manufacture and commercialization of the product candidates.

Bayer AG Amended and Restated Research Collaboration and Option Agreement

On August 28, 2020, Recursion and Bayer entered into a Research Collaboration and Option Agreement, which was subsequently expanded on December 1, 2021, 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 to re-align the collaboration with Bayer's strategic shift in focus to oncology. As a result, the parties wound down their joint work in fibrosis and the exclusivities with respect to the field of fibrosis were terminated.

Under the Restated Agreement, Recursion 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), to initiate up to seven programs in oncology. During certain agreed time periods within the collaboration term, Recursion 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 itself or together with third parties. However, Recursion may continue research and development activities for any such identified genes that it has initiated prior to the date of identification of such gene.

Under each oncology project, Recursion 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 Recursion 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 a project prior to completion, within a specified period of time, Recursion 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 project and backup compounds related thereto, as well as a non-exclusive license under Bayer's background intellectual property necessary for Recursion'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.

Merck KGaA, Darmstadt, Germany Research Collaboration Agreement

In September 2023, we entered into a Research Collaboration Agreement, or the RCA, with the Healthcare Business of Merck KGaA, Darmstadt, Germany, referred to as Merck KGaA, Darmstadt, Germany, pursuant to which we will be responsible for the design process, as well as translational and early non-clinical studies to discover development candidates based on the initial agreed targets. Upon Merck KGaA, Darmstadt, Germany's selection of a compound as a development candidate, Merck KGaA, Darmstadt, Germany will be solely responsible for the non-clinical studies and clinical development, manufacturing and commercialization of such development candidate at its own cost and expense. Under the RCA, Merck KGaA, Darmstadt, Germany has agreed to use commercially reasonable efforts to obtain regulatory approval for at least one product candidate in certain major markets and to commercialize such product if it receives any such regulatory approval.

The research component of the collaboration will be overseen by a joint steering committee comprised of an equal number of representatives from us and from Merck KGaA, Darmstadt, Germany. The collaboration will also have an IP sub-committee comprised of an equal number of patent attorneys from each party that will be the liaison for intellectual property matters that arise in connection with the collaboration.

The RCA allows Merck KGaA, Darmstadt, Germany and us to identify additional targets in oncology and immunology or other mutually agreed disease areas. Should we identify additional targets for the collaboration, we would be responsible for target validation in addition to drug design.

Merck KGaA, Darmstadt, Germany made an upfront cash payment of $20 million to us on signing the RCA, and we remain eligible to receive up to $674 million in discovery, development, regulatory and sales-based milestones, if all milestones for all three initial programs are achieved. Of this amount, up to $113 million is potentially payable on milestones achieved in the discovery phase of development. In addition, we will receive royalty payments ranging from mid-single-digits to low-double-digits on net sales of any products resulting from the initial three targets that are commercialized. If any additional target is identified for the collaboration, we would be eligible to receive additional milestone payments on such target. Pursuant to the RCA, we granted to Merck KGaA, Darmstadt, Germany a worldwide, exclusive, transferable license (with the right to grant sublicenses through multiple tiers) to the intellectual property that is necessary or reasonably useful for development or commercialization of the target compounds and resulting products, if any, in order to develop, manufacture, commercialize and sell the target compounds

and resulting products, if any. Merck KGaA, Darmstadt, Germany has the right to control the prosecution and maintenance of any patent rights related to intellectual property that is the subject of each program.

The RCA will remain in effect from September 20, 2023 until such date that no milestone payments or royalties are, or may become, payable under the RCA, unless the RCA is terminated earlier in accordance with its terms. The RCA contains standard termination provisions, including termination by either party for material uncured breach or insolvency of the other party, by us if Merck KGaA, Darmstadt, Germany breaches certain obligations with respect to regulatory and commercialization activities, and by Merck KGaA, Darmstadt, Germany for convenience. Certain of these termination rights can be exercised in respect of a given target, or in respect of the RCA as a whole. In certain circumstances, upon termination, we have the right to terminate the licenses granted to Merck KGaA, Darmstadt, Germany and to pursue the development and commercialization of the target compounds and resulting products, if any.

During the term of the RCA, we are subject to exclusivity obligations that limit our ability to conduct research and development or commercialization activities (whether ourselves or in conjunction with a third party) with respect to the compounds and targets which are within the scope of the RCA.

The RCA contains standard confidentiality provisions and representations and warranties made by each party to the agreement. The parties also provide mutual indemnification under the agreement and the RCA excludes liability of either party for consequential or similar damages, except to the extent prohibited by law.

Tempus Master Agreement

On November 3, 2023, Recursion Pharmaceuticals, Inc., or the Company, and Tempus Labs, Inc., or Tempus entered into a Master Agreement, or the Tempus Agreement pursuant to which Tempus may provide certain services and deliverables to the Company and/or license certain data to the Company. The term of the Tempus Agreement is five years from the effective date of the Tempus Agreement, or 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 the 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 the Term, and to retain each downloaded record for a period of 180 days from the date of download. After such 180-day period, The 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, the Company will pay Tempus an initial license fee in an amount equal to $22.0 million, or 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 the Company's early termination, which may be triggered only following the third anniversary of the Master Agreement's effective date, and payment by the 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 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 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 Tempus Agreement also grants the 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 the Company may not assign the Tempus Agreement without Tempus's consent if the proposed assignee is a large pharmaceutical company.

REC-994: University of Utah Research Foundation Agreements

In February 2016, we entered into an Amended and Restated License Agreement with the University of Utah Research Foundation, or UURF, pursuant to which we obtained an exclusive license under certain patents and a non-exclusive license under certain know-how, in each case controlled by UURF and related to the drug tempol, or REC-994, to make, have made, use, offer to sell, sell, import and distribute products incorporating REC-994 worldwide for the treatment of cerebral cavernous malformation, or CCM. In partial consideration for the license rights, we issued UURF equity in our company. In addition, we agreed to reimburse UURF for a specified portion of costs associated with the filing, maintenance and prosecution of the licensed patent rights. The Amended and Restated License Agreement will expire on a country-by-country basis upon the expiration of the last-to-expire patent within the patent rights in the applicable country. UURF may terminate the agreement for an uncured material breach, if we cease commercially diligent efforts to develop or commercialize a licensed product or service, or our bankruptcy or insolvency.

REC-2282: Ohio State Innovation Foundation In-License

In December 2018, we entered into an Exclusive License Agreement with the Ohio State Innovation Foundation, or OSIF, pursuant to which we obtained an exclusive, sublicensable, non-transferable, royalty-bearing license under certain patents and fully-paid up, royalty-free, nonexclusive license under certain know-how, in each case controlled by OSIF and related to the pan-histone deacetylase inhibitor, OSU-HDAC42, or REC-2282, to develop, make, have made, use, sell, offer for sale and import products incorporating OSU-HDAC42 worldwide. OSIF also assigned certain assets to us, relating to the pharmaceutical composition known as AR-42. OSIF retains the right to use and allow other academic, nonprofit and government institutions to use the licensed intellectual property for research, non-commercial and educational purposes. OSIF shall not practice, have practiced, or transfer such reserved rights for any clinical purpose other than completion of the existing clinical trials at the time of the license agreement without our prior written consent. We are developing REC-2282 for the treatment of NF2 and are evaluating the utility of the compound in additional disease states using our platform.

Pursuant to the agreement, we must use commercially reasonable efforts to commercialize licensed products and are required to meet certain diligence milestones within two years following the execution of the agreement, including the initiation of clinical trials. The license agreement is also limited by and made subject to certain rights and regulations of the government, including the Bayh-Dole Act.

In consideration for the license, we paid OSIF, an upfront payment of $2.0 million dollars and are obligated to pay OSIF certain milestones, totaling up to $20.0 million dollars, as well as mid-single digit royalties on net sales of the licensed products. In addition, we owe 25% of any non-royalty sublicensing consideration prior to a Phase II clinical trial or 15% of such sublicensing consideration after initiation of a Phase II clinical trial, provided that milestone payments are creditable against these sublicensing fees. In 2022, we paid OSIF $1.0 million dollars upon dosing of the first patient in the Phase 2 study of REC-2282 for the treatment of NF2.

The agreement expires on the expiration of the last valid claim within the licensed patents. We may terminate this agreement on 90 days prior written notice to OSIF. Either party may terminate the agreement on 60 days prior written notice for an uncured, material breach by the other party, or bankruptcy or insolvency of the other party.

REC-4881: Takeda License Agreement

In May 2020, we entered into a License Agreement, or the Takeda In-License, with Takeda Pharmaceutical Company Limited, or Takeda, pursuant to which we obtained an exclusive (even as to Takeda and its affiliates), worldwide, sublicensable under certain conditions, transferable, royalty-bearing license to certain Takeda patents, know-how and materials related to develop, manufacture and commercialize Takeda's clinical-stage compound known as TAK-733, a non-ATP-competitive allosteric inhibitor of MEK1 and MEK2, subject to a non-exclusive, royalty-free, irrevocable, fully paid up, license back to Takeda to use the licensed compounds for non-clinical research purposes. We are currently developing the compound REC-4881 for the treatment of FAP, and patients with spontaneous APC-mutant tumors. We are also evaluating the utility of the compound in additional disease states using our platform.

We are required to use commercially reasonable efforts to develop and commercialize at least one licensed product in each of (a) the US, (b) at least three of the following European countries: the United Kingdom, France, Germany, Italy and Spain and (c) Japan.

Upon execution of the agreement, we paid an upfront fee of $1.5 million to Takeda. Under the Takeda In-License, we are obligated to pay Takeda milestones amounts totaling up to $39.5 million upon achievement of specified development and regulatory milestone events. In addition, we are obligated to pay Takeda low-to-mid single-digit royalties based on net sales of products containing the licensed compounds by us, our affiliates or sublicensees, subject to specified reductions. Our obligation to pay royalties continues on a country-by-country basis until the latest of expiration of the last to expire patent licensed by Takeda that covers the product, expiration of any regulatory exclusivity period for the product and ten years after the first commercial sale of the product, in such country. As of the date of this filing, we have not made any milestone or royalty payments to Takeda.

Each party has the right to terminate the license agreement for the other party's material uncured breach, insolvency or bankruptcy. In addition, we may terminate the agreement without cause any time after May 2023, and Takeda may terminate the agreement if we have not conducted any material activities in support of the development or commercialization of the licensed compounds or any product containing a licensed compound and have not demonstrated that we used commercially reasonable efforts towards the development of such compounds or products for a period of 12 consecutive months and such failure is not due to events beyond our reasonable control. Further, Takeda may terminate the license agreement if we challenge the validity or enforceability of a licensed patent. Upon termination for any reason other than for Takeda's breach of the license agreement, upon Takeda's request we are obligated to negotiate in good faith, for a period of 120 days, terms and conditions of a license to Takeda under certain technology developed by us during the term of the agreement for the purpose of developing, commercializing and otherwise exploiting the licensed compounds and products containing the licensed compounds.

Target Epsilon: Bayer License Agreement

In December 2023, we entered into a License Agreement with Bayer, the Bayer License Agreement, pursuant to which we obtained (a) an assignment of certain compounds, know-how and inventions related primarily to fibrosis, and (b) an exclusive, sublicensable and royalty-bearing license under certain project know-how related to fibrosis to research, develop, manufacture and commercialize products as independent research tools in all fields worldwide, subject to a non-exclusive, royalty-free license back to Bayer to use such licensed project know-how solely for internal research and development purposes.

We are required to use commercially reasonable efforts to develop and commercialize at least one product in one of the following countries: (a) the US, (b) Japan, or (c) a country of the European Union.

Under the Bayer License Agreement, we are obligated to pay Bayer milestone amounts totaling up to approximately $34 million upon achievement of specified development, regulatory and sales milestones. In addition, we are obligated to pay Bayer low single-digit royalties based on net sales of products containing certain compounds by us, our affiliates, or sublicensees, subject to specified reductions. Our obligation to pay royalties continues on a product-by-product and country-by-country basis until the latest of: (a) expiration of the last to expire patent filed by us, our affiliates or sublicensees that covers the product, and (b) ten years after the first commercial sale of the product in such country. As of the date of this filing, we have not made any milestone or royalty payments to Bayer.

Each party has the right to terminate the license agreement for the other party's material uncured breach. In addition, we may terminate the agreement without cause. Upon termination by us without cause or by Bayer for our breach, Bayer would have the right to use, practice, develop and exploit (including the right to sublicense) certain assigned know-how solely for Bayer's internal research and development purposes.

Competition

Our efforts to date have resulted in several clinical-stage programs, an expansive pipeline of differentiated programs in early discovery and preclinical development, several partnerships with large pharma and technology companies, as well as an intellectual property portfolio comprising patents, trademarks, software and trade secrets. We believe that our differentiated approach provides us with a significant competitive advantage. We are a hybrid company, competing within multiple categories of the pharmaceutical, biotechnology, and technology industries where companies are similarly working to integrate rapidly advancing technologies into their drug discovery and development activities and/or are creating scalable scientific platforms. Notable competitors include:

- ***TechBio Companies.*** Such companies apply computational tools to unlock novel insights or accelerate drug discovery and development across different points in the value chain. Representative examples include Relay Therapeutics, Isomorphic Labs, Schrodinger, and AbCellera.
- ***Scalable Platform Companies.*** Such companies are applying novel scientific approaches or engineering novel therapeutic modalities with the potential to seed large numbers of therapeutic candidates. These companies may compete directly with our pipeline of predominantly small molecule therapeutics. Representative companies include Moderna, BioNTech, and Roivant Sciences.
- ***Traditional Biopharma Companies.*** Such companies, while primarily engaged in late-stage clinical development and product commercialization, are increasingly making their own investments in the application of ML and advanced computational tools across the drug discovery and development value chain. Such investments may include partnerships with other biotechnology companies (including Recursion) from which we may benefit. Representative companies include Janssen (a subsidiary of Johnson & Johnson), Merck, and Pfizer.
- ***Large Technology Companies.*** Large technology companies constantly seek growth opportunities. Technology-enabled drug discovery may represent a compelling opportunity for these companies, some of which have research groups or subsidiaries focused on drug discovery and others of which have signed large technology partnerships with biopharma companies. Representative companies include Alphabet, Microsoft, and Amazon.

Intellectual Property

Patents

As of February 2025, the Recursion patent portfolio is balanced between Platform IP and Program IP.

- ***Platform IP:*** Approximately one-half of the patents and patent applications that we own or license worldwide relate to the Recursion platform, including patents and applications related to the Recursion OS IP, as well as many other inventions related to Recursion's machine learning and artificial intelligence capabilities, cell perturbations, gene editing, drug discovery, drug development and hardware solutions. We also pursue a strategy of seeking patent protection on smaller discrete inventions throughout the breadth of our pipeline, ranging from experiment design, operations within our labs, data collection and analysis (including deep learning insights).
- ***Recursion Program IP:*** A breakdown of our Program IP portfolio is below:
    - REC-2282: We exclusively license OSIF's interest in patents and patent applications related to REC-2282 from OSIF; these patents and patent applications relate to composition of matter and methods of use treating cancer cachexia for REC-2282. Currently, we expect our licensed issued patents related to REC-2282 to generally expire between 2030 and 2035, excluding any patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee. With respect to NF-2, orphan drug exclusivity in the U.S. would run seven years from marketing authorization.
    - REC-994: We exclusively license UURF's interest in patents and patent applications related to use of REC-994 for treatment or prevention of CCM from UURF. Currently, we expect our licensed issued patents related to REC-994 to generally expire in 2035, excluding any patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee. With respect to CCM, orphan drug exclusivity in the U.S. would run seven years from marketing authorization.
    - REC-4881: We own patent applications, or exclusively license Takeda's interest in patents and patent applications from Takeda, related to composition of matter and methods of reducing polyp burden in people living with FAP using REC-4881. Currently, we expect our licensed issued patents related to REC-4881 to generally expire in 2029, excluding any patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee. With respect to FAP, orphan drug exclusivity in the U.S. would run seven years from marketing authorization.
    - REC-3964: We own a patent and patent applications related to the composition of matter and methods of inhibiting the toxin produced by Clostridioides difficile in the gastrointestinal tract using REC-3964. Currently, we expect our issued patent related to REC-3964 to expire no earlier than 2042, excluding any patent term adjustment or patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee.

- REC-617: We own patent applications related to REC-617; these patent applications relate to composition of matter and methods of treatment of multiple advanced solid tumor indications for REC-617. Upon issuance, we expect our patents resulting from these patent applications will expire no earlier than 2041, excluding any patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee.
- REC-1245: We own patent applications related to the composition of matter and methods of treating biomarker-enriched solid tumors and lymphoma using REC-1245. Upon issuance, we expect our patents resulting from these patent applications will expire no earlier than 2043, excluding any patent term adjustment or patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee.
- REC-3565: We own patent applications related to the composition of matter and methods of treating multiple hematology indications using REC-3565. Upon issuance, we expect our patents resulting from these patent applications will expire no earlier than 2041, excluding any patent term adjustment or patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee.
- REC-4539: We own a Patent Cooperation Treaty (PCT) application related to the composition of matter and methods of treating multiple hematology and solid tumor indications using REC-4539. Upon issuance of a national phase patent from our PCT application, we expect the resulting patents to expire no earlier than 2043, excluding any patent term adjustment or patent term extension, or other mechanisms for effecting patent term, and assuming payment of all appropriate maintenance, renewal, annuity or other governmental fee.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of biotechnology has emerged in the United States and in Europe, among other countries. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, importing, or otherwise commercializing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending and enforcing patent claims that cover our technology, inventions and improvements. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our platform and drug candidates and the methods used to manufacture them. Moreover, our issued patents and those that may issue in the future may not guarantee us the right to practice our technology in relation to the commercialization of our drug product candidates. The area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, which may prevent us from commercializing our drug candidates and future drug candidates and practicing our proprietary technology.

Our issued patents and those that may issue in the future may be challenged, narrowed, circumvented, or invalidated, which could limit our ability to stop competitors from marketing related platforms or drug candidates or limit the length of the term of patent protection that we may have for our drug candidates, future drug candidates and platforms. In addition, the rights granted under any issued patents may not provide us with complete protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that achieve similar outcomes but with different approaches. For these reasons, we may have competition for our drug candidates. Moreover, the time required for the development, testing and regulatory review of our candidate products may shorten the length of effective patent protection following commercialization. For this and other risks related to our proprietary technology, inventions, improvements, platforms and drug candidates, please see the section titled “Risk Factors—Risks Related to Our Intellectual Property.”

Our commercial success will also depend in part on not infringing upon the intellectual property and proprietary rights of third parties. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies for our products or processes or to obtain licenses or cease certain activities. Our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future products may have an adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference or derivation proceedings in the USPTO to determine priority of invention. For more information, please see “Risk Factors—Risks Related to Our Intellectual Property.”

Some of our pending patent applications in the United States are provisional patent applications. Provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of filing of one or more of our related provisional patent applications. If we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent applications and any patent protection on the inventions disclosed in our provisional patent applications. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents that provide us with any competitive advantage.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a nonprovisional patent application related to the patent. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent. A U.S. patent also may be accorded patent term adjustment, or PTA, under certain circumstances to compensate for delays in obtaining the patent from the USPTO. In some instances, such a PTA may result in a U.S. patent term extending beyond 20 years from the earliest date of filing a non-provisional patent application related to the U.S. patent. In addition, in the United States, the term of a U.S. patent that covers an FDA-approved drug may also be eligible for patent term extension (PTE), which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. However, with respect to patent term extensions granted as a result of the FDA regulatory review period, the restoration period cannot be longer than five years, the total patent term including the restoration period must not exceed 14 years following FDA approval, only one patent applicable to each regulatory review period may be extended and only those issued claims covering the approved drug or a method for using it may be extended. We may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process, fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. There can be no assurance that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

Rapidly evolving patent laws in the United States and elsewhere make it difficult to predict the breadth of claims that may be allowed or enforced in our patents. Moreover, patent offices in general can require that patent applications concerning pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Thus, even if we are able to obtain patents, the patents may be substantially narrower than anticipated.

Our ability to maintain and defend our intellectual property and proprietary position for our drug product candidates, methods of their use, and other proprietary technologies will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own, may receive in the future, or license from third parties may be challenged, invalidated, held unenforceable, narrowed or circumvented, and the rights granted under any issued patents may not provide us with proprietary protection or competitive advantages against third parties, including our competitors, with similar technology. Furthermore, third parties, including our competitors, may be able to independently develop and commercialize similar drugs or products, or duplicate our technology, business model or strategy without infringing our patents.

Trademarks

As of February 2025, our trademark portfolio comprises more than 70 registered trademarks or active trademark applications worldwide, among which we have issued trademarks in the U.S. for “Recursion” and “Recursion Pharmaceuticals.”

Trade Secrets

In addition to our reliance on patent protection for our inventions, drug candidates and programs, we also rely on trade secrets, know-how, confidentiality agreements and continuing technological innovation to develop and maintain our competitive position. For example, some elements of manufacturing processes, proprietary assays, analytics techniques and processes, knowledge gained through clinical experience such as approaches to dosing and administration and management of patients, as well as computational-biological algorithms, and related processes and software, are based on unpatented trade secrets and know-how that are not publicly disclosed. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees, advisors and consultants, these agreements may be breached, and we may not have adequate remedies for any breach. In addition, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. As a result, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party’s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived of by the individual during the course of employment, and which relate to or are reasonably capable or being used in our current or planned business or research and development are our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against the misappropriation of our proprietary technology by third parties. However, such agreements and policies may be breached, and we may not have adequate remedies for such breaches. For more information regarding the risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and

biological products. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the relevant regulatory authority.

U.S. Drug Development

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA. Drugs also are subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or post-market may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

- Our drug candidates are considered small molecule drugs and must be approved by the FDA through the new drug application, or NDA, process before they may be legally marketed in the United States. The process generally involves the following: completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with good laboratory practice, or GLP;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials in the U.S. may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, good clinical practice, or GCP, requirements and other clinical trial-related regulations to establish substantial evidence of the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to accept the filing for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the preclinical study and/or clinical trial sites that generated the data in support of the NDA filing;
- payment of user fees for FDA review of the NDA;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug in the United States; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

The data required to support an NDA is generated in two distinct developmental stages: preclinical and clinical. The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any current and future drug candidates will be granted on a timely basis, or at all.

Preclinical Studies and IND

Before testing any drug product candidate in humans, the product candidate must undergo rigorous preclinical testing. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP and ICH regulations for safety/toxicology studies. The preclinical developmental stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The sponsor must submit the results of the preclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin.

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials, which are generally required for FDA approval of an NDA, to commence. A

separate submission to an existing IND must also be made for each successive clinical trial conducted during product development along with any subsequent changes to the investigational plan. Some long-term nonclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Clinical Trials

The clinical stage of development involves the administration of the investigational product to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB must also approve the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will generally accept a well-designed and well-conducted foreign clinical trial not conducted under an IND if the trial was conducted in accordance with GCP and GMP requirements, and the FDA is able to validate the data through an onsite inspection, if deemed necessary, and the practice of medicine in the foreign country is consistent with the United States.

Clinical trials in the United States generally are conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the drug candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, tolerability and safety of the drug, the side effects associated with increasing doses, and if possible to gain early evidence on effectiveness.
- Phase 2 clinical trials involve studies in disease-affected patients to determine the dose and dosing schedule required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information are collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. These trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. The sponsor is also responsible for submitting written IND safety reports, including reports of serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or in vitro testing that suggest a significant risk for human subjects, and any clinically significant increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated checkpoints based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal safety studies and also must develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process, as performed by the

manufacturing facility, must be capable of consistently producing quality batches of our drug candidates. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that our drug candidates do not undergo unacceptable deterioration over their labeled shelf life.

NDA Review Process

Following completion of the clinical trials, data is analyzed to assess whether the investigational product is safe and effective for the proposed indicated use or uses. The results of preclinical studies and clinical trials are then submitted to the FDA as part of an NDA, along with proposed labeling, chemistry, and manufacturing information to ensure product quality and other relevant data. In short, the NDA is a request for approval to market the drug in the United States for one or more specified indications and must contain proof of safety and efficacy for a drug.

The application must include both negative and ambiguous results of preclinical studies and clinical trials, as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a product's use or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of an NDA must be obtained before a drug may be legally marketed in the United States.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each NDA must be accompanied by a user fee. FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual program fee for each marketed human drug. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews all submitted NDAs before it accepts them for filing and may request additional information rather than accepting the NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months, from the filing date, in which to complete its initial review of a new molecular-entity NDA and respond to the applicant, and six months from the filing date of a new molecular-entity NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also may audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by recommendations of an advisory committee, but it considers such recommendations when making decisions on approval. The FDA likely will reanalyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or non-patent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Orphan Drugs

Under the Orphan Drug Act, the FDA may grant an orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety, or providing a major contribution to patient care or in instances of drug supply issues. However, competitors may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if a drug candidate is determined to be contained within the scope of the competitor's product for the same indication. If one of our products designated as an orphan drug receives marketing approval for an indication broader than that which is designated, it may not be entitled to orphan drug exclusivity. Orphan drug status in the European Union has similar, but not identical, requirements and benefits.

Expedited Development and Review Programs

The FDA has a fast track program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for fast track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting with the FDA.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies.

A product may also be eligible for accelerated approval, if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, which is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. FDA may withdraw drug approval or require changes to the labeled indication of the drug if confirmatory post-market trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it may require such post-marketing restrictions as it deems necessary to assure safe use of the product.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of breakthrough therapy designation include the same benefits as fast track designation, plus intensive guidance from the FDA to ensure an efficient drug development program. Fast track designation, priority review, accelerated approval and breakthrough therapy designations do not change the standards for approval, but may expedite the development or approval process.

Post-approval Requirements

Following approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping requirements, requirements to report adverse events and comply with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations, known as "off-label promotion," and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are

any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the development of additional data or preclinical studies and clinical trials.

The FDA may also place other conditions on approvals including the requirement for REMS, to assure the safe use of the product. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. Manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation, and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, its manufacturer or the NDA holder, including recalls.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market, or product recalls;
- fines, warning letters, or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications;
- suspension or revocation of product approvals;
- product seizure or detention;
- refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

FDA Regulation of Companion Diagnostics

Safe and effective use of a therapeutic product may rely upon an in vitro companion diagnostic for use in selecting the patients that will be more likely to respond to that therapy. If an in vitro diagnostic is essential to the safe and effective use of the therapeutic product and if the manufacturer wishes to market or distribute such diagnostic for use as a companion diagnostic, then the FDA will require separate approval or clearance of the diagnostic as a companion diagnostic to the therapeutic product. According to FDA guidance, an unapproved or uncleared companion diagnostic device used to make treatment decisions in clinical trials of a drug generally will be considered an investigational medical device unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. The sponsor of the diagnostic device will be required to comply with the IDE regulations for clinical studies involving the investigational diagnostic device. According to the guidance, if a diagnostic device and a drug are to be studied together to support their respective approvals, both products can be studied in the same clinical trial, if the trial meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the clinical trial protocol, the investigational product(s), and subjects involved, a sponsor may seek to submit an IDE alone (e.g., if the drug has already been approved by FDA and is used consistent with its approved labeling), or both an IND and an IDE.

Pursuing FDA approval/clearance of an in vitro companion diagnostic would require either a pre-market notification, also called 510(k) clearance, or a pre-market approval, or PMA, or a de novo classification for that diagnostic. The review of companion diagnostics involves coordination of review with the FDA's Center for Devices and Radiological Health.

510(k) Clearance Process

To obtain 510(k) clearance, a pre-market notification is submitted to the FDA demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet required the submission of a PMA application. The FDA's 510(k) clearance process may take three to 12 months from the date the application is submitted and filed with the FDA, but may take longer if FDA requests additional information, among other reasons. In some cases, the FDA may require clinical data to support substantial equivalence. In reviewing a pre-market notification submission, the FDA may request additional information, which may significantly prolong the review process. Notwithstanding compliance with all these requirements, clearance is never assured.

After a device receives 510(k) clearance, any subsequent modification of the device that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, will require a new 510(k) clearance or require a PMA. In addition, the FDA may make substantial changes to industry requirements, including which devices are eligible for 510(k) clearance, which may significantly affect the process.

De Novo Classification Process

If a new medical device does not qualify for the 510(k) pre-market notification process because no predicate device to which it is substantially equivalent can be identified, the device is automatically classified into Class III. The Food and Drug Administration Modernization Act of 1997 established a different route to market for low to moderate risk medical devices that are automatically placed into Class III due to the absence of a predicate device, called the "Request for Evaluation of Automatic Class III Designation," or the de novo classification process. This process allows a manufacturer whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents a low or moderate risk, rather than requiring the submission and approval of a PMA. If the manufacturer seeks reclassification into Class II, the manufacturer must include a draft proposal for special controls that are necessary to provide a reasonable assurance of the safety and effectiveness of the medical device. The FDA may reject the reclassification petition if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk and requires PMA or that general controls would be inadequate to control the risks and special controls cannot be developed.

Obtaining FDA marketing authorization, de novo down-classification, or approval for medical devices is expensive and uncertain, may take several years and generally requires significant scientific and clinical data.

PMA Process

The PMA process, including the gathering of clinical and nonclinical data and the submission to and review by the FDA, can take several years or longer. The applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness, including information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee. In addition, PMAs for medical devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, the applicant must demonstrate that the diagnostic produces reproducible results. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes extensive testing, control, documentation and other quality assurance and GMP requirements.

After a device is placed on the market, it remains subject to significant regulatory requirements. Among other requirements, medical devices may be marketed only for the uses and indications for which they are cleared or approved, device manufacturers must establish registration and device listings with the FDA and a medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the Quality System Regulation, or QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA and the FDA also may inspect foreign facilities that export products to the U.S.

Other U.S. Regulatory Matters

- Our current and future arrangements with healthcare providers, third-party payors, customers and others may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not limited to: the federal Anti-Kickback Statute, which makes it illegal for any person, including a prescription drug or medical device manufacturer (or a party acting on its behalf), to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce or reward referrals, including the purchase, recommendation, order or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. Moreover, the ACA (as defined below) provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- The federal criminal False Claims Act and Civil Monetary Penalties Laws, and the civil False Claims Act that can be enforced by private citizens through civil whistleblower or qui tam actions, prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government and/or impose exclusions from federal health care programs and/or penalties for parties who engage in such prohibited conduct;
- The Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations also impose obligations on covered entities such as health insurance plans, healthcare clearinghouses and certain health care providers and their respective business associates, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- the FD&C Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- The federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to annually report to Centers for Medicare & Medicaid Services, or CMS, information regarding certain payments and other transfers of value to physicians and teaching hospitals as well as information regarding ownership and investment interests held by physicians and their immediate family members; and
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, state laws that require biotechnology companies to comply with the biotechnology industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and require the registration of their sales representatives, state laws that require biotechnology companies to report information on the pricing of certain drug products and state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pricing and rebate programs must also comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA"). If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Manufacturing, sales, promotion and other activities also are potentially subject to federal and state consumer protection and unfair competition laws. In addition, the distribution of pharmaceutical and/or medical device products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical and/or medical device products. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act as well as other applicable consumer safety requirements.

The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant civil, criminal and administrative penalties, including damages, fines, disgorgement, imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, injunctions, requests for recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals or refusal to allow a firm to enter into supply contracts, including government contracts.

U.S. Patent-Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of any future drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Act. The Hatch-Waxman Act permits restoration of the patent term of up to five years as compensation for patent term lost during product development and FDA regulatory review process. Patent-term restoration, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent-term restoration period is generally one-half the time between the effective date of an IND or the issue date of the patent, whichever is later, and the submission date of an NDA plus the time between the submission date of an NDA or the issue date of the patent, whichever is later, and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug, a method for using it, or a method of manufacturing it, is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application

for any patent term extension or restoration. In the future, if and when our products receive FDA approval, we may apply for restoration of patent term for our currently owned or licensed patents covering products eligible for patent term extension to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. Similar provisions are available in Europe and certain other jurisdictions to extend the term of a patent that covers an approved drug. We may seek patent term extension for any of our issued or licensed patents in any jurisdiction where these are available; however, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for a generic version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness or generate such data themselves.

European Union Drug Development

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated, it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical-trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. Recently enacted Clinical Trials Regulation EU No 536/2014 ensures that the rules for conducting clinical trials in the EU will be identical. In the meantime, Clinical Trials Directive 2001/20/EC continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is composed of the 28 Member States of the European Union and three European Free Trade Association States (Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations.

- The Community MA is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced-therapy medicines such as gene-therapy, somatic cell-therapy or tissue-engineered medicines and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific, or technical innovation or which are in the interest of public health in the EU.
- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a

draft summary of the product characteristics, or SOPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SOPC, labeling or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. Similar to the U.S. patent term-restoration, Supplementary Protection Certificates, or SPCs, serve as an extension to a patent right in Europe for up to five years. SPCs apply to specific pharmaceutical products to offset the loss of patent protection due to the lengthy testing and clinical trials these products require prior to obtaining regulatory marketing approval.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the United States, for example, principal decisions about reimbursement for new products are typically made by CMS. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical drug candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific drug candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

In addition, in most foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow the price structures of the United States and generally prices tend to be significantly lower.

Healthcare Reform

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Unlike Medicare Part A and B, Part D coverage is not standardized. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan likely will be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private third-party payors often follow Medicare coverage policy and payment limitations in setting their own payment rates.

The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price-controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was passed which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA contains provisions that may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the U.S. Department of Health and Human Services, or HHS, Secretary as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. The ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs from 15.1% of average manufacturer price, or AMP, to 23.1% of AMP and adding a rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. The ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization and by enlarging the population potentially eligible for Medicaid drug benefits. Additionally, for a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer.

Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have passed.

On November 20, 2020, the HHS Office of Inspector General ("OIG") issued a final rule eliminating the federal Anti-Kickback Statute safe harbors for rebates paid by manufacturers to Medicare Part D plan sponsors, Medicaid managed care organizations, and those entities' pharmacy benefit managers, the purpose of which is to further reduce the cost of drug products to consumers. OIG created two safe harbors for certain point-of-sale reductions in price on prescription pharmaceutical products and certain pharmacy benefit manager service fees. On December 2, 2020, OIG and CMS each issued a final rule that set forth modifications to the federal Anti-Kickback Statute, Civil Monetary Penalties Law and Physician Self-Referral Law (or the Stark Law) (respectively) regulations to remove regulatory barriers to value-based care arrangements. CMS's final rule also clarifies and updates certain long-standing terms that appear throughout the Stark Law regulations.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, effective April 1, 2013, which, due to subsequent legislative amendments, will stay in effect through 2029 unless additional congressional action is taken. The American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny recently over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drug products. For example, the federal Inflation Reduction Act, signed into law on August 16, 2022, contains multiple provisions that could have an adverse effect on our ability to generate revenue, attain profitability, or commercialize our drug candidates if approved, as the statute includes provisions intended to reduce the cost of prescription drugs under Medicare. In addition to the direct impact of the IRA on federal drug reimbursement, the statute may also lead to similar reductions in payments from private payers. Various members of the current U.S. Congress have indicated that lowering drug prices continues to be a legislative and political priority, and some have introduced other proposals aimed at drug pricing. Similarly, at the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Available Information

Our principal executive office is located at 41 S Rio Grande Street, Salt Lake City, UT 84101. Our telephone number is (385) 269-0203.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, or the Exchange Act, are available free of charge on our website as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Our website is www.recursion.com. Investors and others should note that we announce material financial and other information to our investors using our investor relations website (https://ir.recursion.com/), SEC filings, press releases, public conference calls and webcasts. We use these channels as well as social media and blogs to communicate with our stakeholders and the public about our company, our services and other issues. It is possible that the information we post on social media and blogs could be deemed to be material information. Therefore, we encourage investors, the media and others interested in our company to review the information we post on the social media channels and blogs listed on our investor relations website. Information contained in, or that can be accessed through, our website is not a part of, and is not incorporated into, this report.

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