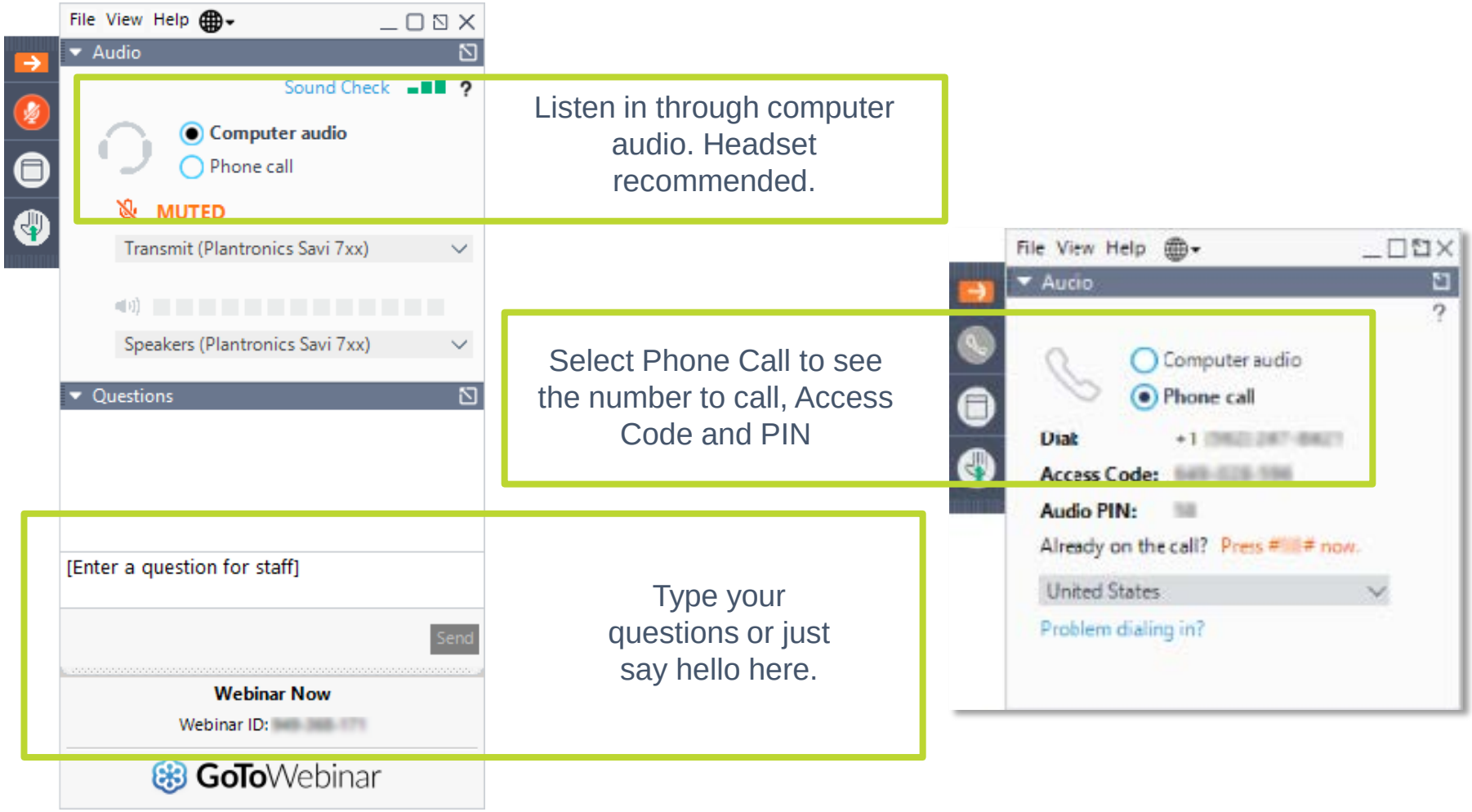
A Glimpse Into the Mind of the Investor

Tips & Tricks to Raising Your Series A

Johnson & Johnson INNOVATION | JLABS

svb Silicon Valley Bank

Livestream Attendees Control Panel



Global Solution to Support Innovation

Join The JLABS Movement

Apply today: jlabs.tv/apply




Company incubation

We understand the challenges of getting a life sciences company up and running, which is why Johnson & Johnson Innovation provides a number of company incubation options for our partners around the globe, through our JLABS and JPODS

- 13 sites across the globe
- 650+ companies, including current resident companies and alumni
- 156+ companies with at least 1 collaboration with Johnson & Johnson

Innovation acceleration

Johnson & Johnson Innovation Centers are focused on accessing innovation from all sources from inception to early stages of development

- 4 Innovation Centers on three Continents
- 500+ collaborations executed over the past seven years
- >$1B deployed since 2013

Strategic Investing

Johnson & Johnson Innovation – JJDC (JJDC) is the strategic venture capital arm of Johnson & Johnson and a long-term investment partner to healthcare entrepreneurs

- 46+ years of strategic healthcare investing
- 40+ investments in 2019
- $500M+ capital deployed in 2019

Business Development

Our goal is to form an active partnership where we can bring the full strength of Johnson & Johnson to bear to create a long and valuable relationship.

- 40+ years leading licensing and M&A deals driving R&D portfolio
- Licensing, M&A Expertise and Alliance Management

Silicon Valley Bank

BEN
JOHNSON
Head of Early Stage
Life Science
Silicon Valley Bank

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Agenda

8:30 am – 8:45 am PT | Introductions

8:45 am – 9:45 am PT | SVB Pitch Challenge

- Endogena Therapeutics
- Gabi Smartcare
- Origami Therapeutics
- Stream Biomedical
- SyntheX
- Vincere

9:45 am – 10:15 am PT | Tips & Tricks to Raising Your Series A

10:15 am – 10:45 am PT | Audience Q&A, Awardees Announced and Closing Remarks

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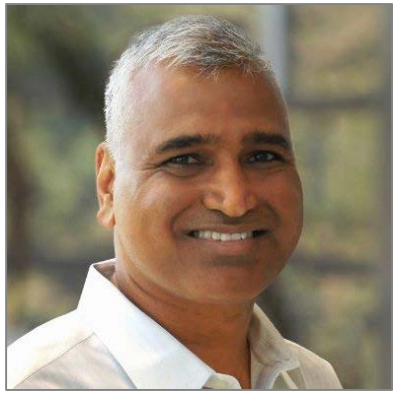
Judges

HEATHER
BEHANNA
Principal
SR One, Ltd



SHAILENDRA
MAHAJAN
Co-Founder and
Managing Director
Maxim Ventures

GAURAV
SATAM
Department of
Business Development
Mayo Clinic Ventures

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Company Pitches

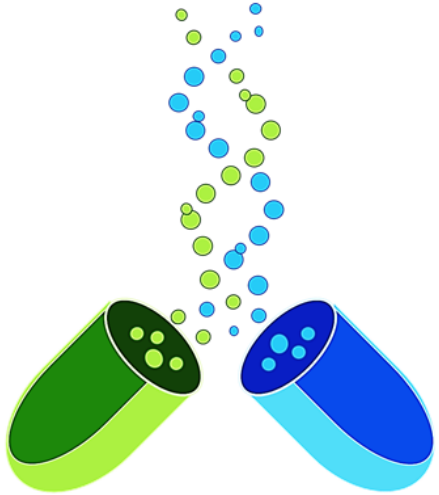
endogena

gabi SMARTCARE

Origami THERAPEUTICS

Reshaping • Restoring • Renewing

Stream BIOMEDICAL



SyntheX

VINCERE

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Event Partner

endogena

MATTHIAS
STEGER, PhD MBA
Co-founder & CEO
Endogena Therapeutics

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endogena

ENDOGENOUS REGENERATIVE MEDICINE

FOR OPHTHALMOLOGY AND BEYOND

ENDOGENA THERAPEUTICS

EXECUTIVE SUMMARY

- Novel therapeutic paradigm - endogenous regenerative medicines
  - AI driven platform, tissue & organ specificity
- Two advanced projects in ophthalmology
  - Retinitis Pigmentosa (RP) – FDA pre-IND meeting scheduled
  - Dry AMD – Clinical candidate selection stage
- High-profile founders, drug discovery expert team and collaborations with world-leading academic labs
- US-incorporated August 2016 / funding raised >$10mio
- Raising Series A of $15mio
  - Clinical proof-of-concept for RP program by 2022
  - Pre-clinical development for dry AMD program

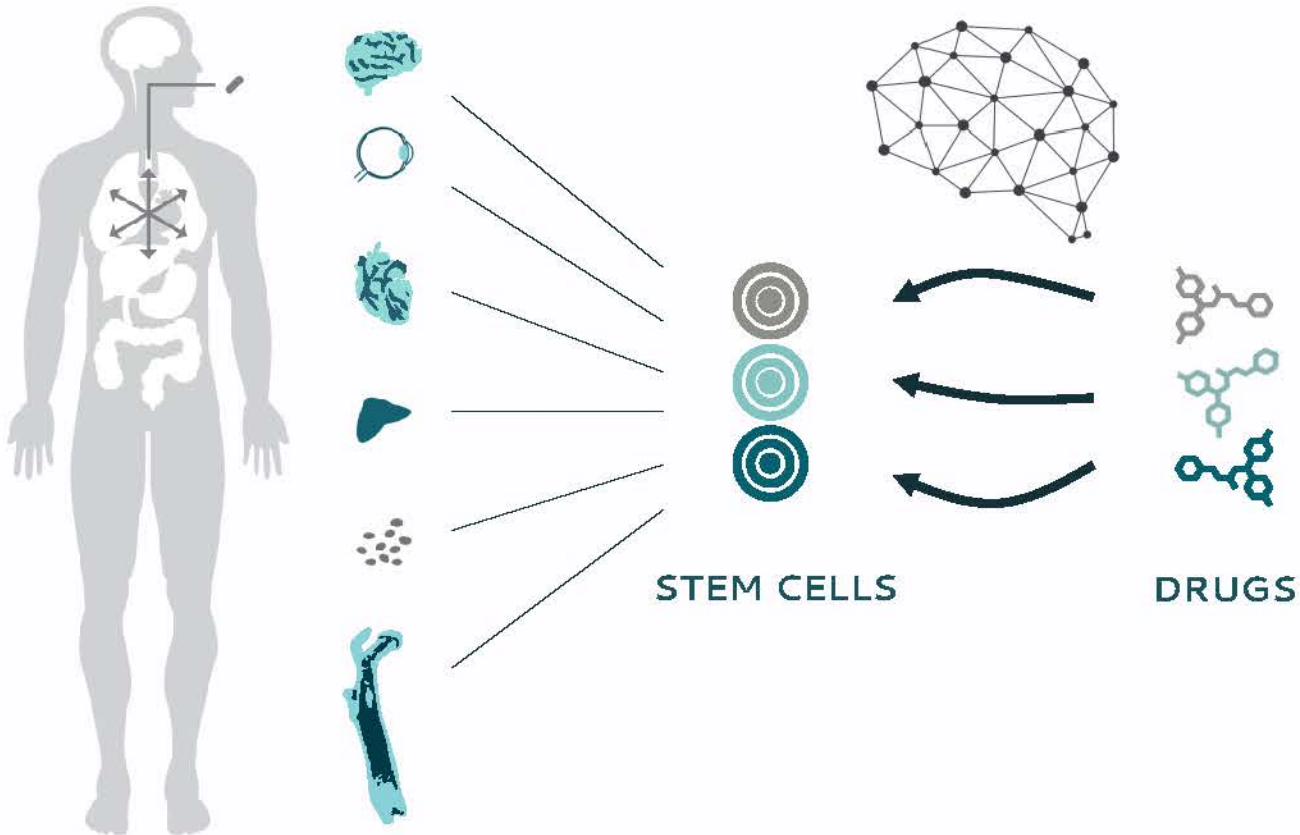
Roche

ETH

Lundbeck

ENDOGENA'S DRUG DISCOVERY PARADIGM

ACTIVATING ENDOGENOUS STEM CELLS FOR REGENERATION



- Endogena discovers & develops drugs that regulate patients' endogenous stem cells to repair and regenerate organs and tissues.

ENDOGENA'S TEAM

LEADERSHIP TEAM

MATTHIAS STEGER
PhD MBA
CEO

- >20 years industry experience
- Entrepreneurial track record
- Former Roche Global Head Research & Technology Partn.
- Built & Lead Roche's Stem Cell Research

MAURO MARIGO
PhD
Medicinal Chemistry

- 15 years experience in drug discovery
- Expert in Fragment- and Structure-Based Drug Discov.
- Former Lundbeck and Nuevolution

MORENO MENGHINI
MD – USZ
CMO

- Vitreoretinal Surgeon
- Nightstar Therapeutics / Biogen RP Trial Investigator
- Former Oxford University (Prof. R. MacLaren)

SUSANNE RAAB
PhD
***In vivo* Pharmacology**

- Leading successful IND application
- 18 years of pharmaceutical industry experience
- Former Roche in vivo pharmacology leader ophthalmology and CVM

DAPHNA MOKADY
PhD
Discovery Biology, Site Head TO

- 15 years of leading biomedical research projects
- Expert in Molecular and Cell Biology
- Former University Health Network, Toronto

MANFRED SCHNEIDER
PhD DABT
ADME / PK, Toxicology

- Certified toxicologist and ADME/PK specialist
- 25 years pharmaceutical R&D experience
- Former Amgen, Merck Serono and Biotech

ADVISORS, ACADEMIC PARTNERS & BOARD DIRECTORS

MARK PENNESI
MD
Casey Eye Inst. Portland

- Lead investigator for Retinitis Pigmentosa program

PETE COFFEY
Prof.
UCSB , UCL & Moorfield's

- AMD Program
- Retinal Pigment Epithelium regeneration

GARY NOVACK
PhD
Regulatory

- Regulatory Expert in Ophthalmology, Clinical Professor Ophthalmology
- Conducted numerous successful IND applications
- Member and advisor of the foundation fighting blindness

DEREK VAN DER KOOY
Prof.
University of Toronto

- Retinitis Pigmentosa Program
- Photoreceptor regeneration

DAN ZABROWSKI
PhD
Director of the Board

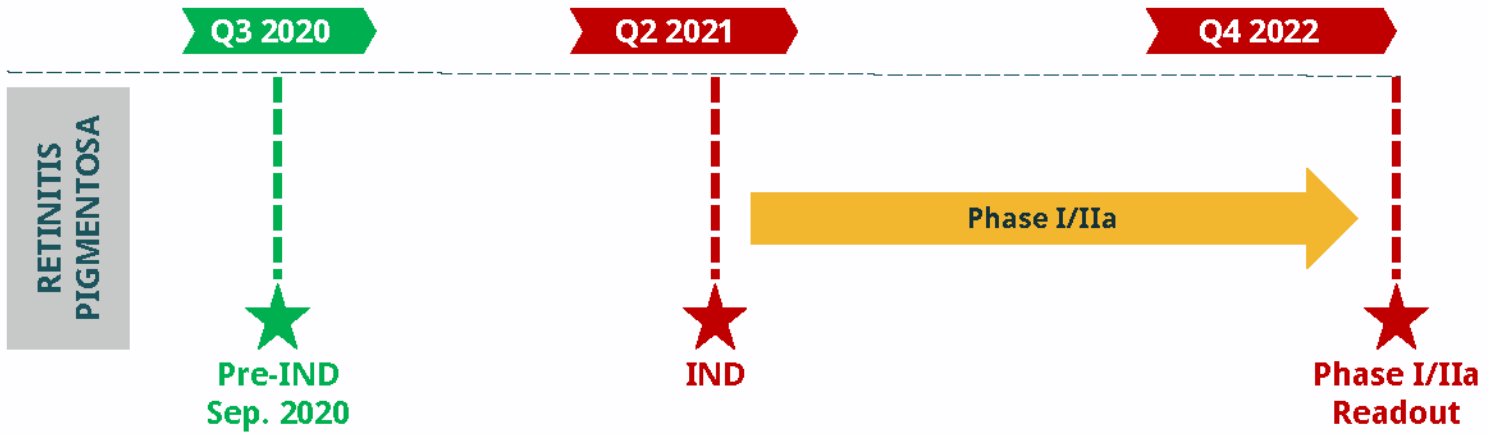
- > 20 years at Roche in executive positions
- Global Head of Regulatory Affairs; Development Operations; Pharma Partnering
- Board Member Chugai Pharmaceuticals

ELONA BAUM
Attorney
Director of the Board

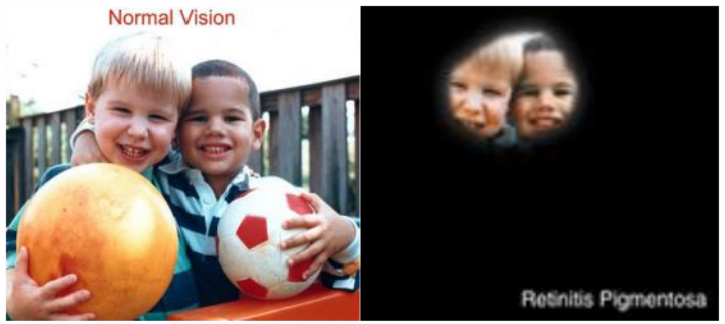
- Managing director at DEFTA Partners
- Former member of CIRM's executive team
- Former Associate General Counsel for legal matters at Genentech

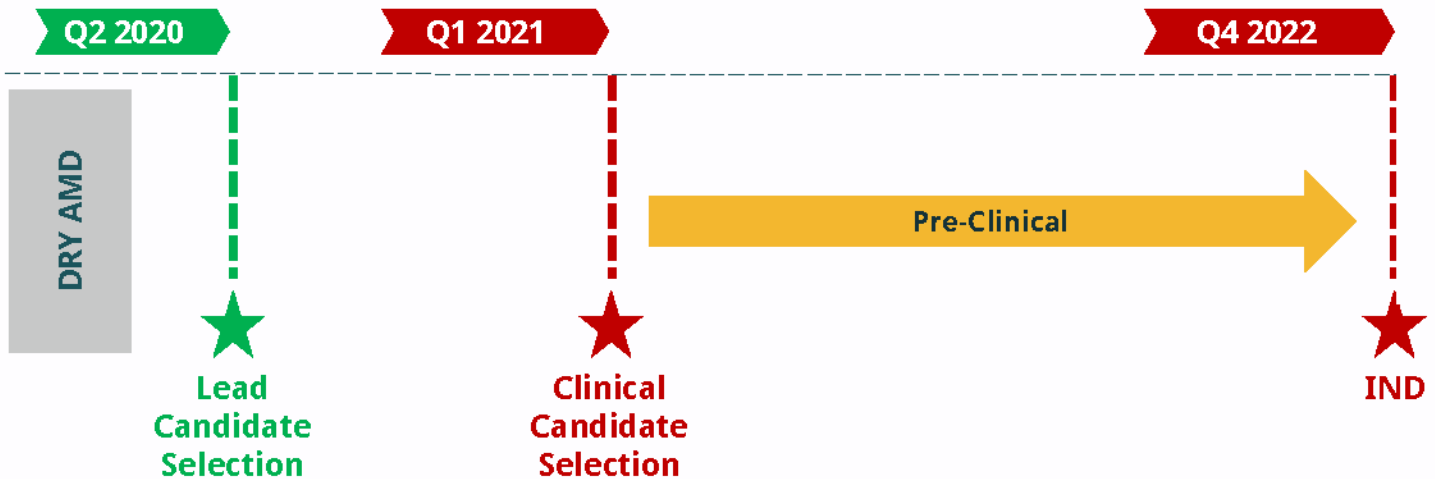
ENDOGENA'S PORTFOLIO

POTENTIAL FOR A MEDICAL TREATMENT PARADIGM CHANGE



RETINITIS PIGMENTOSA



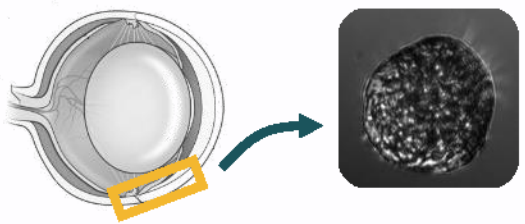


AGE-RELATED MACULAR DEGENERATION

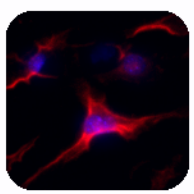
RETINITIS PIGMENTOSA

IND 2021

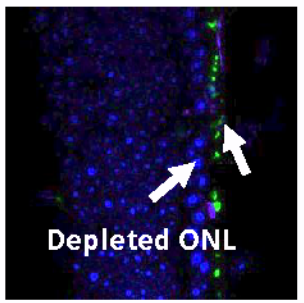
Human (and Mouse)
Retinal Stem Cells



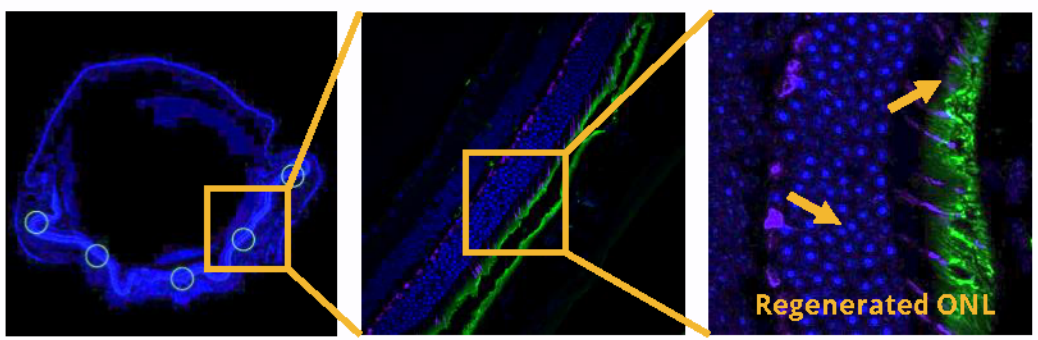
In Vitro



MNU-Induced Retinal Damage



In Vivo



Clinical Candidate

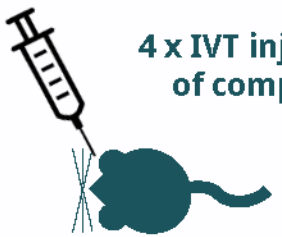
Patents Granted

To Phase 1/2a

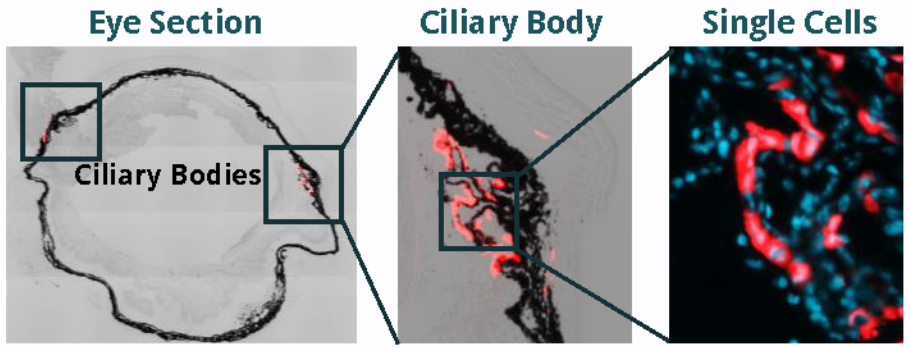
IND-Enabling
Studies
Ongoing

IN VIVO PROOF-OF-CONCEPT

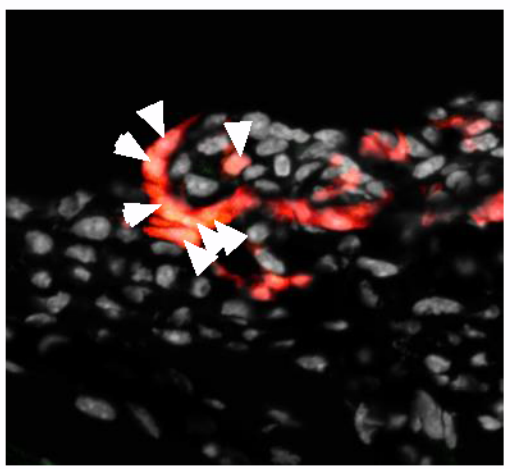
ACTIVATING QUIESCENT RETINAL STEM CELLS IN MICE



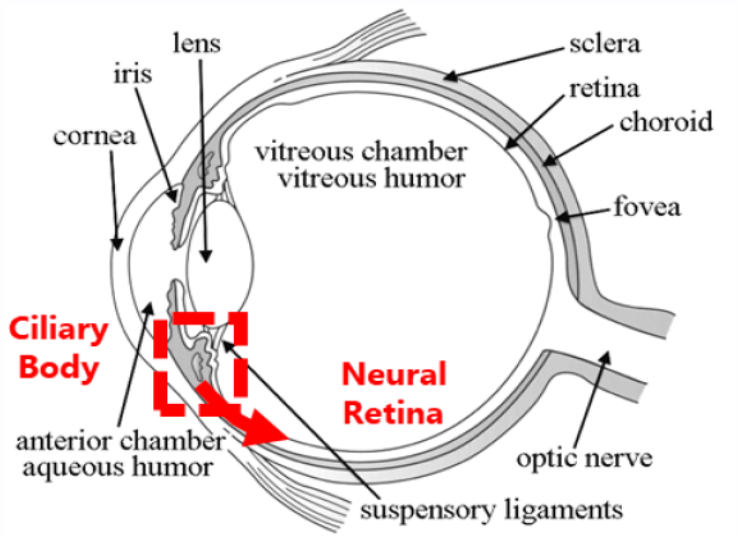
4 x IVT injections of compound



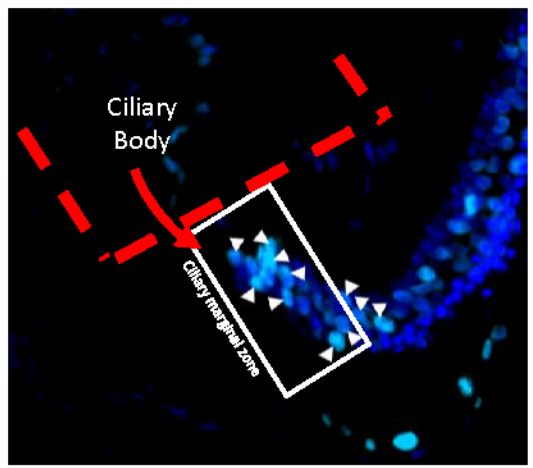
ACTIVATION OF RETINAL STEM CELLS



Stem cells | Proliferation | Nuclei



MIGRATION AND DIFFERENTIATION



Early differentiation marker

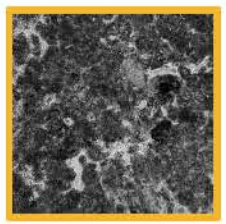
DRY AGE RELATED MACULAR DEGENERATION

IND2022

iPS Retinal Pigment
Epithelial Cells
(and from **Human donor**)

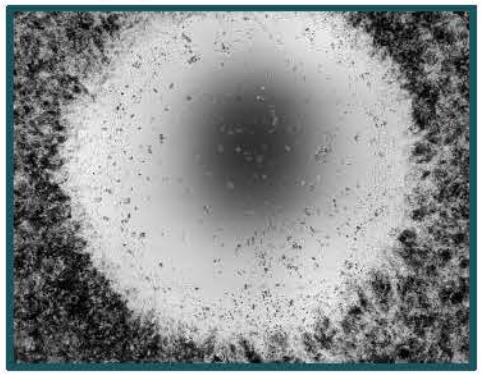
In Vitro Screening

1. Proliferation
2. Pigmentation

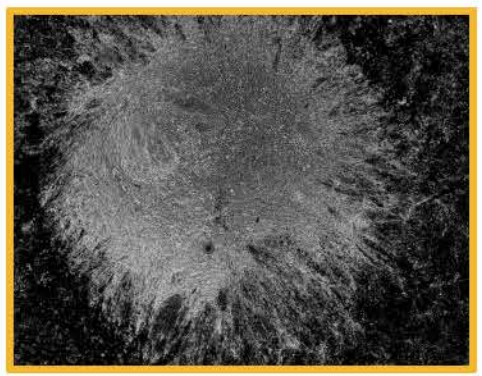


MED < 10nM

In vitro model of GA
Apoptosis cell death

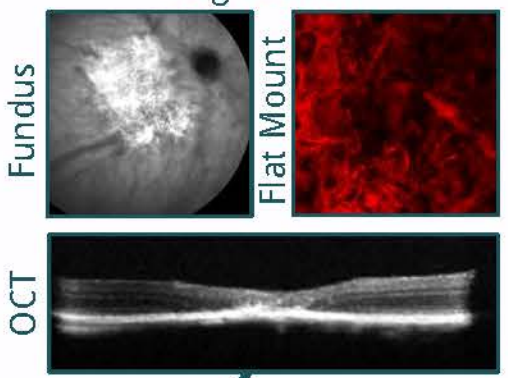


In Vitro Disease Model



In vitro POC

Laser induced
degradation



In Vivo

POC
Enabling studies
Ongoing

SUMMARY

A NOVEL THERAPEUTIC PARADIGM FOR TREATING RETINITIS PIGMENTOSA

- Endogena has successfully discovered a small molecule that activates endogenous retinal stem cells and differentiates them into photoreceptors both *in vitro* and *in vivo*
- Initial hit compounds were further developed into a clinical candidate with desired properties
- Two patents filed protecting two chemical series and their use in treating IRDs
- Preclinical development ongoing, IND planned in Q2-2021
- $15mio required for a phase I/IIa clinical trial to achieve clinical PoC in RP and for preclinical development for AMD

gabi SMARTCARE

JONATHAN
BAUT
Co-founder & CEO
Gabi SmartCare

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BLUE KNIGHT™

Save children's lives

Prevent, Diagnose, Surveil

gabi SMARTCARE

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a premier life science incubator program

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CALIFORNIA CONSUMER PRIVACY ACT OF 2018 · EU GDPR COMPLIANT · FC · CE · bsi. ISO 13485 Medical Devices Quality Management

56% & 32%

ER visits & Hospital admissions are avoidable*

*Consumer Informatics and Digital Health: Solutions for Health and Health Care (Margo Edmunds, Christopher Hass, Erin Holve); Weinick, Billings, & Thorpes, 2003; University of Rochester News, 2008) - *Keeping children out of hospitals: parents' and physicians' perspectives on how pediatric hospitalizations for ambulatory care-sensitive conditions can be avoided - https://www.ncbi.nlm.nih.gov/pubmed/14595 0 - 2003 - * Potentially Preventable 30-Day Hospital Readmissions at a Children's Hospital - doi: 10.1542/peds.2015-4182

Respiratory *

1st cause of hospitalization & ER visit

270m children < 5 – **$120bn** cost – **6%** increase

*Pediatrics. 2003 Nov;112(5):1021-30. Flores G , Abreu M, Chaisson CE, Sun D. Overview of Pediatric Emergency Department Visits, 2015 Kimberly W. McDermott, Ph.D., Carol Stocks, Ph.D., R.N., and William J. Freeman, M.P.H. - Asthma costs and social impact, doi: 10.1186/s4073301600293 - The Global Burden of Respiratory Disease, DOI: 10.1513/AnnalsATS.201311-405PS - Respiratory diseases in the world, Realities of Today – Opportunities for Tomorrow, Print ISBN: 978-1-84984-056-9; e-ISBN: 978-1-84984 057-6

Market size

ER visits

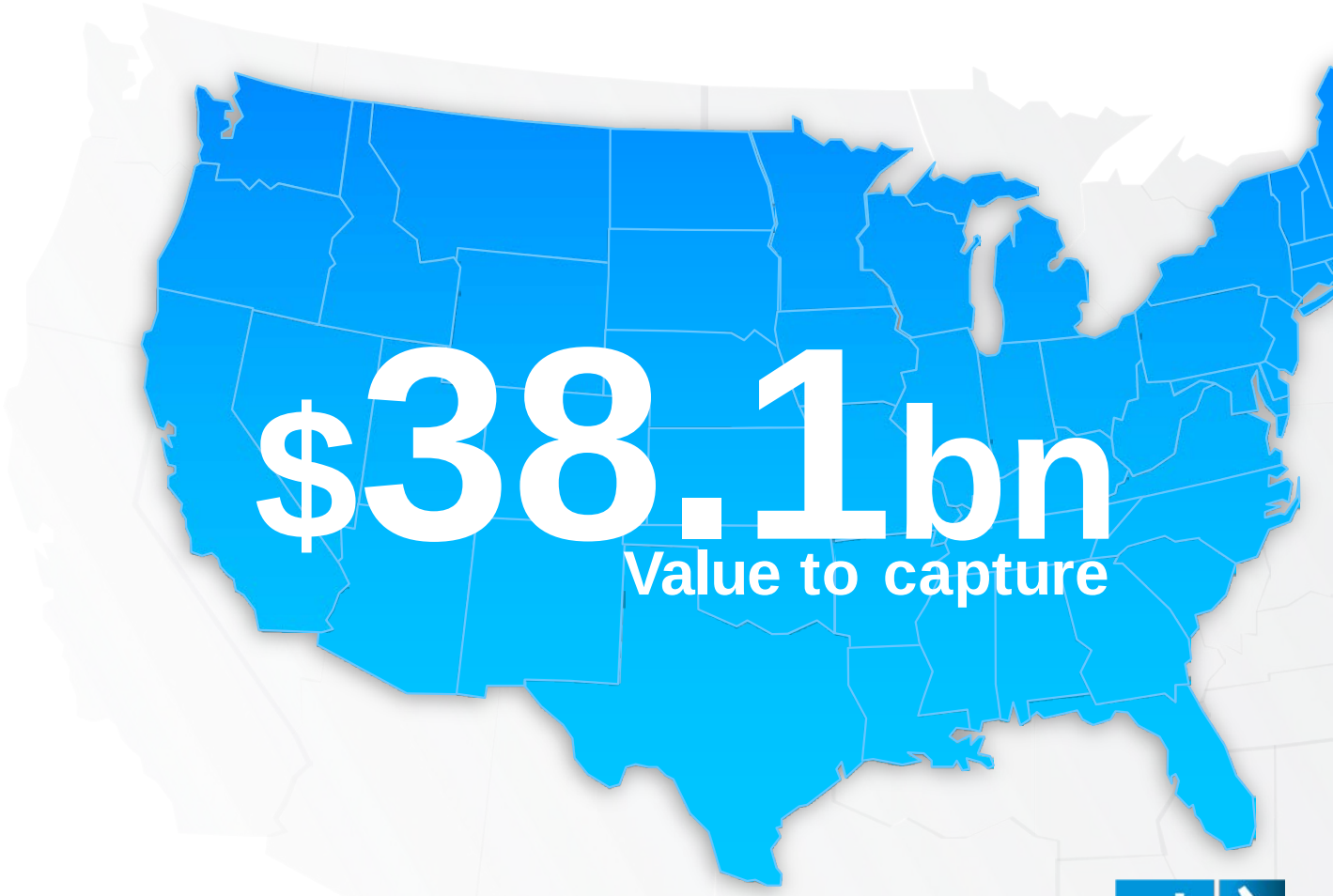
30 million pediatric ER visits / year in the US[1]
56% ER visits avoidable
$1500 average cost / admission[2]

$25.2bn

Hospital admissions

3 million pediatric hospital admissions / year in the US[3]
32% hospital admission avoidable
$13,400 average cost / stay[4]

$12.9bn



[1] https://www.hcup-us.ahrq.gov/reports/statbriefs/sb242-Pediatric-ED-Visits-2015.pdf [2] https://consumerhealthratings.com/healthcare_category/emergency-room-typical-average-cost-of-hospital-ed-visit/#:~:text=Summary%20report%20shows%20average%20cost,pediatric%20ER%20visit%20was%20%243%2C420.– [3] https://cthosp.org/advocacy/quality-and-patient-safety/patients-guide-to-quality-hospital-care/pediatric-hospitalization/#:~:text=Each%20year%20more%20than%203,treatment%20for%20a%20chronic%20illness.; [4] HCUP – UC; Cost of pediatric hospital stay, 2016;

Why?

- 80%Parents struggling to assess their child's condition correctly[1]
- Common tests are not applicable on young children
- Up to 40% of assessment errors[2] and up to 3 years of diagnosis period[3]

Lack of actionable data!

[1] 250 parents Gabi SmartCare survey; [2] A survey from Boulay & Boulet; [3] Asthma.uk

Gabi SmartCare

empowers physicians & parents

thanks to **data driven technologies**

to **disrupt** pediatric healthcare

& **improve children's lives**

How?

By developing

Smart digital platform enabled by hardware

providing unique actionable data to physicians to better

- **Prevent**
- **Diagnose**
- **Surveil**

1st Pediatric fully integrated solution

With a first focus on respiratory

Web Analytics

Interface for Doctors

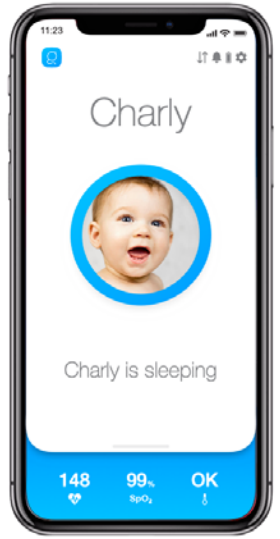
Band

Monitors patient vitals

(SpO2, HR, HRV, RR, Temp.)

Mobile App

Interface for Users



Achievements

✓ 2nd product version
(preclinically validated, 75 patients

✓ ISO13485

✓ 1 international Patent Pending

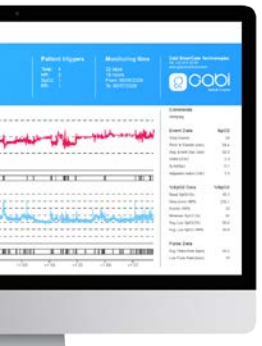
✓ Proven traction
(7 hospitals, 50 doctors, 1000 users, 400 pre-orders)

✓ Awarded

BLUE KNIGHT™ Johnson & Johnson INNOVATION – JLABS – Children's National biopôle MATTER svb Silicon Valley Bank

What's unique?

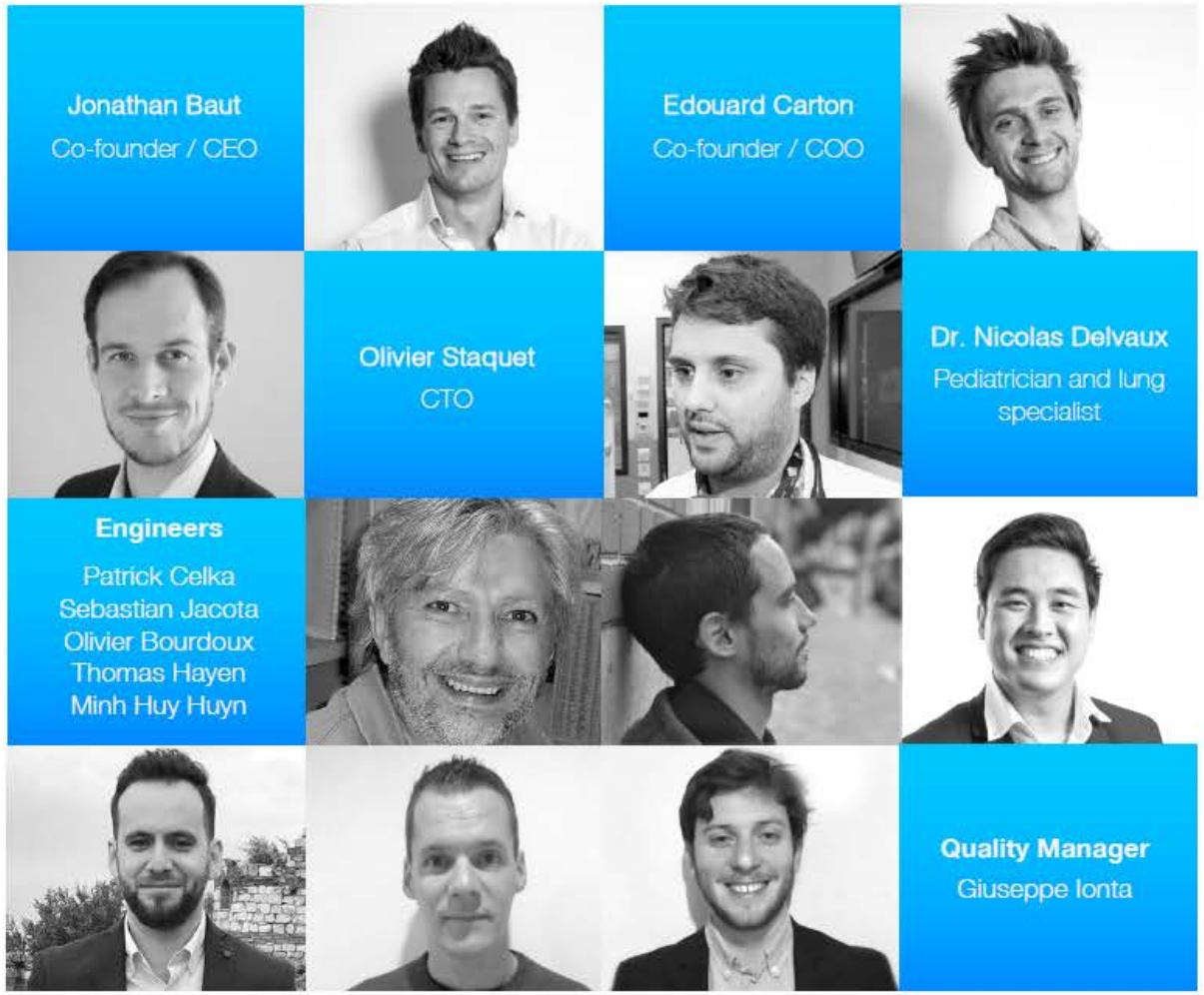
Gabi SmartCare combines the most advanced technologies and tailors them to pediatrics



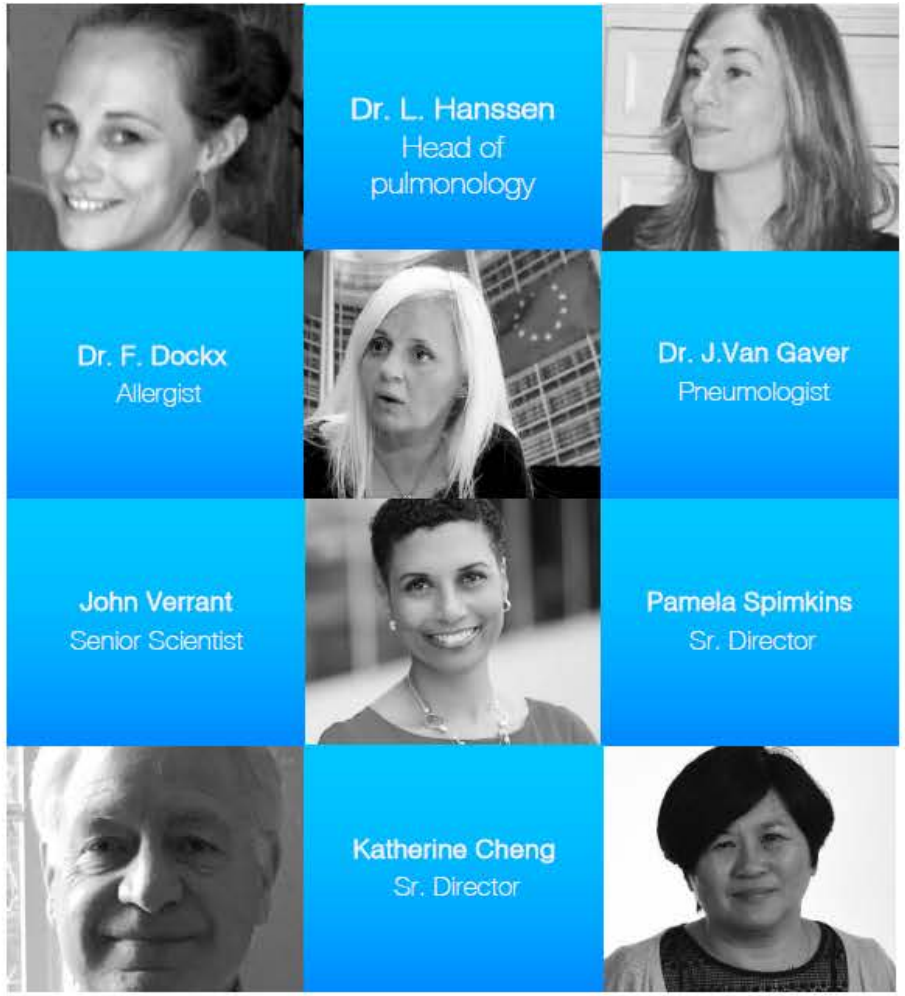
- Full set of vitals
- Suitable from premature babies
- Non-invasive & connected
- Hazardous event detection
- Life-threatening event prediction
- Health assessment report

Team

Core Team



Medical Advisory



Johnson & Johnson's JPALs

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Product Roadmap

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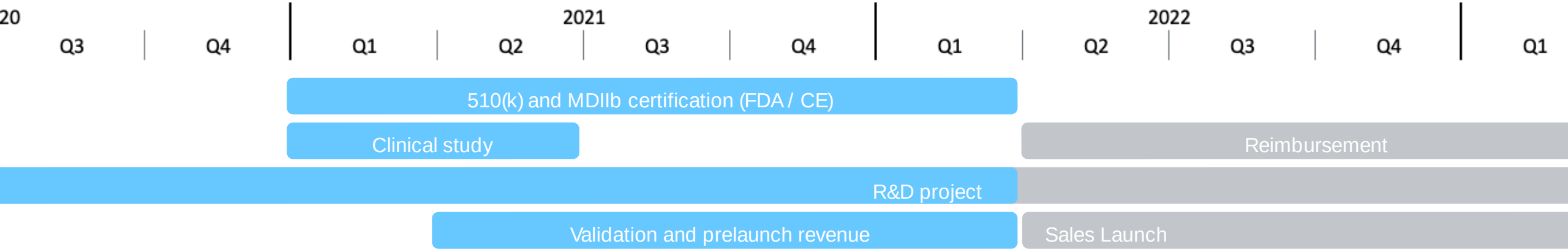
BLUE KNIGHT™



18 months - 510(k)

$2.000.000 Needs

✓ $900.000 Grant committed
✓ $300.000 Invested already

$800.000

Investment Opportunity

Key Milestones

- R&D
- Clinical study
- 510(k)

Hires

- 4 software profiles (Ops, Signal, Firmware)
- 2 Data scientists
- 1 Marketeer

Funding Allocation

- R&D: 50%
- Employees: 45%
- OPEX: 5%

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Improving children's lives

Prevent, Diagnose, Surveil

- ✓ **Disrupt pediatric healthcare**
- ✓ **Preclinical Research-Prototype**
- ✓ **Fully integrated solution**
- ✓ **Proven stakeholders' adoption**
- ✓ **Strong advisory**
- ✓ **Supported by KOL & industry leaders**

ü CALIFORNIA CONSUMER PRIVACY ACT OF 2018 · EU GDPR COMPLIANT · FC · CE · bsi. ISO 13485 Medical Devices Quality Management

jonathan.baut@gabismartcare.com

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Origami THERAPEUTICS

Reshaping • Restoring • Renewing

BETH

HOFFMAN, PhD

Founder, President & CEO

Origami Therapeutics

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Origami Therapeutics, Inc.

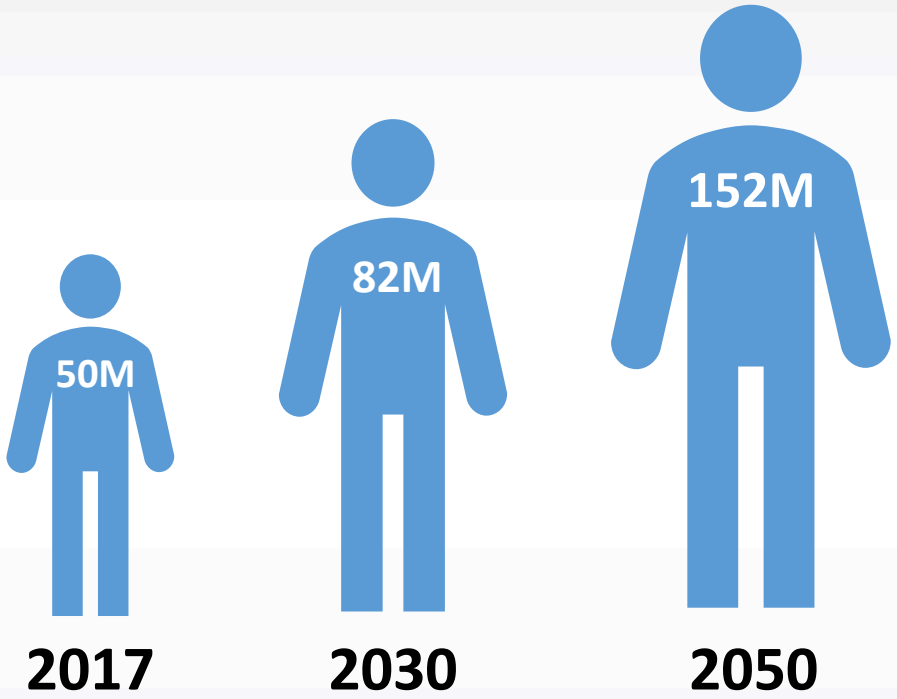
Origami THERAPEUTICS

Reshaping • Restoring • Renewing

JLABS SVB Pitch Competition
September 10, 2020| San Diego

The Threat:

Increasing Burden of Chronic Neurological Patients Worldwide



Devastating Consequences

Economic Societal Cultural

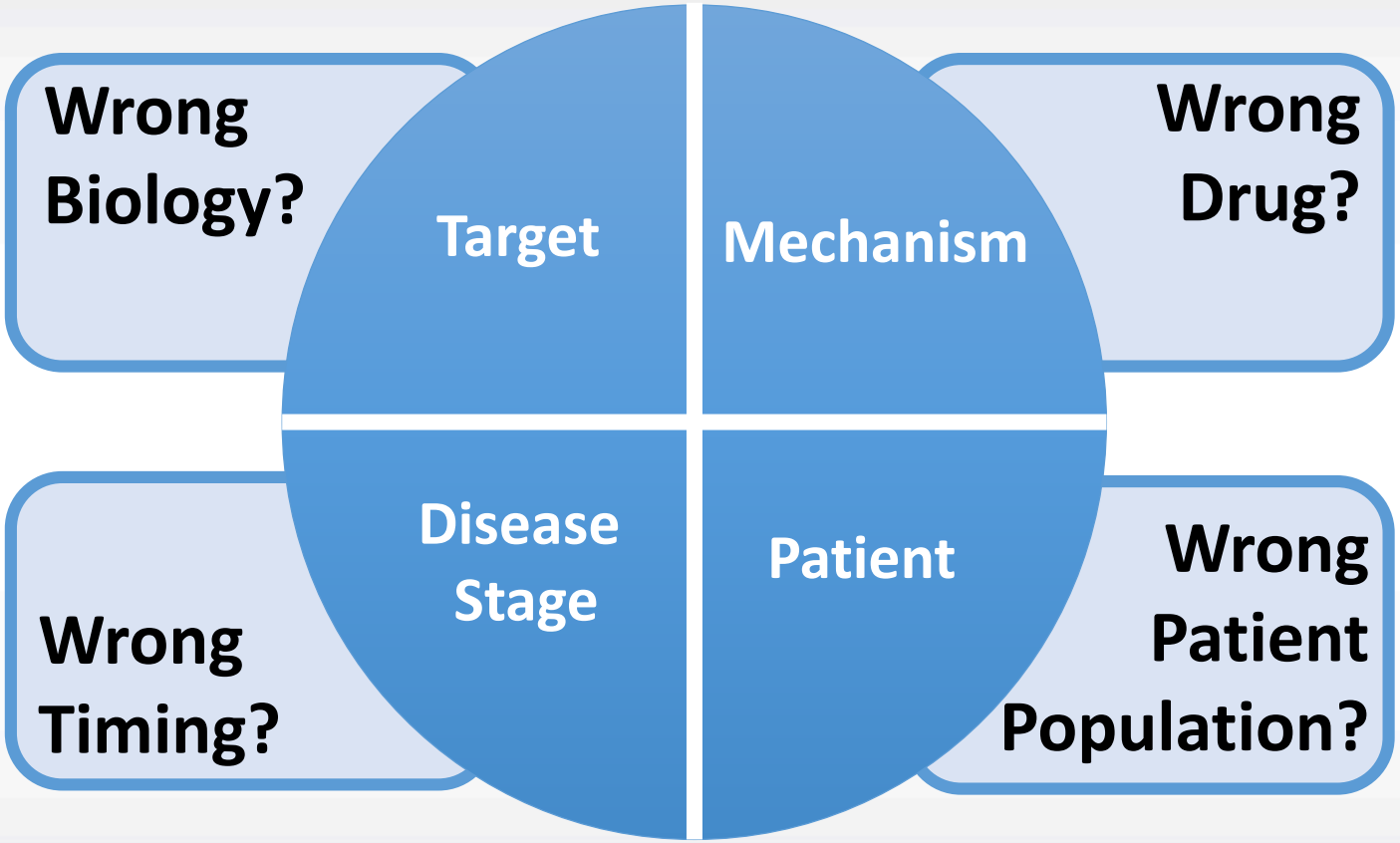
WHO fact sheet 2017

The Problem:

No Drugs Alter Progression of Neurodegenerative Diseases

20 years
100's clinical trials
0 drugs

Why Have Neurodegenerative Disease Trials Failed?

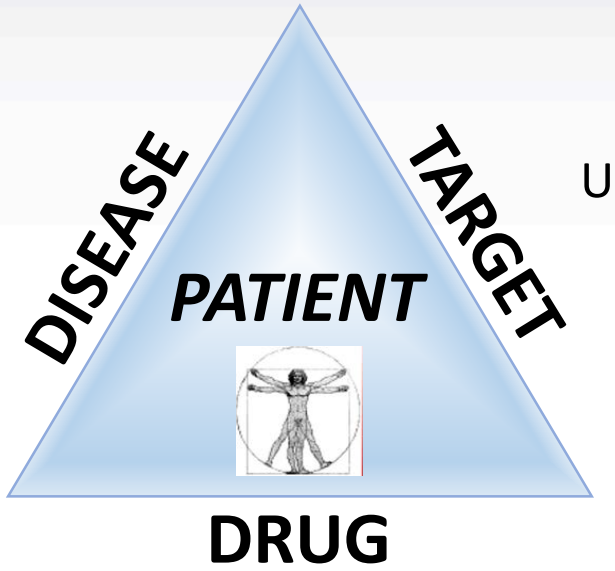


Adapted from S.M. Paul

The Solution: Origami's Precision Medicine Approach

Patient-centric

<u>Disease Selection</u>
Natural History
Who to Treat
When to Intervene
Which Outcome Measures



<u>Target Selection</u>
Underlying Cause of Disease/ Genetics
Mechanism/ Activity

<u>Drug</u>
Modality
Accessibility
Confirm Mechanism/Activity in Clinic

Disease-Modifying Treatment

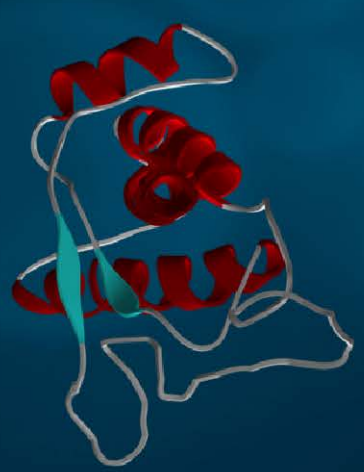
Right drug
Right patients
Right time
Right measures

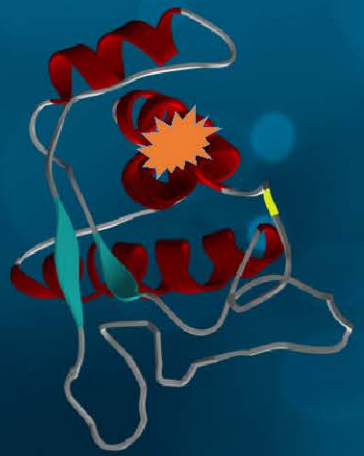
Discovering Drugs That Reshape Proteins To Restore Health

- Vision: Intervene in disease progression to maintain normal productivity & quality of life
- Precision medicine approach to treating neurodegeneration by targeting the underlying genetic cause of disease
  - ❖Efficacy
  - ❖Safety
- Focus: Directly modulating pathogenic proteins with small molecules
- Discovery platform:
  - ❖Enables the discovery of both *protein degraders* and *conformation correctors*
  - ❖Allows us to match the best mechanism to treat each disease
  - ❖Uses patient-derived disease models to ensure translation to the clinic
- Current status: Selecting the optimal protein degrader (lead asset) to advance into pre-clinical studies for Huntington's disease (HD) and initiating programs for additional indications.
- Seeking Seed Funding: To advance HD protein degrader to clinical trial

Origami's Technology: Protein Conformation Modulators

Two Different Approaches to Protein Misfolding





Conformation Corrector

Protein Degrader

Degradation Pathways

Normal Protein

Properly Folded Disease Protein

Misfolded/ Unfolded Disease Protein

N.B. This is a single snap shot of a dynamic kinetic process

= Mutation

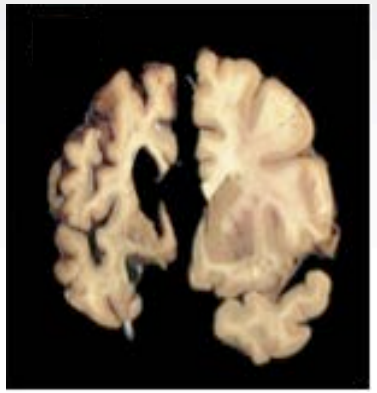
= Origami Drugs

Unmet Medical Need In Huntington's Disease (HD)

No drugs effectively treat symptoms or modify disease progression

Monogenic disease: Huntingtin (*HTT*) gene
Autosomal Dominant: 50% progeny affected
Average age of onset: 35 yrs (range: 30-50 yrs)
Duration: 10 - 25 yrs
Affected: 185,000 WW (***Orphan Status***)

HD Brain



Normal Brain

Standard of care: Supportive care
Drugs partially treat motor symptoms with significant side effects

Unmet need: Cognitive deficits / dementia
Behavioral / psychological symptoms
Motor / physical symptoms
Disease progression

Current Market- Symptomatic	
2020	$1.3B
	Austedo
	Xenazine
	Tetrabenazine

Huntingtin-Lowering Is A Proven Target

Decrease in pathogenic protein by multiple modalities leads to reversal of disease in multiple models of HD

Cell, Vol. 101, 57–66, March 31, 2000, Copyright ©2000 by Cell Press

Reversal of Neuropathology and Motor Dysfunction in a Conditional Model of Huntington's Disease

Ai Yamamoto,[†] José J. Lucas,[†‡] and René Hen[*]

Sustained Therapeutic Reversal of Huntington's Disease by Transient Repression of Huntingtin Synthesis

Holly B. Kordasiewicz,[1] Lisa M. Stanek,[2] Edward V. Wancewicz,[3] Curt Mazur,[3] Melissa M. McAlonis,[1] Kimberly A. Pytel,[1] Jonathan W. Artates,[1] Andreas Weiss,[4] Seng H. Cheng,[2] Lamya S. Shihabuddin,[2] Gene Hung,[3] C. Frank Bennett,[3] and Don W. Cleveland[1,*]

Neuron 2012

An Intrabody Drug (rAAV6-INT41) Reduces the Binding of N-Terminal Huntingtin Fragment(s) to DNA to Basal Levels in PC12 Cells and Delays Cognitive Loss in the R6/2 Animal Model

Amaro & Henderson 2016

2019

The NEW ENGLAND JOURNAL of MEDICINE

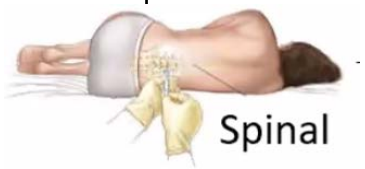
ORIGINAL ARTICLE

Targeting Huntingtin Expression in Patients with Huntington's Disease

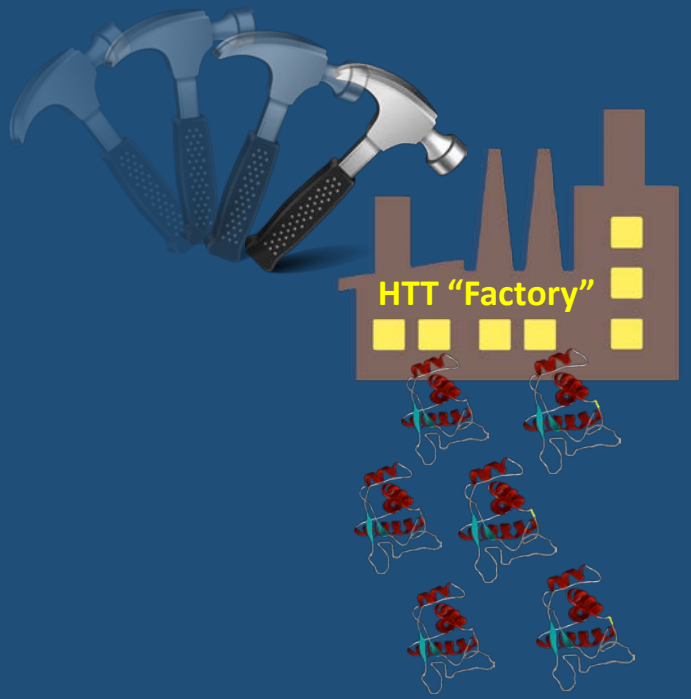
Sarah J. Tabrizi, M.B., Ch.B., Ph.D., Blair R. Leavitt, M.D., C.M., G. Bernhard Landwehrmeyer, M.D., Edward J. Wild, M.B., B.Chir., Ph.D., Carsten Saft, M.D., Roger A. Barker, M.R.C.P., Ph.D., Nick F. Blair, M.B., B.S.,* David Craufurd, M.B., B.S., Josef Priller, M.D., Hugh Rickards, M.D., Anne Rosser, M.B., B.Chir., Ph.D., Holly B. Kordasiewicz, Ph.D., Christian Czech, Ph.D., Eric E. Swayze, Ph.D., Daniel A. Norris, Ph.D., Tiffany Baumann, B.S., Irene Gerlach, Ph.D., Scott A. Schobel, M.D., Erika Paz, B.S., Anne V. Smith, Ph.D., C. Frank Bennett, Ph.D., and Roger M. Lane, M.D.

- ✓ **Disease – Who, When, What to Measure**
- ✓ **Target – Genetics, Mechanism, Activity**
- ✓ **Drug – Modality, Accessibility, Confirm Mechanism/Activity in the Clinic**

Comparison of HTT-Lowering Approaches

	Roche Genentech	WAVE Life Sciences	uniQure	Novartis PTC Therapeutics	Frigami Therapeutics
Delivery	 Spinal		 Brain surgery		
Approach	ASO Total HTT	ASO Mutant HTT	AAV Virus Total HTT	Small molecule ? Total HTT	Small molecule Mutant HTT
Target	mRNA	mRNA	mRNA	mRNA	Protein
Target Organ(s)	Brain	Brain	Brain	Brain + Body	Brain + Body
Phase	Phase III	Phase I/II	Phase I/II	Preclinical	Discovery

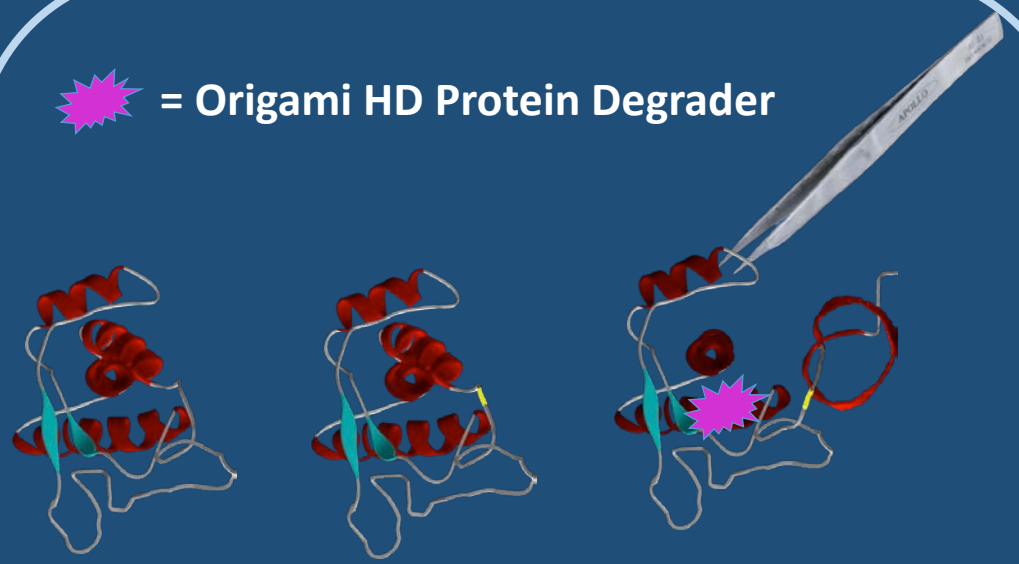
Origami's Technology: Not All "Knock-downs" Are The Same



Suppress production of all HTT or mHTT selectively

Minimizes toxic protein
Reduces functional protein

= Origami HD Protein Degrader



Normal protein

Properly folded Disease protein

Misfolded/ Unfolded Disease protein

Origami's Approach: Protein Degraders
Selectively binds misfolded mHTT for degradation

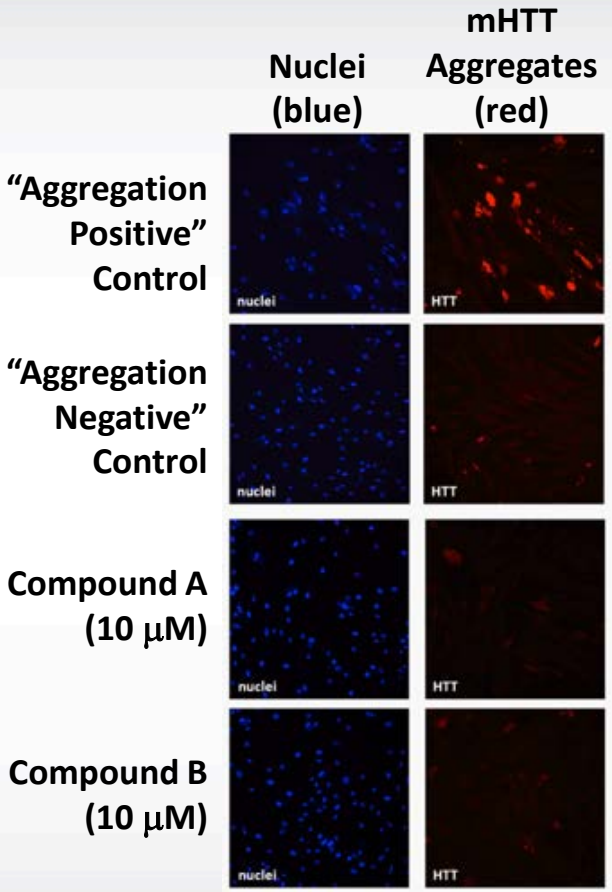
Minimizes toxic protein
Maximizes functional protein
Maintains normal physiology

Activate degradation pathways removing all HTT forms

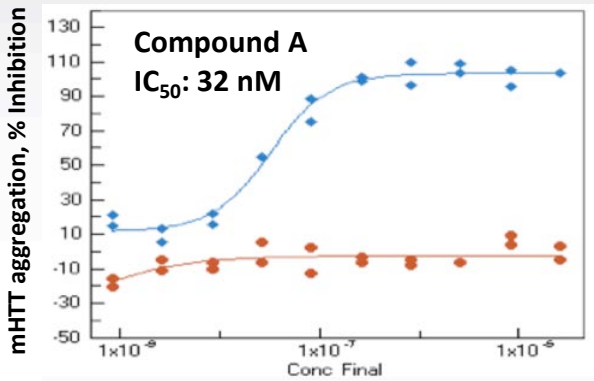
Minimizes toxic protein
Reduces functional protein

Lead Molecules Prevent HD Pathology Via Protein Degradation

Proprietary Cell-based High Content Assay



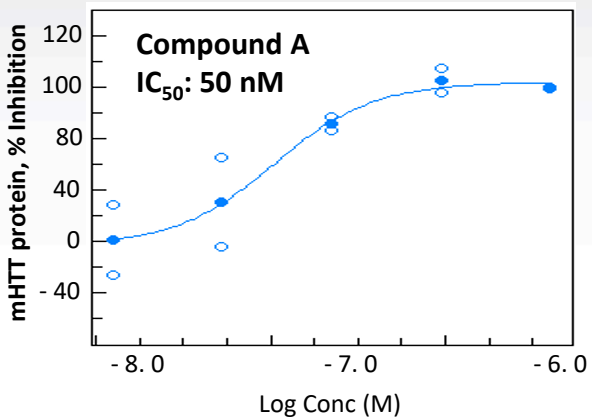
Images from high throughput (HTS) screen



X-axis: compound concentration
Y-axis: % prevention of aggregates (blue)
& % cell toxicity (orange)

Compounds prevent mHTT aggregation (HD Pathology)

mHTT Protein Assay

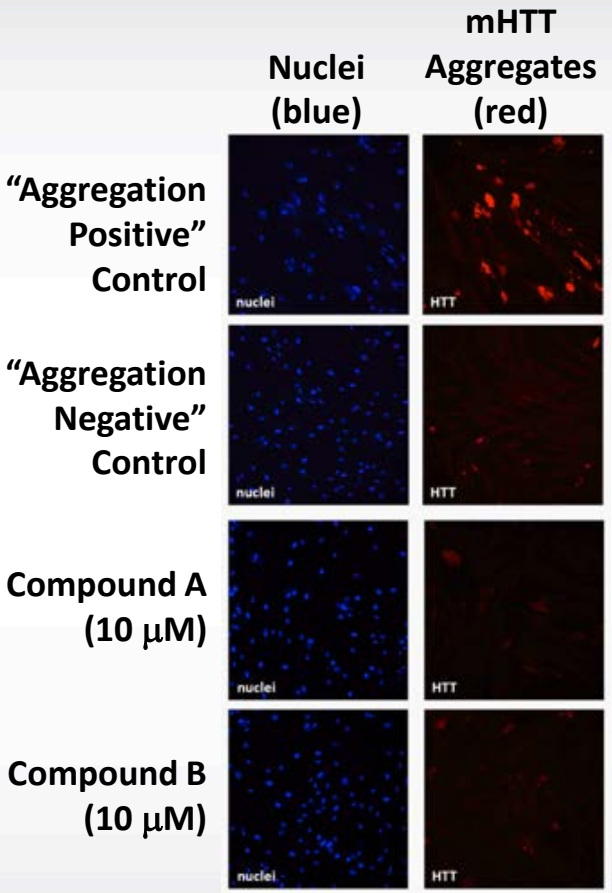


Compounds reduce mHTT protein levels (Protein degraders)

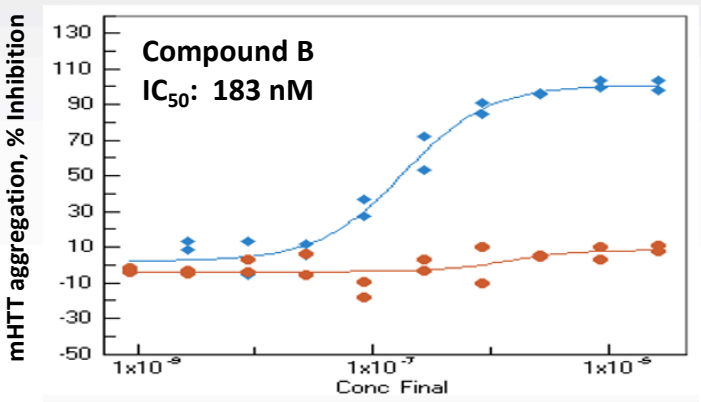
HD: Huntington's disease
HTT: huntingtin protein
mHTT: mutant huntingtin protein (pathogenic)

Conformation Corrector Prevents Aggregates, No Change In mHTT Levels

Proprietary Cell-based High Content Assay



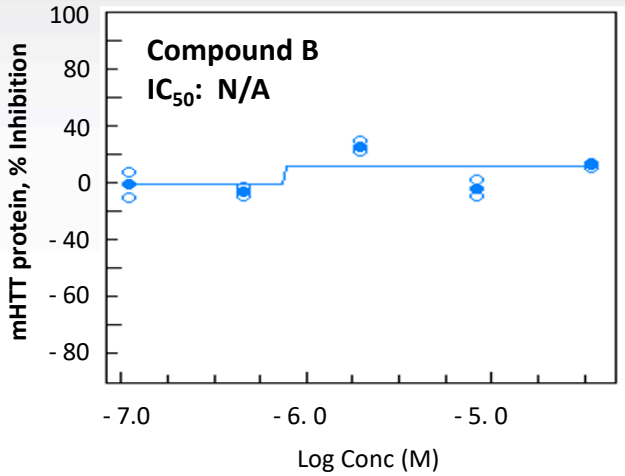
Images from high throughput (HTS) screen



X-axis: compound concentration
Y-axis: % prevention of aggregates (blue)
& % cell toxicity (orange)

Compound B prevents mHTT aggregation with no cell toxicity (HD Pathology)

mHTT Protein Assay



Compound B does not alter mHTT protein levels (Potential conformation corrector)

HD: Huntington's disease
HTT: huntingtin protein
mHTT: mutant huntingtin protein (pathogenic)

Comparison Of Top Five Chemical Scaffolds: Emerging SAR

Scaffold	IC50 (nM)	LE	CNS MPO
A	32	0.43	4.98
B	28	0.46	4.26
C	305	0.41	5.42
D	211	0.40	4.65
E	461	0.39	4.7

- Green: Excellent
- Shaded green: Good
- Orange: Acceptable

- Preliminary Freedom to Operate (FTO)
- Most potent compound shown for each scaffold
- IC50: Prevention of aggregates in HTS cell assay
- LE: Ligand Efficiency, indicates the strength of compound binding, >0.4 desirable
- CNS MPO: > 4.5 suggests CNS permeability

Intellectual Property (IP):

Patent filings include composition of matter (5 scaffolds), method of use and methods for identification (2040 expiry)

Origami's Accomplishments Through Mid-2020

Science

- ✓ Proprietary high throughput screen (HTS)
- ✓ Hit expansion/ mechanism of action (MoA)
- ✓ Molecules with therapeutic potential
- ✓ Pipeline - multiple assets
- ✓ Collaborators
- ✓ IP: Provisional patent applications

charles river

StemoniX

PhenoVista Biosciences
phenotypic assay services

Selected as CONNECT w/ SDVG Cool Company 2020

Operations

- ✓ Accepted into incubator: JLABS San Diego
- ✓ Wet bench laboratory operational
- ✓ 2 Bench Scientists

Johnson & Johnson INNOVATION | JLABS

Team

- ✓ Team (6)
- ✓ Advisory Board (4)
- ✓ Consultants (3)

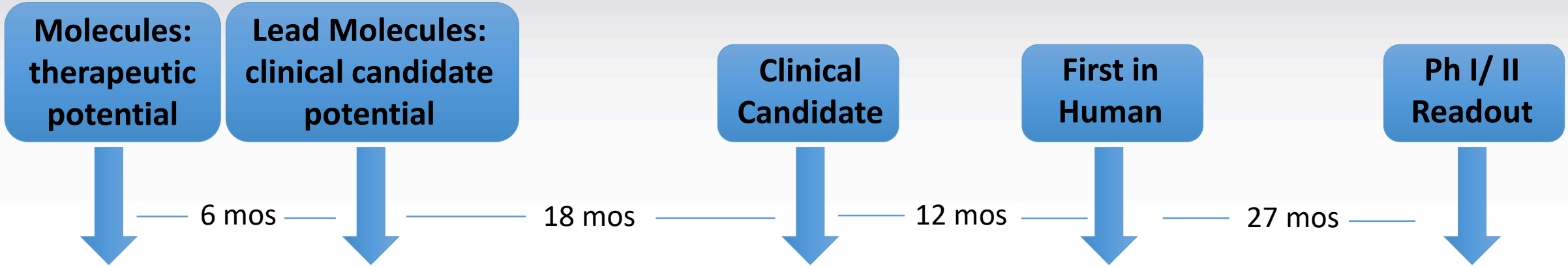
Origami THERAPEUTICS
Reshaping • Restoring • Renewing

Pipeline

	Discovery	Preclinical	IND Enabling	Ph I / Ph II
HD - Degrader	→			
HD - Corrector	→			

Use of Funding & Milestones

Milestones



Seed: $3-4M | **Series A: $10M**

- Lead Selection
  In vivo POC
- Advance Lead Asset and Backup
  Non-GLP Tox
  Clinical Candidate Selection
- IND-Enabling
  API & CMC
  IND Approval
- Phase I/ Phase II
  (Patients)

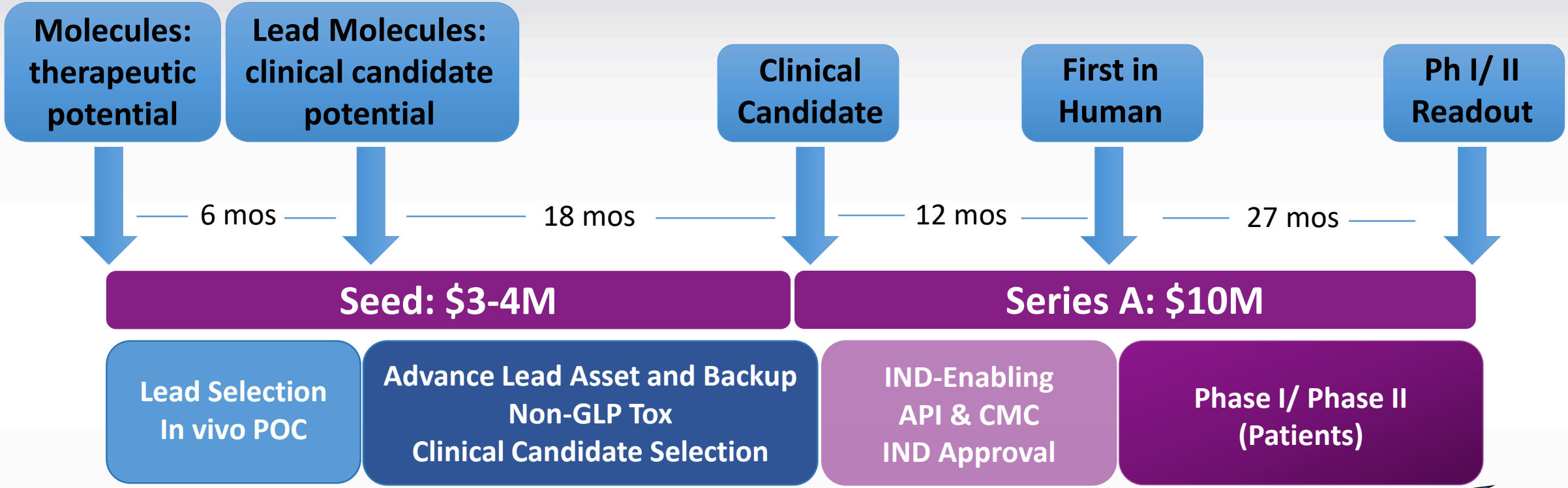
Activities

- Build out science and management teams

Rev 08212020

Potential Exit Strategies

Milestones



Activities

Multiple Ways to Leverage Value

- License/Partnering
- Acquisition/Merger
- Public Capital

Rev 08212020

Management Team & Advisors

> 100 years of drug discovery experience including multiple launched drugs

Beth J. Hoffman, Ph.D.
Founder, CEO

Leslie J. Schulze, CPA, CGMA
Co-Founder, CFO

Christopher Smith, Ph.D.
VP, Chemistry

Lucia Mokres, DVM
VP, Regulatory, Clinical and Medical Affairs

Advisors:

Jody Corey-Bloom, M.D.: Director, HD & AD Clinical Centers, UCSD, ***KOL***

David H. Crean, Ph.D., MBA: Business Advisor, healthcare investment partner

Steven Finkbeiner, M.D., Ph.D.: Professor, UCSF & Gladstone Institutes, ***KOL***

Kalpana Merchant, Ph.D.: CEO & CSO roles at start-ups; formerly Eli Lilly, Pharmacia; ***KOL***

Risks and Mitigations

Risk	Mitigation
• Lead molecule cannot be adequately optimized	• Multiple backup scaffolds available as replacements
• Clinical candidate may not translate from preclinical to clinical	• Use of patient-derived disease models, including 3D organoids

• Protein degradation mechanism is invalidated due to:
  • Associated toxicities
  • Lack of efficacy
	• Conformation correctors available as backup mechanism

• Competitor HTT-lowering treatments achieve regulatory approval	• Origami small molecule modality
	  • Superior delivery and cost-effectiveness
	  • Enables systemic treatment
	  • Opportunity to augment CNS-directed competitors

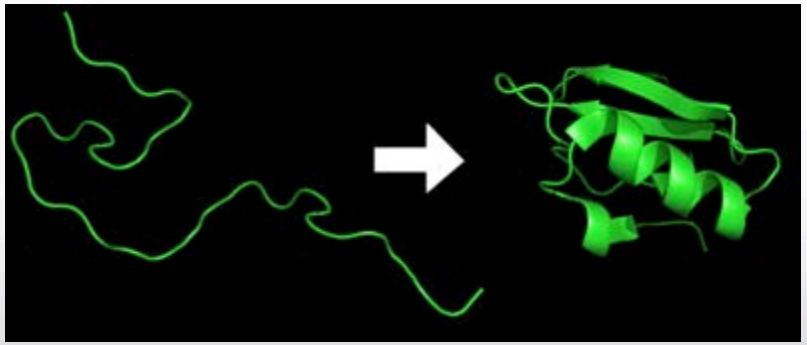
• Sufficient capital to accomplish goals	• Continue to actively raise funds

Origami Therapeutics, Inc.

- Founded October 2015 in San Diego
- Resident company at JLABS @ San Diego (March 2018)
- Platform: Technology platform to generate small molecule conformation modulators
- Seeking: $3-4M Seed Funding:
  - ❖Advance lead asset and back-up to Clinical Candidate/ IND-enabling
  - ❖Prepare for Series A to achieve Ph I/ Ph II readout

Contact Information: Beth J. Hoffman, Ph.D., President & CEO
Mobile: 805.558.2664
beth@origamitherapeutics.com

Origami:
The art of folding paper



Origami Therapeutics:
The science of folding proteins

Stream BIOMEDICAL

GARY

GAGE, PE, MBA

Founder & CEO

Stream Biomedical

Johnson & Johnson INNOVATION | JLABS

svb Silicon Valley Bank

Stream BIOMEDICAL

Silicon Valley Bank – JLABS Event

September 2020

Gary Gage

Key Topics

1) POTENTIAL IMPACT ON HUMAN HEALTH

2) UNIQUENESS OF IDEA / PRODUCT

3) IDENTIFICATION OF KEY RESOURCES AND PLAN TO FURTHER IDEA

4) UNDERSTAND DIFFICULTIES. HAVE PLAN TO AVERT ROADBLOCKS

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1) POTENTIAL IMPACT ON HUMAN HEALTH

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The Unmet Need(s)

Nothing on the market has proven or been approved to:

- Preserve injured brain cells

- Regenerate damaged brain

Neuroprotection and neurorepair are unmet needs

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Stroke Incidence: US and Worldwide

800,000 Strokes / year

15 Million Strokes / year

10% of Survivors return to normal activity

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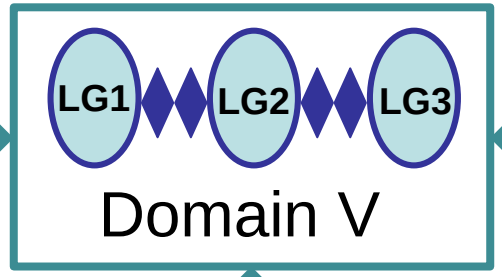
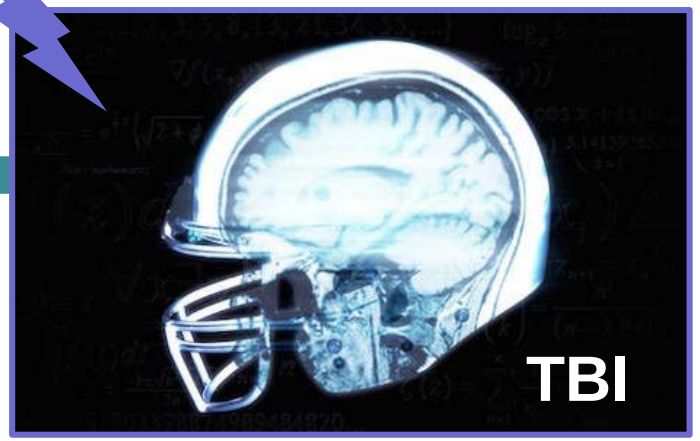
Stroke is the most debilitating condition on the planet

2) UNIQUENESS OF IDEA / PRODUCT

Stream BIOMEDICAL

The Body's Attempt at Self-Repair… Perlecan Domain V (DV)



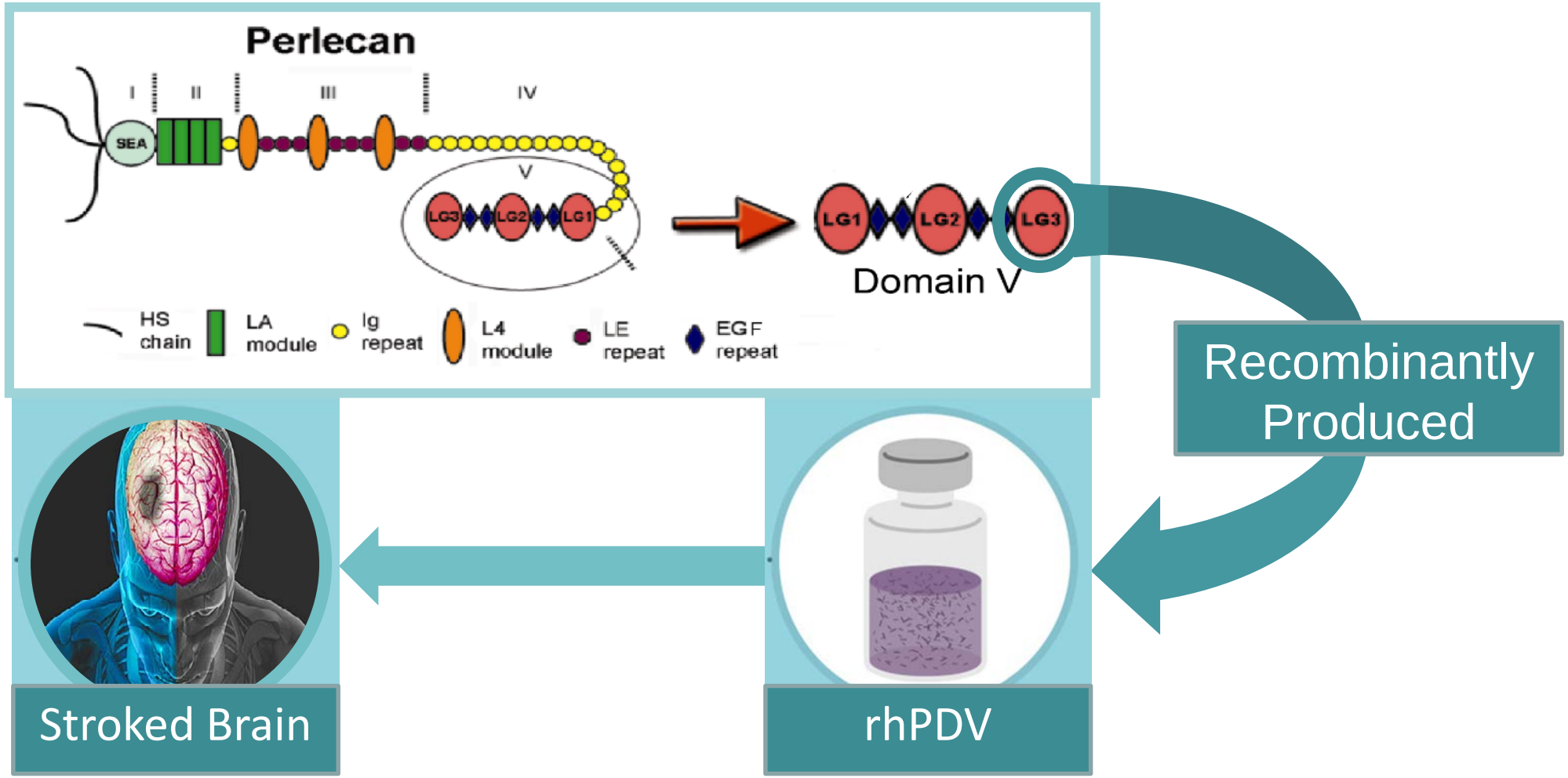


DV is actively generated by vigorous activity, traumatic brain injury (TBI) & stroke

*DV is a critical component of the body's post-stroke attempt at self-repair **

* Per Lee et al, 2011

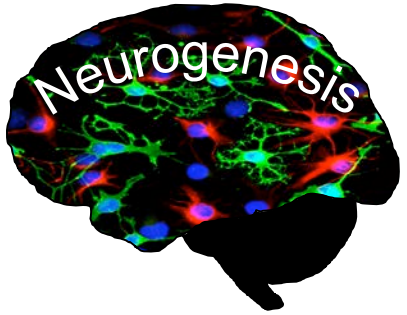
Our Product… Recombinant Human Perlecan Domain V (rhPDV, or DV)



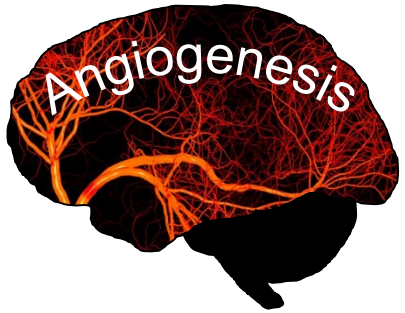
DV is a naturally occurring protein, which we synthesize in a high-yield biological process

DV: for Neuroprotection & Neurorepair

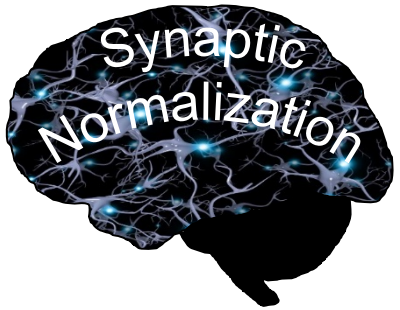
Neuroprotection: the preservation of neurons (nerve cells) compromised by injury or degeneration



Neurogenesis: the biologic process by which new neurons are generated



Angiogenesis: the development of new blood vessels

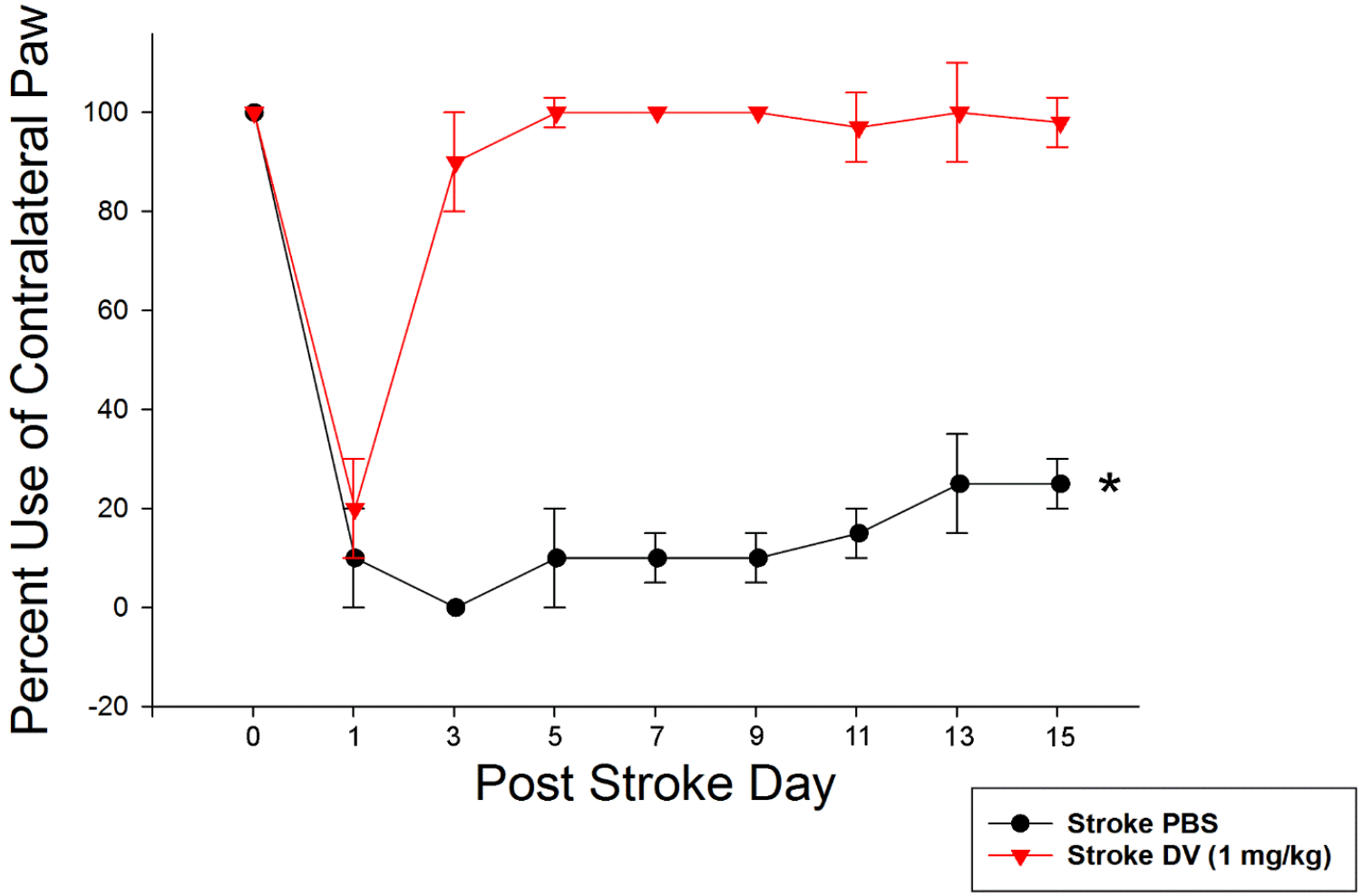


Synaptic normalization: the elimination of seizure-like activity

DV is significantly neuroprotective, angiogenic, neurogenic & significantly normalizes synaptic dysfunction

Stream BIOMEDICAL

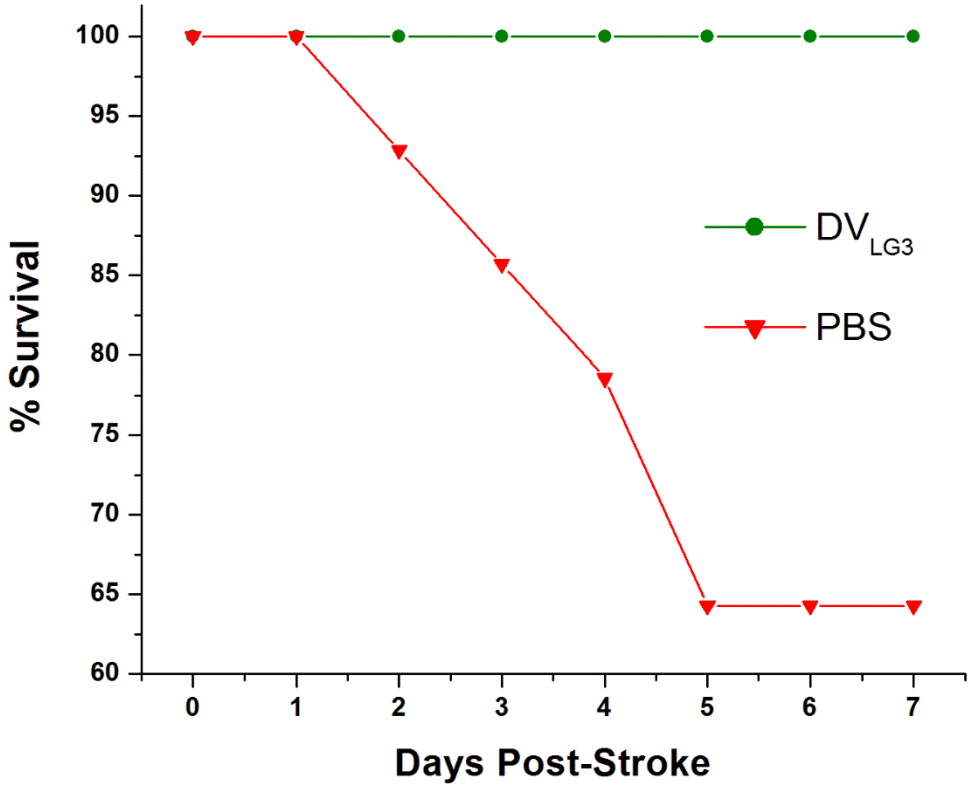
DV: for Dramatic Functional Improvement



DV SIGNIFICANTLY improves post-stroke function

* Per Lee et al, 2011; rodent stroke model

DV: as Potential Life-saving Therapy



Kaplan Meier survival curve and statistical significance illustrating the unique life-saving potential of DV_{LG3}

P=0.005

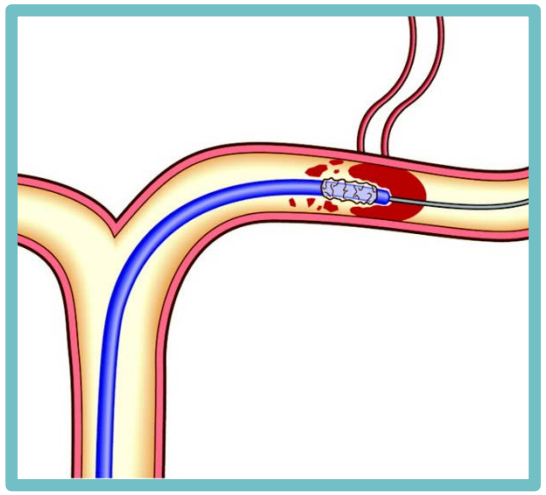
DV SIGNIFICANTLY rescues subjects from post-stroke mortality

* Internal data 2020; severe rodent stroke model

Stroke Standard of Care

Genentech

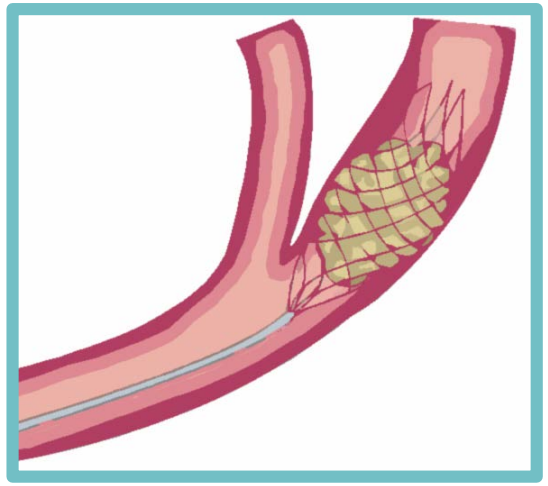
- tPA…Tissue Plasminogen Activator
  - Clot Dissolution



Not Neuroprotective
Not Neuroreparative

Medtronic stryker Penumbra

- Thrombectomy Devices
  - Mechanical Clot Removal



Not Neuroprotective
Not Neuroreparative

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Neuro protection and repair are unmet needs

3) IDENTIFICATION OF KEY RESOURCES AND PLAN TO FURTHER IDEA

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Overview: Plan & Key Resources

PLAN: KEY ACTIVITIES

- File IND in Q1
- Produce GMP DV
  - For Phase 1 human trial
- Execute Phase 1 Trial
  - In stroke patients

KEY REOURCES

- Capital
  - Equity Raise: current raise $4M
    - Fund GMP, Ph1 clinical, Ops
  - Non-dilutive Funding: leverage/expand
    - PH 1-2 FastTrack
- Personnel
  - Stream Team: leverage
  - Clinical Research Associate: hire
  - SAB: establish/expand
- Outside Services
  - CDMO: Hired
  - CRO: Selection process near completion

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Stream Background

PUBLICATIONS	**20+ scientific peer reviewed publications**	Stroke Dementia Mechanism of Action
INTELLECTUAL PROPERTY	**20+ issued patents**	Stroke, Traumatic Brain Injury, Alzheimer's, Parkinson's, Spinal Cord Injury, Other
COMPELLING PRODUCT DATA	**Recombinant Human Perlecan Domain V (rhPDV or "DV")**	Neuroprotective Angiogenic Neurogenic

Stream BIOMEDICAL

Evidence & IP are extensive, data are compelling

Where We Are

- Identified Preferred DV Construct for Stroke
  - Developed 20+ recombinant DV constructs. Chose top 7 producers. Evaluated top 3 in severe stroke model
  - Selected construct elicits functional improvements *and* life-saving potential
- Developed Process for Preferred DV Construct
  - Scaled DV synthesis from milligram to gram quantities
  - Established purification process up to 99% purity
- Initiated IND-Enabling Toxicology Studies
  - Rat & primate injections initiated
  - Initial injections at 25x therapeutic dose show no deleterious effects
- Completed FDA PreIND Meeting
  - Phase 1 Clinical trial design confirmed: escalating dose in stroke patients
- New IP Filed
  - Patent application filed July 2020, with potential to significantly extend patent protection
- IND Filing projected Q1 2021
  - IND clearance will enable subsequent initiation of first–in-human trials

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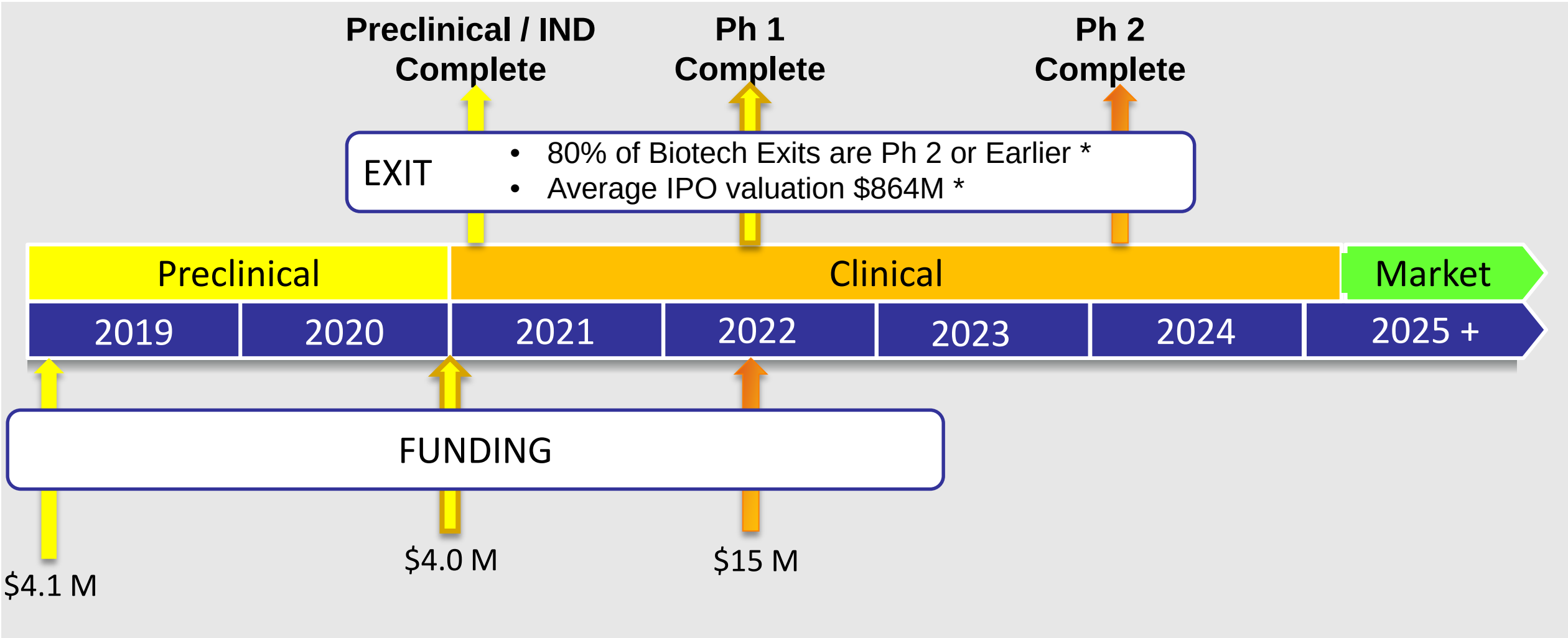
Stream is building on success to drive to a Phase 1 Trial

Timeline: Funding v. Development v. Exit



High return & exit opportunities exist prior to market entry

* E&Y 2014 and 2015 Biotech Reports

Non-Dilutive Funding

NIH National Institute of Neurological Disorders and Stroke

Acute Stroke

- SBIR Ph 1-2 Fast-Track Application
- Notice of Award June 6, 2019
- $3.0M : Ph 1 = $770k; Ph 2 = $2.3M

NIH National Institute on Aging

Alzheimer's

- SBIR Phase 1 Application
- Notice of Award Sep 9, 2019
- $393k

Stream BIOMEDICAL

Non-dilutive funding awarded… Stream to continue applications

Stream Team… since the beginning

Gary Gage, PE, MBA
Founder & CEO

25+ yrs Biotech, Medtech ●
Sr Staff $280MM Acquisition by Medtronic ●

Davis Adkisson, PhD
CSO

20 yrs Biotech, Medtech ●
Experienced CSO ●

Greg Bix. MD, PhD
Chief Neuroscientist

Discoverer/Inventor of DV ●
Director Neuro Center, Tulane ●

Justin Fraser, MD
Chief Clinical Advisor

● Neurosurgeon. Clinical Researcher
● Board of Neurointerventional Society

Bill Schwieterman, MD
Regulatory, Clinical

● CEO Public Biotech Company
● Branch Chief FDA CBER

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Good looks are overrated

Stream Team… with new faces

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Expanded expertise

4) UNDERSTAND DIFFICULTIES. HAVE PLAN TO AVERT ROADBLOCKS

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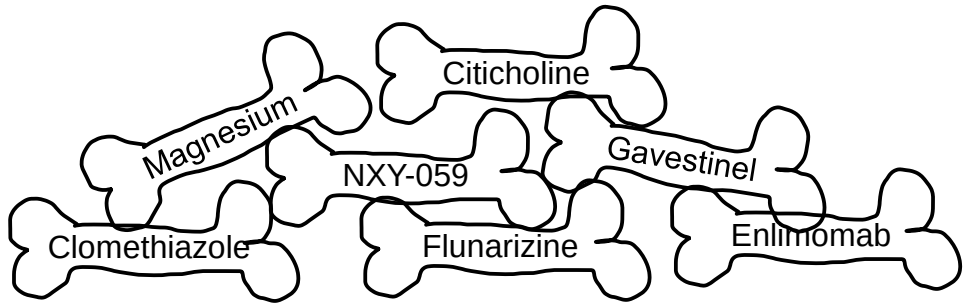
Boneyard (Historical Roadblock)

- The Historical Roadblock is Clinical Trial Failure
- The Neuroprotective Drug Boneyard is Understood
  - Two of Stream Team Members have Published on this Topic
- Expect Stroke Severity & Drug Treatment Outcomes to Differ if…
  - … the patient has small occlusions versus large occlusions
  - … the patient is treated within hours instead of days
  - … the patient has a hemorrhagic stroke versus an ischemic stroke
  - … the patient encounters a stroke of the cerebrum versus a stroke of the brainstem
  - … the occlusion is removed and the vessel is recanalized vs occlusion remaining



Stream BIOMEDICAL

DV Differences & Averting Roadblocks

- Vast Majority of Previous Failures were NOT
  - … biologics
  - … shown to be an endogenous critical component of self-repair
  - … treating homogeneous population

- Animal/ Human Bodies Produce DV in Response to Stroke
  - Mouse, rat, sheep, NHPs, humans…

- To Avert Roadblock Stream Trial will…
  - Maximize Homogeneity of Population
  - Couple with Recanalization

Stream BIOMEDICAL

Stream product and plan is leveraged to avert known roadblocks

Phase 1 Clinical Trial Design

- 3 Escalating Dose Groups
- 24 Patients Total
- All Stroke Patients

Dose 1: Low
- 6 Treated with DV_{LG3}
- 2 treated with Saline

Dose 2: Medium
- 6 Treated with DV_{LG3}
- 2 treated with Saline

Dose 3: High
- 6 Treated with DV_{LG3}
- 2 treated with Saline

Design provides early read of DV-treated stroke patient outcomes

Summary

- *Large Market(s)*
- *Unmet Need*
- *Compelling Product Evidence*
- *Strong Patent Protection*
- *Experienced Team*
- *Strong Return Potential & Early Exit Options*

Stream BIOMEDICAL

Thank You !

Stream BIOMEDICAL

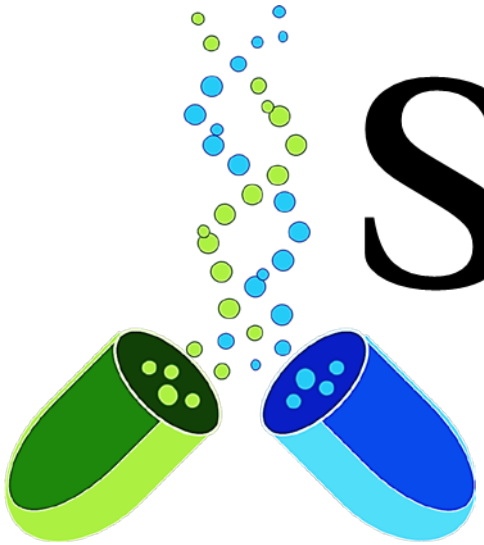
Contact: Gary Gage
gg@streambiomed.com

SyntheX

MARIA
SOLOVEYCHIK, PhD
Co-founder & CEO
SyntheX

Johnson & Johnson INNOVATION | JLABS

svb Silicon Valley Bank



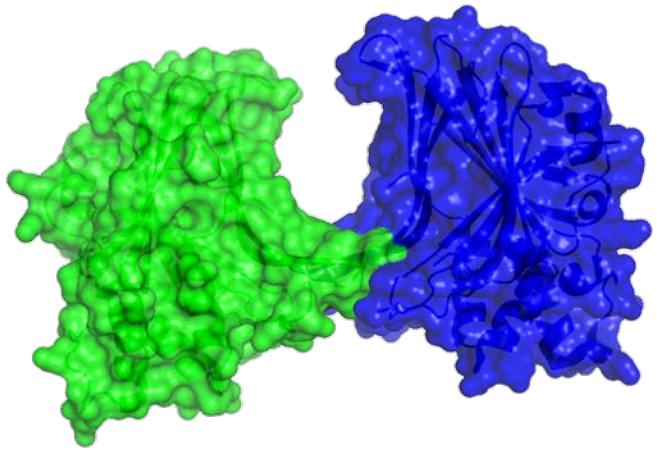
SyntheX

Targeting the undruggable

Maria Soloveychik, PhD
CEO

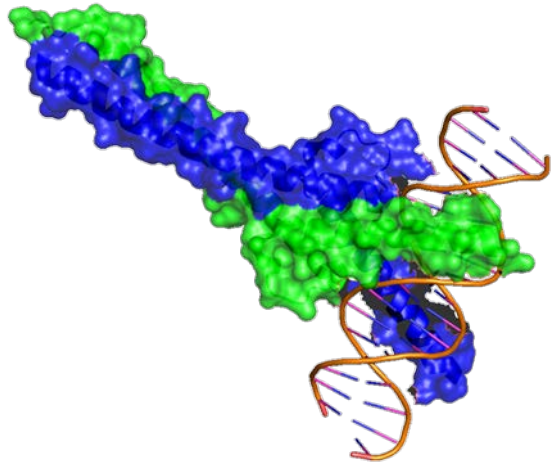
At SyntheX, we are building a collection of synthetic biology technologies to enable us to produce and functionally select potent compounds to target conventionally undruggable proteins.

What do we mean by undruggable targets?



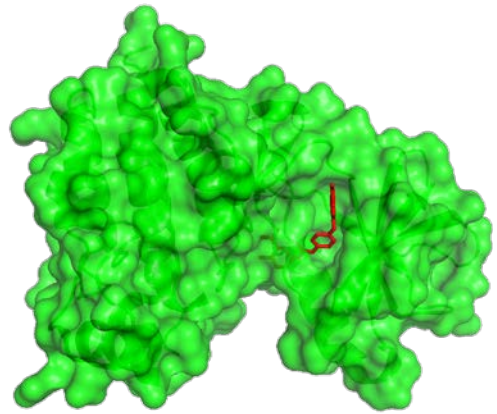
Protein-protein Interactions (PPIs)
(homodimers, heterodimer, complexes, aggregates, etc.)

e.g. Ras/Raf, YAP/TEAD



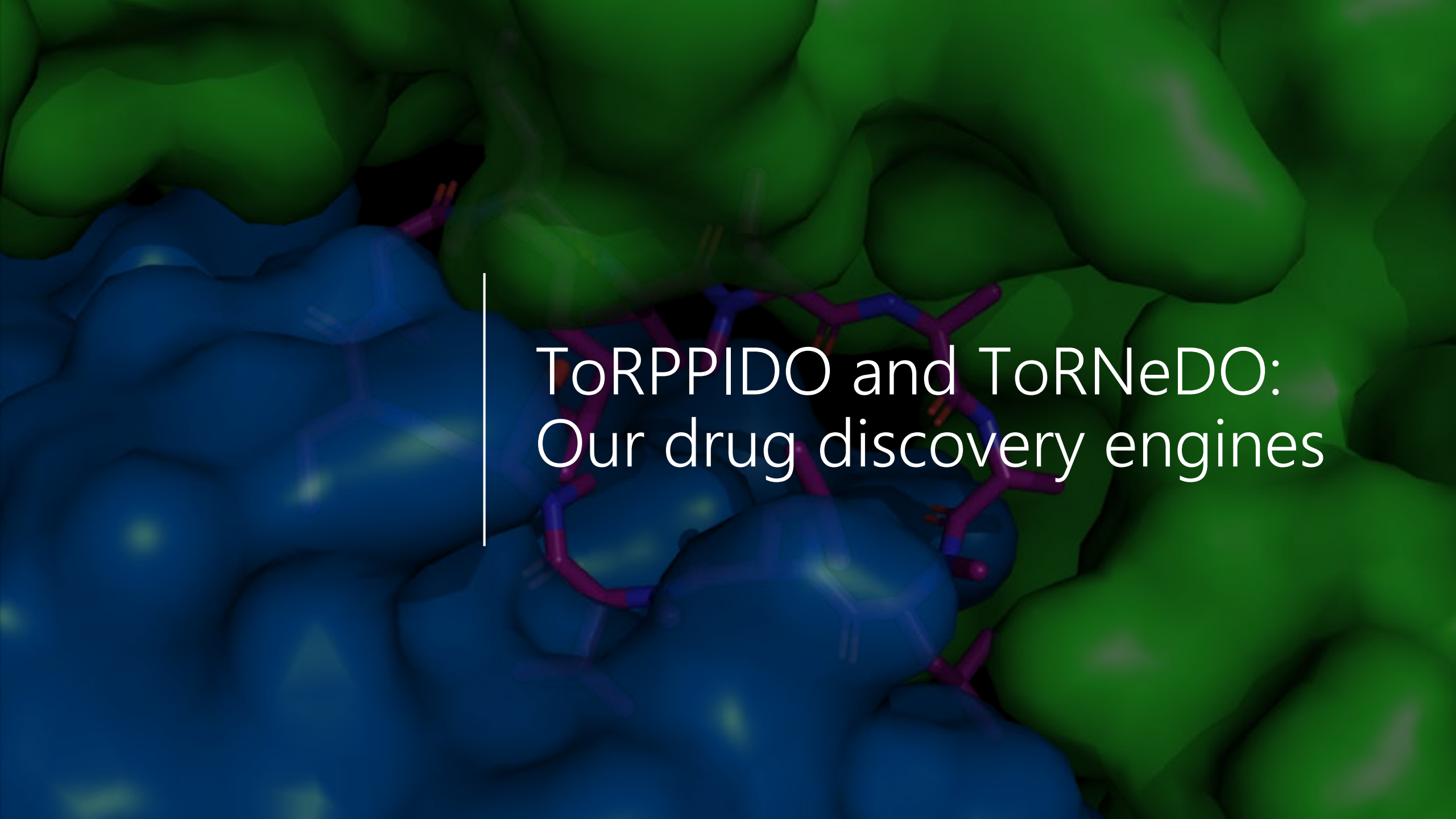
Protein-nucleic acid interactions
(transcription or splicing factors)

e.g. Myc, Ets TFs



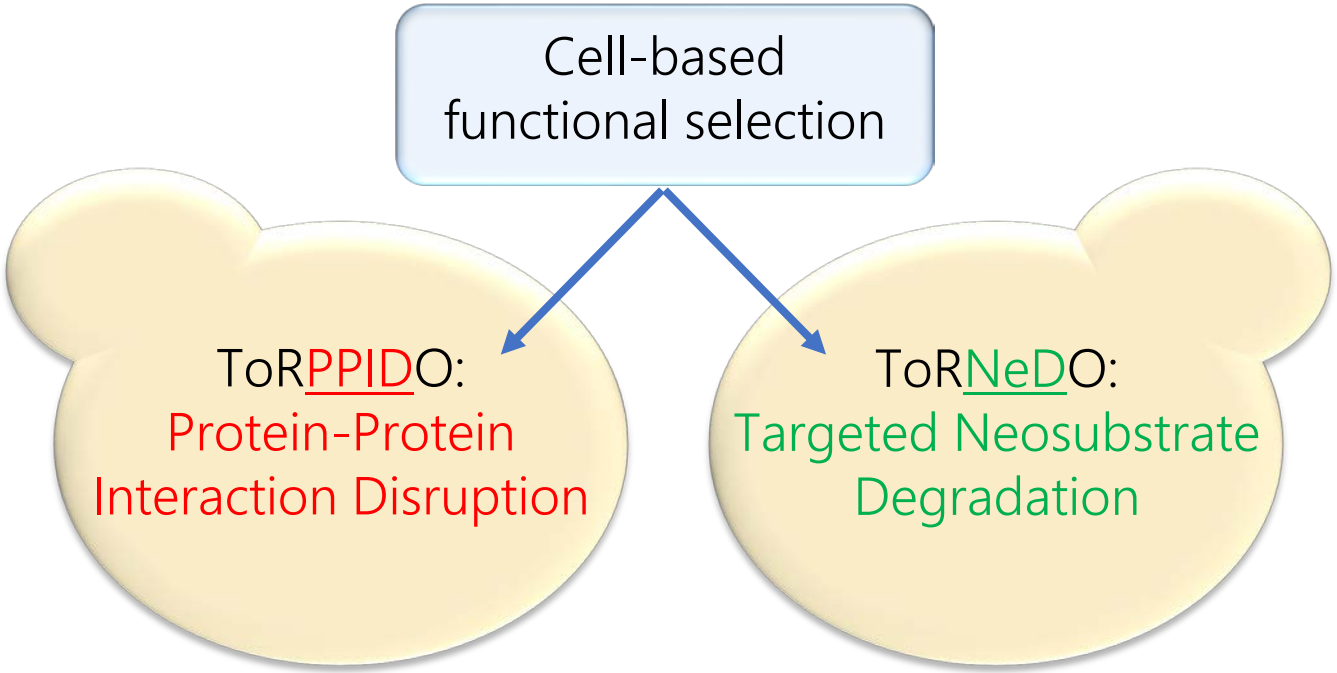
Low specificity enzymes
(phosphatases, nucleases, proteases etc.)

e.g. Shp1/2, Trex1

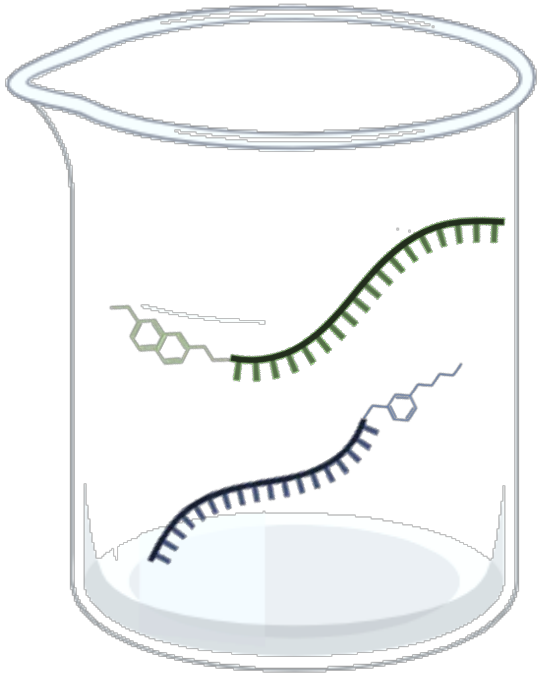


ToRPPIDO and ToRNeDO: Our drug discovery engines

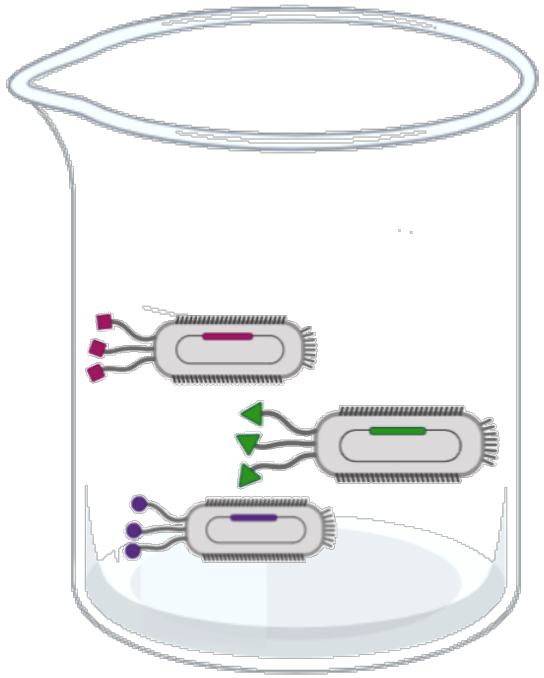
Platform technologies overview



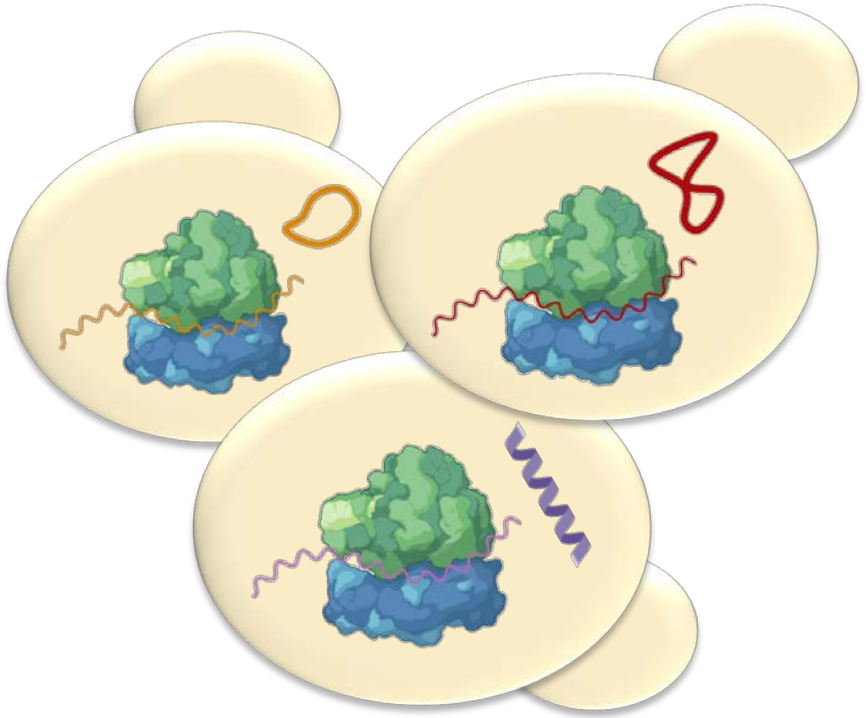
SyntheX libraries are ribosomally encoded and provide expanded chemical diversity and built in functional selection



Traditional DNA-barcoded libraries:
Used in *in-vitro* binding assays

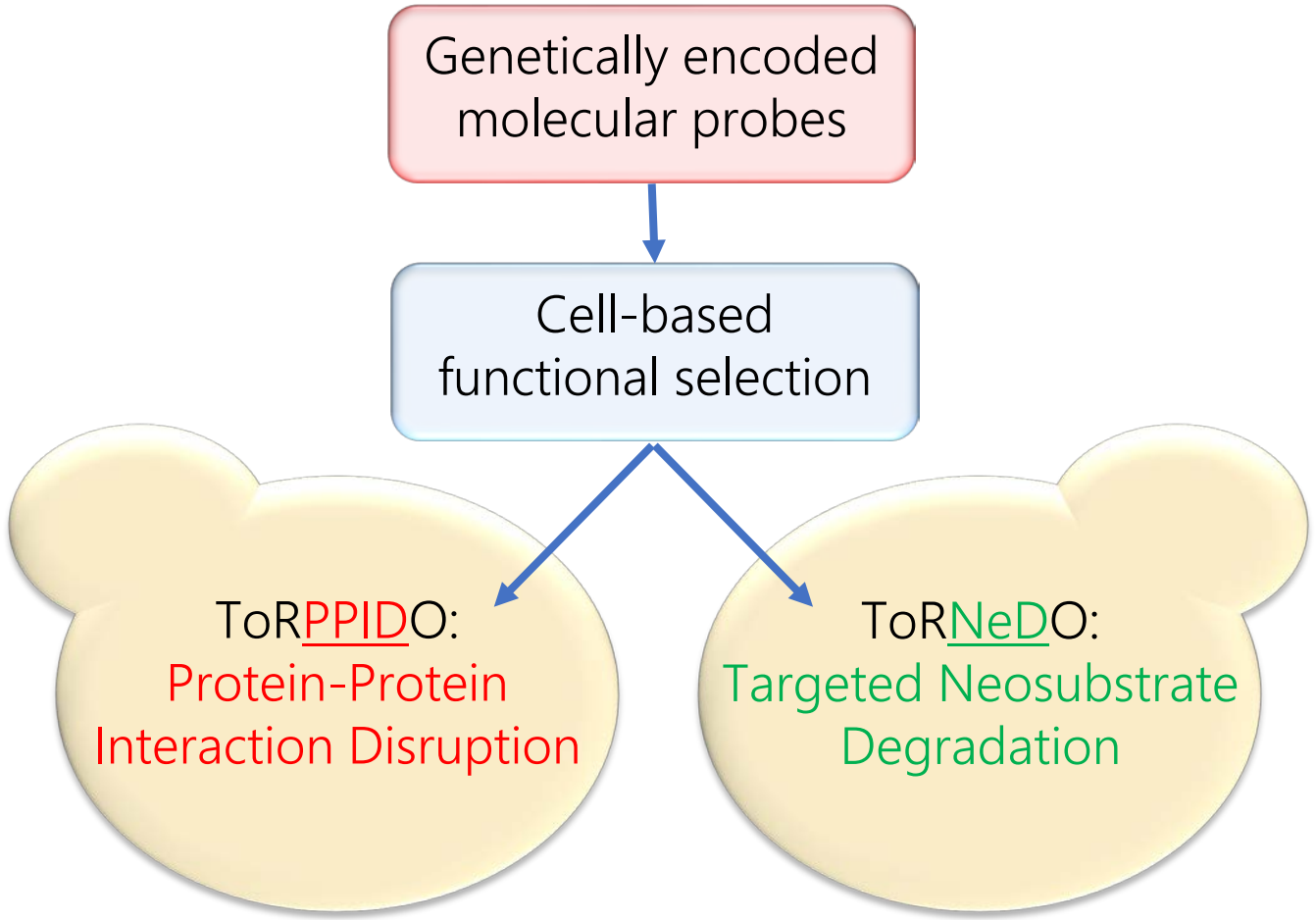


DNA-encoded displayed libraries:
Used in *in-vitro* binding assays
(e.g. phage/ mRNA/ yeast displays)

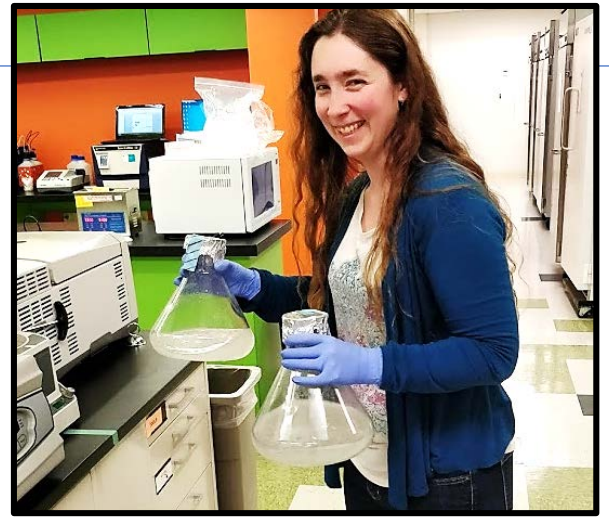


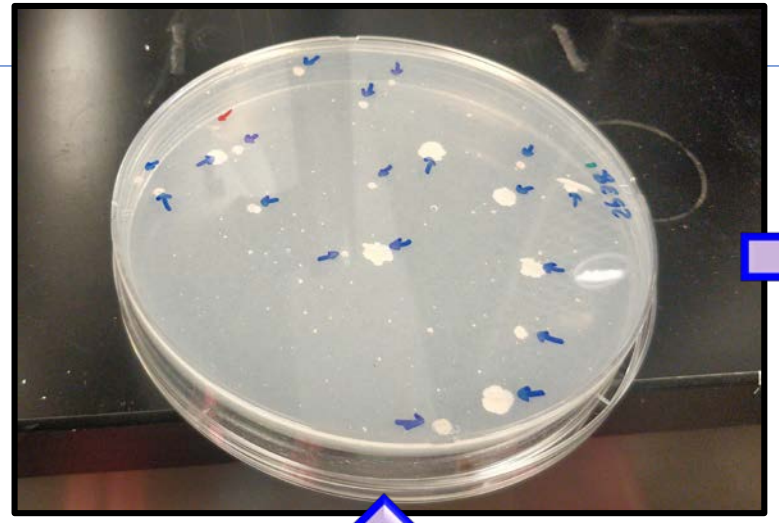
Intracellular Genetically-encoded libraries:
Our libraries of peptides and macrocycles are used in cell-based functional selection assays

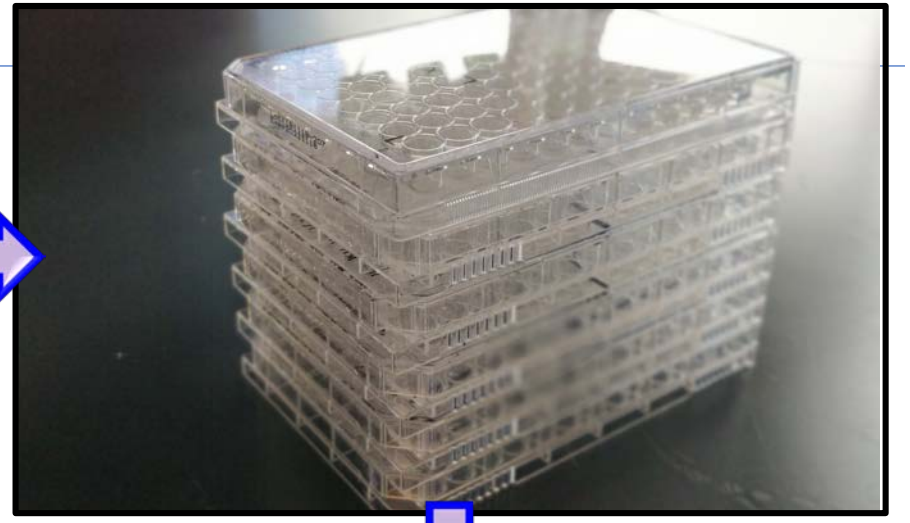
Platform technologies overview

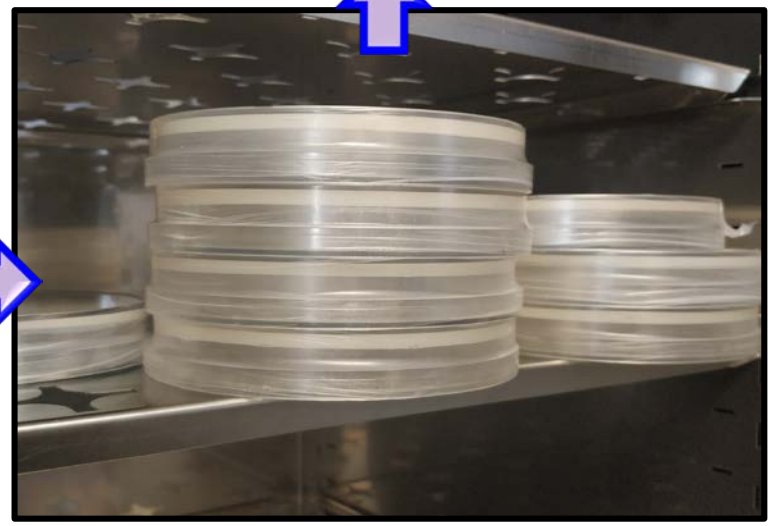


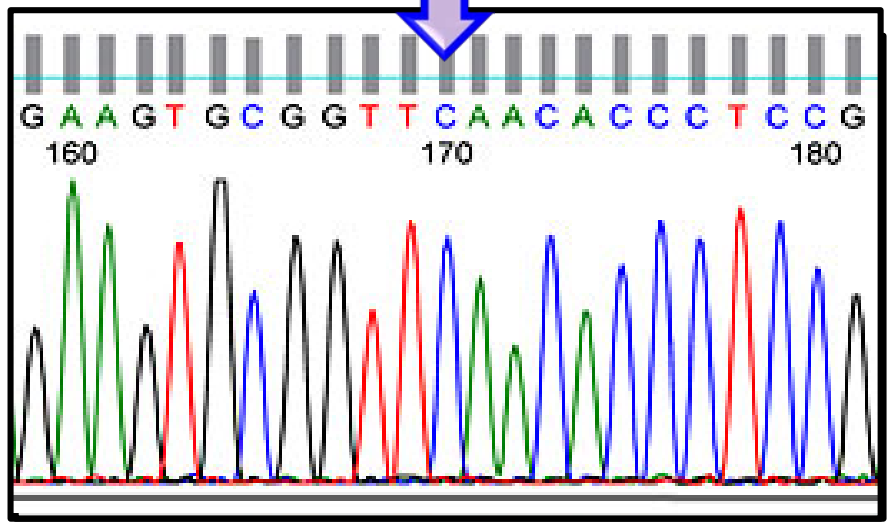
Screening process



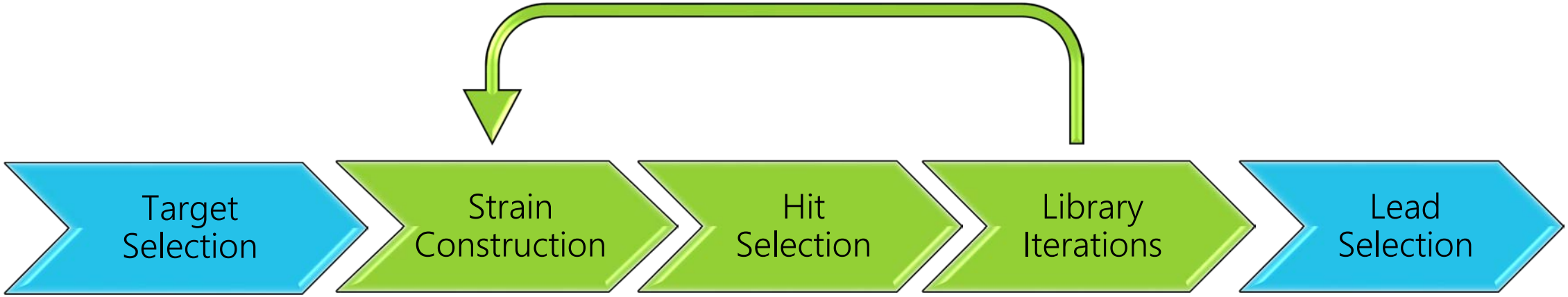




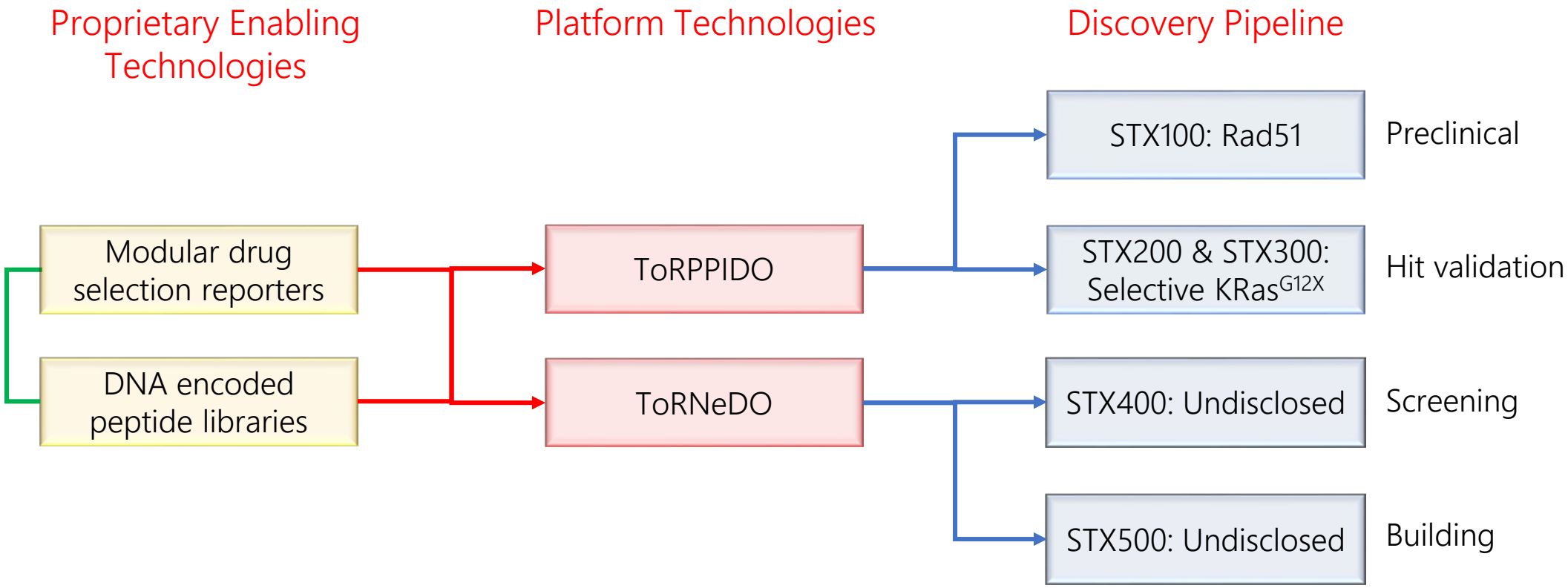




Our screening process selects for potent hits



SyntheX strategy overview – building our pipeline



We create synthetic biology-based tools to accelerate and improve drug discovery

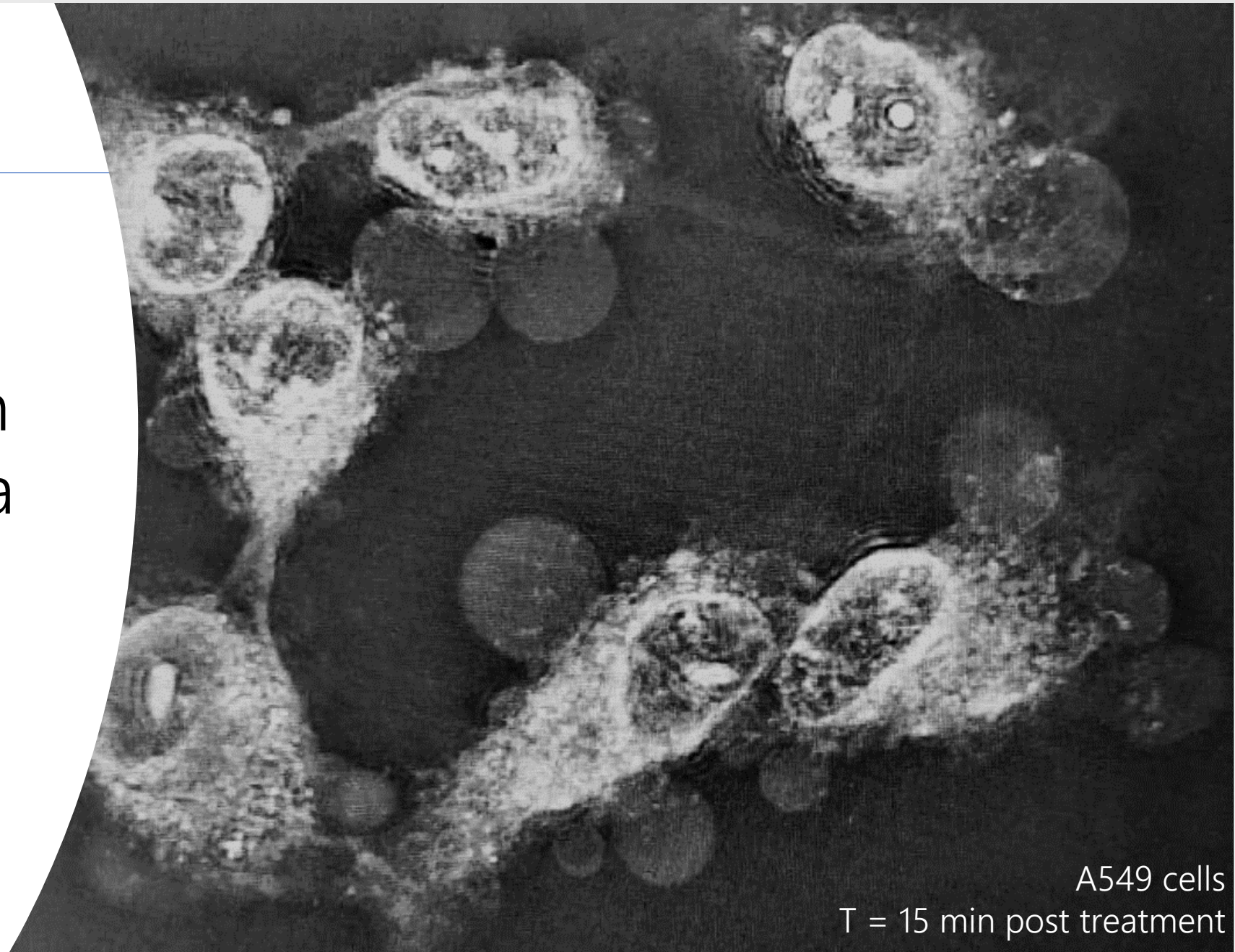
Our technologies are combined to generate our powerful cell-based drug discovery platforms

Using our internal discovery engines, we built a pipeline of oncology assets

STX100: Targeting the BRCA2/RAD51 Homologous Recombination (HR) DNA repair pathway

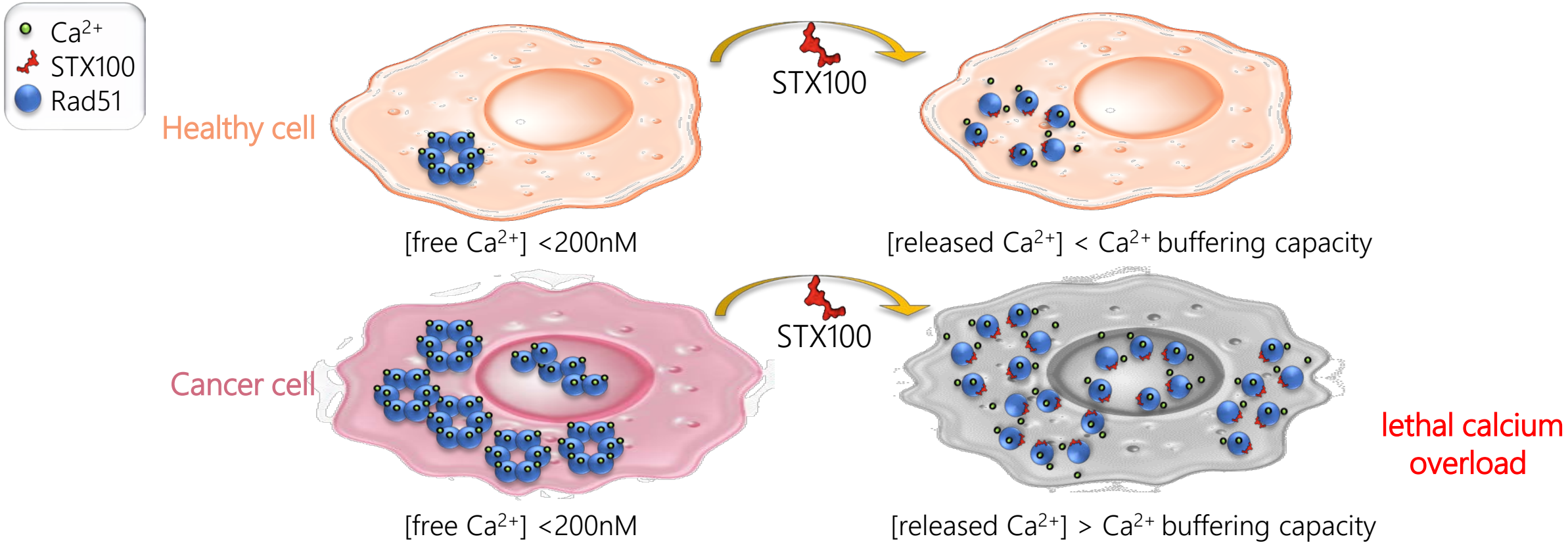
SyntheX

STX100 works with acute kinetics via a novel cell death mechanism

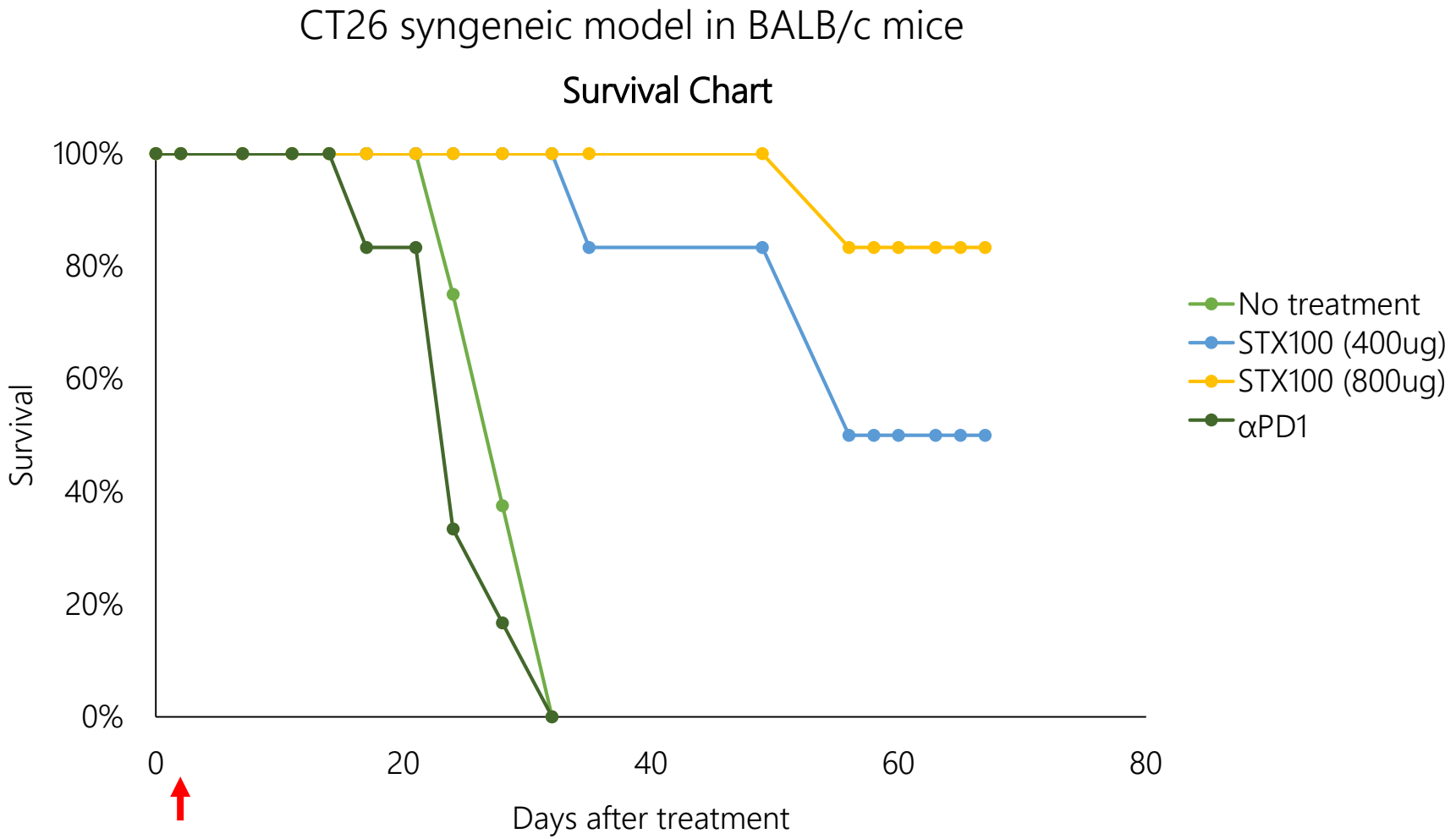


A549 cells
T = 15 min post treatment

STX100 kills cancer cells via a calcium surge released from the cancer's over-expressed Rad51



STX100 exhibits single agent activity in a CT26 model

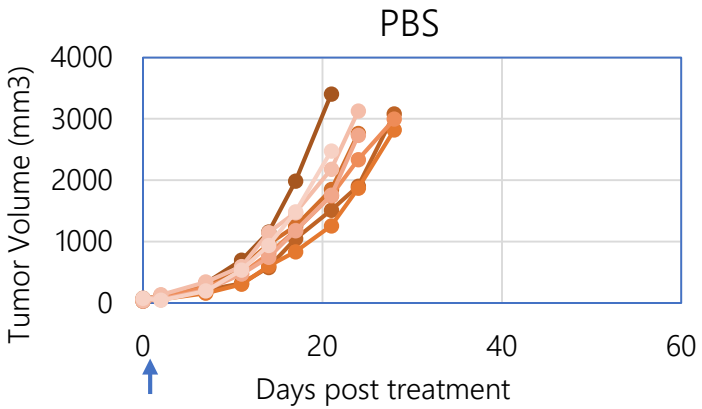


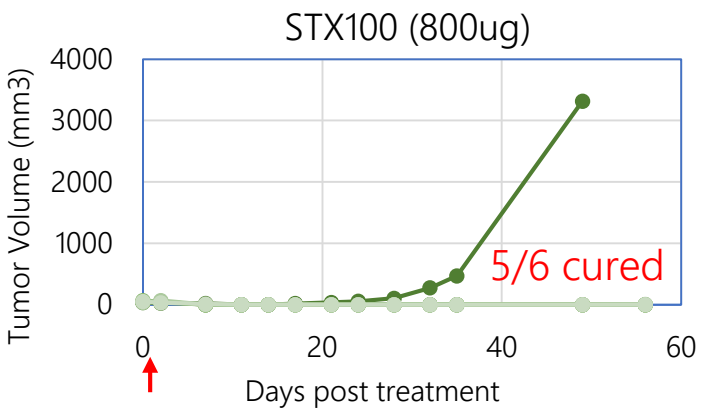
n=6-8 mice
Day=0 refers to 1st day of treatment with tumor volumes ranging between 50-100m^3

STX100 IT
10mg/kg αPD-1 IP

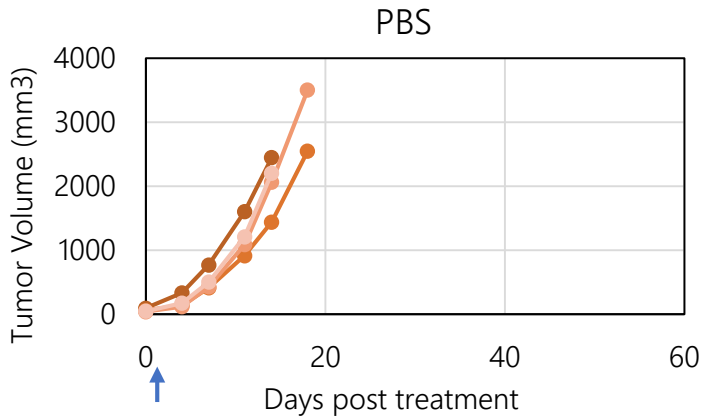
STX100 activity requires an intact immune system

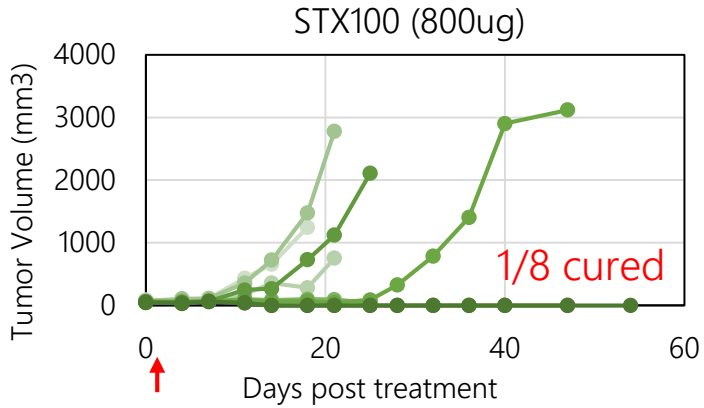
CT26 model in BALB/c mice





CT26 model in NSG mice

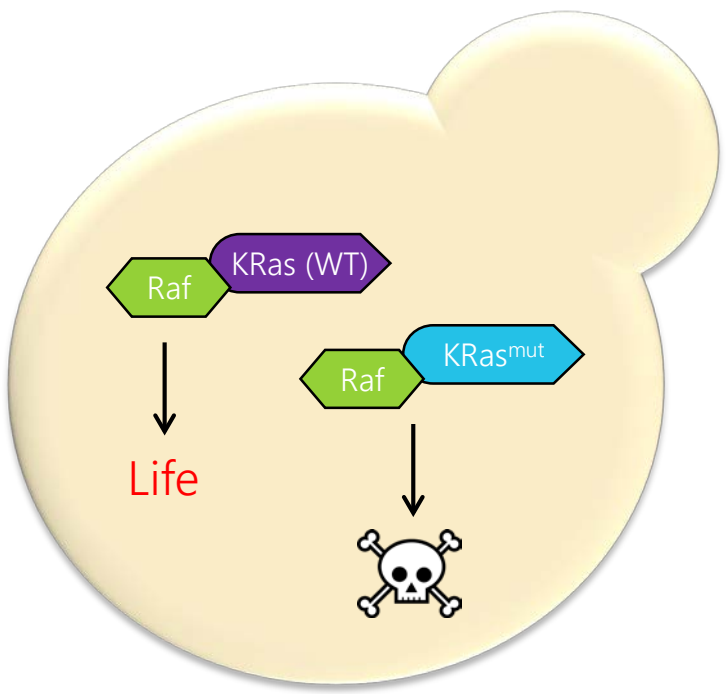




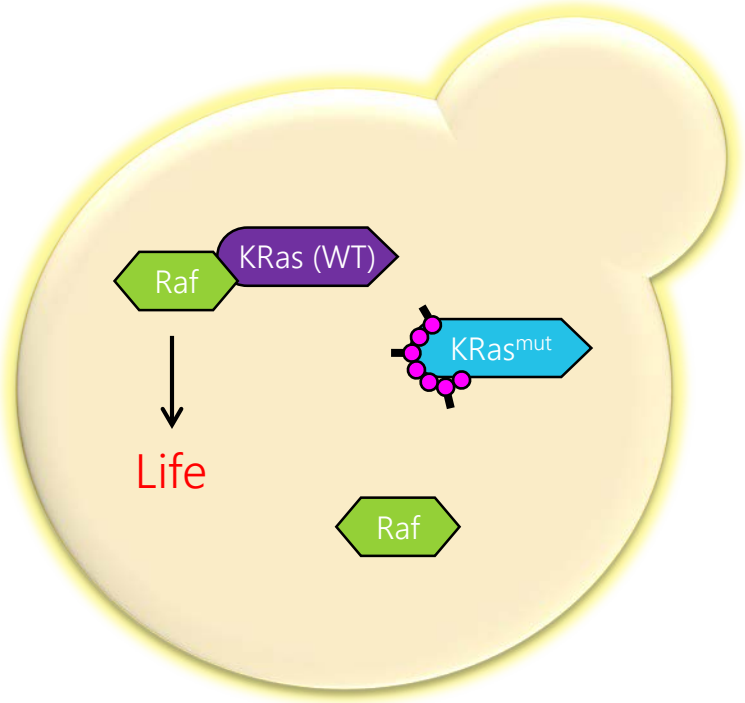
Day=0 refers to 1st day of treatment with tumor volumes ranging between 50-100m^3

STX200 & STX300: Selectively targeting oncogenic KRas signaling

STX200: Distinguishing KRas^{mut} signaling from WT



Interaction: cell death



PPI disruption: cell survival

Survival only possible If Raf preserves binding to KRas WT but NOT Kras^{mut}

Using ToRPPIDO, we discovered two different mechanisms of disrupting oncogenic KRas signaling

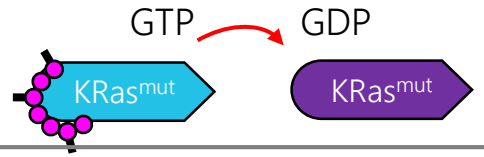
Potential disruptor classes:

- $KRas^{mut}$ binding peptides
- Non-productive KRas dimers

Both of these classes constitute novel insights and tools for probing KRas biology

- Disrupting peptides

- $KRas^{mut}$ selective GTPase activating peptides



Currently undergoing biochemical characterization and compound optimization.

Our core team

Maria Soloveychik ,PhD
Co-Founder, CEO

Charly Chahwan
Co-Founder, CSO

Tri Luong, MBA
Head of Finance and Operations

Rachel Bond, PhD
ToRPPIDO Scientist

Michal Olszewski, PhD
Biochemistry Scientist

Shirin Jenkins, PhD
ToRNeDO Scientist

Daniel Nielsen, PhD
Peptide Med Chemist

Pin-Joe Ko, PhD
Cell Biology Scientist

Sabrina Lin, BSc
Research Assistant

Our advisory teams

Leonard Post, PhD
Drug Development
SAB

Andrew Perlman, MD, PhD
Clinical Development
SAB

Diane Hollenbaugh, PhD
Immuno-Oncology
Advisor

Lesley Stolz, PhD
Corporate Development
Advisor

Arvind Gupta
Board Member

Esther Chung, JD
Corporate Counsel

Maya Skubatch, JD
IP Counsel

Mary Wheeler, PhD, MBA
Business Development
Advisor

info@synthexlabs.com
@SyntheX_Inc
www.synthexlabs.com

VINCERE

SPRING

BEHROUZ, PhD

CEO

Vincere

Johnson & Johnson INNOVATION | JLABS

svb Silicon Valley Bank

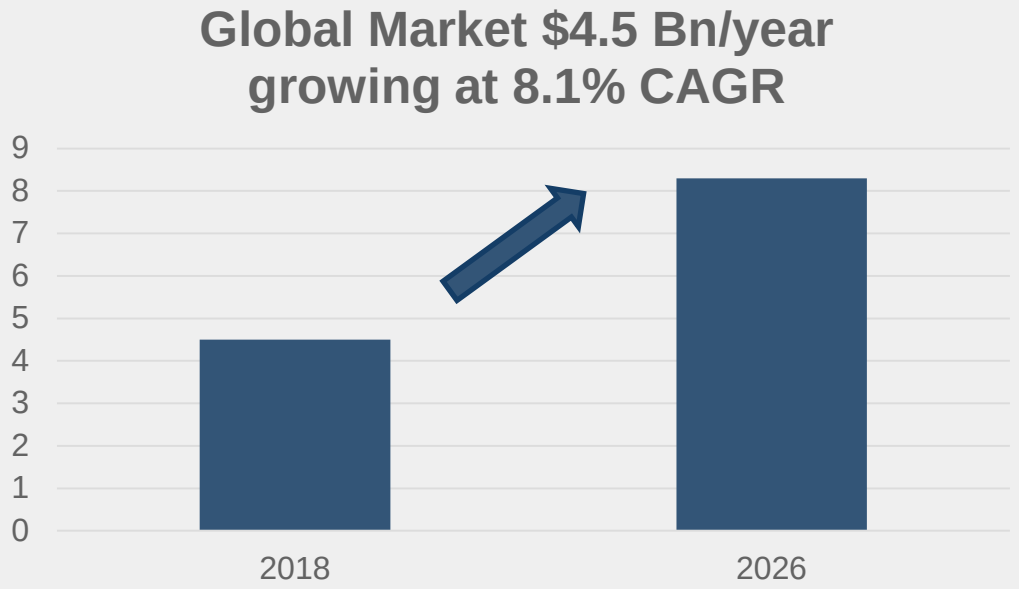
VINCERE

Invent the Future

Sept 2020

Parkinson's Disease is a Large and Growing Unmet Need

- No disease modifying therapy
- 10 million patients worldwide – 1 million in US
- $2B/year spent on therapeutics in US and growing



Fortune Business Insights report FBI100655

Additional Health Impact: Compounds Have Potential for Rare Diseases and Diseases of Aging

- Mitochondria important for many diseases
- Mitochondria important for healthspan and lifespan

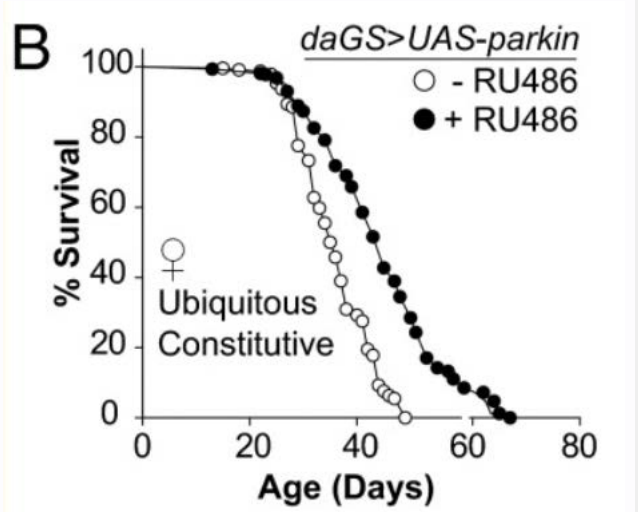
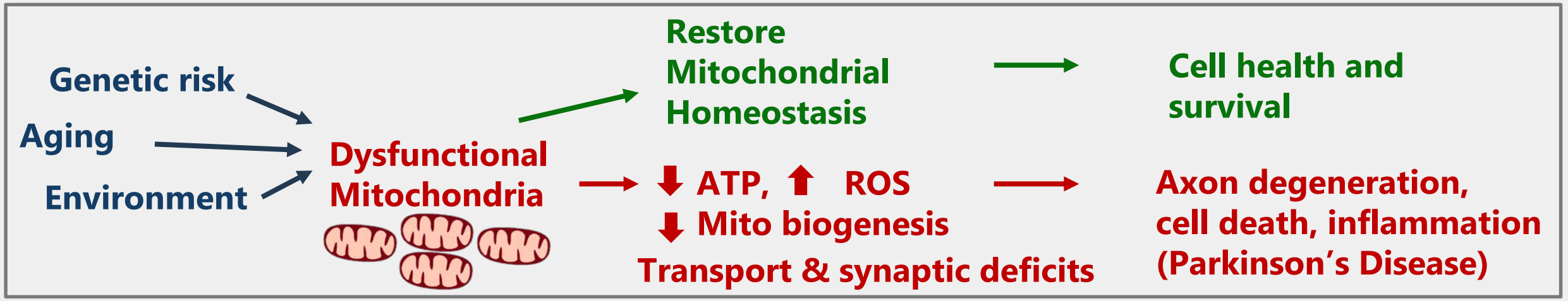


Figure from Rana et al, 2013

Indication	Market Size (US)	Prognosis	Standard of Care
Idiopathic Pulmonary Fibrosis	200,000	Fatal within 3 years	Do not improve prognosis or symptoms
Acute Kidney Injury	~2M deaths/year	~50% hospital mortality	supportive
Mitochondrial Rare Diseases	80,000	Varies	Symptomatic or palliative

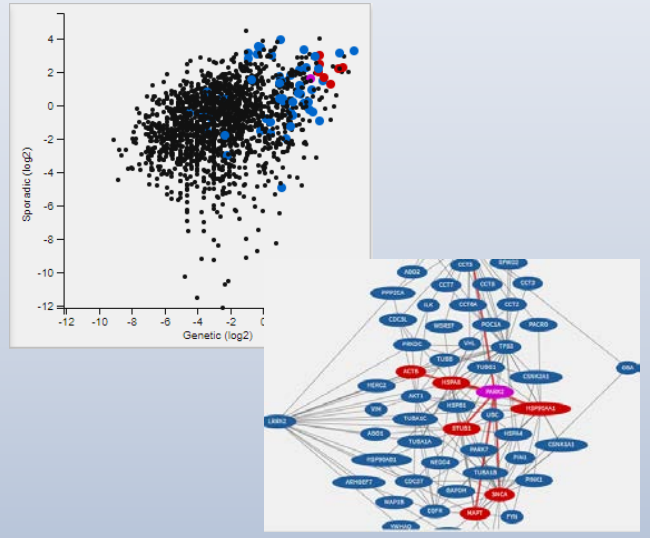
Unique Approach: No Similar Therapies in the Clinic or Clinical Trial



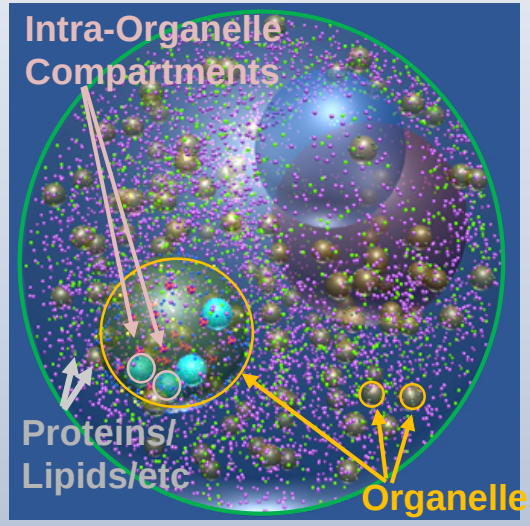
- No therapies in clinical trial that remove damaged mitochondria
- Preclinical competition from a few companies but we have technical advantages

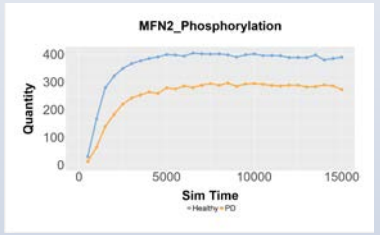
Unique Innovative Technology:
Software Aids Target Validation, Patient Enrichment, and Biomarker ID

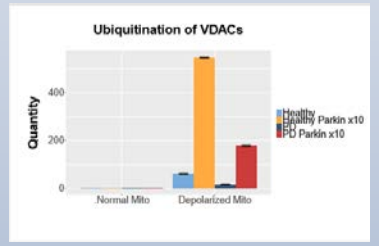
1. Target ID with network analytics and AI



2. Target validation using patented simulation of patient cells

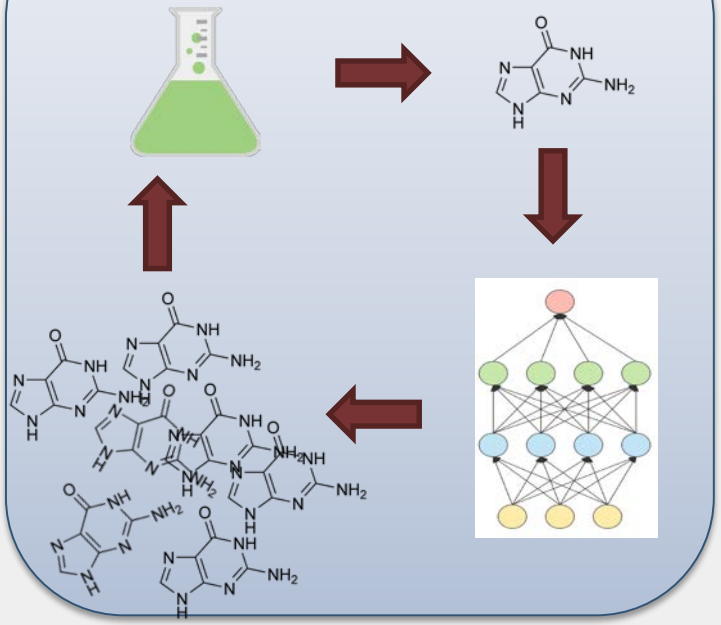






U.S. Patent No. 9,805,159

3. Compound ID using suite of med-chem and AI



Key Resources: Accomplished Team Skilled in Advancing Drugs to Clinic

Management Team:

Spring Behrouz, Ph.D.
Chief Executive Officer

Neuroscientist. Mayo alumna with >15 years Parkinson's R&D experience

Andy Lee
Chief Operations Officer

Computer scientist. Former VP of Engineering at Black Knight

Jim Liang
Board Director

Former IBM chief strategy officer and Morgan Stanley tech banker

Science Team:

Donna Romero, PhD
Lead Medicinal Chemist

Former Pfizer and Pharmacia Sr Director of Med-Chem with 35 patents, an approved drug, and many discovery to clinic projects

Chris Fanger, PhD
Head of Biology

Stanford alumnus with over 15 years at startup biotechs, including Hydra and Cadent

Ed Fritzen, MS
Medicinal Chemist

Over 25 years of experience at biotech and pharma with 11 patents

Scientific Advisory Board:

Dario Alessi, PhD
SAB – Dundee University

Enzymology expert and one of most cited biochemists in the world

Stephen Burley, MD, Dphil
SAB – Protein Data Bank, Rutgers

Expert in structural biology who successfully founded and partnered SGx with Eli Lilly

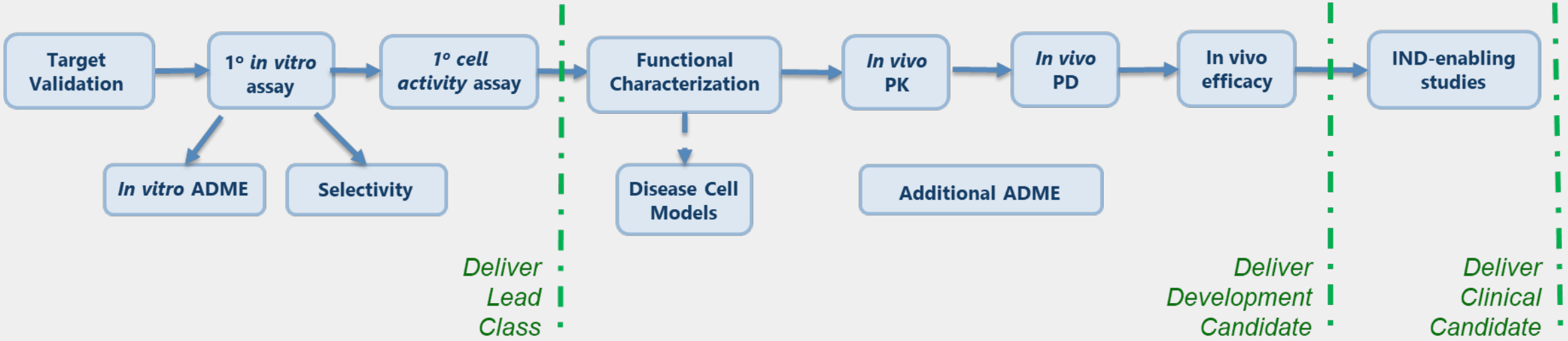
Peter Lansbury, PhD
SAB– Harvard, Lysosomal Tx

Serial Biotech founder who has delivered a Parkinson's disease therapeutic molecule to clinic

Key Resources: Funding from Expert Agencies
Plan: Clear Inflection Points Drive Value Increase and Reduce Risk

NIH National Institute of Neurological Disorders and Stroke

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH



This slide contains forward-looking statements

Traction: Target Validation to Patent Filing for Lead Class in 9 Months

Target Validation

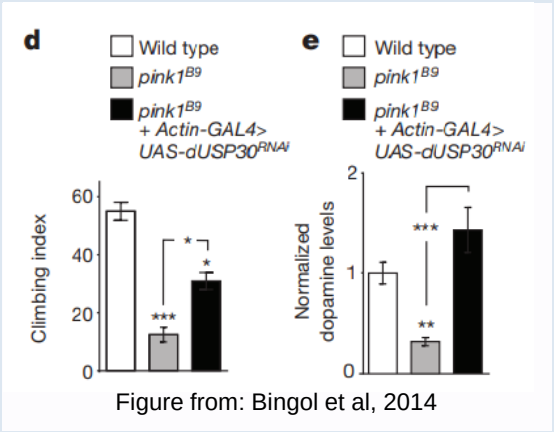
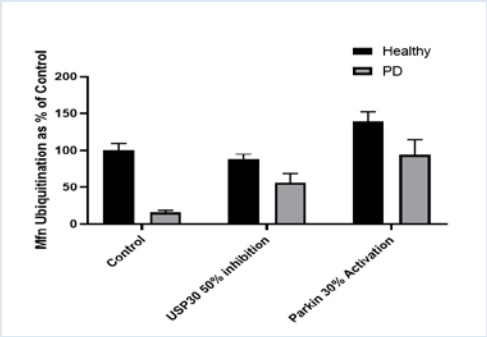
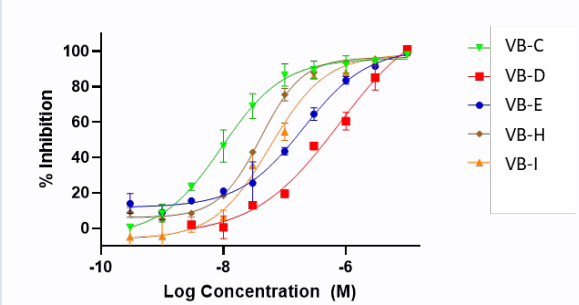


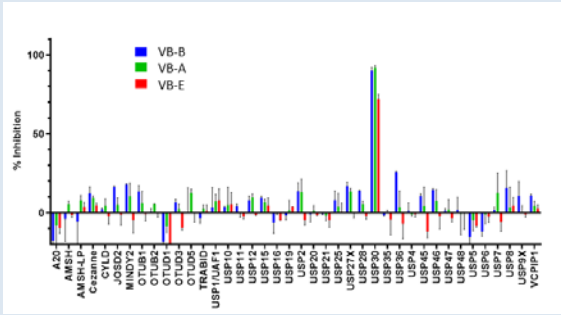
Figure from: Bingol et al, 2014



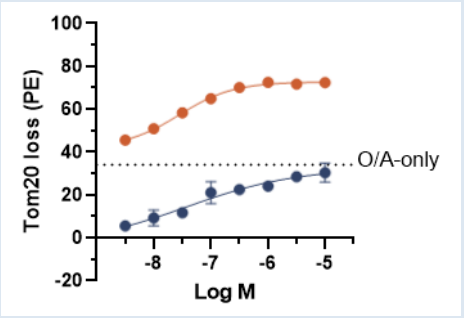
1° *in vitro* assay



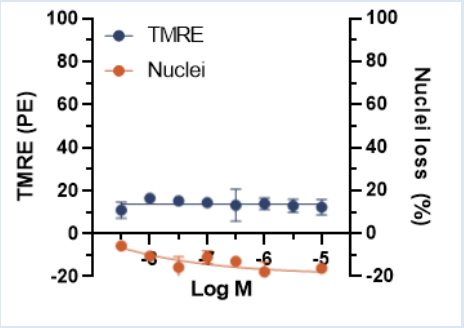
Selectivity



1° Cell Assay



Functional Characterization



Potential Roadblocks and Action Plan

	Roadblock	Solution
Scientific	• No clinical precedence for targets • Lack of good animal models for PD	• Experienced med-chem & learn from similar successes • Simulation and Patient cell validation
Execution	• Milestone “no-go”	• Multi-asset pipeline • Track record of hitting milestones
Financial	• Significant capital required • Market risk	• Large market justifies investment • Building early relationships with institutional investors and pharma

Impact*: *First-in-class small molecules to halt/slow **Parkinson's Disease** & **other age-related disorders**

Competitive Advantage:

- **Patent-pending, potent, and selective inhibitors of USP30**
- **Patented** software technology
- **Multiple assets** in pipeline

Resources and Plan:

- **Accomplished** drug discovery team
- Funding from **NIH and MJFF**
- Clear flow-scheme demonstrating **value created** and upcoming **inflection points**

Panelists

JEFF
CALCAGNO
Head of JLABS San Francisco Bay Area
Johnson & Johnson Innovation - JLABS

WILLIAM
HYUN
Venture Partner
Genoa Ventures

LAURA A.
LANE
Associate
Advent Life Sciences

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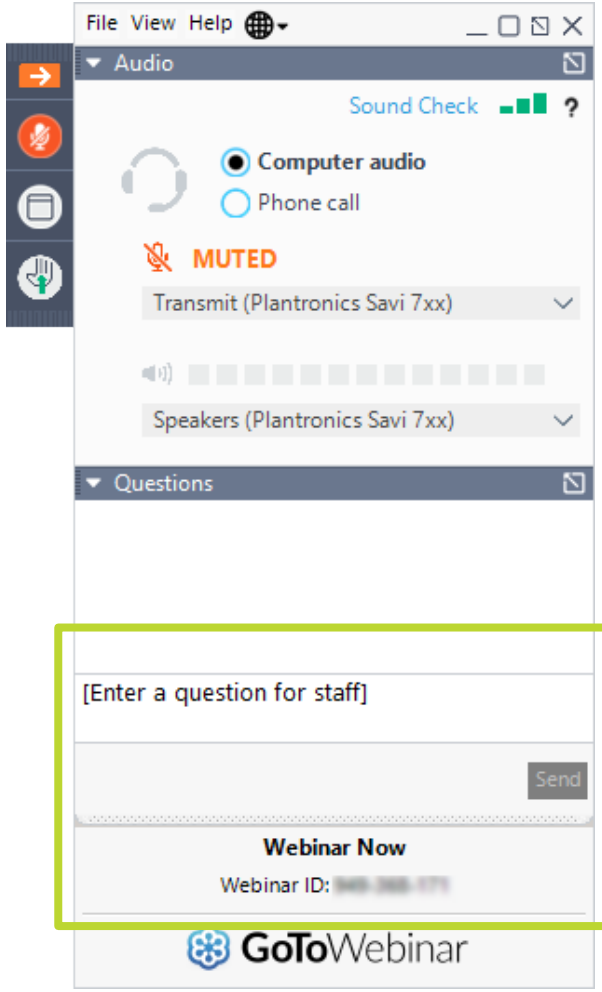
Audience Q & A



Type your questions or just say hello here.

AWARDEE RESULTS

BEN
JOHNSON
Head of Early Stage
Life Science
Silicon Valley Bank

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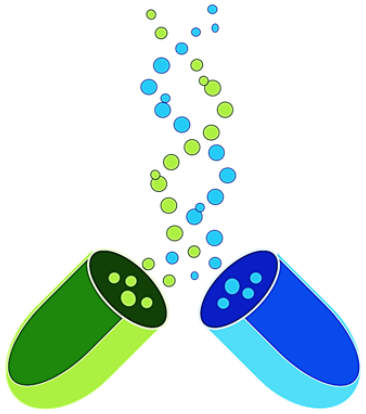
CONGRATULATIONS AWARDEES!

1ST

Stream BIOMEDICAL

2nd



SyntheX

3rd

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Upcoming JLABS Webinars

SEPT 14 | Catalyzing Innovation in TB Care: Solutions During COVID-19 and Beyond

SEPT 15 | Next in Naturals: A Look at the Future of Dietary Supplements and Their Potential Role in Our Health and Wellness

SEPT 16 | A Step Forward: Development of Effective Allogeneic CAR-T Strategies

SEPT 17 | A Master Introduction to Developing Cell and Gene Therapies

SEPT 18 | A Breath of Fresh Innovation: Advancing Remote Respiratory Monitoring

SEPT 22 | Precision Medicine and AI: Collaborating to Transform Biomedical Research and Development

OCT 8 | The Great Debate: Debt vs. Equity - with Silicon Valley Bank

For more information on JLABS events, please visit https://jlabshub.splashthat.com

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QuickFire CHALLENGE

Next in Naturals QuickFire Challenge on Immune-Support

Innovators are invited to submit breakthroughs ideas aiming to support healthy immune systems in babies, children, or adults. Ideas must be supported by scientific data and on track for commercialization in existing retail channels within 6-18 months.

APPLY AT jlabs.buzz/immune-support

BY SEPTEMBER 18, 2020

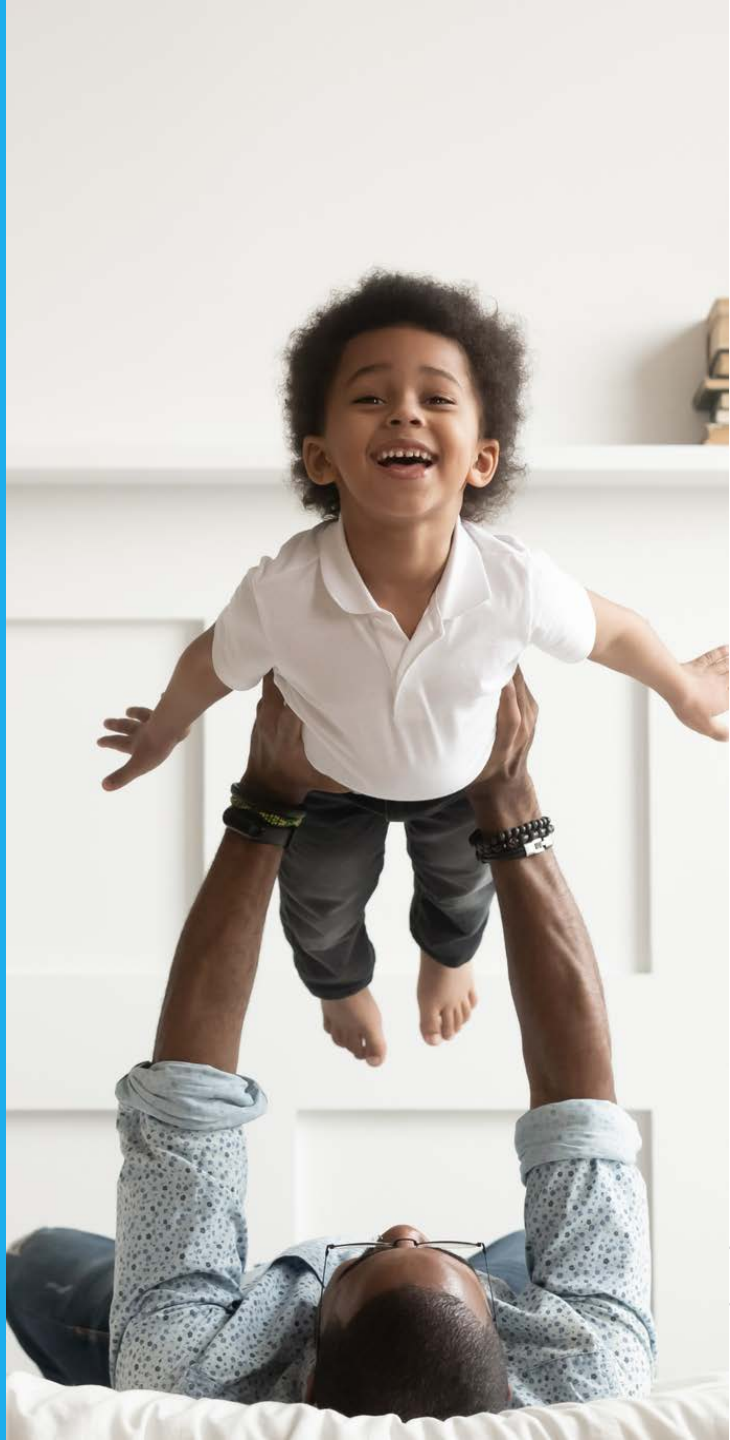
Johnson & Johnson INNOVATION | JLABS

Awardee(s) will receive:

UP TO
$50,000
IN GRANT FUNDING

ONE YEAR
OF RESIDENCY AT JLABS

MENTORSHIP
FROM EXPERTS AT JOHNSON & JOHNSON FAMILY OF COMPANIES



Thank You for Attending!

You will receive the recording within 24 – 48 hours.

Additional questions, please send them to:

Ro Rabanillo
rrabanil@its.jnj.com

Interested in applying to JLABS? https://jlabs.tv/apply

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