Hybridex Biosciences

# Antispacer Peptide Nucleic Acids

## Enabling the next generation of precision gene editing

Nicholas Economos, PhD
Jem Atillasoy
Peter Glazer, MD, PhD

# Founders

Nucleic Acids Research

**Antispacer peptide nucleic acids for sequence-specific CRISPR-Cas9 modulation**

Nicholas G. Economos [1,2], Elias Quijano [1,2], Kelly E.W. Carufe[1,2], J. Dinithi R. Perera[1] and Peter M. Glazer[1,2,*]

Nucleate

MassBioDrive
Accelerating the next generation of life sciences companies

## Peter Glazer, MD, PhD

Peter Glazer is Robert E. Hunter Professor and Chairman of Therapeutic Radiology, and Professor of Genetics at Yale University. As a physician-scientist Dr. Glazer has spun out multiple successful companies. He is currently co-founder and advisor to Cybrexa Therapeutics and Gennao Bio.

Yale

Gennao

CYBREXA THERAPEUTICS

## Nicholas Economos, PhD

Nicholas Economos is a 8th year MD/PhD candidate at Yale University with 10+ years experience investigating nucleic acid biology and gene editing technologies. Trained in the laboratory of Peter Glazer.

Tufts UNIVERSITY

Yale

SCIENTIA · PRO · BONO · HUMANI · GENERIS
The Rockefeller University
1901

OCR

## Jem Atillasoy

Jem Atillasoy is a 3nd year medical student at Yale University with prior experience in life science consulting, focusing on strategy & business development. Additionally worked in various roles across the biopharmaceutical industry.

PRECISION MEDICINE GROUP

MERCK

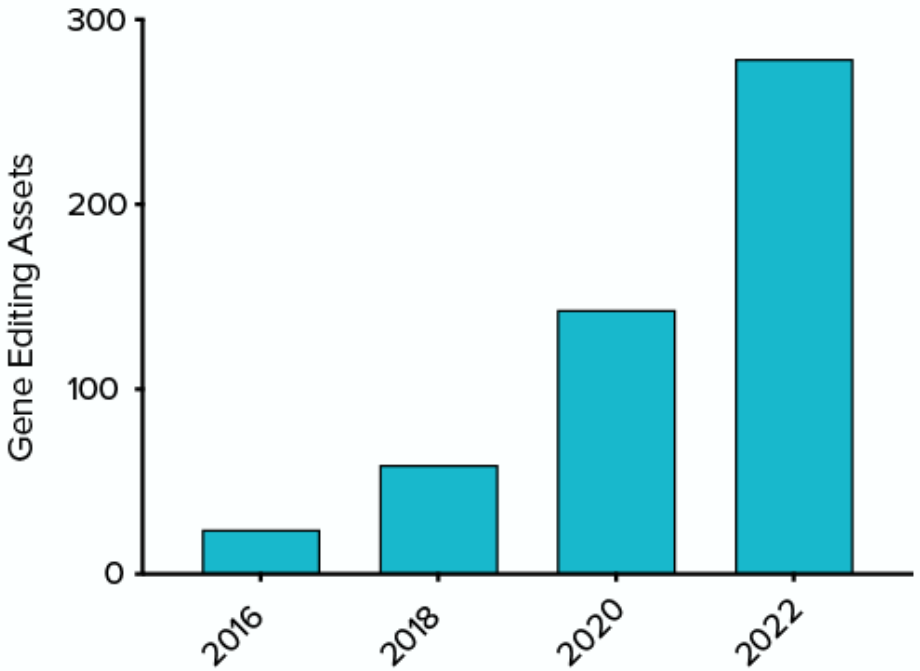
biohaven pharmaceuticals

gsk

OCR

# Gene editing market overview

## Gene Editing Assets in Development




~17% CAGR

$18B

Mammoth Biosciences
Beam Therapeutics
life edit
an elevatebio company
SPOTLIGHT THERAPEUTICS
metagenomi
Intellia THERAPEUTICS
editas MEDICINE
CRISPR THERAPEUTICS
GRAPHITE BIO
verve THERAPEUTICS
prime medicine
CARIBOU BIOSCIENCES
code bio
VERGE genomics

Pharmaprojects: Editing the Future Report. Jan 2022; *Biospace Market Reasearch*

# *Real Cures*

CRISPR medicines: Definitive genetic cures to a range of diseases not otherwise treatable

# *Real Limitations*

CRISPR-Cas9 has difficulty discriminating between similar genomic sequences resulting in:

- Off-target effects, leading to clinical trial holds
- Inaccessible indications due to target sequence homology

# Tools for precision and control

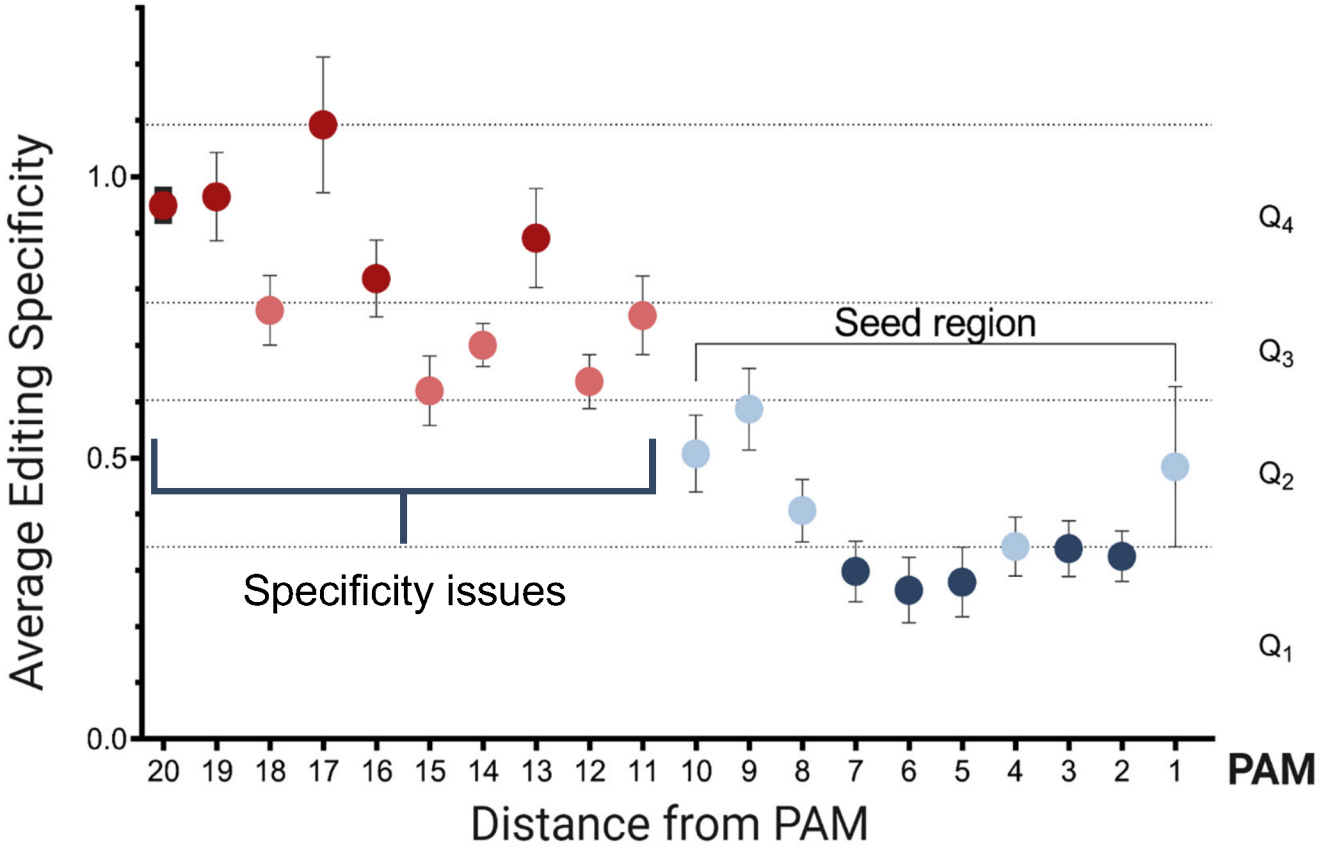
Improve CRISPR system accuracy to overcome sequence limitations and optimize patient health

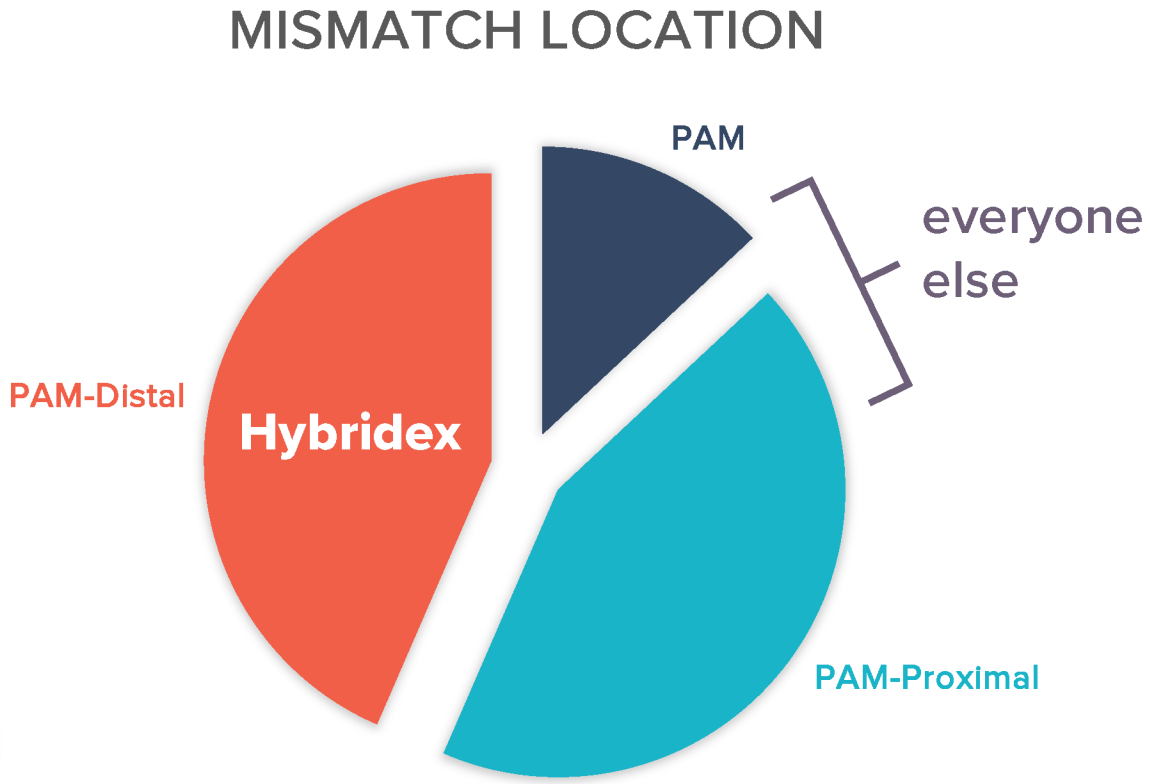
# Unlock and de-risk indications

Our antisense platform pushes beyond CRISPR specificity limitations to:

- Unlock new indications for therapeutic editing
- De-risk assets held back by off-target editing

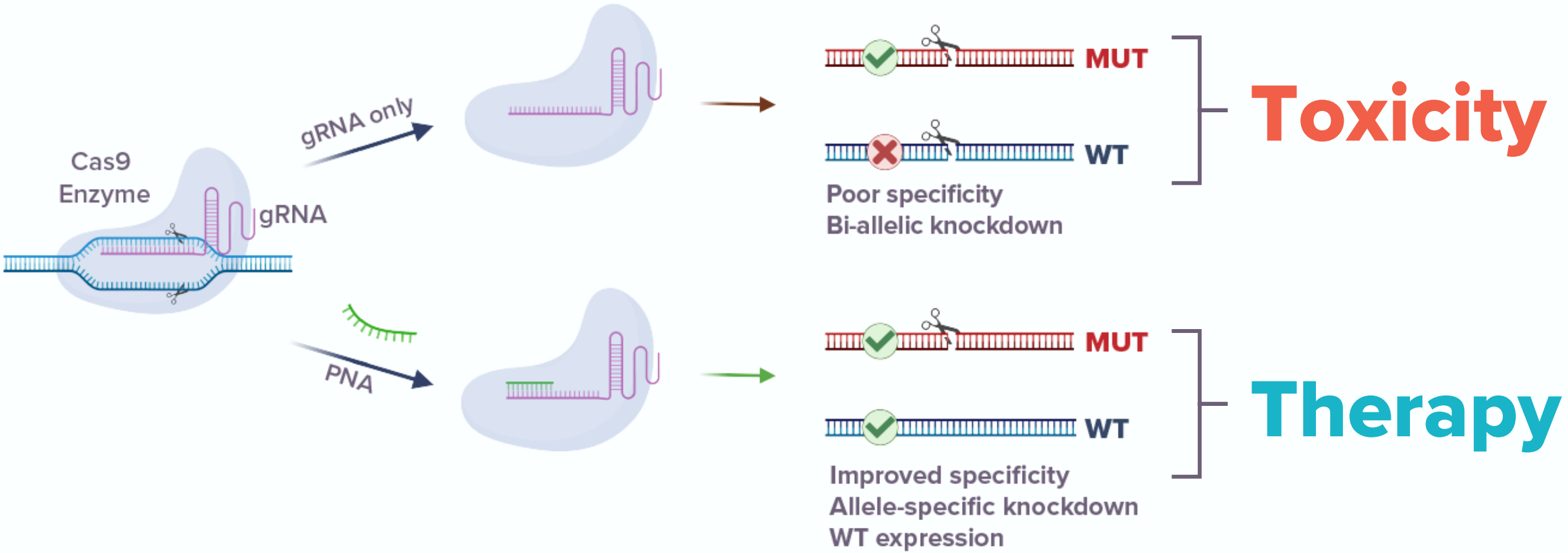
# Unlock 100% of the CRISPR guide RNA



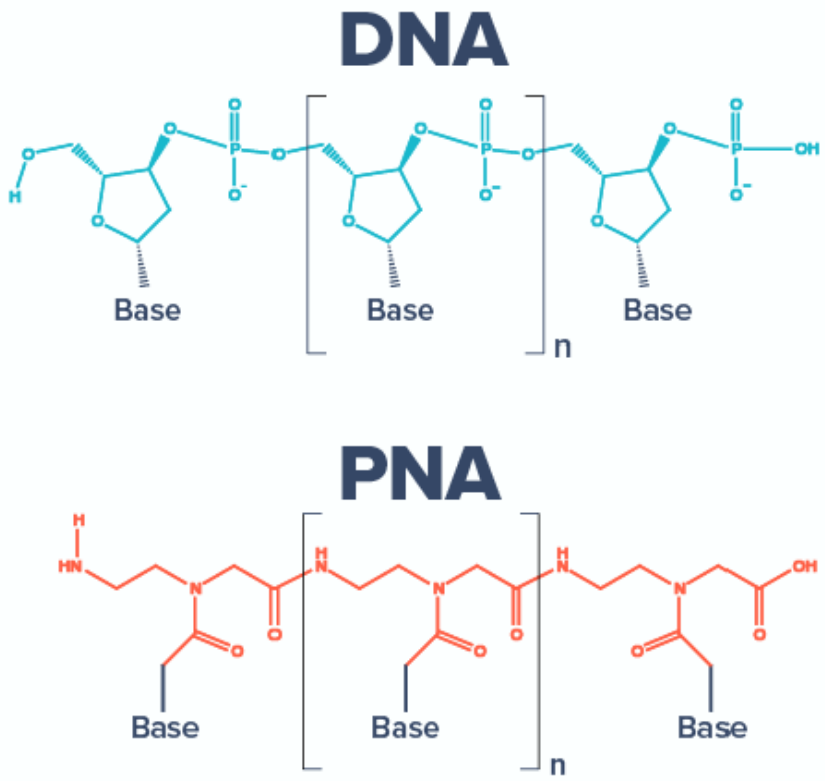




Rabinowitz and Offen, *Molecular Therapy*, 2021

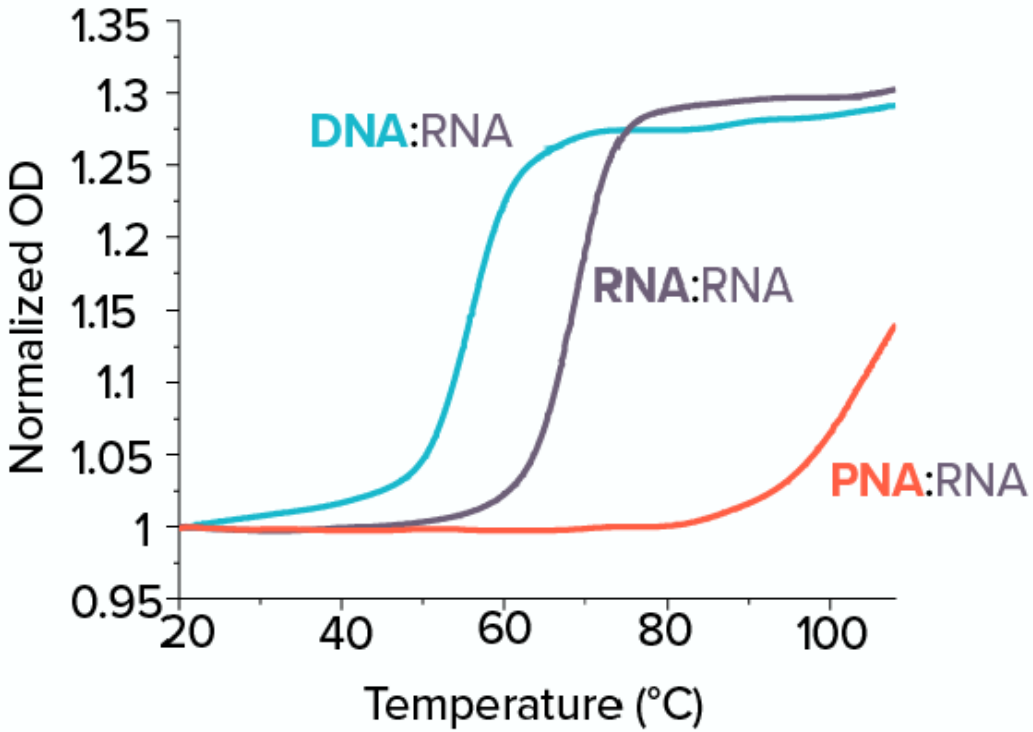
# PNAs for precise allele-specific gene editing in autosomal dominant disease



# PNAs bind RNA with extremely high affinity

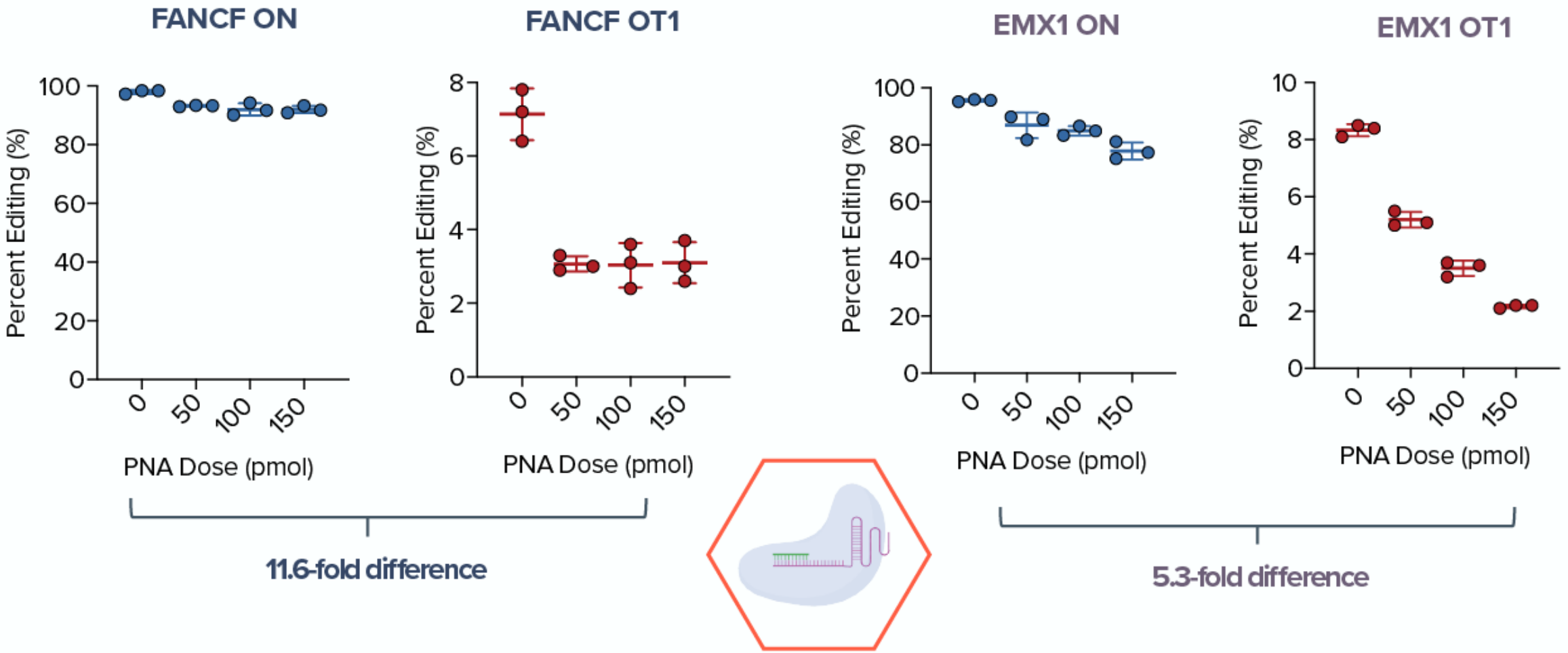



**Engineered nucleic acid with peptide backbone**




**Ultra high-affinity gRNA binding Tm > 100° C**

# Tunable tools for single-nucleotide precision



# CRISPR-PNA Platform

Ultra-precise gene editing medicines engineered for:

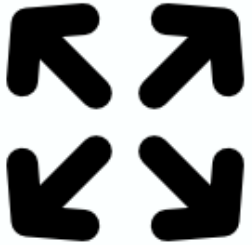
**Superior Specificity**

**Tolerability**

**Potency**

**Broad Delivery**

**Durability**



**Universal Applicability**

# Hybridex Biosciences Growth Strategy

## New IP Generation

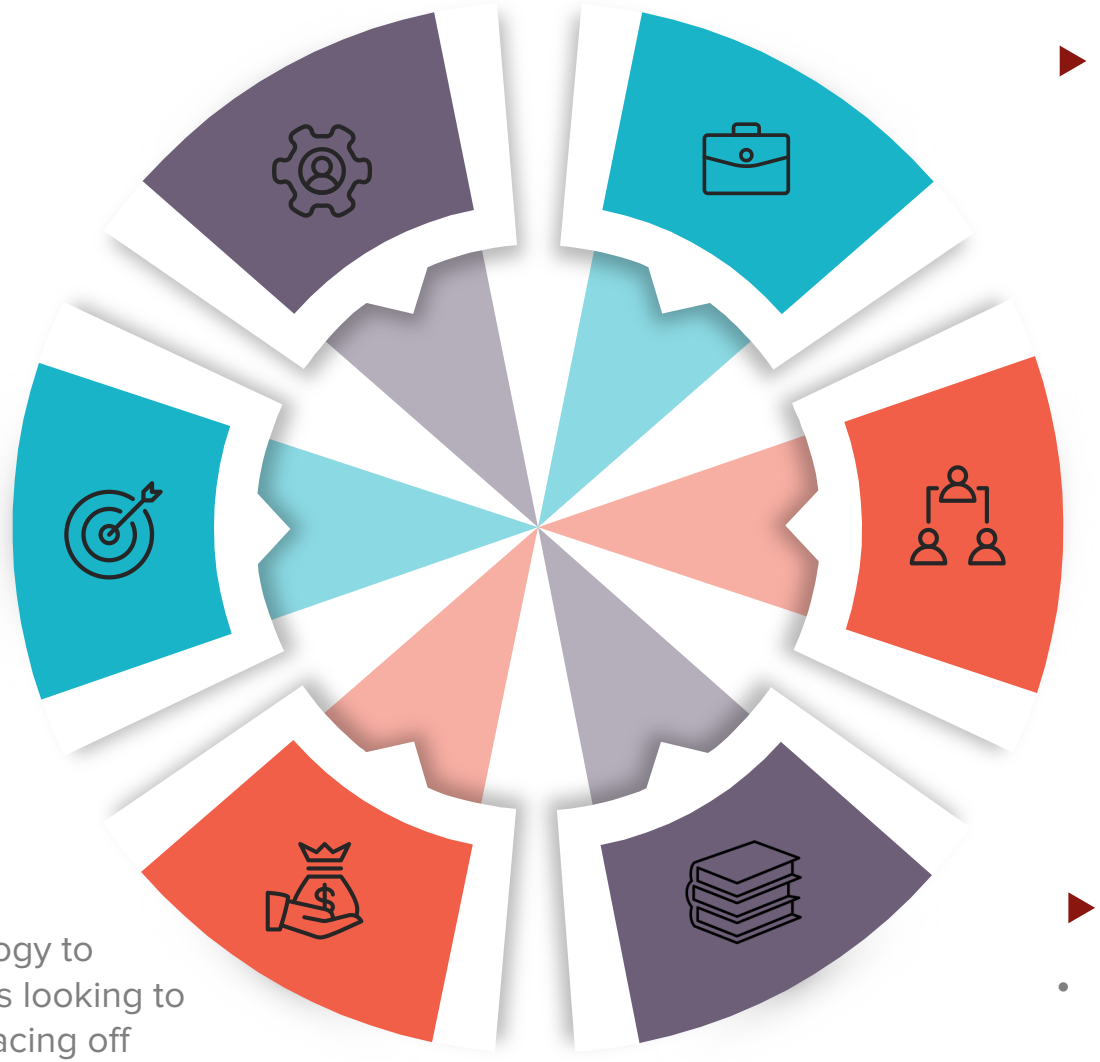
- Demonstrate utility of PNAs across cas orthologs & new editing modalities
- Currently pursuing new research to expand applications of PNAs

## Pipeline Development

- Develop Crispr/PNA therapeutics to target allele specific autosomal dominant diseases with a high unmet need

## Out License Agreements

- Out license PNA technology to biotechnology companies looking to de-risk assets currently facing off target issues



## Maintain and Hire Key Talent

- Build a world class SAB
- Collaborate with scientific leaders and experts in our target indications
- Hire experienced gene therapy consultants

## Co-Development Opportunities

- Engage with pharma/biotech companies with interest in rare disease and precision medicines to co-develop new products

## Academic Collaborations

- Utilize SBIR and STTR grants for non dilutive fundings
- Partner with expert scientists including those at Yale to optimize delivery

# Operational Plan and Blavatnik Funding

| | Milestones | 1H 2023 | 2H 2023 | 1H 2024 | 2H 2024 | 1H 2025 |
|---|---|---|---|---|---|---|
| Technical RD | Lead Screening and Identification | | | | | |
| | Lead Optimization | | | | | |
| | POC in Vivo | | | | | |
| | IND enabling studies | | | | | |
| Clinical Trial | | | | Pre-IND meeting | ★ | |

**Pilot Grant (100K)**

- PNA Synthesis (30K)
- Lead Screening and Identification (20k)
- PNA formulation optimization (30k)
- Off-target and sequencing analyses (20K)

**Development Grant (200K):** Evaluation of in vivo PNA/Cas9 lead compounds identified in pilot grant (200k)

- In vivo efficacy
- Preliminary Tox
- Preliminary biodistribution

**Series A and Beyond**

- NHP/large animal studies
- IND-enabling studies
- CMC activities
- IND-filing and first-in-human

**Indications currently under investigation:**

 Ocular

 Heme/Onc

 Otologic

 Dermatologic

★ Submit IND

# Financing Plans and Use of Proceeds

| Financing Round | Description of Milestones |
|---|---|
| Seed<br>3 Million<br>Q2 2023 | ▪ Identify and optimize lead candidates for POC indication<br>▪ Conduct in vivo pre-clinical POC trials for 3 indications<br>▪ Advance lead program to IND enabling stage<br>▪ Pursue non dilutive grant opportunities for further development of CRISPR-PNA drug candidates<br>▪ Engage potential industry partners to out license PNA technology on indication-by-indication basis<br>▪ Form collaborations with Yale faculty who are experts in drug delivery |
| Series A<br>~30 Million<br>Q4 2024 | ▪ NHP safety studies for lead and secondary indications<br>▪ Submit IND and initiate Ph1 trial for lead developmental candidate<br>▪ Submit IND for 2nd developmental candidate<br>▪ Establishment of R&D team to leverage PNA platform for expanded applications<br>▪ Lab/office with ~18-20 employees in CT |

# Questions

**Hybridex** Enabling the next generation of **precision** gene editing

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