Professional Development Program

Neoclease Pitch
Chelsea Trengrove, Ph.D.

Presenting Your Pitch for Expert Feedback
BIO Bootcamp

neoclease

gene-specific editors

the cutting edge against Parkinson's

Lab Central ignite · Chiesi

Golden Tickets

MilliporeSigma · All Things Innovation

In-Kind + Cash Awards

NVIDIA · aws

Engineering Support

Nucleate · The Michael J. Fox Foundation for Parkinson's Research · Johnson & Johnson Innovation | JLABS

Cohort + Consortium Invitations

genetic medicines today

limitless potential, limited precision

the opportunity

Gene editing unlocked curative potential, but today's tools can't deliver

Limitations

Editors **too large to deliver** & need for DNA recognition sequence (PAM)

Risks

Immunogenicity, **toxicity** & **mutations**

Precision Gap

Off-target & **incomplete edits**

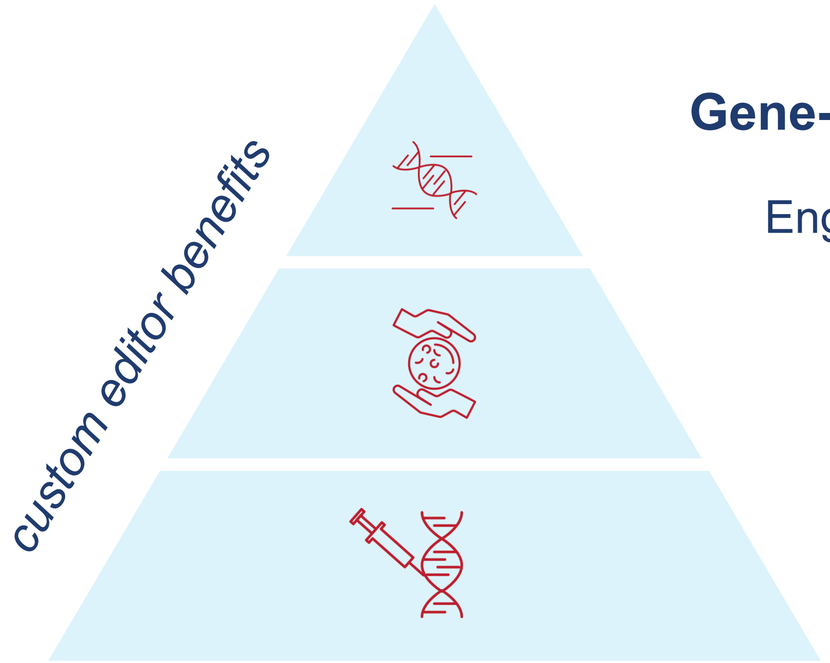
You wouldn't ask a small molecule to treat every disease why are we doing this with gene editors?

the next generation of gene editors

one gene. one editor.

our solution

Small-molecule approach to gene editing:
optimizing every therapeutic for a single target



Gene-Specific

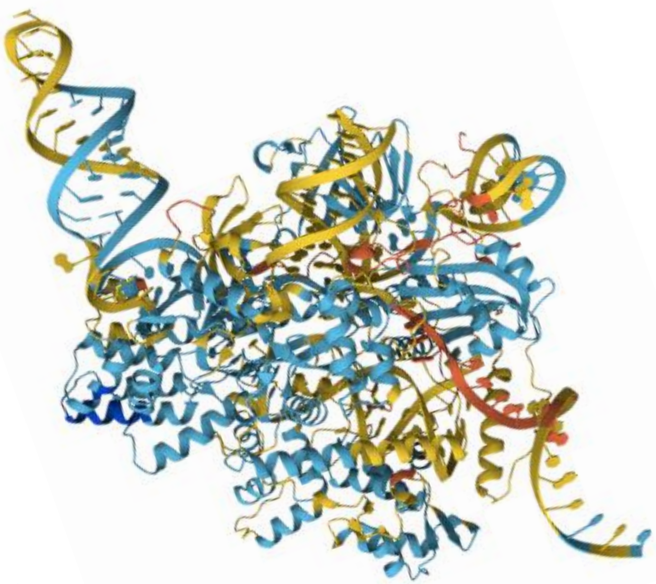
Engineered to target only one gene

Enhanced Safety

Minimizes off-target risks

Improved Efficacy

Miniaturized for delivery to any tissue



Neoclease is the only company customizing gene editors to target a specific gene

scientific foundation

AI-optimized editors

CTO and Cofounder, Prof. Jin Liu - builds miniaturized and more specific CRISPR editors

AI-designed libraries with millions of *mini* nucleases

Trained on Cas-Φ, Cas9, Cas12a:

- **30-50% smaller nucleases**
- equivalent efficacy *in vitro*
- **minimal off-target edits** compared to commercial Cas9

The CRISPR Journal
Volume 5, Number 2, 2022

DOI: 10.1089/crispr.2021.0076

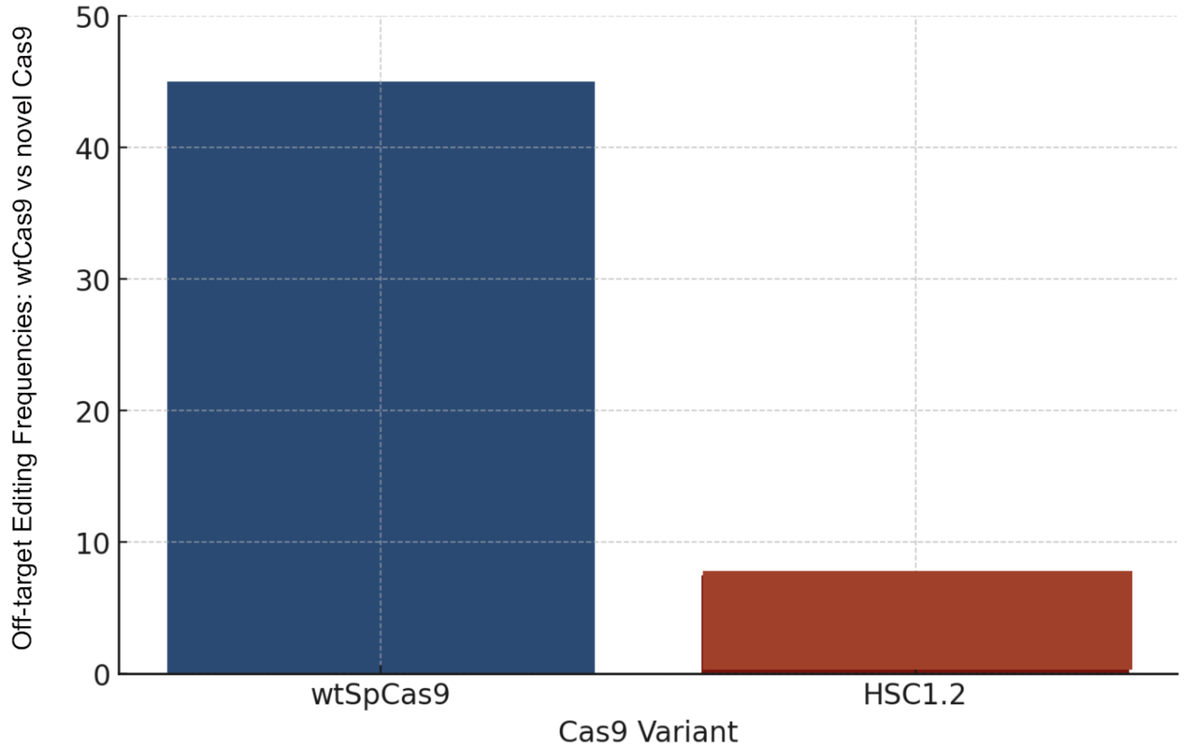
The CRISPR Journal

RESEARCH ARTICLE

Rational Engineering of CRISPR-Cas9 Nuclease to Attenuate Position-Dependent Off-Target Effects

Zhicheng Zuo,[1,2,3] Kesavan Babu,[4] Chhandosee Ganguly,[4] Ashwini Zolekar,[3] Sydney Newsom,[4] Rakhi Rajan,[4] Yu-Chieh Wang,[3,5] and Jin Liu[3,*]

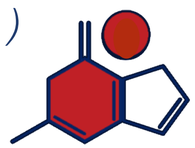
Enhanced specificity: Cas9 variant reduces off-target edits by 6-fold



market landscape

unlimited potential

target for initial validation
(PD therapeutics market)



monogenic disorders

polygenic disorders

prophylactic and multiplex

$5.1B

1 - 3 targets

$8.7B

5k - 10k
estimated disorders

$52.4B

8k - 15k
estimated disorders

$$$B

Millions
estimated disorders

Initial Targets

Near Future Opportunities

Select targets

1. Parkinson's disease
2. HPV
3. Pancreatic Cancer

in silico pipeline milestones

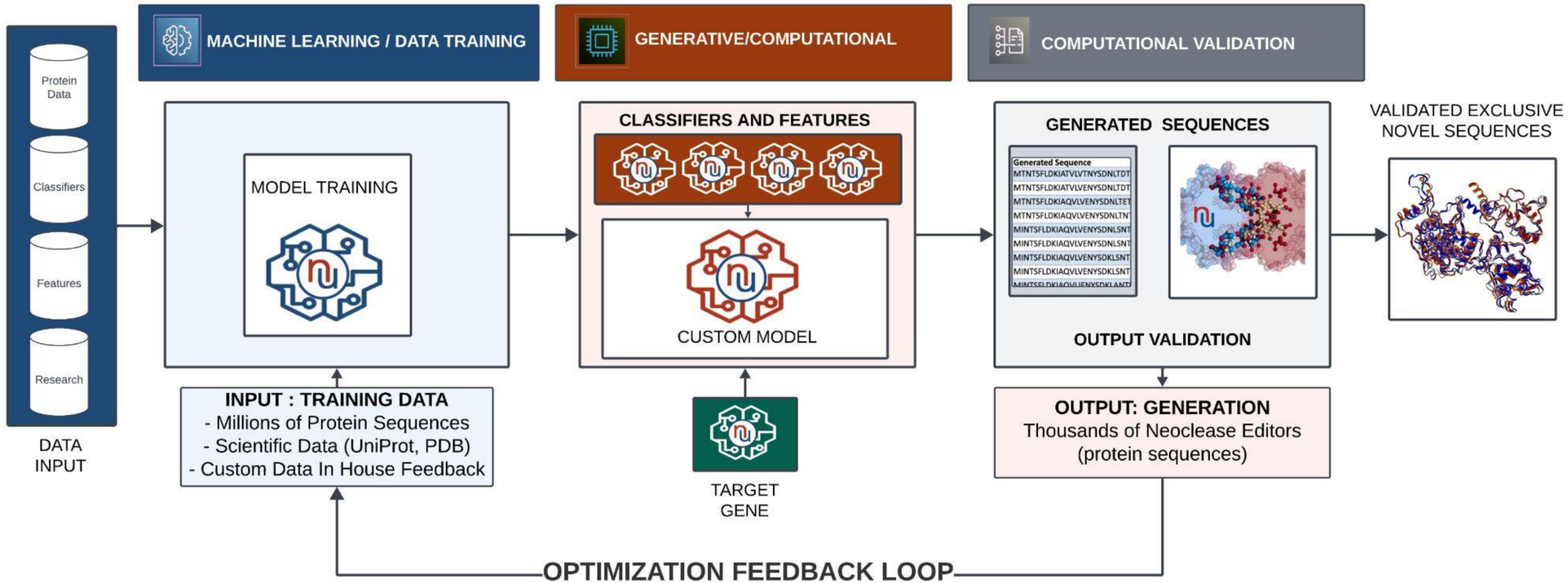
we built a ChatGPT for proteins

Generative Model

Trained on **millions** of editing proteins to generate new, **gene-specific** nucleases

Computational Evaluation Pipeline

Series of checks and gates to screen **smaller**, **precise**, and **efficient** editors for target gene

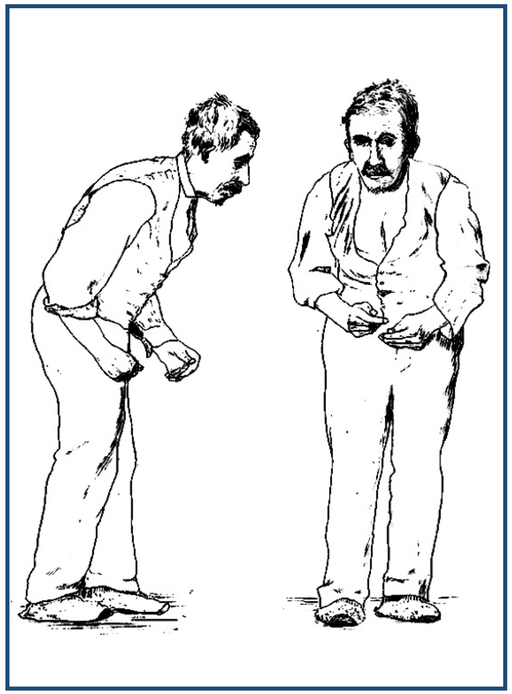


Parkinson’s-specific editor

our lead program

neoclease

*Parkinson's disease affects **10M + people worldwide***



Unmet Medical Need:
Current treatments manage symptoms without addressing underlying neurodegeneration

LRRK2 is a Key Driver in Parkinson’s: Causing both familial and sporadic PD *(opportunity to treat all patients with PD)*

Neoclease’s Differentiator

One-time, brain-specific therapy with higher safety and efficacy

- **Miniaturized** for *in vivo* delivery, **no PAM constraints**, targeting **unique sequence** within LRRK2 (untargetable by current CRISPR systems), **first-in-class**, **novel IP**

AI-designed LRRK2 nuclease

Screened, ranked, and prioritized top editors from a pool of 100k **as small as 350 a.a.**

in vitro validation

translating AI-design into therapeutic candidates

timeline: critical step toward preclinical translation

unlocking preclinical and BD milestones

On Target | ***Off Target*** | **Pre-Clinical Studies**

June 2025

PCR and Sanger sequencing to quantify on-target editing for top 50 candidates

July 2025

NGS to assess genome-wide off-target effects for top 10% of editors

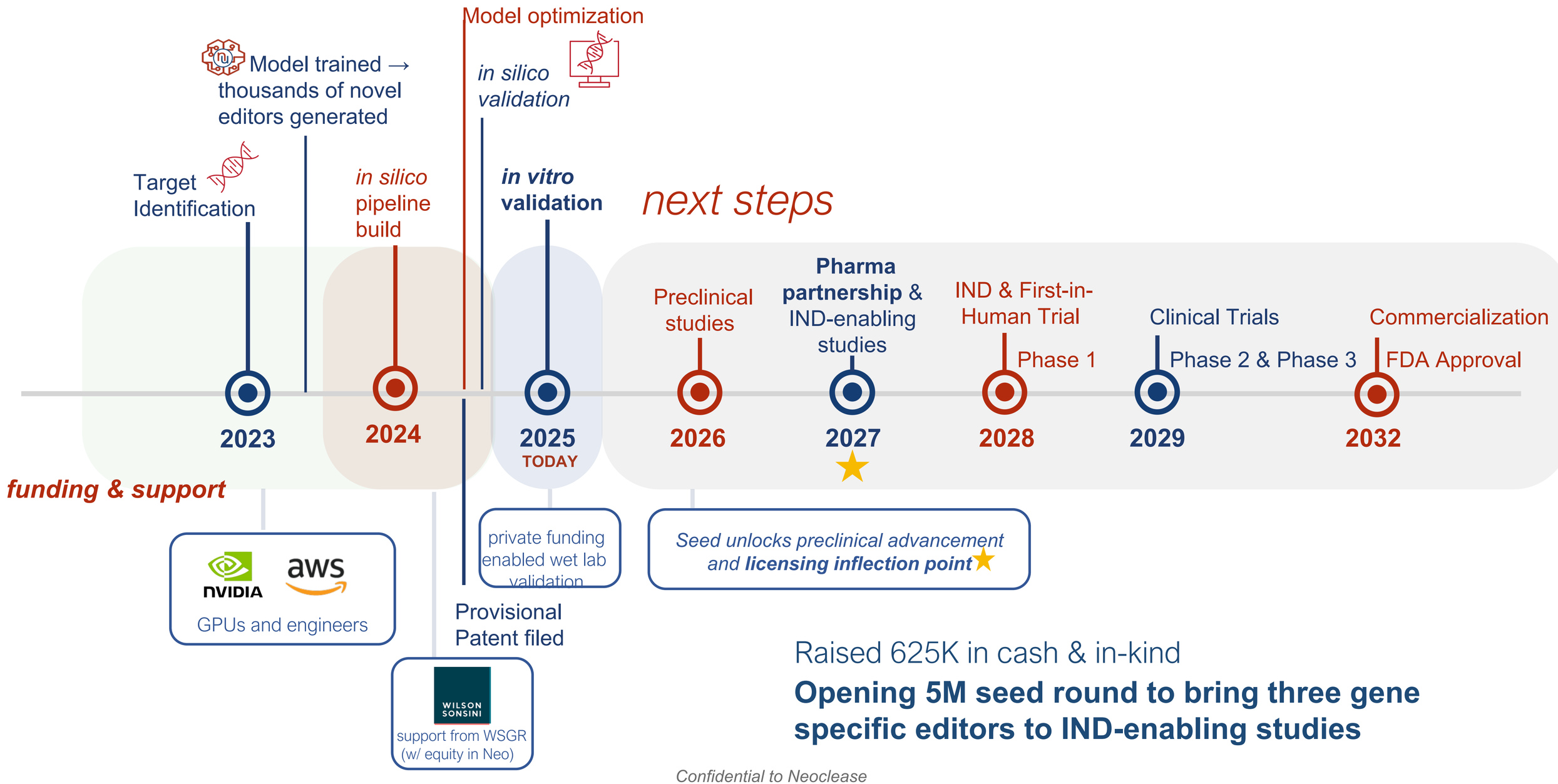
Summer 2025

Top 5 LRRK2 editors advanced into PD mouse models for preclinical development

neoclease roadmap

neoclease

from platform build to clinical impact



Raised 625K in cash & in-kind

Opening 5M seed round to bring three gene specific editors to IND-enabling studies

business model + financials

enables early licensing deals

Use of Proceeds	Timelines	Funding / In-Kind	What this looks like
Pre-seed	Q4 2023 – Q2 2025	**SAFE Investors** - $100k **Amazon** – engineers ($100k) **NVIDIA** – GPUs ($100k) **Chiesi** - Lab Space ($75k) **Lab Central** - Lab Space + Cash ($65k) **FEI** - $25k	**Generative AI model**, **computational evaluation pipeline**, **LRRK2-targeting nuclease library**, & **on/off target in vitro studies**: • 3 scientists, • GPUs • 2 FTEs
5M seed	2025 - 2027	$5M	**Progress lead candidate to IND-enabling studies** • 4 scientists (computational and wet lab) • Large compute clusters • *in vitro* wet lab work • 3 FTEs: finance, business dev., operations • IP lawyer (WSGR) • CRO for *in vivo* mouse work

Pharma Co-Development Model

- Genetic medicines historically licensed for **$1-2B (total deal value)**
- Targeting three licensing deals by 2028

Deal Structure with Pharma / Biotech

- **Upfront** - develop gene-specific nuclease to IND-enabling studies **($10-60M)**
- **Milestones** - Ph1 and Ph3 human trials **($100Ms)**
- **Royalties** - commercialization revenue

competitive landscape

lock-and-key vs. one-size-fits all

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Instead of workhorse editors, Neoclease optimizes every therapy for an individual target

Technology	Company
Generative AI to Build Custom Gene Therapies	neoclease **(Generative AI to build new nucleases for specific genes)**
Generative AI for Protein Design	Absci (AI-driven protein drug design)
	Profluent (Generative AI for a workhorse Cas protein)
AI Modifications to a Known Gene Editor	Inscripta Therapeutics (Cas9 and MAD7 tools)
	Scribe Therapeutics (CasX for genetic diseases)
	Beam Therapeutics (Base editors for liver, blood, and eye diseases)
	Prime Medicine (Prime editors for liver, blood, and eye diseases)
Developing CRISPR Therapies	CRISPR Therapeutics (Cas9 protein for blood disorders)
	Intellia Therapeutics (Cas9 for liver and ex-vivo editing)
	Editas Medicine (Cas9 and Cas12s for genetic disorders)
	Caribou Biosciences (Cas9 for multiple industries)
	Mammoth Biosciences (Cas12, Cas13, Cas14 mainly for diagnostics)
	Verve Therapeutics (Base editors for cardiovascular diseases)

neoclease advantage

platform for precision, designed to partner

PROCESS

Partner-Ready

Progression toward IND-enabling studies, making us an attractive partner for pharma.

INTELLECTUAL PROPERTY

Freedom to Operate

New IP opens doors to unique licensing deals with pharma. Circumvents foundational CRISPR patents.

GENERATIVE AI ENGINE

Custom Nuclease Design

Design of highly specific gene editors tailored to, which off-the-shelf CRISPR tools can't target.

DATA

End-to-End Pipeline Iteration

Rapid design-test-refine cycles, grows a proprietary database of novel biology and AI-generated nucleases.

progress highlights

engine built, traction gained

neoclease

milestones and momentum

Supported: Amazon & NVIDIA
Engineered AI-generated nuclease libraries with ***AWS*** + ***NVIDIA*** support

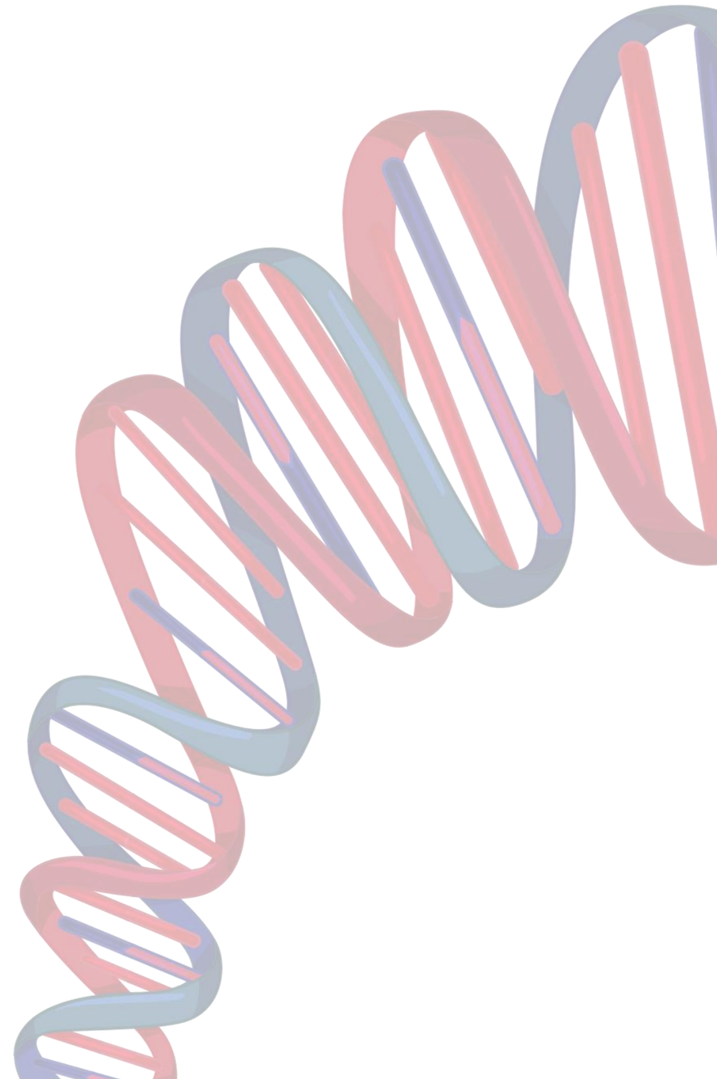
Built: Computational Pipeline
Designed and *in silico* validated 100k+ novel editors for Parkinson's

Filed: Wilson Sonsini Provisional Patent
Filed foundational IP with ***WSGR*** for AI-driven design and evaluation platform

Awarded: Golden Tickets
Won Golden Tickets from ***Chiesi*** + ***LabCentral***—2 years of funded lab space

Invited: Michael J. Fox Initiative
Joined the ***Michael J. Fox Foundation****'s* LRRK2 Therapeutics Exchange.

Announcing: In-Kind Resources Award
To be presented at BIO 2025 at Startup Stadium, June 17th



leadership team

neoclease

experts in CRISPR, AI, and biotech, driving bold cures

on a mission to cure genetic diseases

Chelsea Trengrove, PhD
CEO & Cofounder

REGENERON · sware · empatica

- Drove **multi-million dollar biotech partnerships**
- Led MIT startup's **yearly doubling of revenue**
- **Negotiated contracts with top Pharma**, CROs, NASA, US Army, and BARDA
- PhD in Neuroscience

Prof. Jin Liu, PhD
CTO & Cofounder

NIH · BHSAI · hsc · UTSouthwestern Medical Center

- **Tenured professor**, 40+ publications, **multiple patents** in AI/ML, gene editing, and synthetic biology
- Pioneer in AI-driven synbio, receiving multiple scientific awards
- Led teams in **drug discovery at the DoD**
- **PhD in Quantum Chemistry**, **NIH Postdoc**

Vivek Gowda
Head of Research

CRISPR THERAPEUTICS

- **10+ yrs gene-editing** at Harvard Medical School and **CRISPR Therapeutics**
- **Led R&D** programs to CTA/IND, including contributions to **first FDA-approved gene editor**
- Authored multiple regulatory reports for genome-editing filings
- Advisor on multimillion-dollar biotech investments

director and advisory board members

Vern Norviel
Scripps Research · WILSON SONSINI · Stanford Medicine · affymetrix · NEUVIVO

Andrew Hessel
HUMANE GENOMICS · GP-write

John Mattison, MD
UC San Diego · KAISER PERMANENTE · Arsenal Capital Partners

Justin Yang, MBA
BARDA · LYNDRA THERAPEUTICS · Global Health Investment Corporation

contact

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CEO & Cofounder
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APPENDIX

supporting slides

neoclease

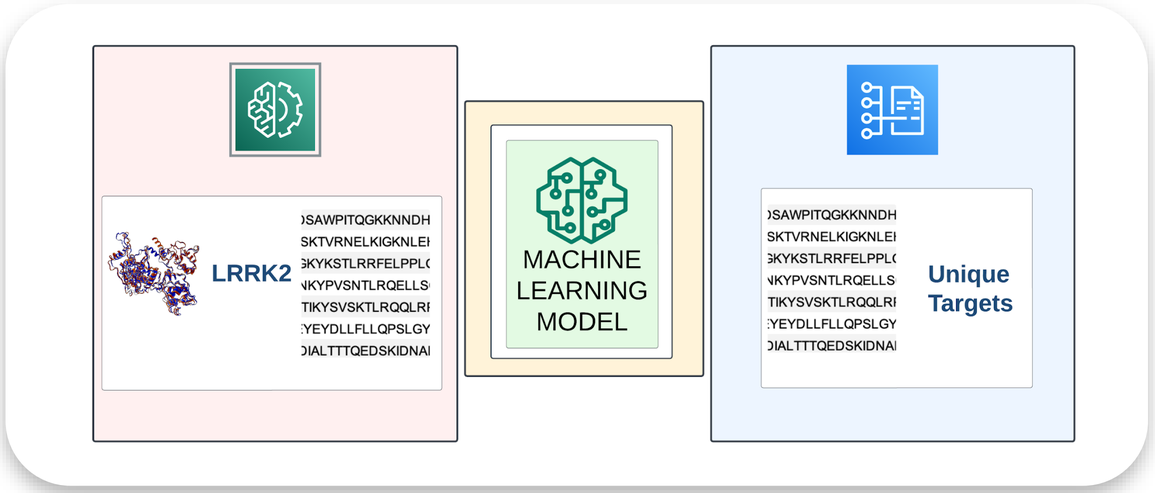
wet lab validation

confirming editing efficiency, specificity, and superiority

Step	Purpose / Outcome
1. Transfection	Assess gene editor activity in human cells (HEK293T + SH-SY5Y)
2. On-Target Validation	Quantify on-target LRRK2 knockout via PCR + Sanger
3. Optimization Cycle	Refine and select top candidates through iterative screening
4. Off-Target Analysis	Genome-wide off-target detection via NGS to assess safety
5. Benchmarking	Benchmark against spCas9 + OpenCRISPR-1 to demonstrate platform advantage

LRRK2 unique targets

Our model identifies sequences in LRRK2 found nowhere else in the genome, ensuring build specificity



Precision Targeting - A unique target ensures that the editing tool only binds to the intended location

Reduced Off-Target Effects - Reduce the risk of altering other genes or regulatory elements that could lead to harmful consequences or unintended mutations.

Enhanced Safety - Potential for unintended edits in other genes is minimized, making the editor safer for therapeutic and *in vivo* applications.

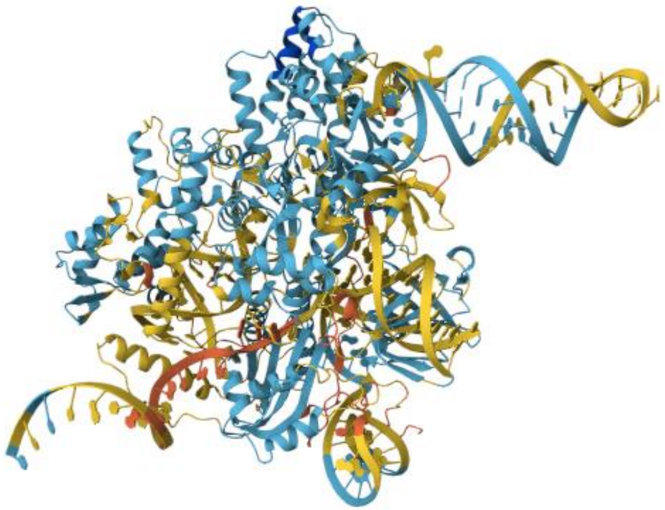
We have identified unique targets within LRRK2

Creating a model to predict efficiency scores of target sequences

novel AI-generated sequences

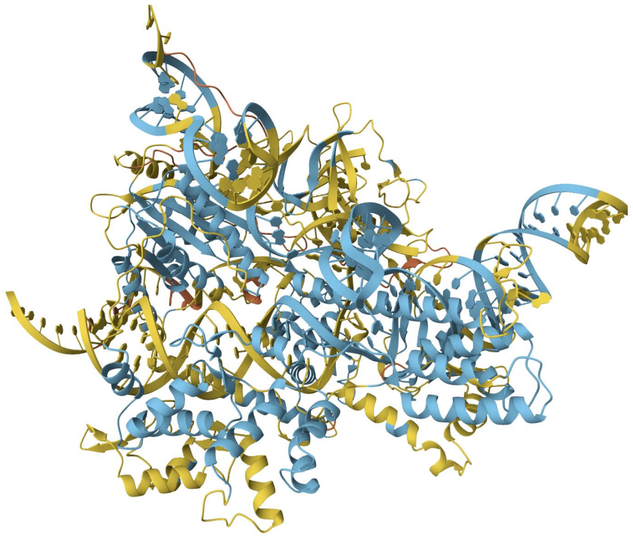
atomic level binding predictions

ipTM= 0.78 pTM= 0.81
25% Identity with SpCas9



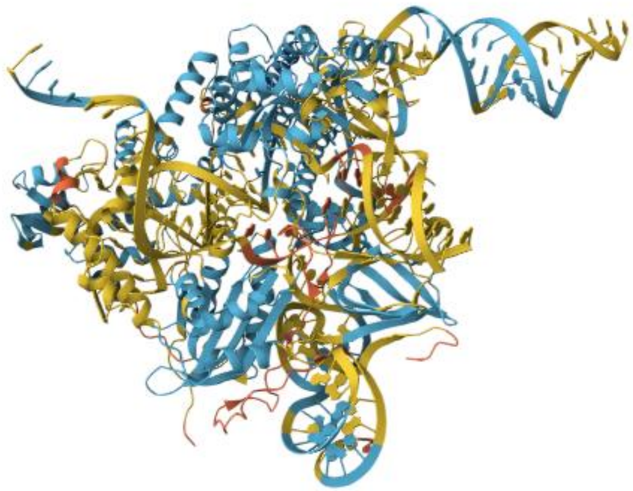
Novel SeqID7
Unique Target 1

ipTM= 0.8146 pTM= 0.8361
24.44% Identity with SpCas9



Novel SeqID58
Unique Target 1

ipTM= 0.76 pTM= 0.7854
24.79% Identity with SpCas9



Novel SeqID9122
Unique Target 3

DNA/RNA binding prediction with unique targets to LRRK2 gene sequence

commercial opportunity & partner landscape

neoclease

why now: first-mover advantage in LRRK2 editing

First-in-Class
AI-designed genetic medicine targeting LRRK2 in Parkinson's

Market Potential
Unlocks $5B+ Parkinson's therapeutic market

De-Risked Approach
In vitro validation **attracts early pharma engagement**

Accelerated Pathways
Fast Track, RMAT, Breakthrough Therapy designations

Validated Market: Active Acquirers + Partners

Company	Focus Area	Key Investments in Gene Editing
Biogen	Neurodegeneration, Parkinson's	$1B+ LRRK2 inhibitor (Denali)
Denali	Parkinson's, CNS Disorders	LRRK2 therapies, Biogen deal
Voyager	Gene therapy, AAV Delivery	Deals with Novartis, Neurocrine, AbbVie
Novartis	Gene Therapy, Rare Diseases	Up to $1.3B partnership with Voyager
AbbVie	Neuroscience, Parkinson's	Partnered with Voyager on AAV
Lilly	CNS & Neurodegeneration	$1.4B investment in AAV gene therapies to the CNS

All invest in Parkinson’s, LRRK2, or gene therapy - clear fit for Neoclease licensing or M&A

novel editors

neoclease

Demonstrated ability to generate novel editors.
Generating low sequence similarity while conserving structural and functional domains.

Model Inputs

Classification training

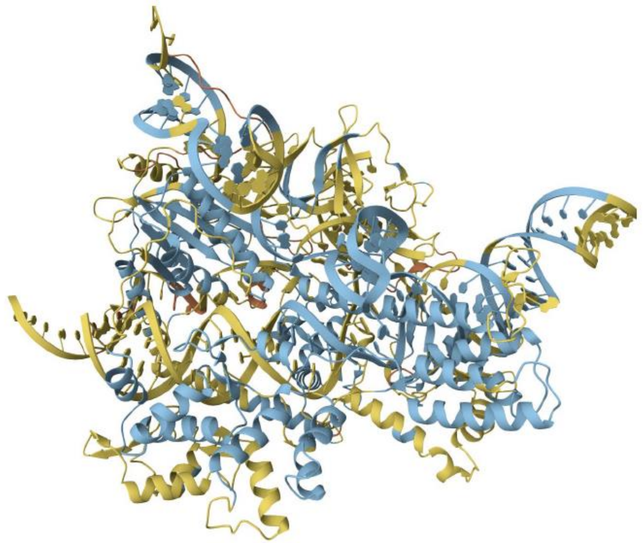
- Cas-like nucleases (i.e. cas9, cas12a, etc.)
- TALENs
- Zinc fingers
- Meganucleases
- Base editors
- Novel nucleases

Feature training

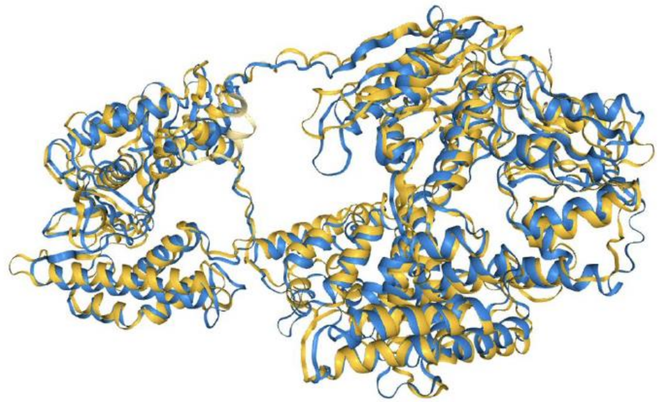
- Size, sequence identity, domains, polarity, charge, binding energies, cleavage efficacy, metal-ion dependence, etc.

Novel AI-Generated Outputs

ipTM= 0.8146 pTM= 0.8361



TM-Score= 0.907 RMSD= 3.13



Strong folding and DNA/RNA binding prediction with target to **unique Parkinson's gene sequence.** Domain functionality similar to **Cas9**.

Overlay of our generated nuclease with *high structural similarity* and only **70% sequence identity** to known **Cas12**

We have generated and are evaluating 10,000s of novel Cas-like editors

top oncology candidate - HPV E6/E7

viral oncogenes

HPV-Driven Cancers, chiefly Cervical Cancer (and other anogenital cancers, HPV-positive head & neck cancers). HPV16 and HPV18 E6/E7 oncoproteins are ideal targets for gene knockout.

Knock out the HPV E6/E7 genes in tumor cells. By using CRISPR/Cas to introduce cuts within E6 or E7 DNA sequences, we can disrupt their function. Without E6/E7, the cancer cell's cell-cycle brakes (p53, Rb) would be restored, likely triggering growth arrest or apoptosis.

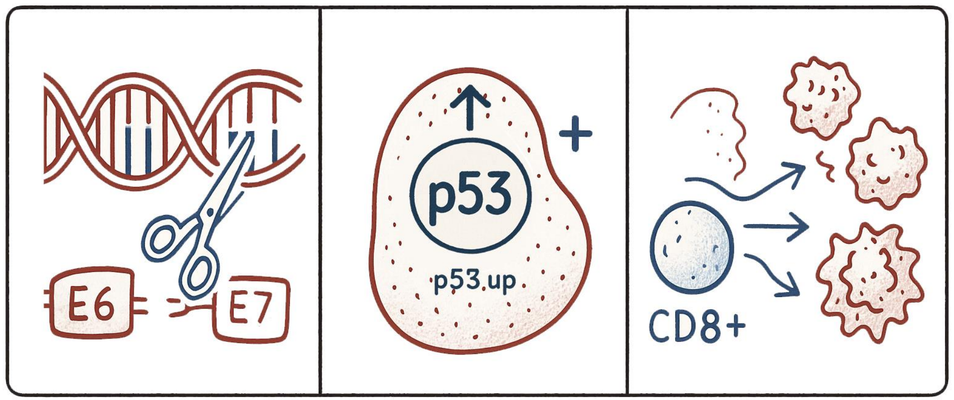
Cancer Indication	Oncogenic Driver	HPV Etiology	Annual Incidence (Global)	Annual Incidence (U.S.)
Cervical Cancer (advanced)	HPV16/18-derived E6 and E7 viral genes (integrated)	~95% of cases caused by high-risk HPV	~604,000; ~660,000 (2022)	~13,000 (2025)

HPV program

turning viral oncogenes into self-destruct buttons

Edit E6/E7 ➜ Reactivate p53/Rb ➜ Immunogenic tumor collapse

- AI-designed mini-nuclease (<900 aa) + dual guides targeting HPV16/18 E6/E7
- Frameshift knockout restores tumor-suppressor brakes within hours
- Immunogenic cell death releases viral neoantigens – natural I-O booster
- One-time dose, no chronic drug resistance, no viral integration issues



Three-step pathway