INVEST IN **ORIGAMI THERAPEUTICS, INC.**

Unfolding Precision Medicine to Slow Brain Aging and Extend Healthspan

origamitherapeutics.com San Diego, CA Y Combinator

Highlights

Y Combinator
Raised from Y Combinator

1. $6.8M raised to date; entering key value inflection point ahead of human trials

2. Founder led discovery of 4 approved CF drugs and 1 approved pain drug; $50B+ in lifetime sales

3. First-in-class drug shows disease reversal of Huntington's symptoms in human & mouse disease models

4. Targeting $9B+ Huntington's market; Alzheimer's next with tau degrader

5. Strong pharma interest; approach validated by recent $2.9B Novartis–PTC deal

6. Multiple patents filed; proprietary ORICISION drug discovery platform

7. Prepping IND submission for ORI-003; clinical trials on the near horizon

8. Lean team; 80%+ of capital goes straight into advancing the science

Featured Investors

NuFund Venture Group Follow Invested $450,000

NuFund Venture Group is a new wave of investors with a new fund model investing in technology leaders. Founded in San Diego, CA, NuFund is one of the largest, most active and most successful early-stage investor groups over the past 20+ years. We represent diverse backgrounds and perspectives, and work together to foster a culture of excellence, respect, innovation, and fun.

Ashok Kamal, Co-Fund Manager

"I am an enthusiastic supporter of Origami Therapeutics and their efforts to bring impactful therapies to patients with neurological disorders, an area of tremendous unmet need for human health and massive opportunity for innovation. Origami's screening technology has identified a completely new mechanism to treat devastating diseases like Huntington's disease and Alzheimer's-related dementias. The leadership of Origami has demonstrated incredible commitment and resourcefulness along with past success in developing treatments that transformed how genetic diseases are treated. They have data showing great promise in treating neurological diseases with an oral pill and this is the ideal time to join in their journey toward developing important new medicines."

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Syndicate Lead

Follow

Invested $5,000

"I am an enthusiastic supporter of Origami Therapeutics and their efforts to bring impactful therapies to patients with neurological disorders, an area of tremendous unmet need. They use patient cells to identify the most effective compounds and at the same time increase the likelihood of success in clinical trials. Their screening technology has identified a completely new mechanism to treat devastating diseases like Huntington's disease. The leadership of Origami has demonstrated past success in developing treatments that completely change how genetic diseases are treated, and they have data showing great promise in treating neurological diseases with an oral pill. I am excited to join Origami in their journey to provide transformative treatments for those affected by neurodegenerative diseases and their families."

Other investors include Y Combinator Notable , Catalytic Impact Foundation, Princeton Alumni Angels

Our Team

Beth J Hoffman CEO

Veteran biotech executive who led the discovery of four FDA-approved drugs for Cystic Fibrosis, now used by over 100,000 patients worldwide. A proven biotech innovator, she founded Origami to bring that same precision to neurodegenerative disease.

Leslie Schulze CFO

Ms. Schulze has over two decades of financial and operational leadership across early- to late-stage biotech companies. She specializes in fundraising strategy, financial planning, and scaling companies from inception through commercialization.

Martin Eglitis Strategy Advisor

Dr. Eglitis has held senior roles in business development and R&D at Teva, Amgen, Eli Lilly, and the NIH. He advises VC-backed therapeutics companies on corporate strategy, partnerships, and translational research alignment.

Katherine Widdowson Chemistry Advisor

Dr. Widdowson is a medicinal chemist with 30+ years of experience at GSK and biotech startups. She's a co-inventor on 35+ patents and helped advance over a dozen drug candidates, including the marketed COPD treatment Incruse®.

Help Us Reimagine Brain Health

Neurodegenerative diseases are one of the greatest fears of aging—and if you've watched someone struggle with Alzheimer's or Parkinson's, you know how urgently we need better solutions.

ORIGAMI Therapeutics

Pioneering a new way to treat neurodegenerative diseases by targeting the *root causes*, not just managing symptoms.

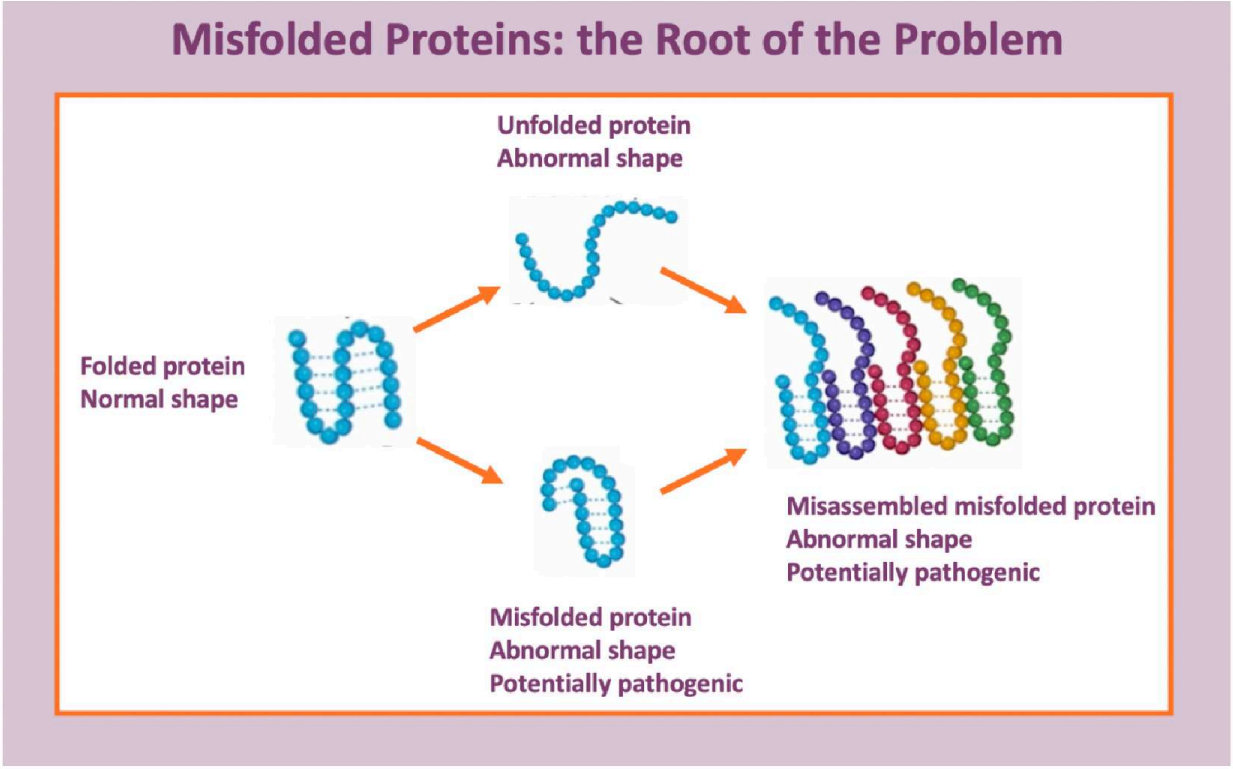
We fix what goes wrong at the cellular level *before it's too late.*

Our founder and CEO, Dr. Beth Hoffman, led the discovery of the first FDA-approved protein correctors for Cystic Fibrosis, now used by ***100K+ patients*** and **generating over *$10B annually***. Her work helped establish one of the most successful precision medicine programs in biotech history. Now she's applying that same expertise to one of medicine's toughest frontiers: brain health.

We've built a platform to unlock a new generation of treatments for millions of people facing Huntington's, Alzheimer's, Parkinson's, and other age-related brain diseases. These diseases spare no one and touch nearly every family, and Origami is developing breakthrough solutions to stop them.

Misfolded Proteins Drive Brain Aging

Proteins are the workhorses of our cells—but to do their job, they must be folded into precise shapes. Imagine a string of pearls that must be knotted just right. If the knot is wrong, the protein can't work—or worse, it clumps up, damages cells, and spreads disease.



This breakdown in protein folding is a key driver of aging and over 100 diseases—including Huntington's, Alzheimer's, Parkinson's, and ALS.

For a more technical overview, view our investor deck here: **Origami Investor Deck**.

Precision Tools to Restore Brain Health

Most treatments today for neurodegenerative diseases only try to clean up the mess after it's made. Origami is fixing the problem at its source by developing small molecule drugs that find and destroy toxic proteins *before* they cause harm.

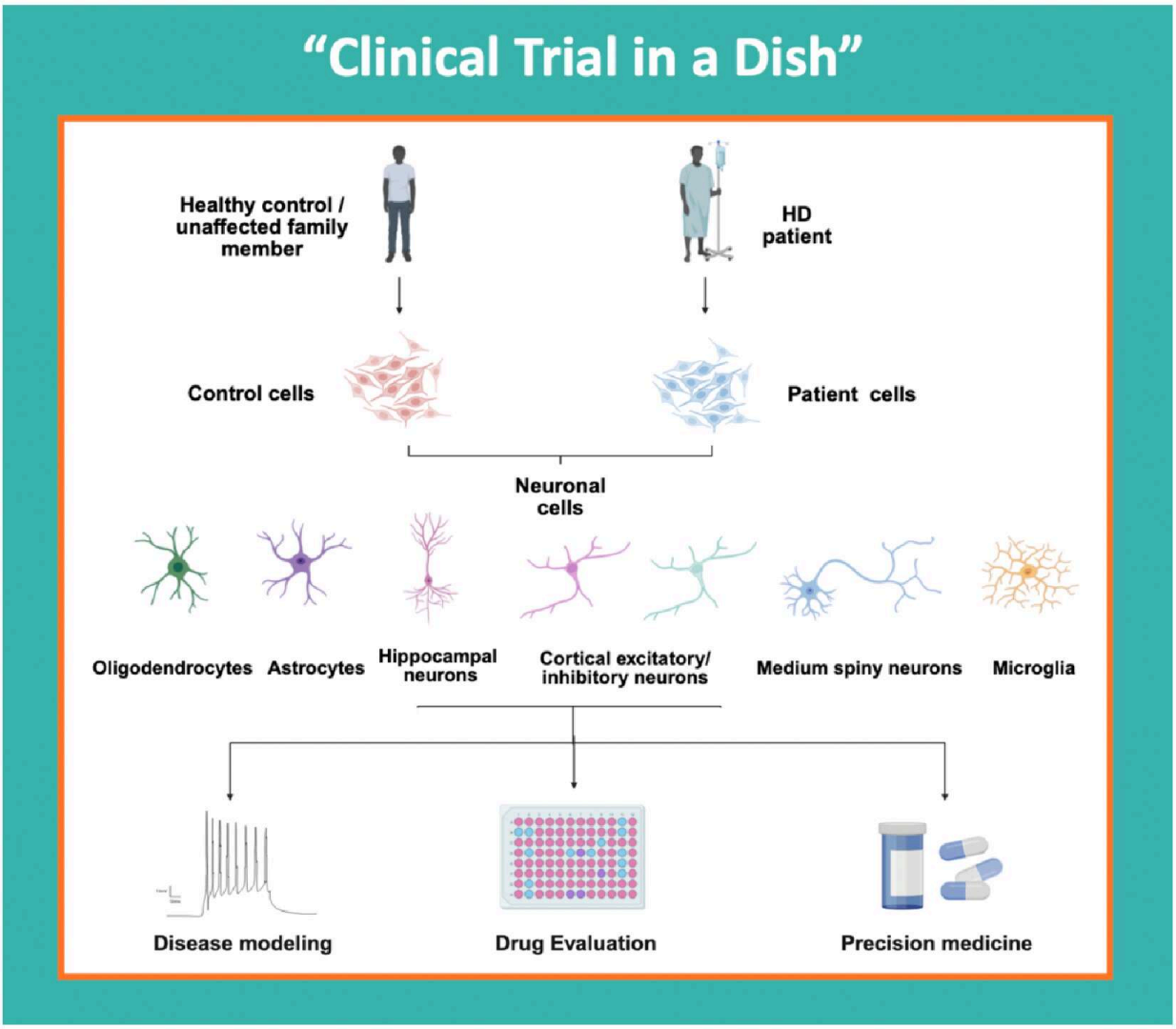
Our proprietary platform, ORICISION™, is our discovery engine to find small molecules that either:

- ***Tag misfolded proteins for destruction,*** or

- *Correct their shape so they function properly*

These drugs harness the body's own clean-up system, a process called *selective autophagy*—a kind of cellular recycling that removes toxic proteins. Our novel approach aims to prevent, reverse, or slow neurodegenerative disease by restoring brain health.

We test our candidates in patient-derived cells – a "clinical trial in a dish" approach that lets us study safety and effectiveness in human biology before entering a human trial. This helps us choose better drug candidates, faster, and increases the chances they'll work in people. To learn more, read **Dr. Hoffman's article on clinical trials in a dish**.



Why it matters:

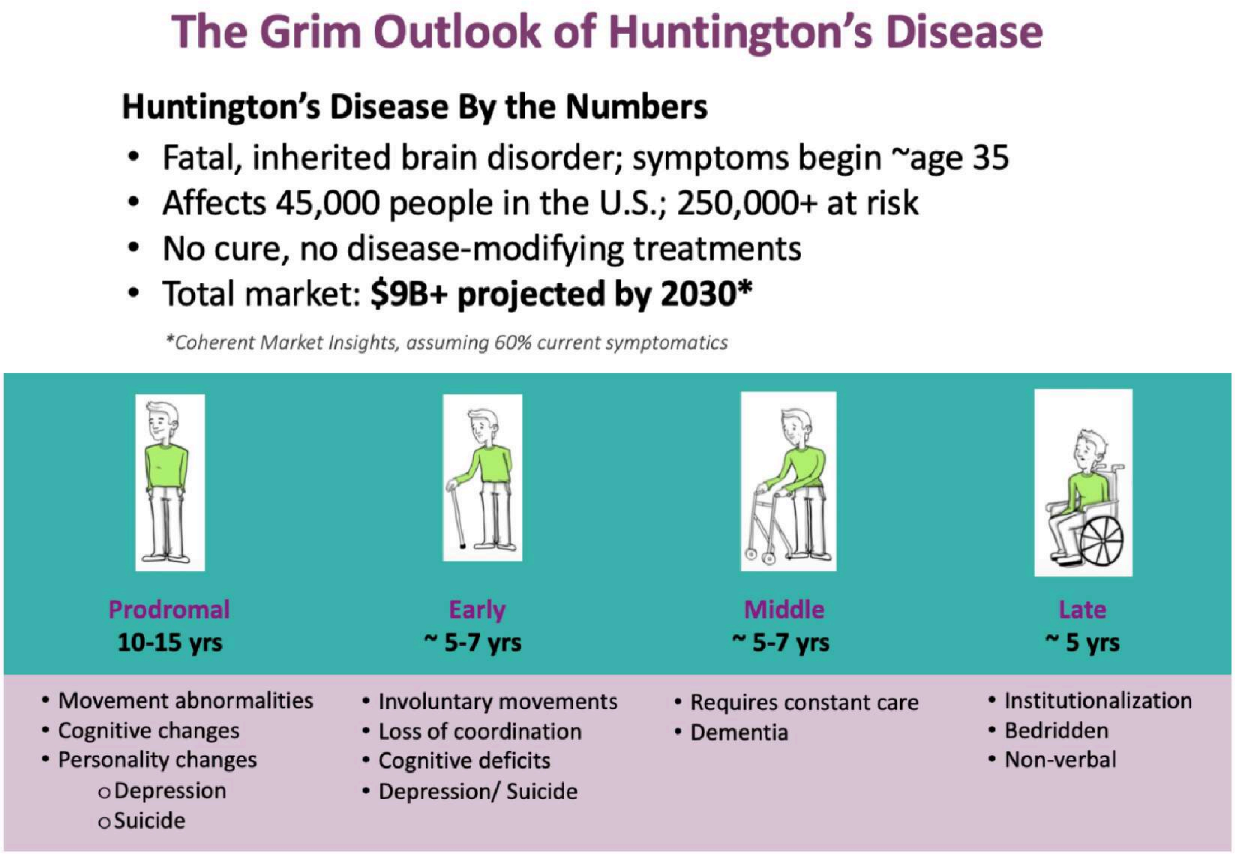
- Our drugs are designed to be orally available and brain-penetrant, so they can treat both the brain and body effectively and easily.

- We're able to go after targets that most others can't—even those considered "undruggable."
- Small molecules are generally easier and more cost-effective to produce compared to larger biologic therapies.

The platform is already delivering results.

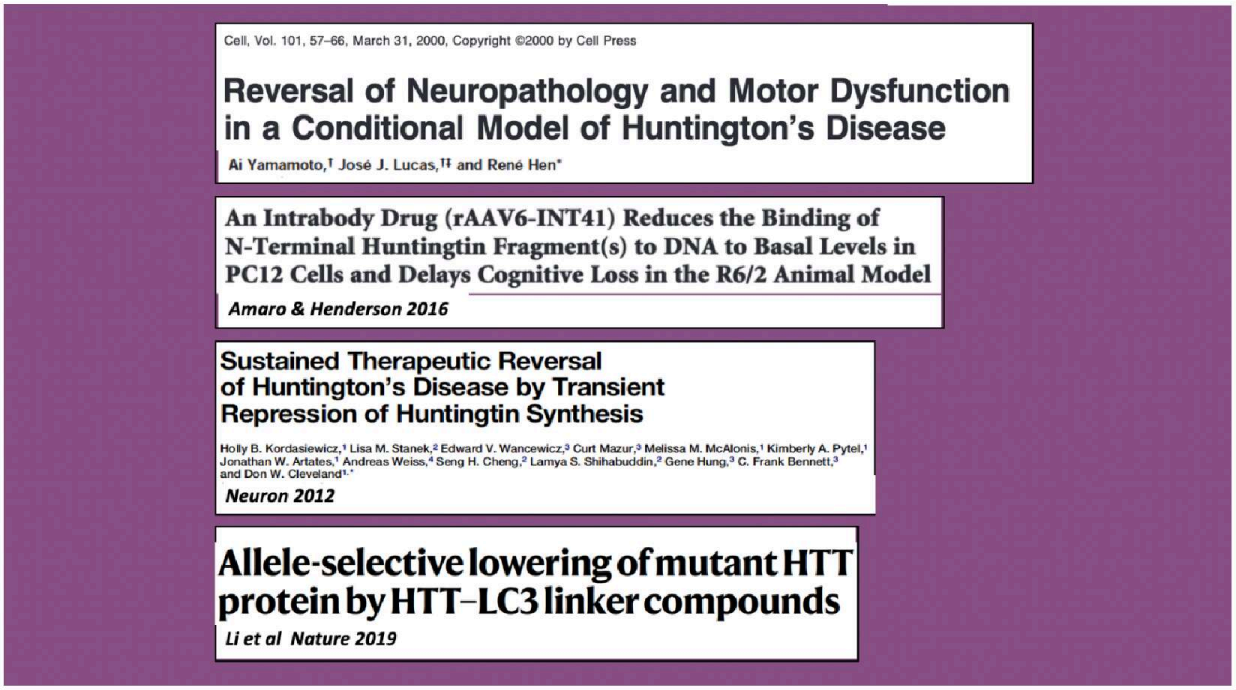
Why Huntington's Is the Right Beachhead

Our lead program focuses on Huntington's Disease – a rare, devastating genetic disorder caused by a mutation in a single gene called huntingtin (HTT). The mutant huntingtin (mHTT) misfolds and becomes toxic. There are no disease modifying treatments for Huntington's, and the few available drugs only partially ease movement symptoms with considerable side effects to help these patients.



We're starting with Huntington's because it's purely genetic—***we know who to treat, what to measure, and how to move quickly.*** With well-validated science showing that lowering mHTT improves outcomes in models, ***we know what an effective drug should do.***

Research Shows Reducing the Cause Can Reverse the Disease

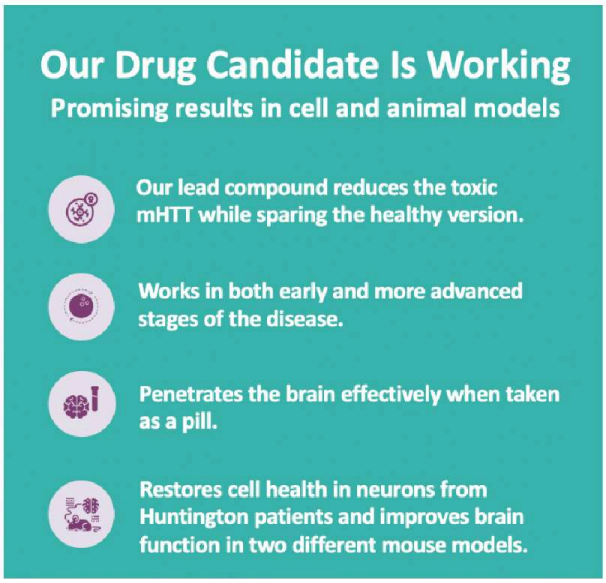


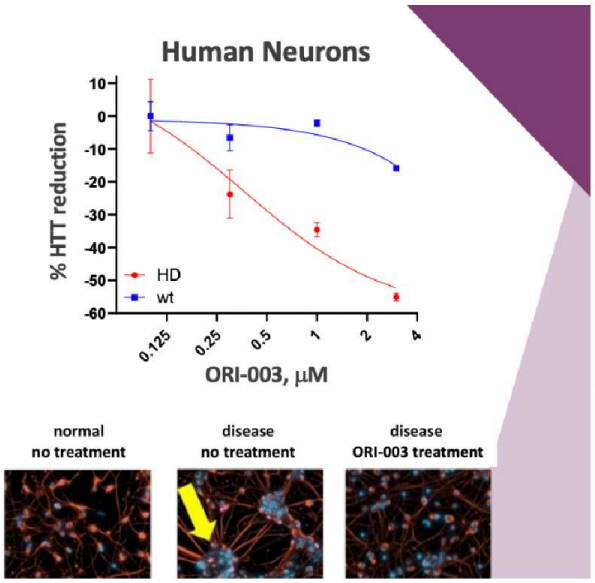
It's the ideal proof-of-concept to demonstrate our platform in action.

Once we show safety and early effectiveness, we unlock a pipeline of treatments for far more common diseases tied to misfolded proteins, like Alzheimer's and Frontotemporal Dementia, ***creating tremendous value through the same underlying method.***

ORI-003 for Huntington's Disease

ORI-003 is our first-in-class small molecule designed to target this root cause of Huntington's disease.





Here's why we're excited about ORI-003:

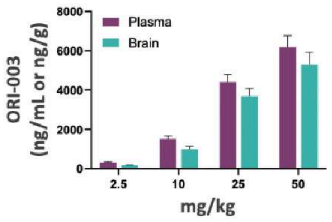
- It works in human-derived neurons—not just lab models
- It reverses disease damage in both cells and animals
- It reaches the brain and is taken orally—no injections or gene therapy required

ORI-003: A Strong Candidate Approaching the Clinic

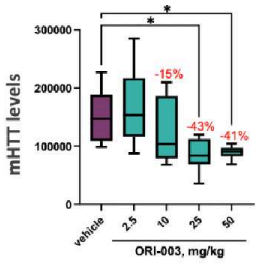
- ORI-003 is over 85% orally bioavailable
- Highly brain penetrant
- Shows no adverse effects after two weeks of daily dosing
- IND-ready; prepares us to start safety studies and apply for orphan drug status

We're moving quickly toward human trials and the potential first disease-modifying treatment for Huntington's

Well-distributed in brain and body



Dose-responsive lowering of mHTT protein



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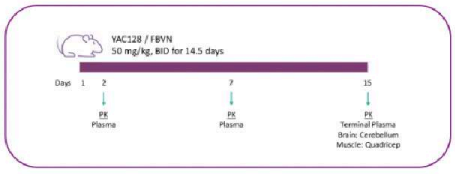
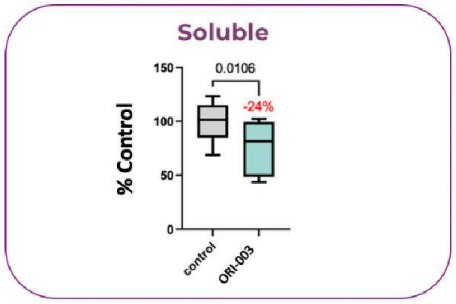
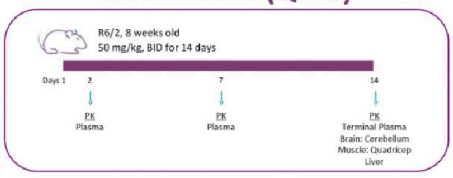
Lead Drug Shows Efficacy in 2 Huntington's Models

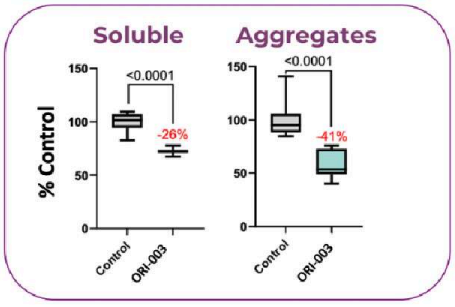
Full length mHTT (Q128)





Symptomatic Exon1 mHTT (Q120)





ORI-003 reduces mHTT proteins and fragments before and after symptoms appear

It's now moving into preclinical safety studies (IND-enabling studies). If these are successful, we'll apply to the FDA to begin clinical trials—***a major inflection point in value and impact.***

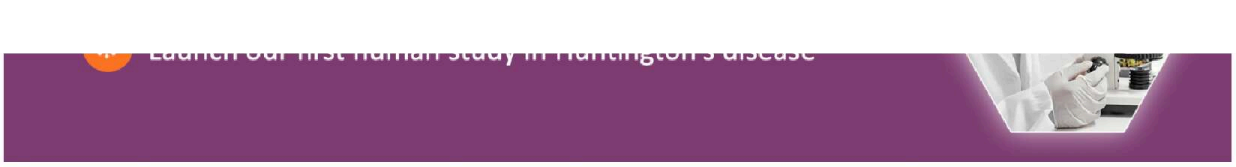
Traction and What's Next

Founded in 2015, we have made significant accomplishments:

- $4.8M raised to date from Founders, Y Combinator, Catalytic Impact Foundation, Princeton Angels, NuFund Ventures
- Discovered, developed and tested our lead development candidate, ORI-003
- Shown strong results in both human patient-derived cells and animal models
- $2M non-dilutive funding received as cash ($1.1M from NIH SBIR Phase I grant) and medicinal chemistry services ($0.9M from Kickstarter awards)
- BIO Start-up stadium finalist 2024 & 2025
- Selected as Peter Como HD Research Symposium presentation at 2023 Huntington's Study Group Annual Meeting
- Filed multiple patents protecting both our lead drug and proprietary discovery platform

Major pharmaceutical companies are already paying attention—***Origami is in early discussions with potential partners***, with interest expected to accelerate once safety data is complete.

Our Momentum Puts Us in a Strong Position to Scale



Beyond Huntington's — A Platform That Grows

Origami's approach isn't just about one drug or one disease. ORICISION™ gives us a scalable way to treat dozens of neurodegenerative diseases caused by protein misfolding.

With each success, we grow our reach—from rare genetic disease to widespread conditions tied to aging and brain health. ***It's a significant advancement that offers hope for treating these devastating diseases.***

Targeting Tau

Our next focus is already in motion: a program targeting tau, a toxic protein that plays a key role in diseases like Alzheimer's. By developing a tau-targeted protein degrader, Origami aims to provide a new therapeutic option in a space with huge unmet need and global impact.

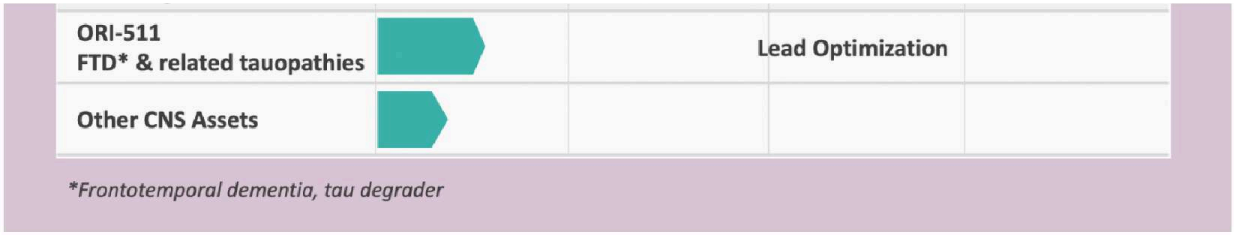
We're early in this program, but we've already demonstrated success in degrading tau in patient-derived neurons—and we're actively advancing this into preclinical studies.

Success Stacking

Every success unlocks new paths forward to a new class of medicines for some of the world's most feared brain diseases:

- Huntington's proves the science
- Tau expands us into Alzheimer's and related dementias
- Future targets include Parkinson's, ALS, and beyond

Origami's Current Pipeline



These build value and open doors to partnerships, licensing, and acquisition opportunities following key clinical milestones.

Large Markets Growing Fast

Neurodegenerative diseases are one of the largest and fastest-growing healthcare markets in the world. And they're only becoming more urgent.

- Huntington's represents a projected ***$9B+ global opportunity*** due to the high cost and burden of care
- Alzheimer's alone is a ***$5B+ market today***—and expected to grow to ***$13B+ by 2030***
- Tau-targeting therapies are attracting ***major pharma interest*** and ***billion-dollar partnerships***

We're not just following the science. We're leading it.

As populations age, demand for therapies that protect and restore brain healthspan is skyrocketing.

Targeted protein degradation is one of the most promising frontiers in medicine—and Origami is pushing the boundaries of what's possible.

ORIGAMI Therapeutics

Big Pharma Is Watching

Origami isn't alone in the massive opportunity in targeting neurodegeneration at the protein level. Recent pharma deals show just how much value is being placed on new approaches in this space:

- **$2.9 Billion — Novartis & PTC Therapeutics:** Novartis inked a deal with PTC for a Huntington's disease program, highlighting the appetite for new therapies in even rare neurodegenerative diseases.
- **$1 Billion+ — Biogen & Ionis:** Biogen entered into a broad partnership with Ionis around neurological diseases including the license of a Tau-lowering antisense therapy targeting Alzheimer's and frontotemporal dementia.
- **$1.4B — Abbvie & Aliada:** Abbvie acquired Aliada for its brain-penetrant novel Alzheimer's therapeutic
- **$500M+ — Sanofi & Vigil:** Sanofi acquired Vigil's oral small molecule for treatment of Alzheimer's disease

These deals set a clear precedence for a future acquisition and validate what Origami is building:

- A new therapeutic class with broad disease reach
- Precision-targeted molecules that address the cause, not the symptoms
- A platform model that can scale across multiple programs and partnerships

With a compelling pipeline and an experienced founder who's done this multiple times before, Origami is positioned to be a serious player—and an attractive partner—as the space continues to heat up.

Future projections are not guaranteed.

How We're Different (and Better Positioned)

Most drug companies working in this space:

- Focus on symptoms, not causes
- Use complex delivery methods, like gene therapy
- Target toxic proteins but also hit healthy ones, disrupting normal cell function

Origami is different.

We go after the root cause of neurodegeneration, misfolded proteins that

We go after the root cause of neurodegeneration: misfolded proteins that accumulate with age and trigger disease. Our drugs are small molecules taken as pills—***easy to deliver, easy to scale***—and designed to work across the brain and body.

Origami's Differentiation

	ORIGAMI Therapeutics	Alnylam	VICO Therapeutics	SKYHAWK THERAPEUTICS	Roche	WAVE LIFE SCIENCES	uniQure	PTC THERAPEUTICS
Delivery		 Spinal	 IV inpatient		 Spinal	 Spinal	 Brain Surgery	
Approach	Small molecule *Mutant HTT*	siRNA Total HTT	ASO *Mutant HTT*	Small molecule Total HTT	ASO Total HTT	ASO *Mutant HTT*	siRNA / AAV Vector Total HTT	Small Molecule Total HTT
Target	*Protein*	mRNA	mRNA	mRNA	mRNA	mRNA	mRNA	mRNA
Target Organ(s)	*Brain + Body*	Brain	*Brain + Body*	*Brain + Body*	Brain	Brain	Brain	*Brain + Body*
Phase	Preclinical	Phase 1	Phase 1	Phase 1	Phase 2	Phase 2	Phase 2	Phase 2

We've built in key advantages:

- ***Precise targeting:*** Our lead compound removes only the toxic form of the huntingtin protein (mHTT), while sparing the healthy form (HTT) to help restore normal cell function.
- ***Thorough clean-up:*** It eliminates toxic protein fragments already in the brain, including one called Exon1, which is especially damaging.
- ***No new problems:*** Unlike some other therapies, our approach doesn't generate new harmful protein pieces as a byproduct.
- ***Whole-body reach:*** Because it's taken orally and reaches the brain, our drug treats both central and systemic symptoms of disease.

The Team Behind the Breakthrough

Origami's team combines deep scientific expertise with real-world drug development success.

A Founder Who's Delivered – Beth Hoffman, Ph.D.

Our founder and CEO, Dr. Hoffman, brings 30+ years of experience advancing drugs from discovery through approval.

At Vertex Pharmaceuticals, she led the early-stage discovery for four approved drugs for Cystic Fibrosis—precision medicines that correct misfolded proteins, now transforming lives and generating $10B+ annually. That success helped establish the model for Origami's approach today.

Dr. Hoffman knows how to move breakthrough science from lab bench to patients—efficiently and effectively. She founded Origami to apply that same precision to neurodegenerative diseases, with a clear focus: treat the root cause, not just the symptoms. With her at the helm, we know how to turn promising science into real-world impact.

Capital-Efficient by Design

Origami is lean by choice.

- We outsource non-core functions to avoid fixed overhead
- We use human-derived cell models to streamline early testing and reduce risk
- We focus every dollar on de-risking the science, not inflating the org chart

This model lets us advance with speed and discipline—giving investors more science per dollar

Board of Directors:
Beth Hoffman, Ph.D./ Mohamedi (Mo) Kagalwala, Ph.D., Co-founder & COO, Alleo Labs/ *open position*

Leadership Team

Beth J. Hoffman, Ph.D. – Founder, CEO/CSO -- Dr. Hoffman is a veteran biotech executive who led the discovery of four FDA-approved drugs for Cystic Fibrosis, now used by over 100,000 patients worldwide. A proven biotech innovator, she founded Origami to bring that same precision to neurodegenerative disease.

Leslie J. Schulze, CPA, CGMA – Co-founder, CFO -- Ms. Schulze has over two decades of financial and operational leadership across early- to late-stage biotech companies. She specializes in fundraising strategy, financial planning, and scaling companies from inception through commercialization.

Martin Eglitis, Ph.D. – Strategy Advisor -- Dr. Eglitis has held senior roles in business development and R&D at Teva, Amgen, Eli Lilly, and the NIH. He advises VC-backed therapeutics companies on corporate strategy, partnerships, and translational research alignment.

Katherine Widdowson, Ph.D. – Chemistry Advisor -- Dr. Widdowson is a medicinal chemist with 30+ years of experience at GSK and biotech startups. She's a co-inventor on 35+ patents and helped advance over a dozen drug candidates, including the marketed COPD treatment Incruse®.

Board & Advisors

Jody Corey-Bloom, M.D., Ph.D. – Clinical Advisor -- Dr. Corey-Bloom is a neurologist and longtime director of the HDSA Center of Excellence at UC San Diego. She brings deep expertise in neurodegenerative diseases and clinical trial leadership, with a focus on Huntington's and Alzheimer's.

Steven Finkbeiner, M.D., Ph.D. – Key Opinion Leader -- Renowned neuroscientist at UCSF and the Gladstone Institutes, Dr. Finkbeiner is a leading expert in neurodegenerative disease and patient-derived cellular models with focus on protein misfolding.

Kalpana Merchant, Ph.D. – Key Opinion Leader -- Neuroscience advisor with decades of pharmaceutical experience, including at Eli Lilly, where she led CNS biomarker strategy.

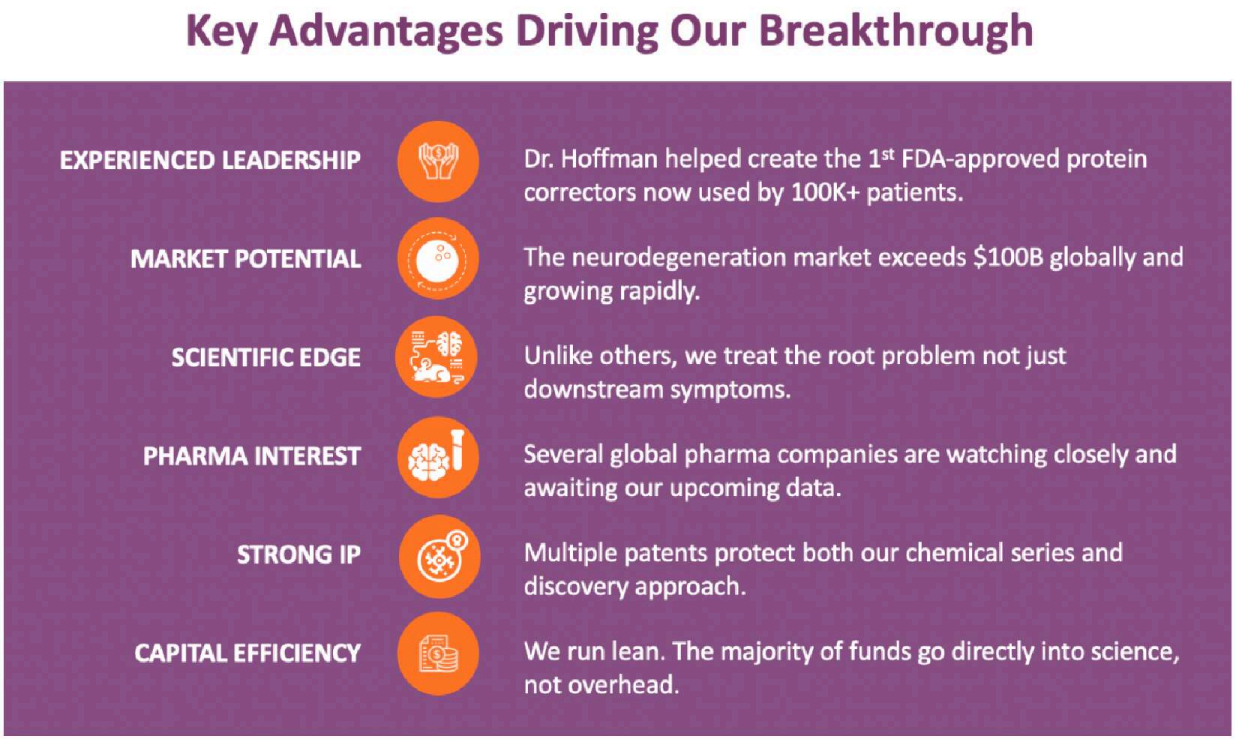
Robin Mansukhani – Business Strategic Advisor -- Currently CEO, Deciduous Therapeutics, previously Co-founder, CEO at Alzeca Biosciences, previous experience in venture capital and investment banking.

Mohamedi (Mo) Kagalwala, Ph.D. – Board Member -- NuFund investor, co-founder, COO at Alleo Labs, formerly COO at Immuneering, is a scientist, founder, and venture partner with a strong track record in drug discovery.

neuroscience, and AI/ML applications.

Let's Change the Story on Brain Aging

We're on the cusp of a major breakthrough and we need support to cross the next milestone.



Origami is raising on Wefunder to fund critical IND-enabling safety studies for our drug candidate, ORI-003. This is the final step before we apply to begin human trials—***a key value inflection point that's already drawing attention from potential pharma partners.***

And we're doing it with a lean, capital-efficient model that puts your investment to work on the science—not overhead.

Your investment will help us:

- Complete preclinical toxicology studies
- Prepare for our IND submission to FDA
- Lay the groundwork for our first clinical trial in Huntington's disease
- Expand our platform into more neurodegenerative diseases

Most of us know someone affected by Alzheimer's, Parkinson's, or another

devastating brain disease. These conditions rob people of who they are and today's treatments just aren't enough.

Origami is tackling the root cause. Not managing decline, but working to restore brain health, extend healthspan, and change what's possible as we age.

Join Us

Invest in the science that could help millions hold on to who they are.

ORIGAMI Therapeutics