ORIGAMI Therapeutics

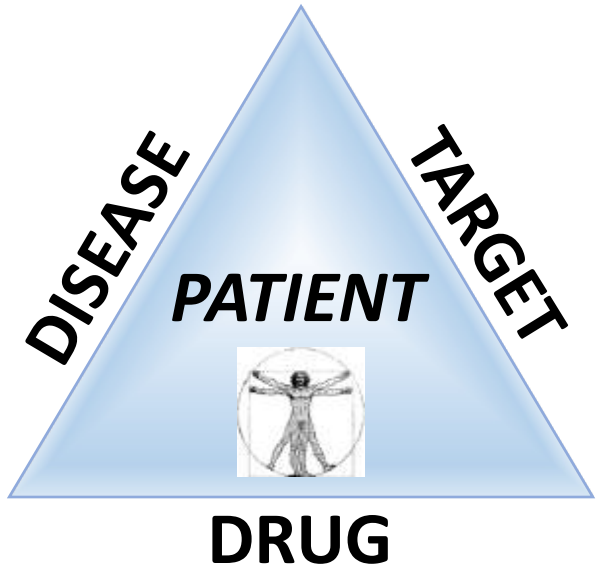
Developing oral drugs to halt neurodegeneration

BIO Biotechnology Entrepreneurship Bootcamp
13 June 2022
Session 14: Pre-seed/Seed Funding Pitch

No drugs alter progression of neurodegenerative diseases

20 years
100's clinical trials
0 drugs

Origami's concept: A precision medicine approach



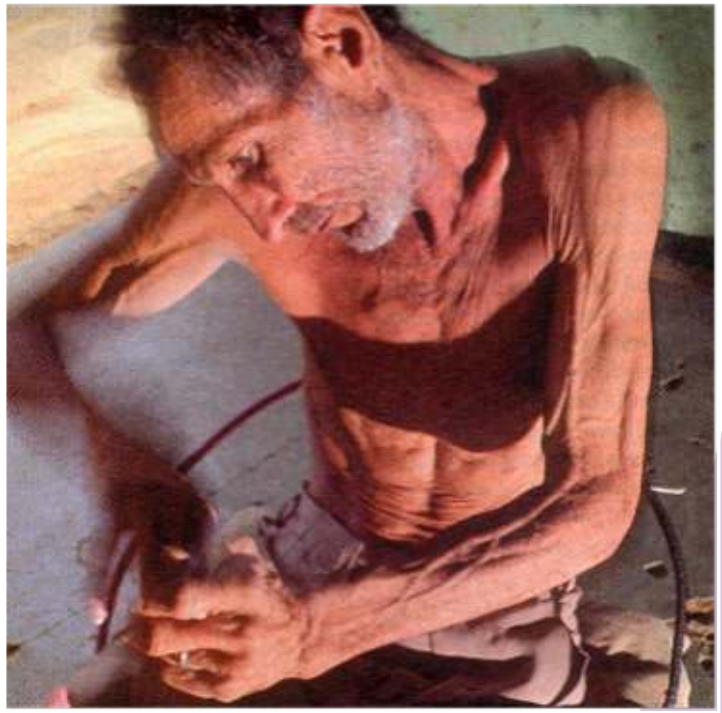
Disease-Modifying Treatment

Right drug
Right patients
Right time
Right measures

- Disease selection: Clinical trials feasible & Patient population accessible
- Target selection: Fix the root cause of disease
- Drug selection: Choose best therapeutic modality

Despite $2.8B spent on drugs for HD in 2021 alone, we still can't effectively treat Huntington's disease (HD)

- Caused by mutation in Huntingtin protein (mHTT)
- Characterized by loss of brain cells
- Affects all cells in the body
- Huntingtin protein is critical for normal function
- Lowering mHTT halts & reverses disease in animal models



HD is an orphan disease with $9B projected revenue in 2030

- Affected: 185,000 WW
- Orphan Disease designation provides an expedited regulatory path
- Current symptomatic drugs: $100K/annum/patient
- Estimated revenue for disease-modifying drug:
  - 185K patients x 25% market share x $100K/patient/ yr = $4B*
- Projected Industry Revenue in 2030: $9.2B WW**

* Medical Market Economics evaluation for Origami, 8/2019
**Coherent Market Insights, assuming 60% current symptomatics, 8/2021

Leadership team: >30 assets advanced into clinic, 4 marketed drugs in Cystic Fibrosis

Beth Hoffman, Ph.D.
Founder & CEO

25 years of CNS drug discovery experience, with over 30 assets advanced into the clinic and 4 marketed drugs for Cystic Fibrosis

Leslie Schulze
Co-Founder & CFO

Over 20 years of finance experience in life sciences, including VC financing, non-dilutive funding, licensing and M&A

Christopher Smith, Ph.D.
Advisor, Chemistry

20 years of industrial experience in neuroscience, oncology, immunological and metabolic disease therapeutic areas

Scientific advisors: World class key opinion leaders

Jody Corey-Bloom, M.D., Ph.D.
Professor, UCSD
Director, HD & AD Clinical Centers
Translational research & clinical trials

Steven Finkbeiner, M.D., Ph.D.
Professor, Neurology & Physiology, UCSF
Director, Taube/Koret Center of Neurodegenerative Disease Research & Center for Systems and Therapeutics, Gladstone Institutes

Kalpana Merchant, Ph.D.
President & CEO, TransThera Consulting
Adjunct Professor, Feinberg School of Medicine, Northwestern University
CEO & CSO roles at start-ups

Pharmacia &Upjohn

Lilly

Lucia Mokres, DVM
Regulatory, Clinical and Medical Affairs
Founder & Principal, Araneae Biotech Consulting

evalve

EPIBIOME
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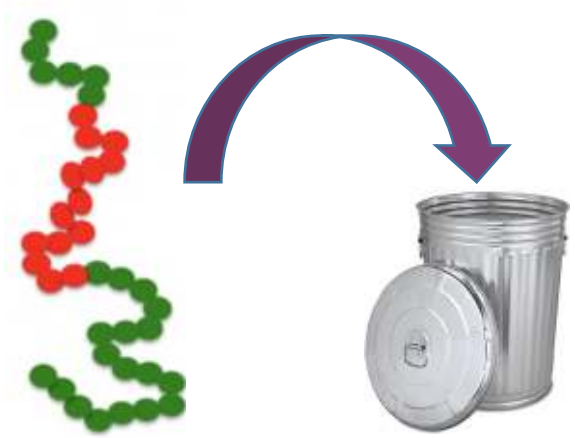
ORIGAMI Therapeutics

Origami's solution: protein degraders selectively destroy mHTT protein

Selectively destroy mutant protein

Mutated Huntingtin protein (mHTT)



Spare normal protein

Normal Huntingtin protein (HTT)

- Goal: Remove toxic protein to enable restoration of normal function
- Targeted protein degradation (TPD): a powerful way to silence errant proteins
- Origami's approach is tailored to diseases of the brain

Origami has identified promising molecules

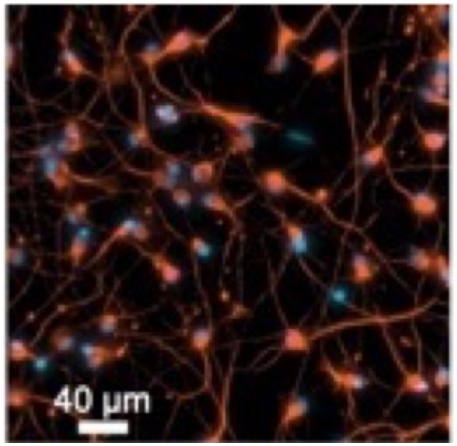
- Unique proprietary high throughput screen identified multiple small molecules
- Developed human HD neuronal models: Use enhances probability of success in clinical trials
- Our small molecules prevent HD pathology in human neurons

Origami molecules prevent disease pathology in human HD neurons in cell culture

- **Use of patient-derived cells enhances probability of success in the clinic**
- **Machine learning generates human disease models by integrating multiple layers of data**
- **Drives compound optimization and biomarker discovery**

Origami molecules prevent disease pathology in human HD neurons in cell culture

Normal
No Treatment



Blue = cell body
Red = neurites

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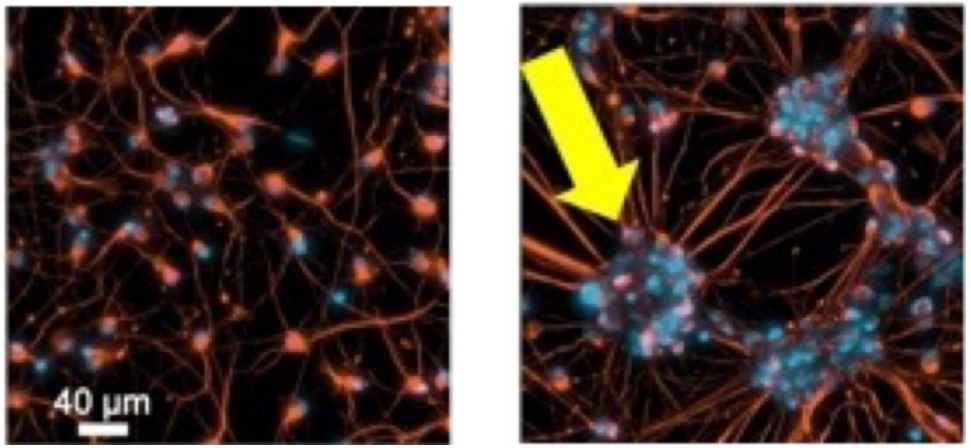
Origami molecules prevent disease pathology in human HD neurons in cell culture

Normal
No Treatment

Disease
No Treatment



= points to cluster of cells

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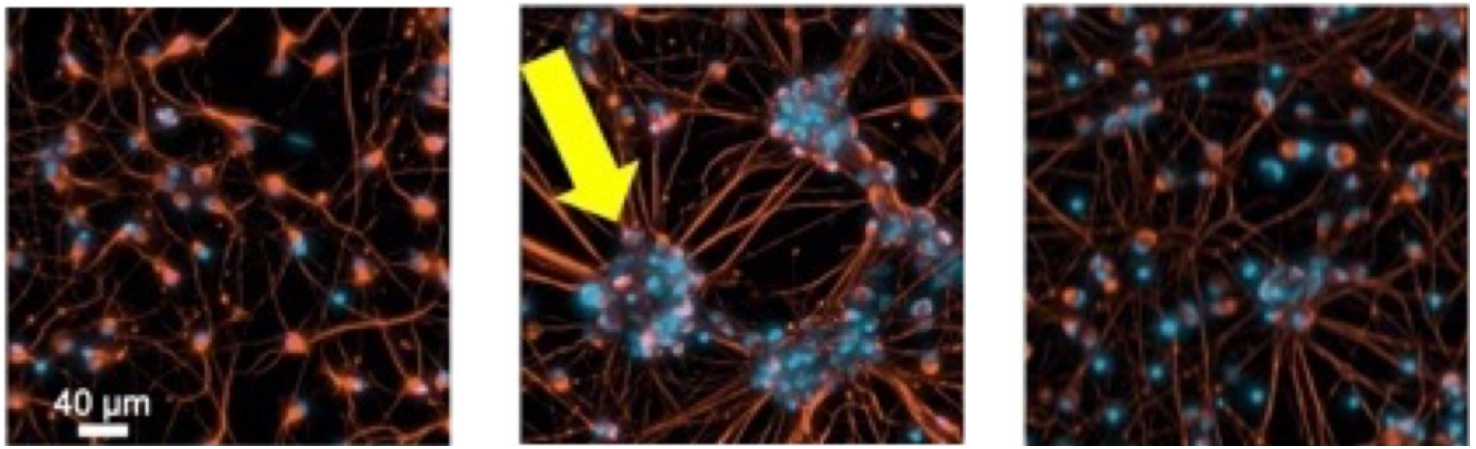
Origami molecules prevent disease pathology in human HD neurons in cell culture

Normal
No Treatment

Disease
No Treatment

Disease
ORI-113 Treated



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Multiple chemical assets have therapeutic attributes

ORI-113 and ORI-110 represent distinct chemical classes of mHTT protein degraders

ATTRIBUTE	ORI-113	ORI-110
Prevents mHTT protein aggregation	✓	✓
Reduces mHTT protein levels	✓	✓
Selective for mHTT over wtHTT	✓	✓
Efficacious in human disease neurons	✓	✓
Brain penetrant	✓	✓
Efficacious in mouse HD model	In progress	In progress

Origami is pursuing a robust intellectual property strategy

- All assets discovered by Origami
- Patent filings include:
  - Composition of matter (5 scaffolds)
  - Method of use
  - Expiry not before 2040
- Methods of selection (proprietary know-how) held as trade secrets

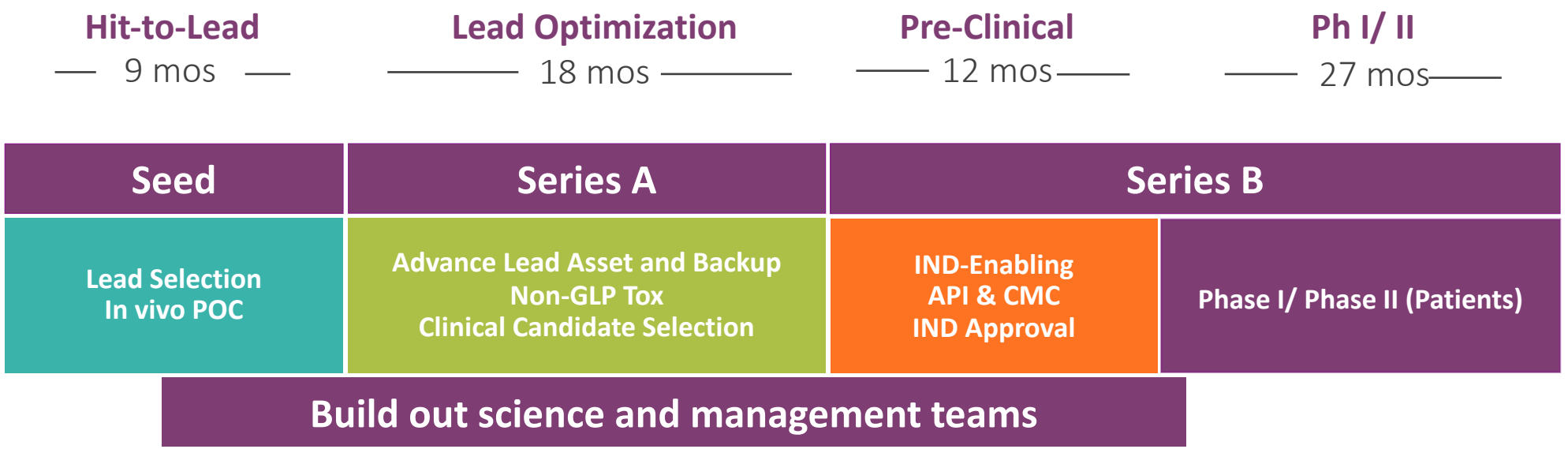
We have Preliminary Freedom to Operate (FTO)

Compared to competitors, Origami molecules selectively reduce mHTT and are systemically available

Origami Protein Degraders	Competitors
Reduces mutant HTT Spares normal HTT	Reduces both normal and mutant HTT
Systemic exposure Treats whole body, entire disease	Brain only, may be limited to parts of brain Partially treats disease
Oral delivery Democratization of access	Invasive delivery Requires neurosurgeon & neurosurgical suite

Reducing normal HTT may contribute to dose-limiting side effects

Huntingtin Protein Degrader Development Timeline



Hit-to-Lead Milestones:

1. Efficacy in human HD neurons
2. Efficacy in rodent HD model
3. Lead Selection

Origami's business thesis

Origami intends to generate clinical stage drug programs through internal research

- License most with large global pharmaceutical companies
- Develop a limited number of clinical programs independently
- Exit via large pharma acquisition or public capital

Recent Deals in Similar Spaces:

	Pharma Partnerships	Institutional Investment	Public Markets
Targeted Protein Degradation	**Pfizer/Arvinas** **$350M upfront, $1B milestones**	**PAQ Therapeutics** **$30M Series A**	**Monte Rosa Therapeutics** **IPO (preclin), $850M valuation**
Rare Diseases	**Eli Lilly/ProQR** RNA Therapeutic **$50M upfront, $1.3B milestones**	**Kelonia Therapeutics** Gene Therapy **$50M Series A**	**Parvaris** Small molecules **IPO (Phase 1), $575M valuation**
Neurodegenerative Diseases	**UCB/Neuropore (pre-IND, PD)** Small Molecule **$20M upfront, $460M milestones**	**LEXEO Therapeutics** Gene Therapy **$85M Series A**	**Vigil Neuroscience** Small molecule **IPO (Phase 1), $395M valuation**

ORIGAMI Therapeutics

$2M Seed to show our drugs work in HD animal brains, select lead molecules using human disease models and make key hires

Goal: Select the best compounds to advance

Funding History:

$3.3M raised

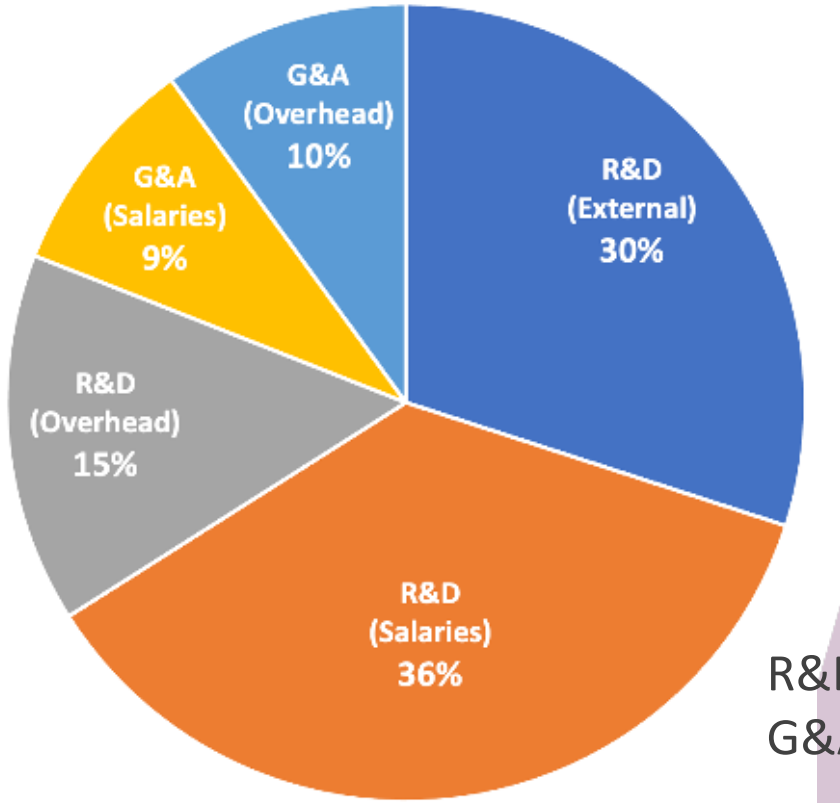
- Founders: $2.8M
- Y Combinator: $0.5M

Seeking:

$2M Seed Raise (9-12 month runway)

- $0.2M raised to date
- $12M post-money SAFE, 20% discount

Seed Raise ($2M)
9-12 month runway



R&D: 81%
G&A: 19%

Investment opportunity

- Origami has created an entirely new way to treat neurodegeneration
  - Starting with Huntington's Disease
- Origami team has extensive experience in advancing drugs through clinical trials
- Multiple exit opportunities with excellent ROI
- If successful, this approach can be applied to other neurodegenerative disease such as Alzheimer's, Parkinson's, ALS, Frontotemporal Dementia.

Developing next-generation disease-modifying protein degraders

ORIGAMI Therapeutics

Origami has potential to impact millions of lives

Impact

Patients who would be plagued by neurodegeneration will not become symptomatic and will live healthy productive lives.

Scalability

Our drug discovery engine can scale to address the > 30 million patients with neurodegenerative diseases worldwide.

Origami Therapeutics: Oral drugs to halt neurodegeneration

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