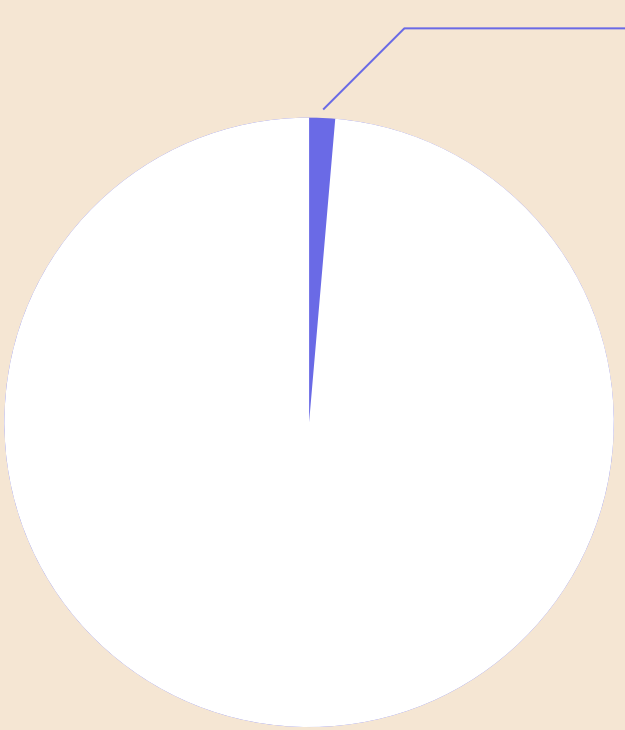
Dyno Therapeutics: Advancing AI & Delivery Frontiers to Empower Patients with Genetic Agency

Eric Kelsic, CEO & Cofounder

ASGCT 2026 SCIENTIFIC SYMPOSIUM

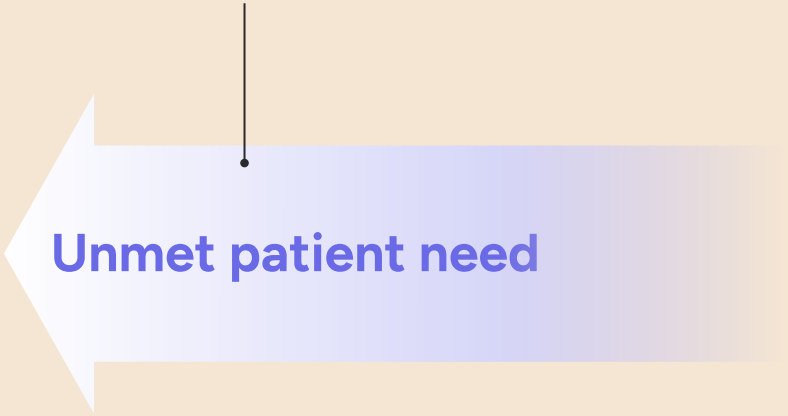
The challenges and massive opportunities for genetic medicine



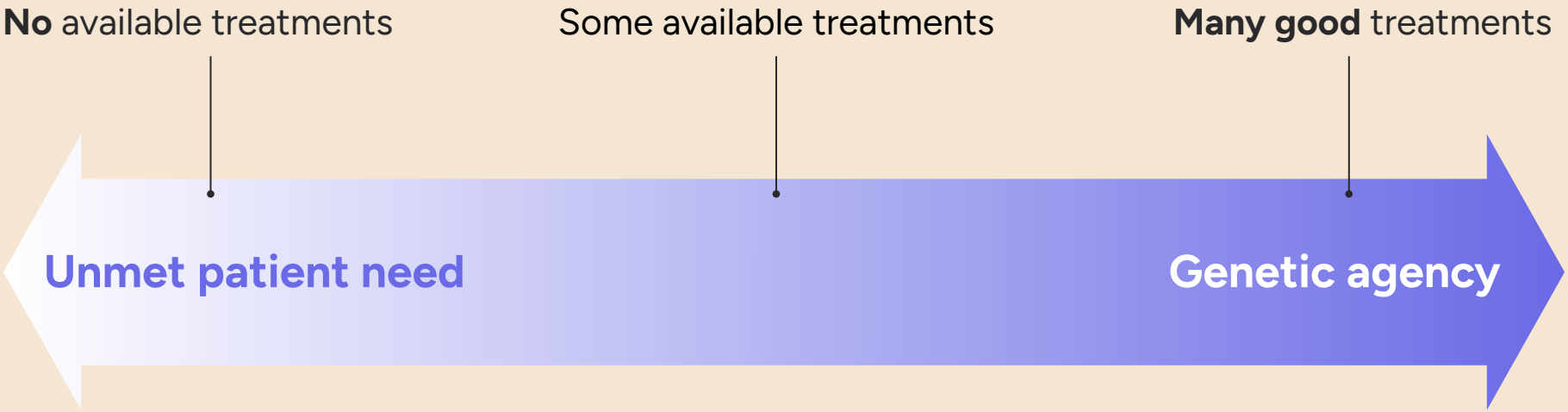
Effective treatments

Known genetic illnesses affecting 100’s of millions of people, with no ability to take action yet...

No available treatments




No available treatments
Some available treatments
Unmet patient need

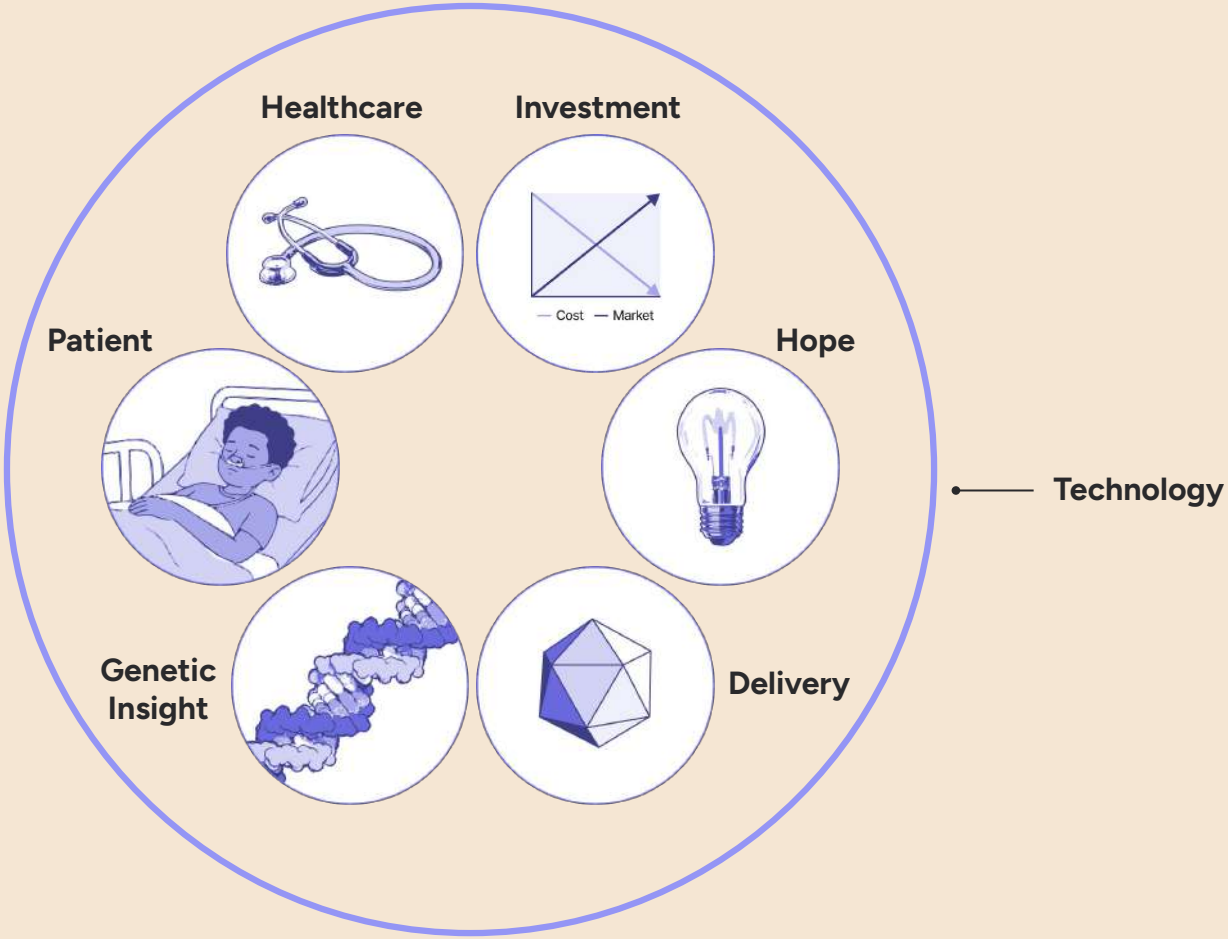


*"An **individual's** ability to take **action** at the **genetic** level to live a **healthier** life"*

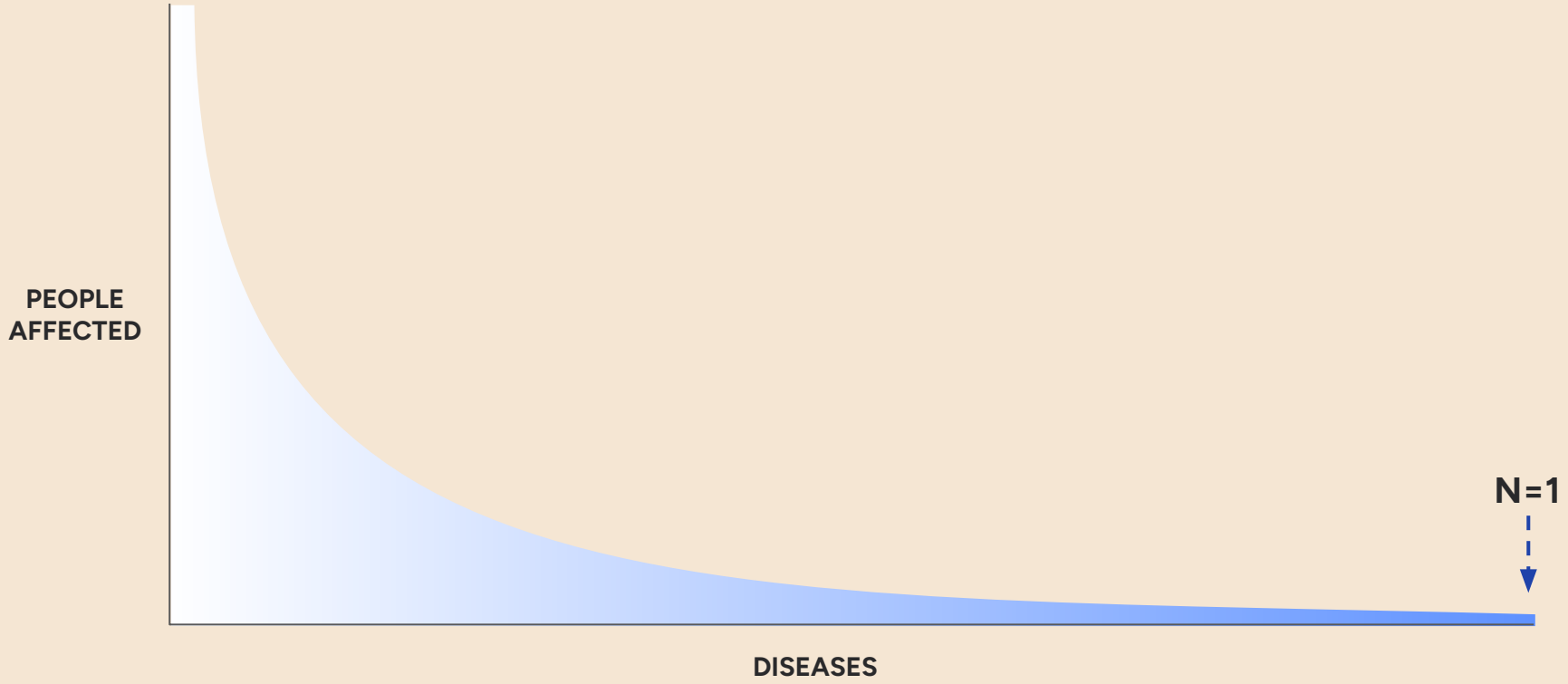
At Dyno, we are 100% focused on building genetic technologies to empower patients with genetic agency



Achieving Genetic Agency



Solving for the “long tail” of rare and ultra-rare diseases



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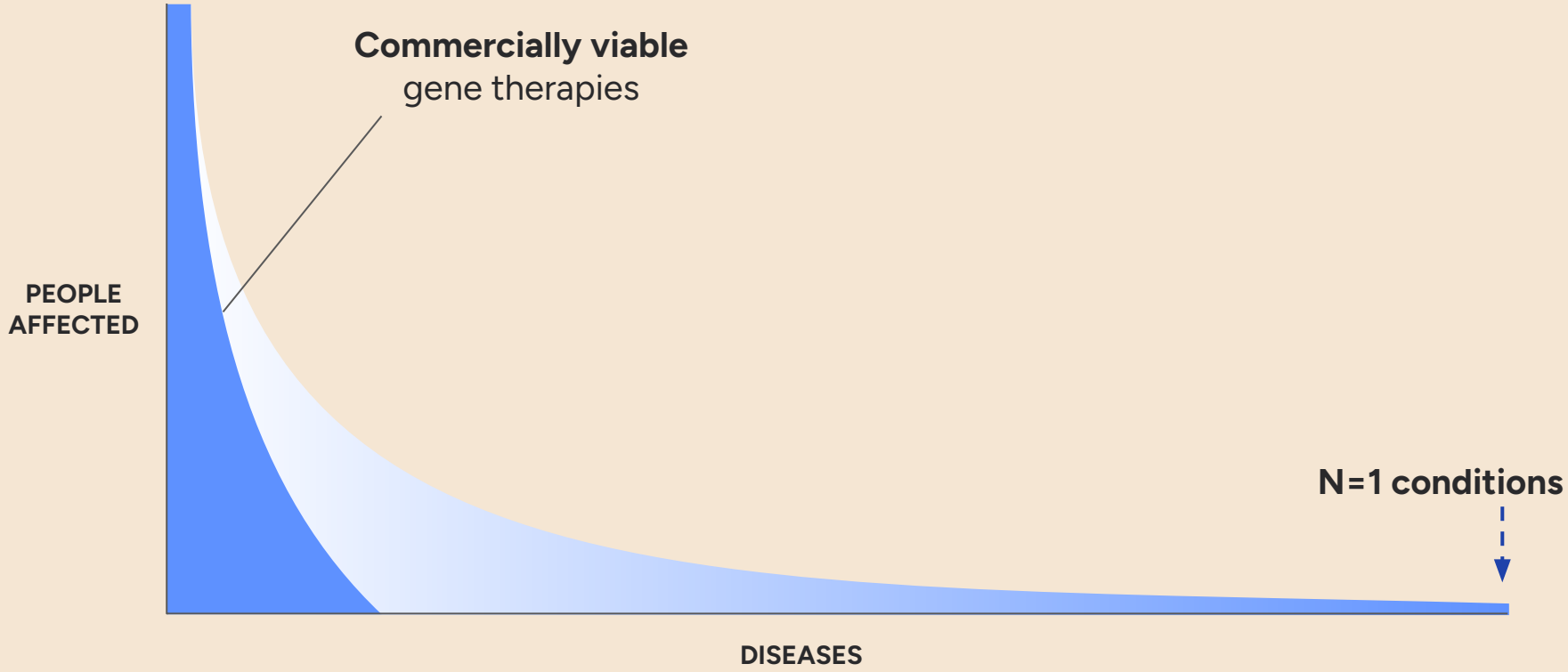

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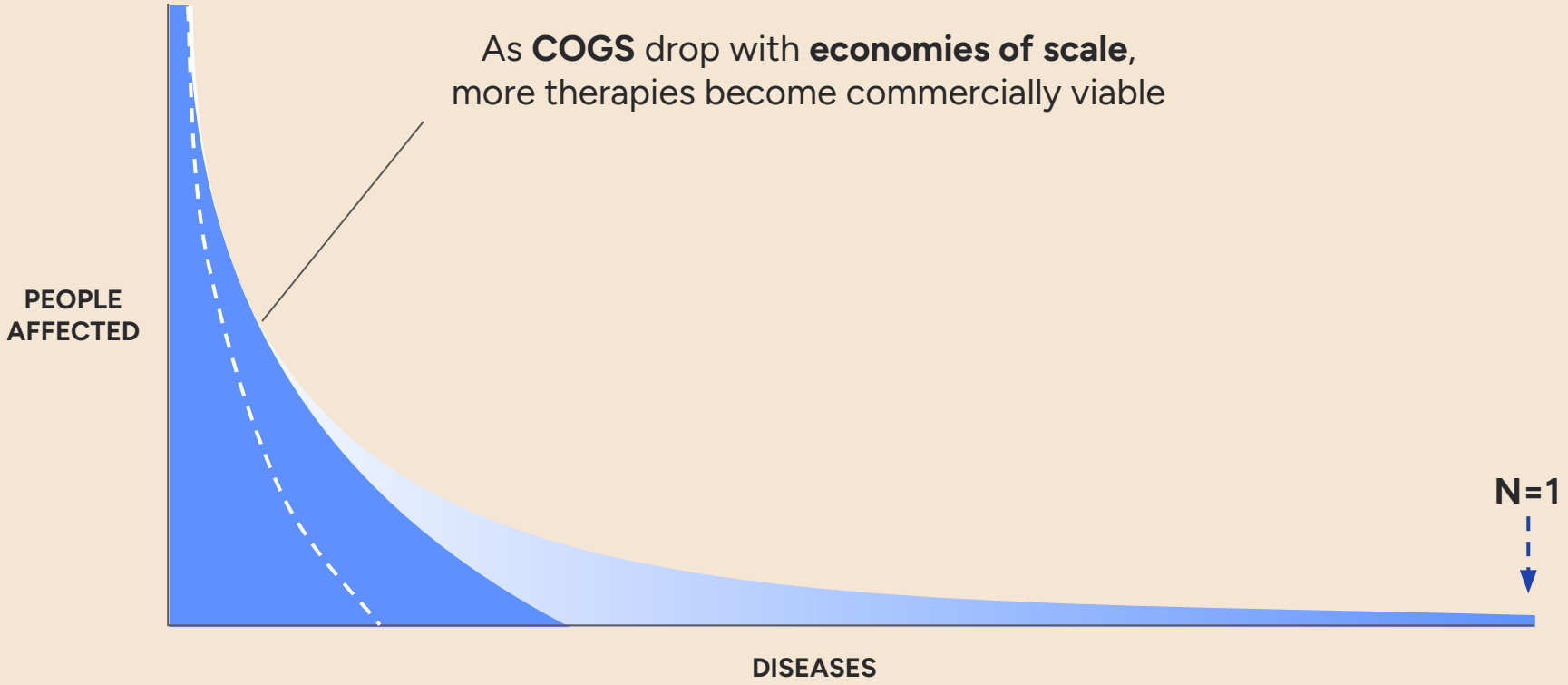


Solving for the “long tail” of rare and ultra-rare diseases



DELIVERY

opens the path to genetic agency

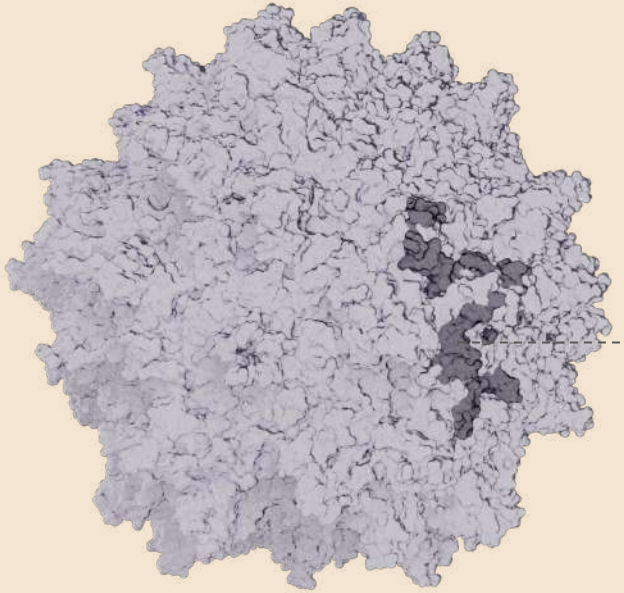


Dyno:

(noun) in climbing, a powerful jump across a rock face to reach a hold



AAV capsid: a ~736 letter sequence design problem



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HADAEFQERLKEDTSFGGNLGRAVFQAKKRLLEPLGLVEEAAKTAPG
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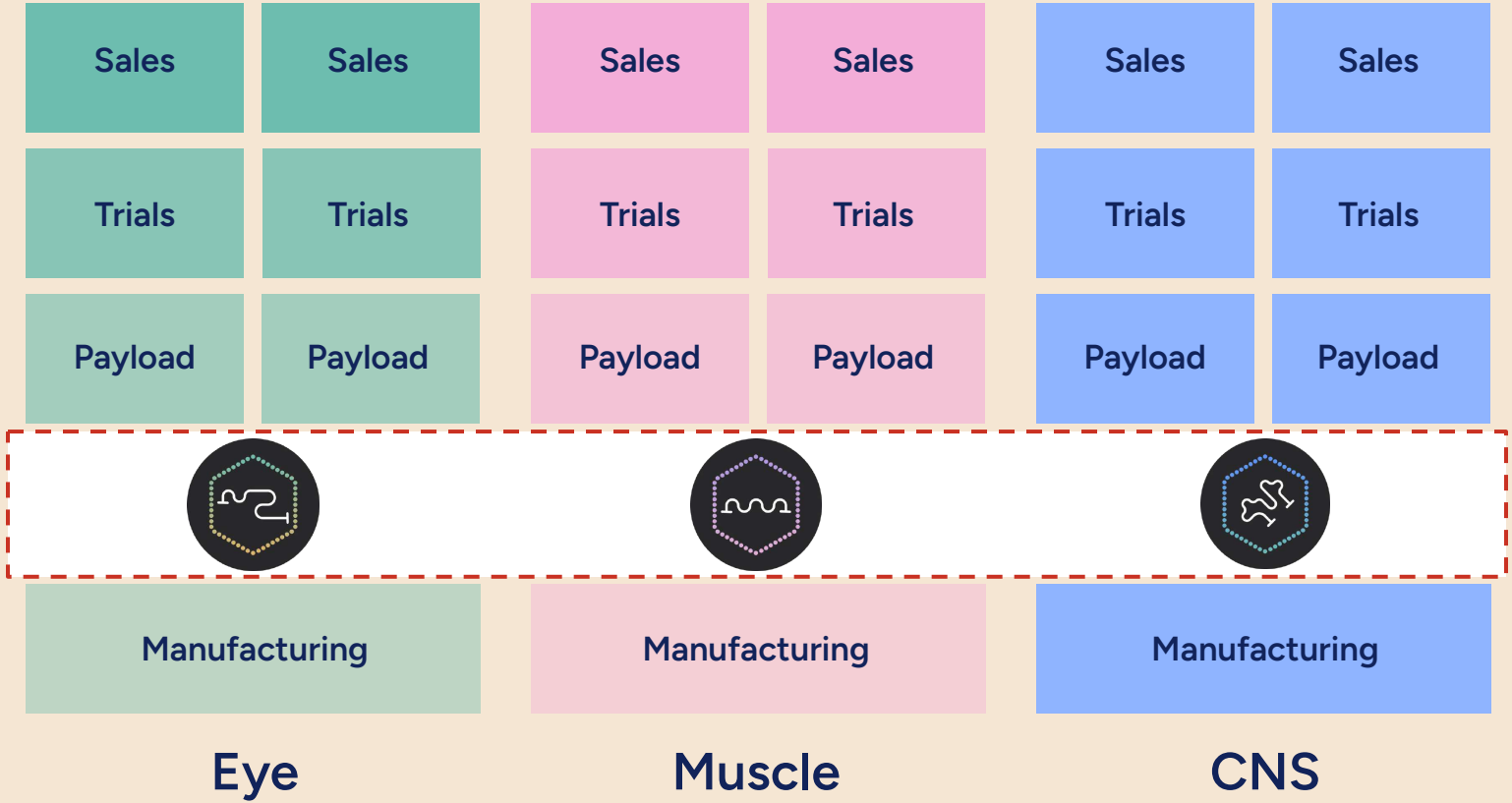
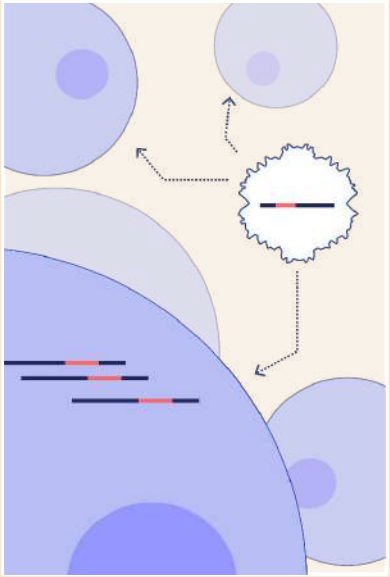
PTAFNKDKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY
YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL*

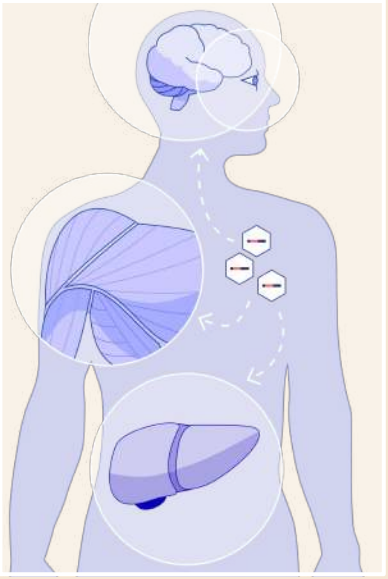
Dyno's focus has been to solve delivery generally and broadly



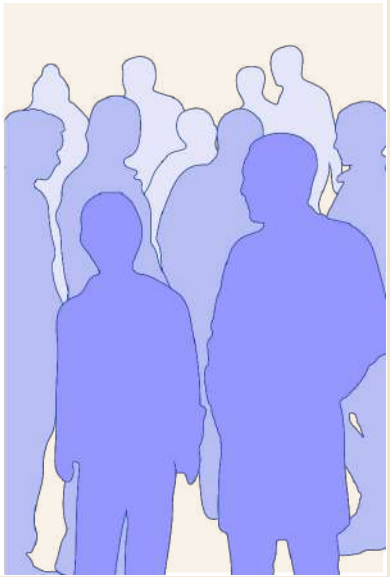
Every cell



Every organ



Every patient



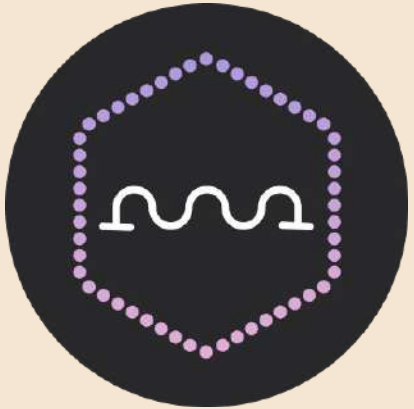
The capsids you need



Muscle



Neuromuscular



CNS

The capsids you need



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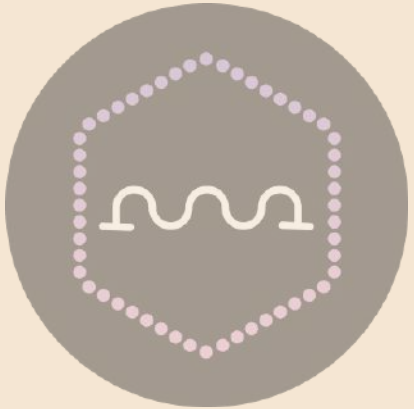


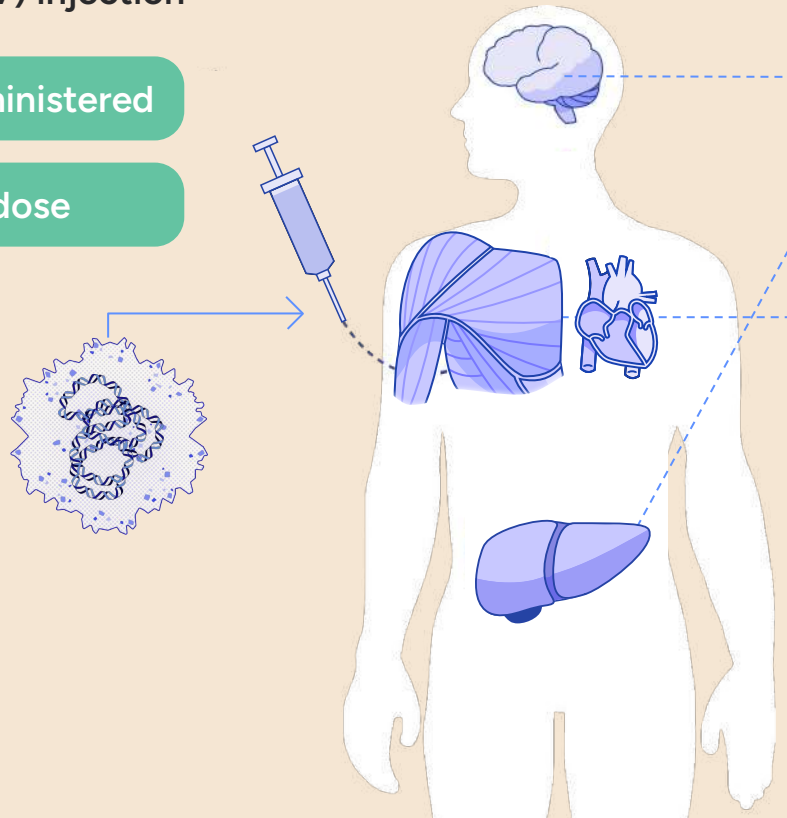
CNS

Challenge: safe and effective IV gene delivery

Intravenous (IV) injection

Easily administered

Low dose

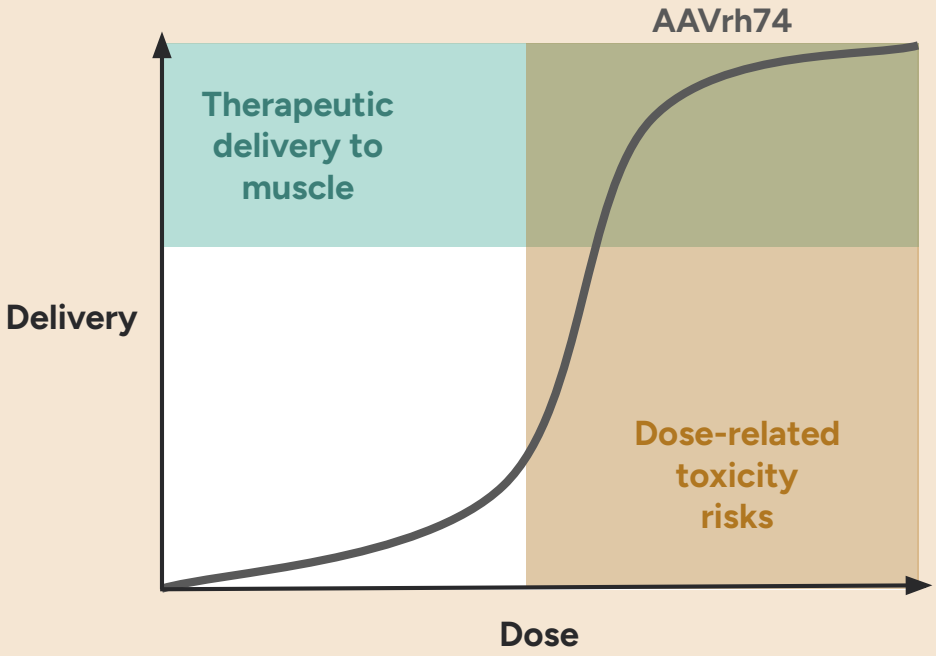


De-targeting peripheral organs

Transducing heart and skeletal muscle

Gene delivery for muscle remains challenging

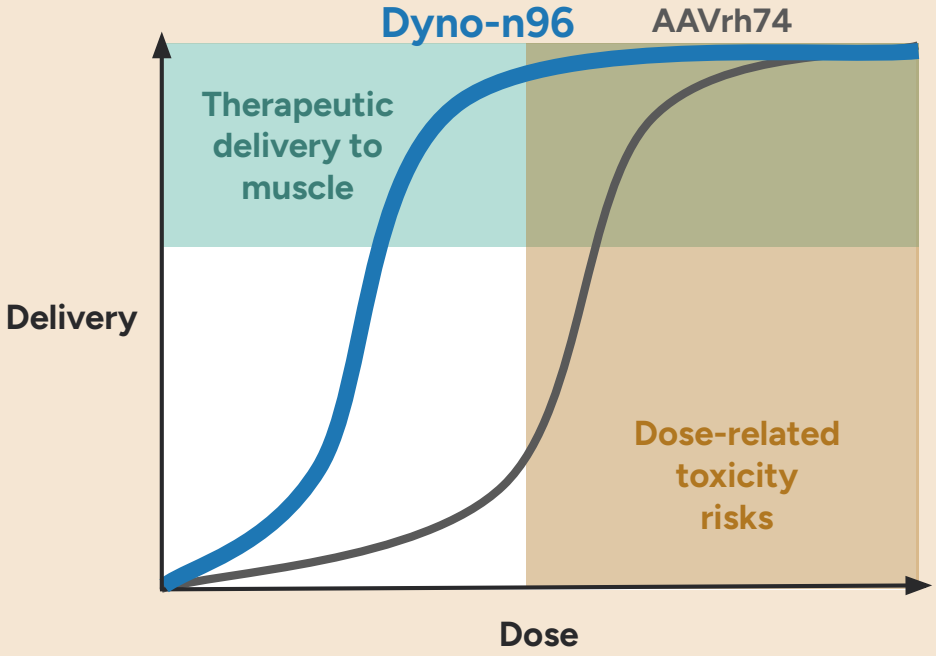
ELEVIDYS, the only FDA-approved gene therapy for muscular dystrophies, is an AAVrh74-based gene therapy that requires a high systemic dose of 1.33e14 vg/kg to reach efficacy



goal:

- Safer
- More effective

AI-designed Dyno-n96 achieves therapeutic delivery at a low dose, improving safety and reducing costs

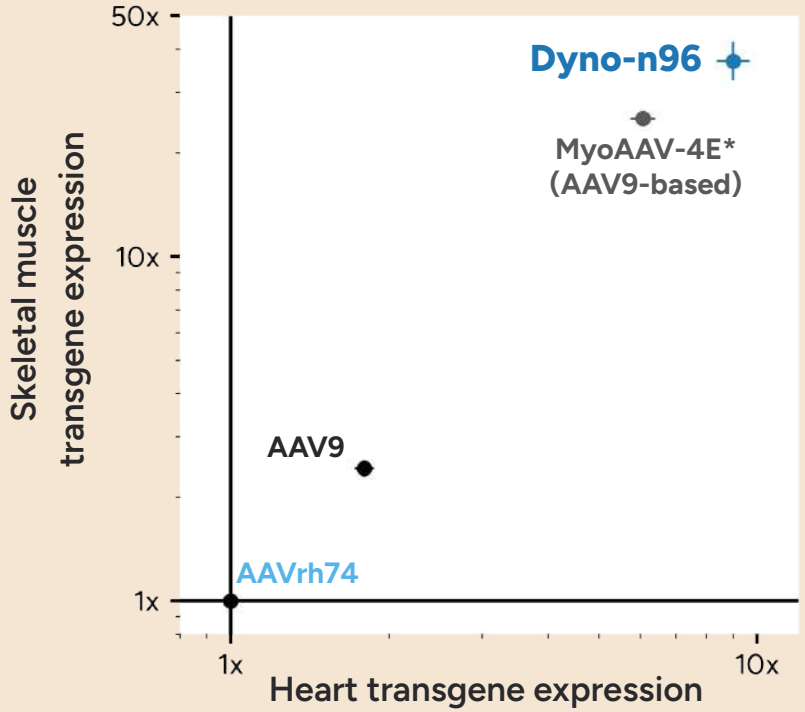


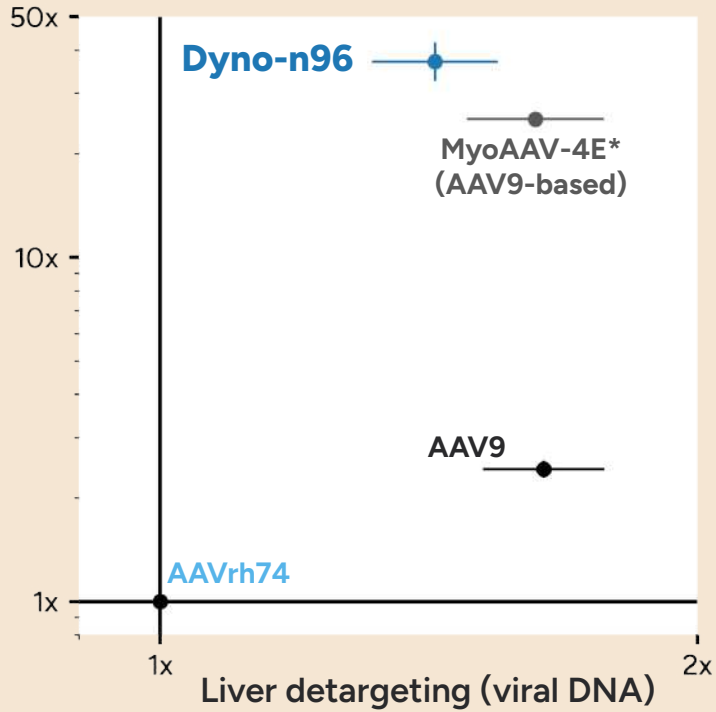
Dyno-n96

- Safer
- More effective

Optimized design of Dyno-n96 enables targeting skeletal muscle and heart while detargeting liver in NHP vs AAVrh74

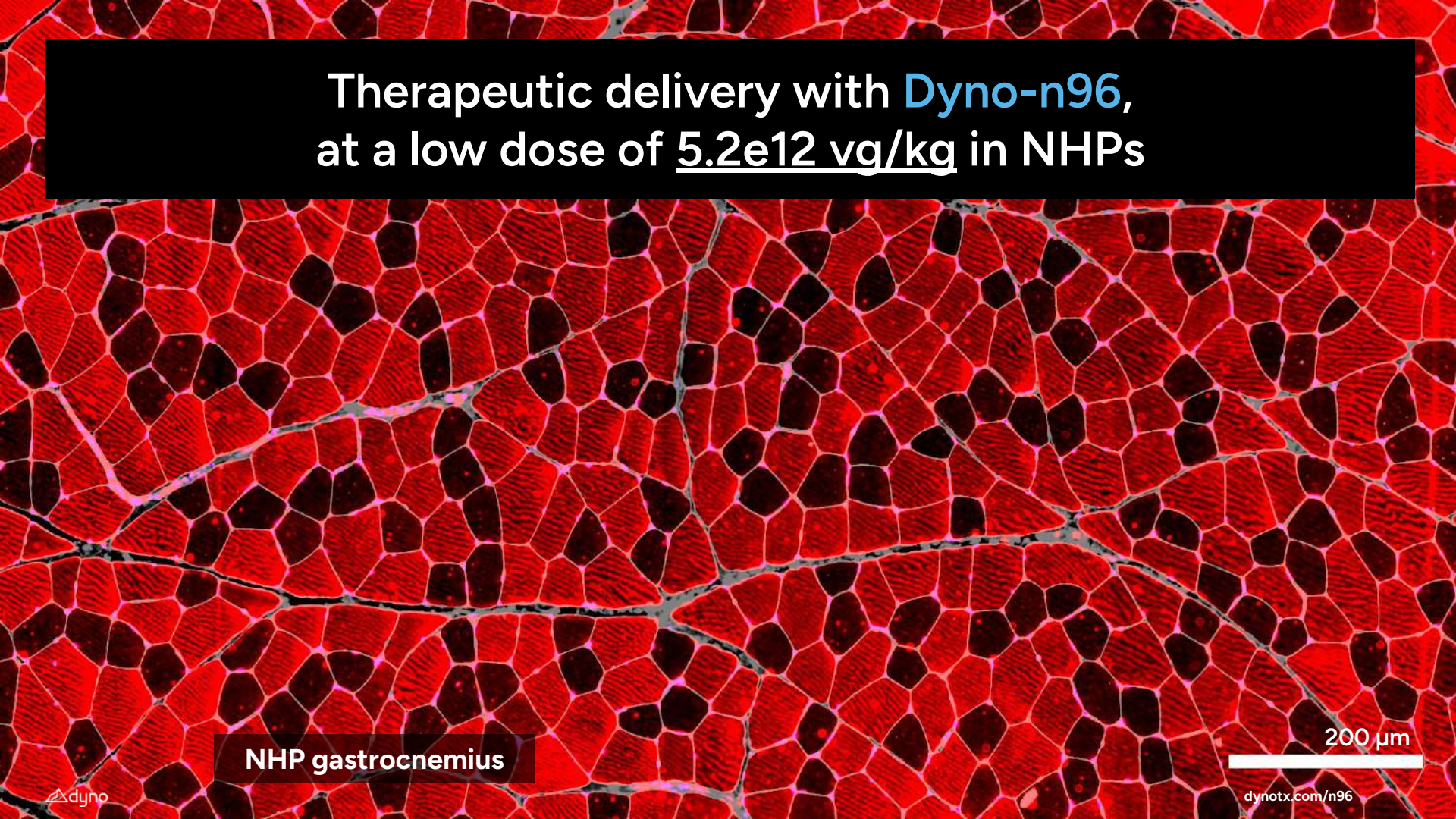
Data from small, pooled capsid study in NHPs

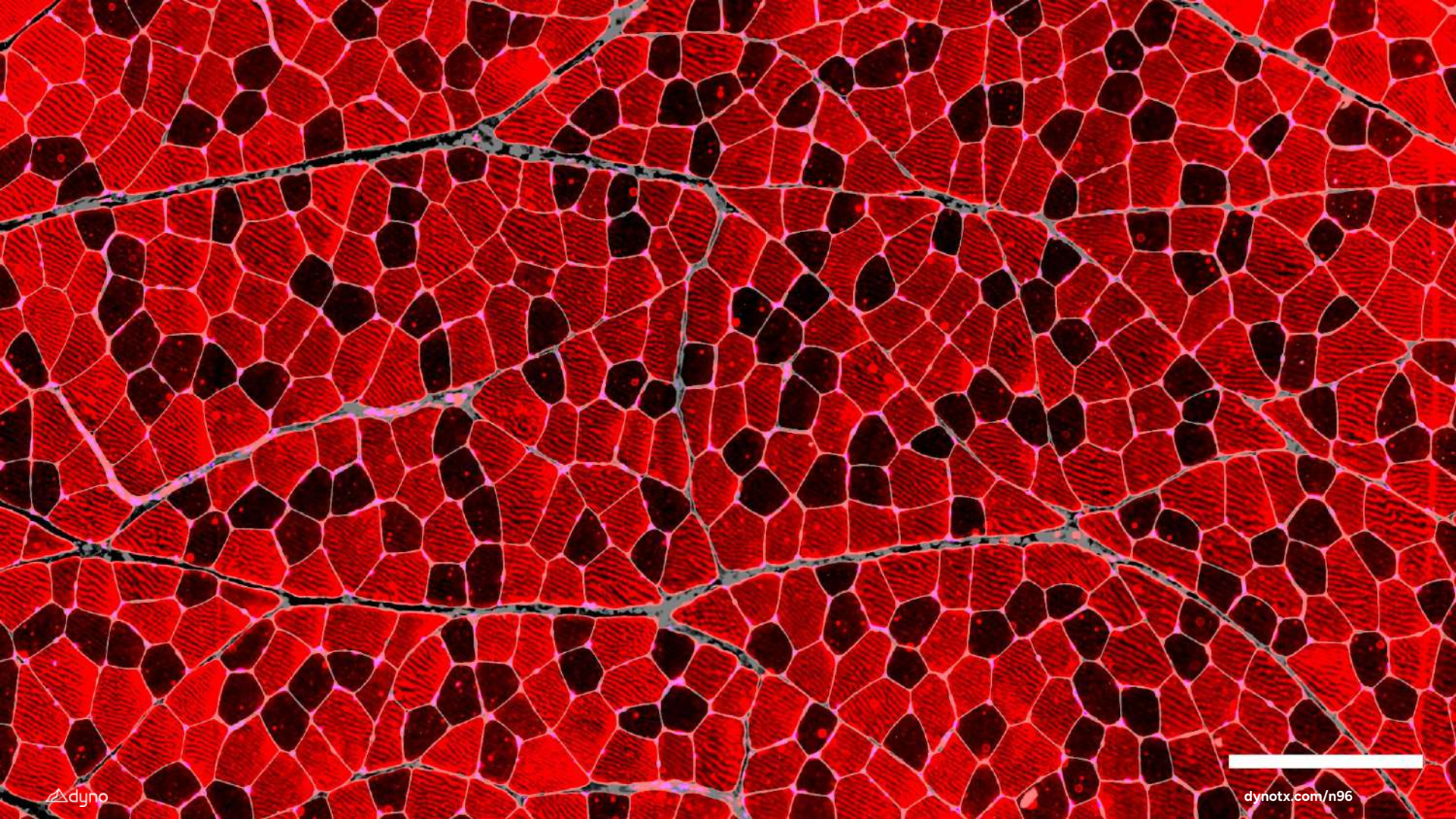




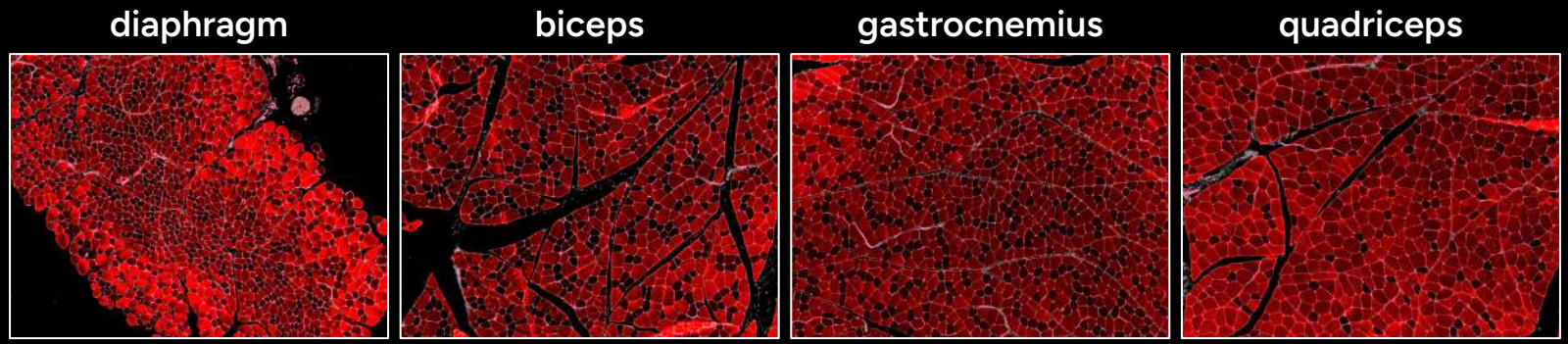
*MyoAAV-4E, Tabebordbar et al. 2021. *Cell*

Therapeutic delivery with Dyno-n96, at a low dose of 5.2e12 vg/kg in NHPs



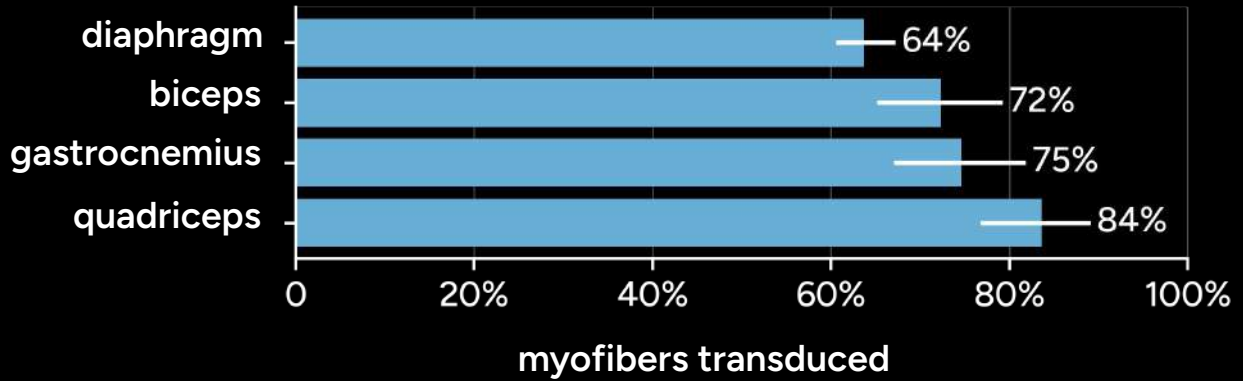

dyno
dynotx.com/n96

At 5.2e12 vg/kg, Dyno-n96 evenly transduces an average of 74% of skeletal myofibers across several tissues



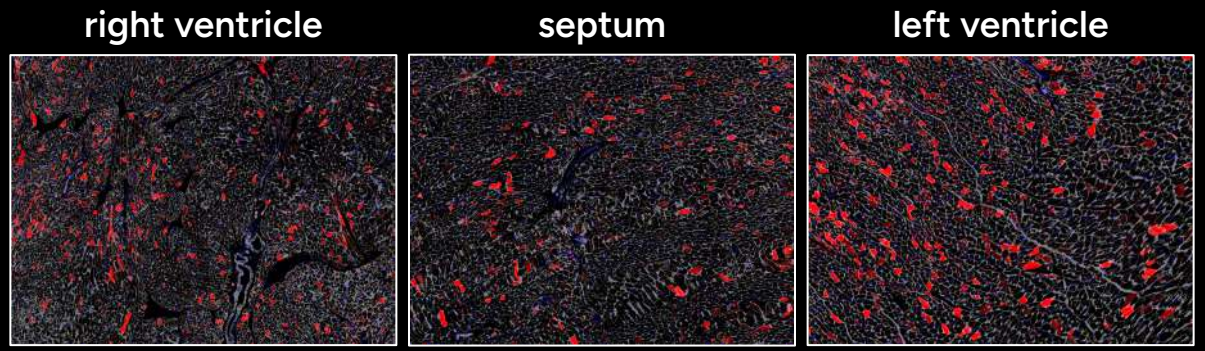
WGA, mCherry (Dyno-n96), DAPI

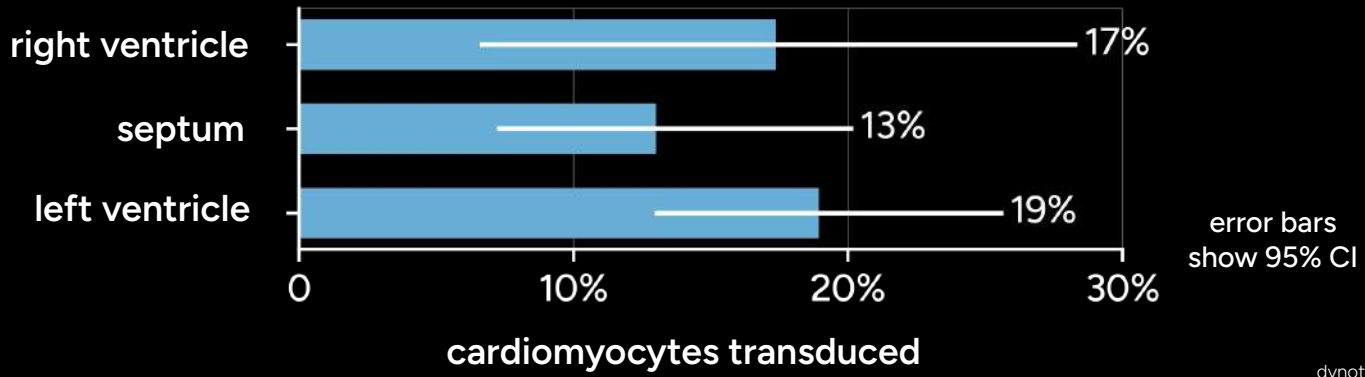
Scale = 200 µm



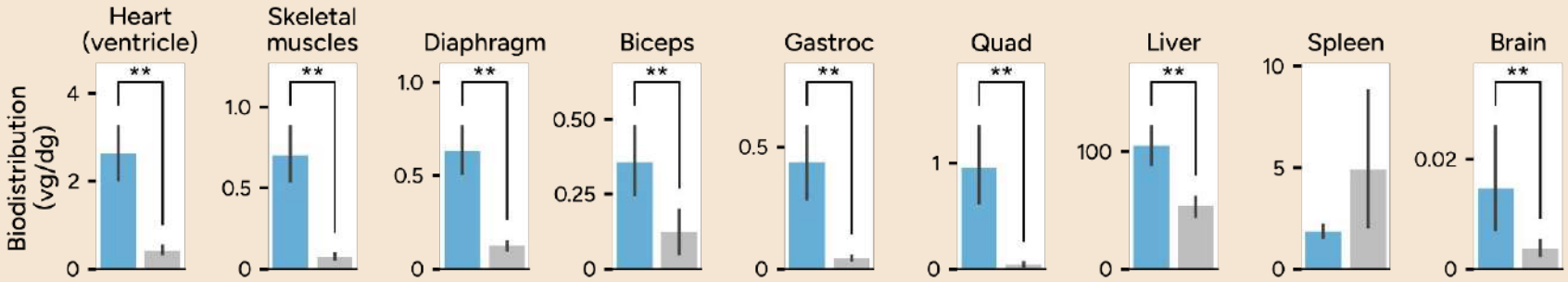
error bars show 95% CI

At 5.2e12 vg/kg, Dyno-n96 delivery to ventricular cardiomyocytes remains efficient, though variable





Dyno-n96 more potent than MyoAAV-4E in muscle and heart



Dyno-n96, 5.2e12 vg/kg

MyoAAV-4E, 5.2e12 vg/kg

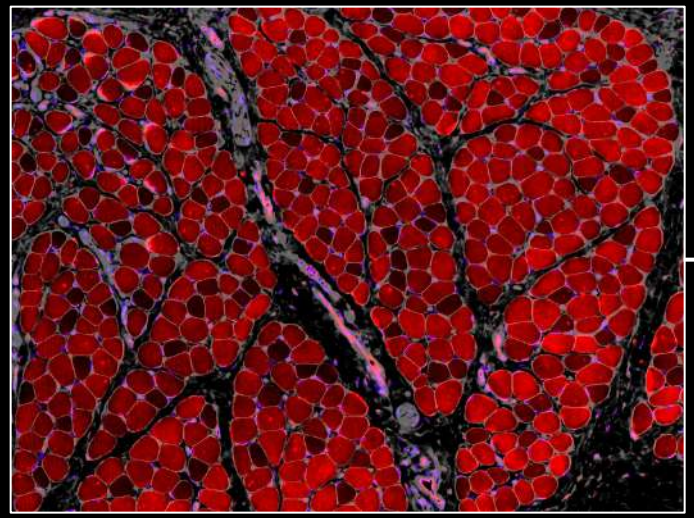
Error bars show 95% CI

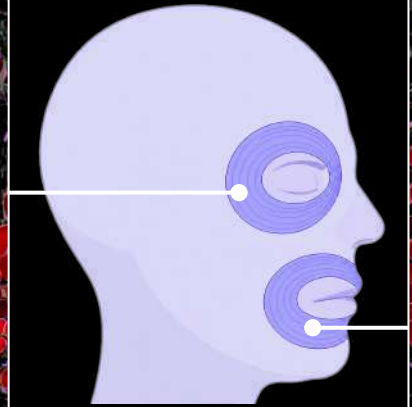
* p < 0.05

** p < 0.01

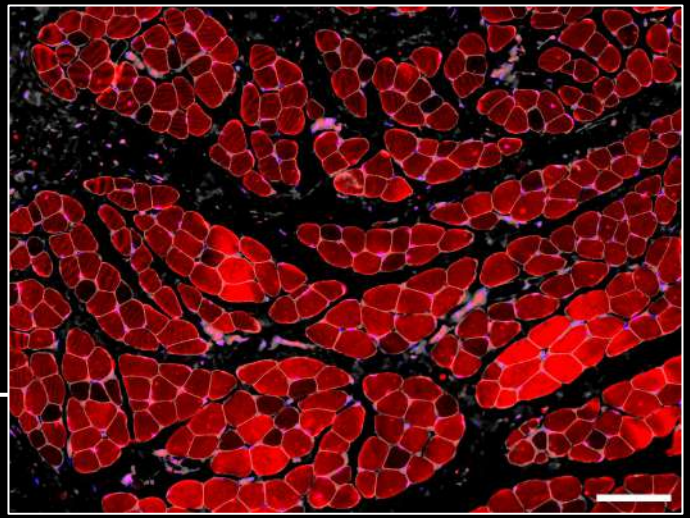
At 5.2e12 vg/kg, Dyno-n96 delivers efficiently to facial muscles in NHP, key targets for disorders such as FSHD

orbicularis oculi





orbicularis oris



WGA, mCherry (Dyno-n96), DAPI

Scale = 100 µm

Dyno-n96 transduces around 50% of satellite cells, positioning it as a promising candidate for gene editing applications

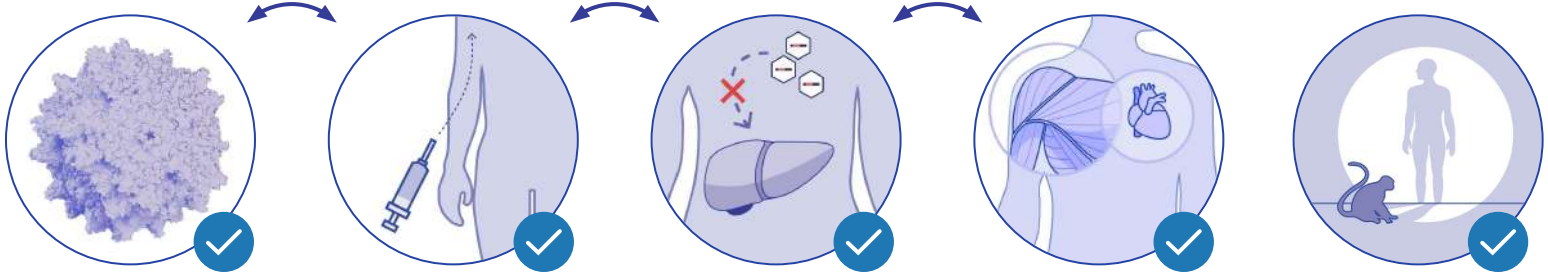


WGA, PAX7, mCherry (Dyno-n96), DAPI
5.2e12 vg/kg IV

Scale = 10 µm

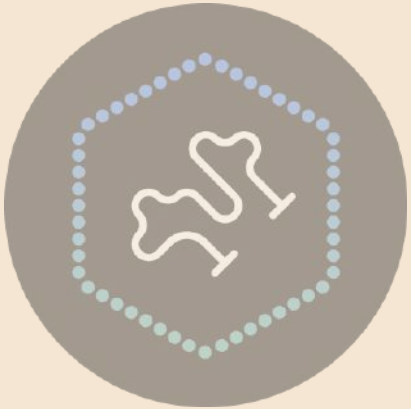
Dyno-n96 achieves therapeutic delivery to muscle at significantly lower doses and with improved liver detargeting

Lower cost | **Safety** | **Efficacy** | **Translation**



Efficient production	Efficient at low doses	Detargeted from liver	Targeted delivery to multiple organs	Predict performance in humans
similar production vs AAV9	**5.2e12vg/kg**	**1.4x** < AAVrh74 in liver	**74%** avg muscle **16%** avg heart at **5.2e12vg/kg**	**Enhanced transduction** in relevant human cell lines

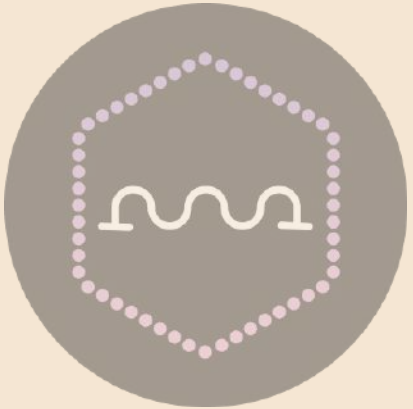
The capsids you need



Muscle



Neuromuscular



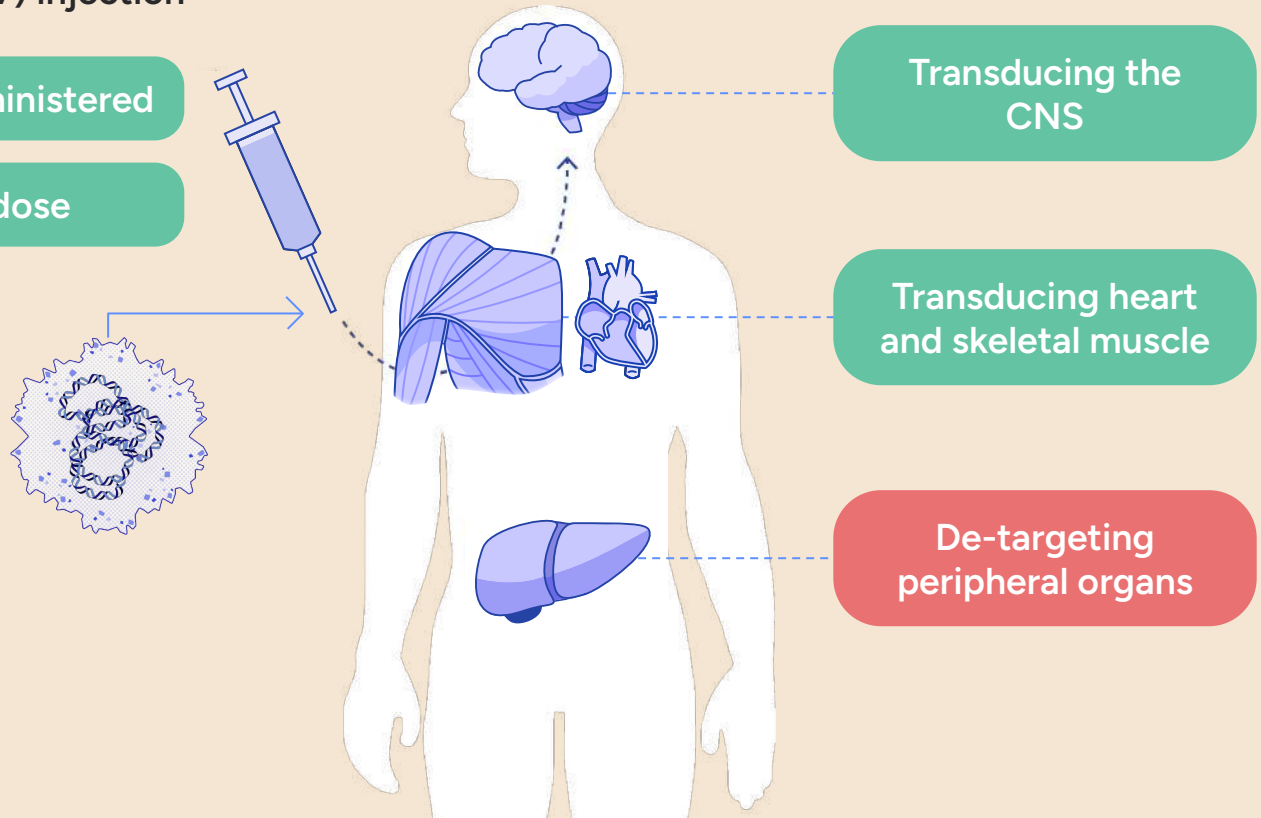
CNS

Challenge: safe and effective IV gene delivery

Intravenous (IV) injection

Easily administered

Low dose

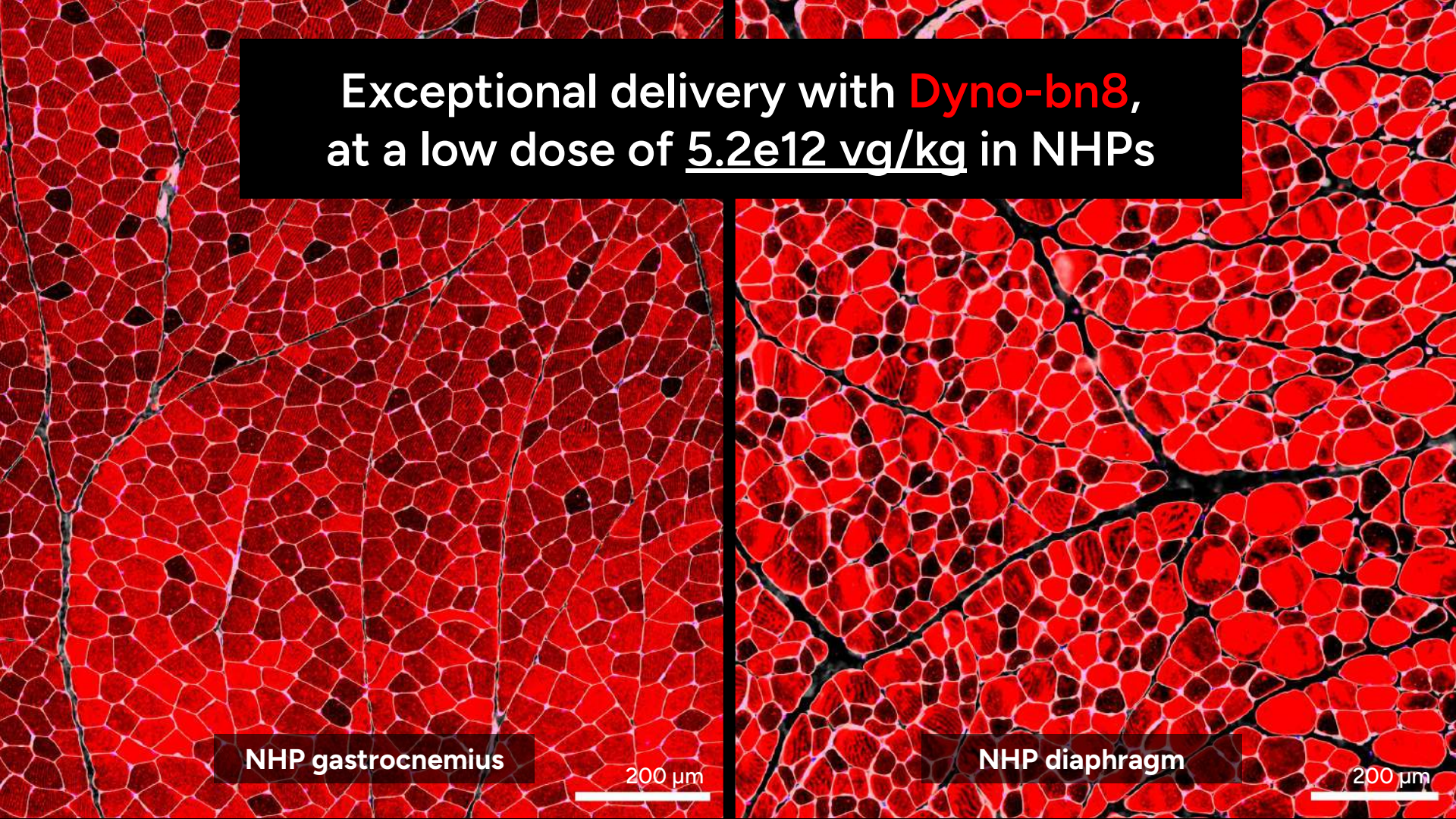


Transducing the CNS

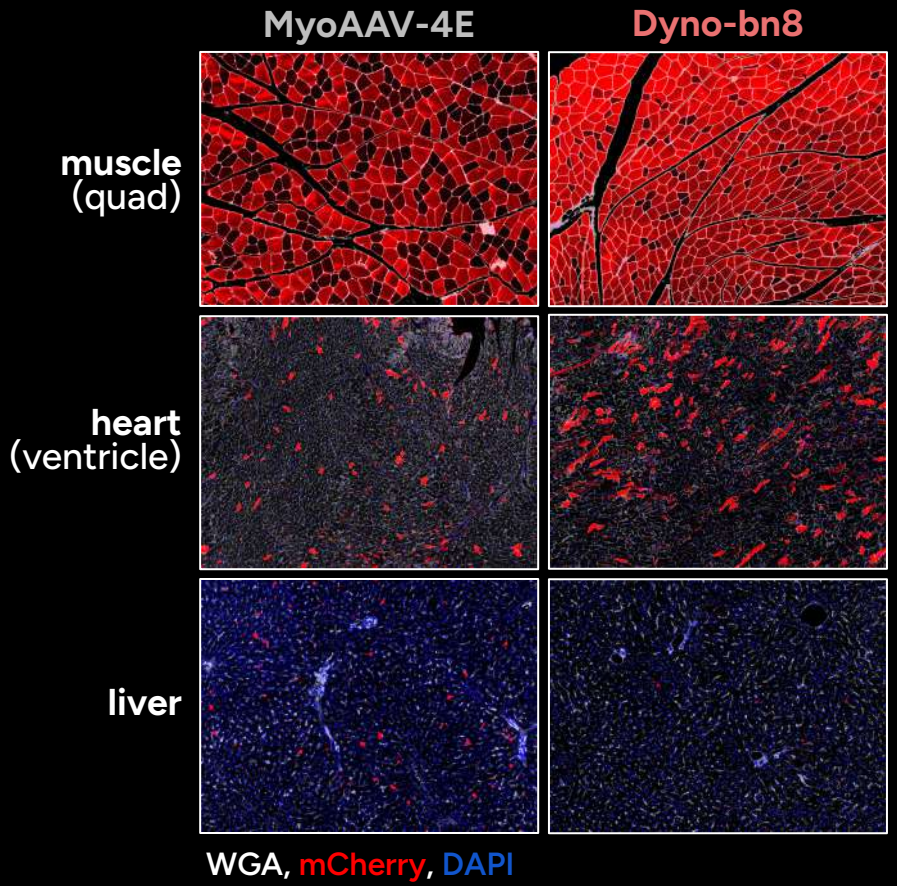
Transducing heart and skeletal muscle

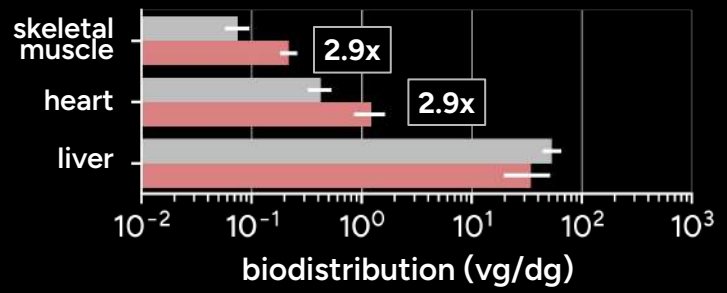
De-targeting peripheral organs

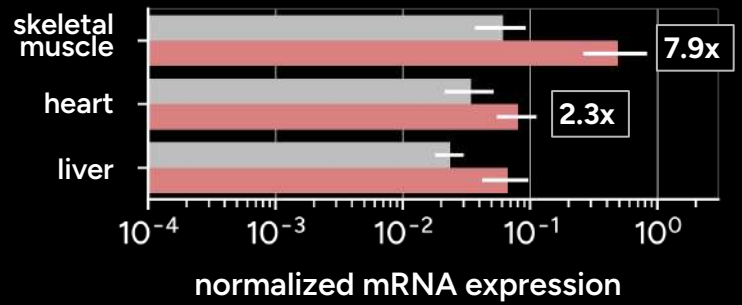
Exceptional delivery with Dyno-bn8, at a low dose of 5.2e12 vg/kg in NHPs

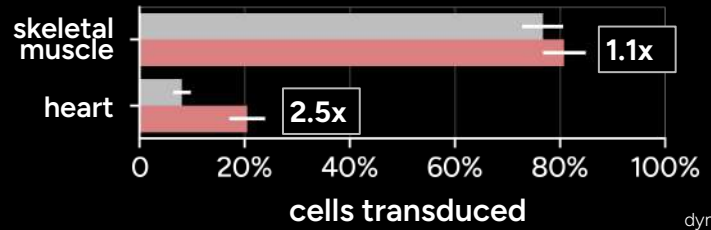


Dyno-bn8 outperforms MyoAAV-4E in muscle, heart, and liver



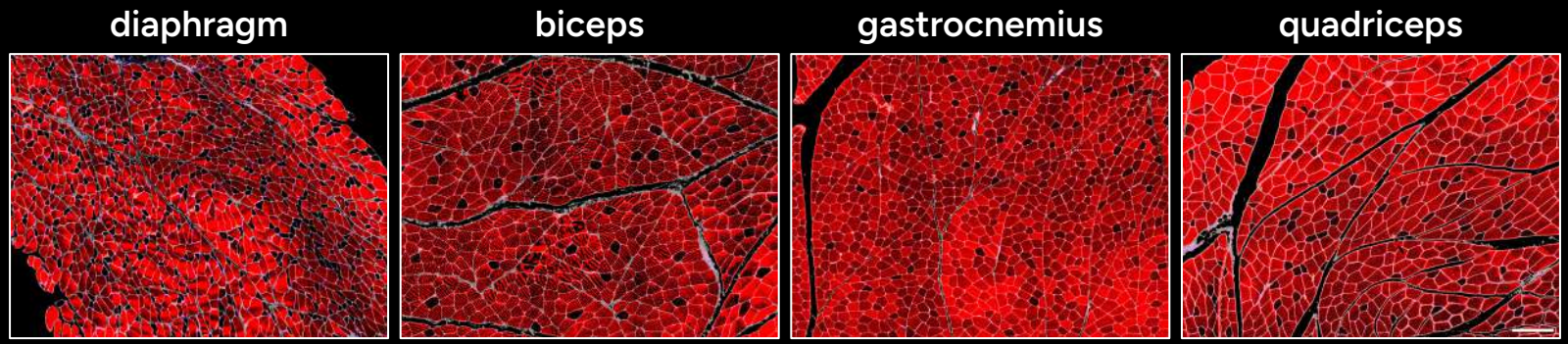


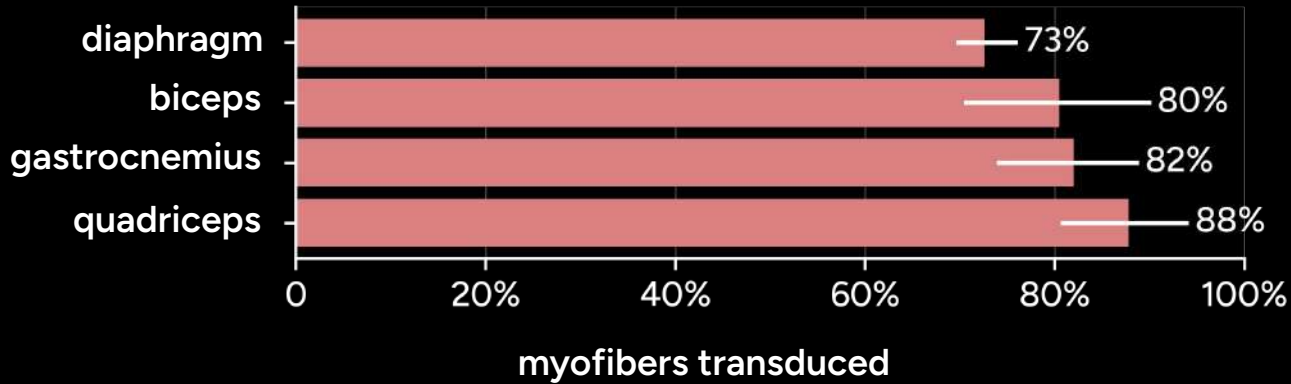




error bars show 95% CI

At 5.2e12 vg/kg, Dyno-bn8 evenly transduces the vast majority of skeletal myofibers in all tested tissues





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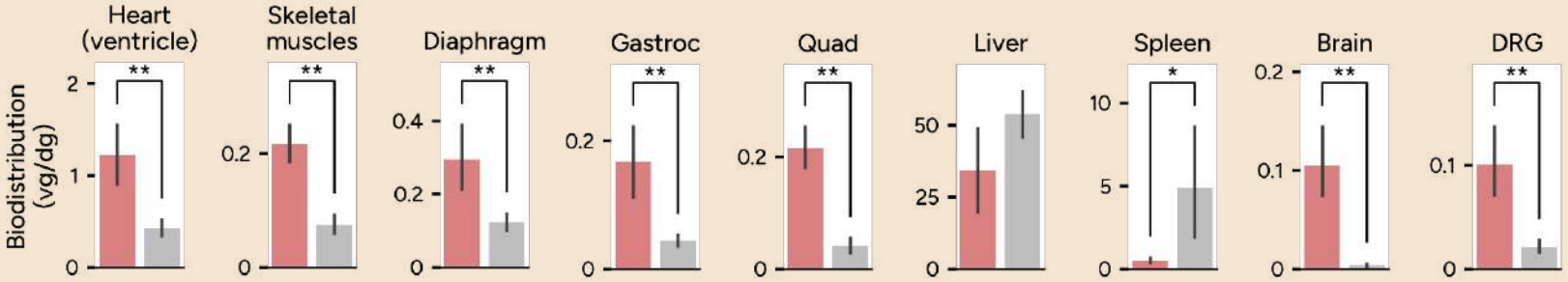


Dyno-bn8, 5.2e12 vg/kg

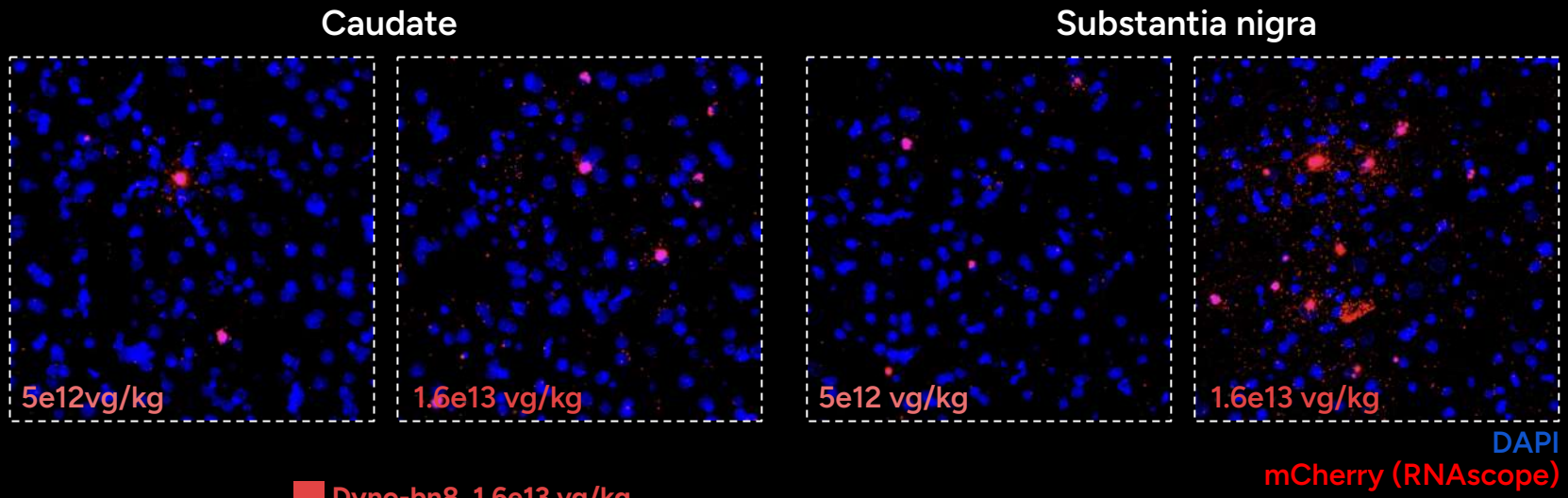
MyoAAV-4E, 5.2e12 vg/kg

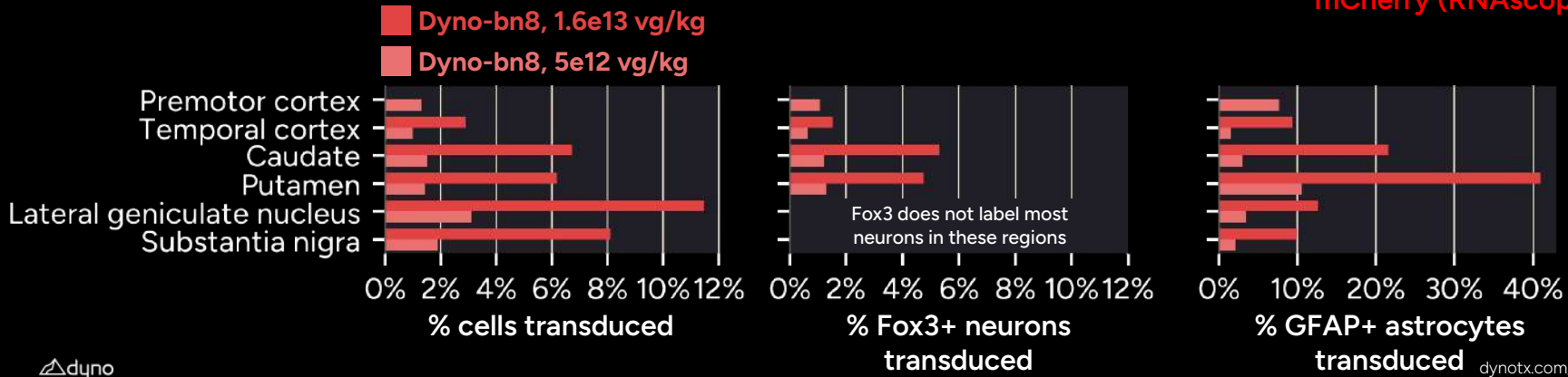
Error bars show 95% CI

* p < 0.05

** p < 0.01

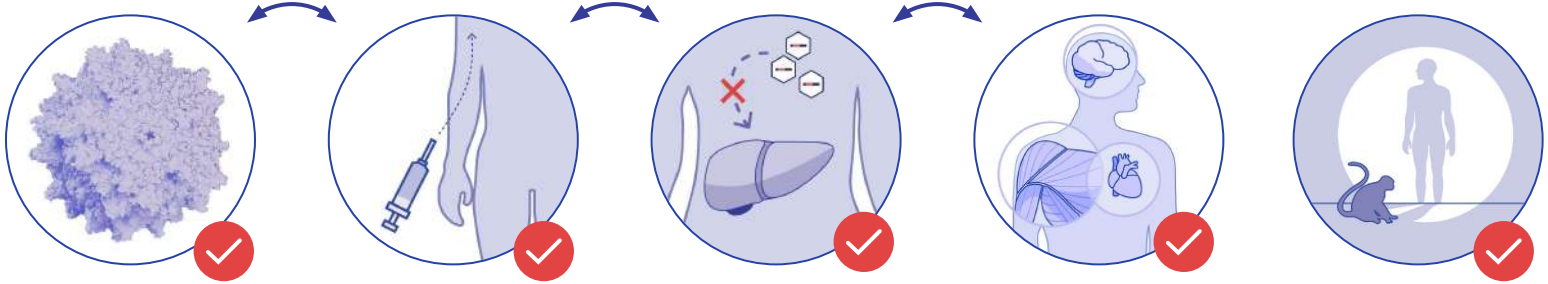
Dyno-bn8 transduces neuronal cells in the CNS





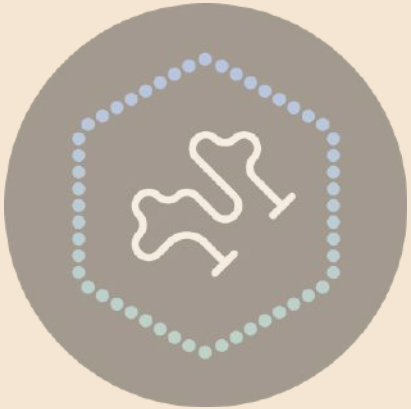
Dyno-bn8 achieves therapeutic delivery to muscle at lower doses and with improved liver detargeting

Lower cost | **Safety** | **Efficacy** | **Translation**



Efficient production	Efficient at low doses	Detargeted from liver	Efficient delivery to target organs	Predict performance in humans
similar production vs AAV9	1.6e13 vg/kg 5.2e12 vg/kg	34 vg/dg liver at 5.2e12 vg/kg	81% avg muscle at 5.2e12 vg/kg 40% avg heart at 1.6e13 vg/kg	Conserved receptor in NHP and humans

The capsids you need



Muscle



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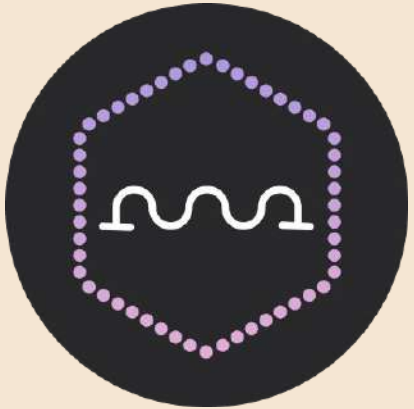

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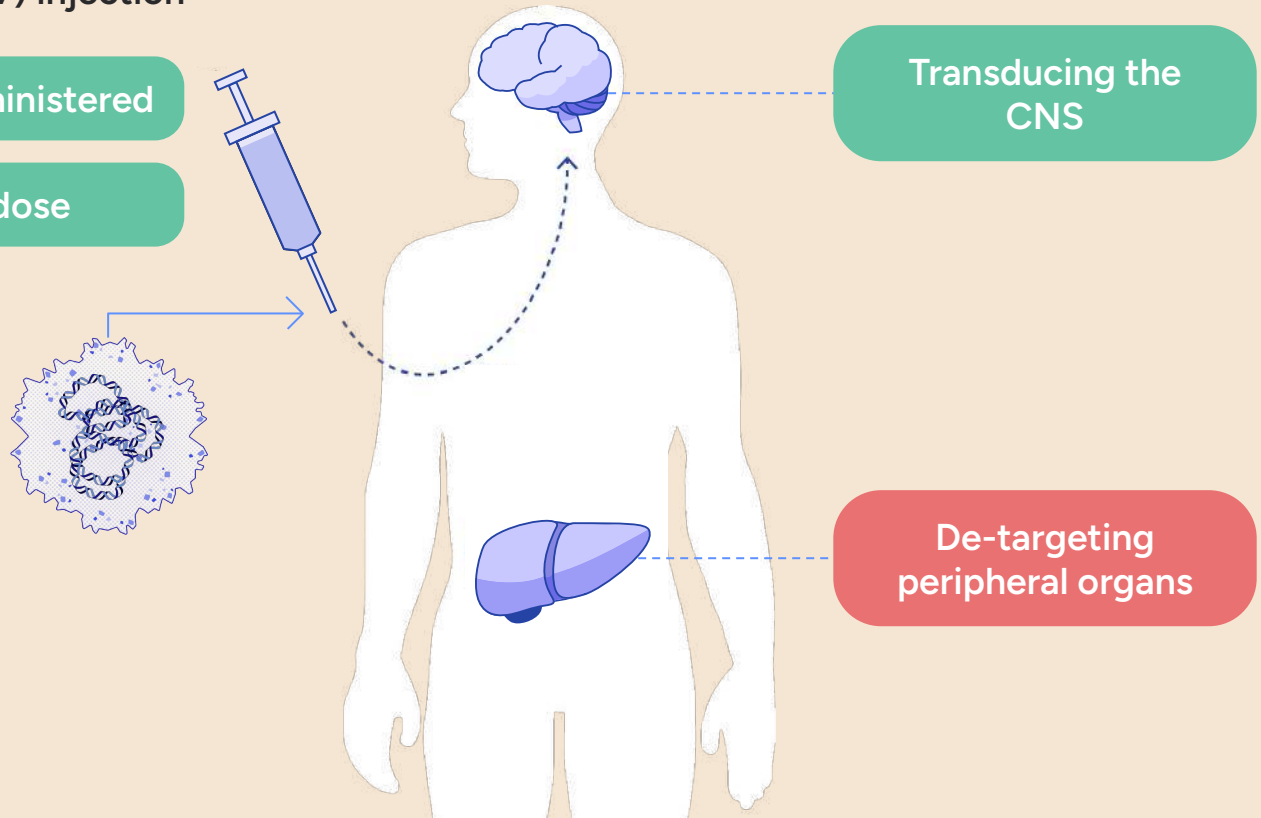


Transducing the CNS

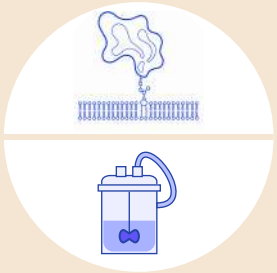
De-targeting peripheral organs

Understanding mechanism informs human translatability *and* improves design capabilities

Sequence



In vitro function

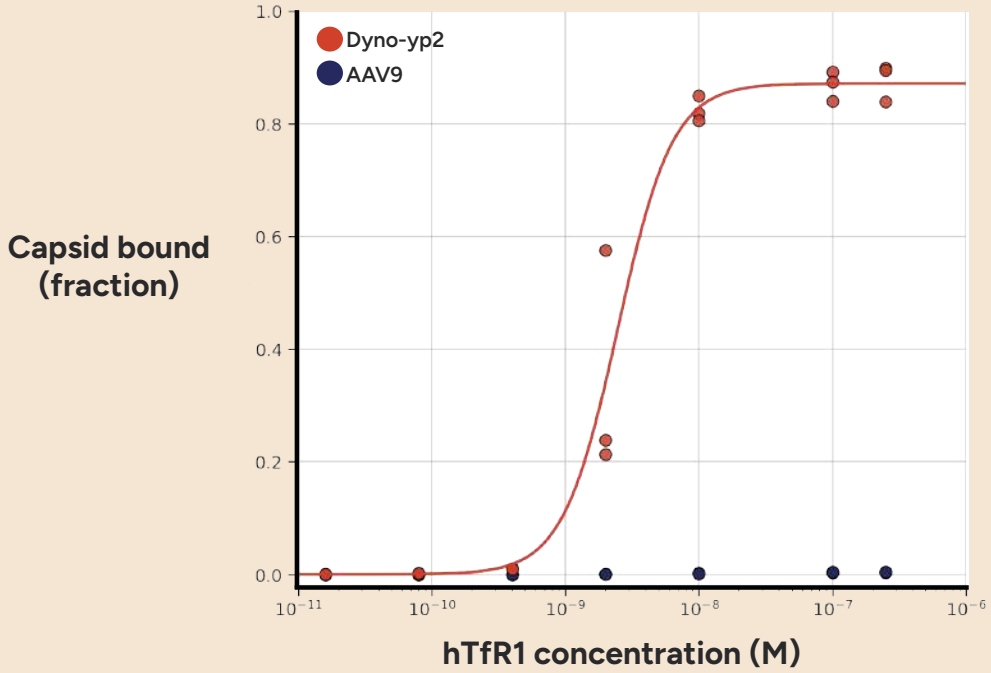


Receptor binding to human, NHP orthologs

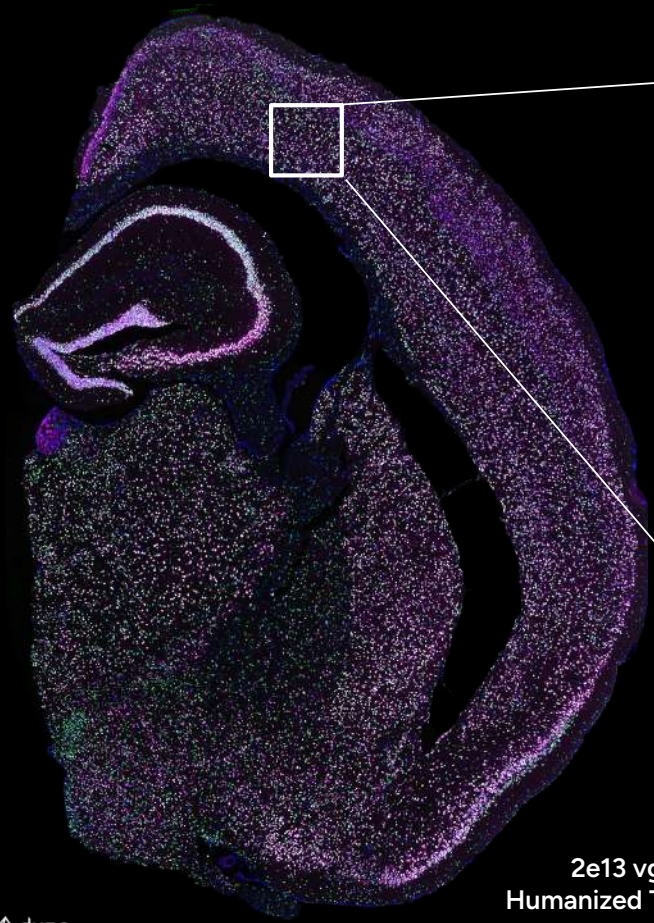
Manufacturability

AI models trained on in vitro data to predict receptor binding enable rapid capsid improvement

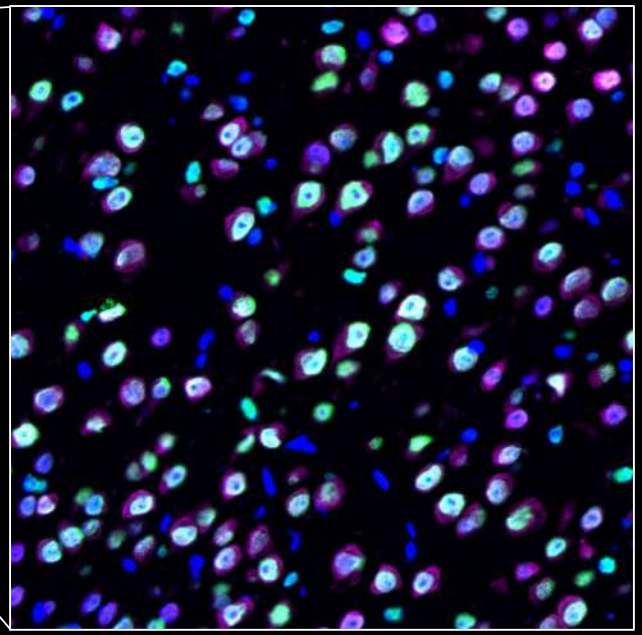
Dyno-yp2 binds the human TfR1 receptor

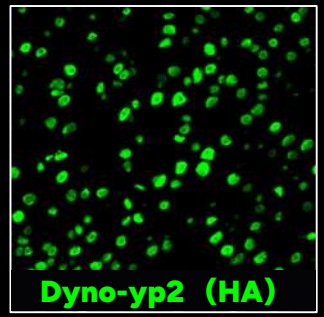


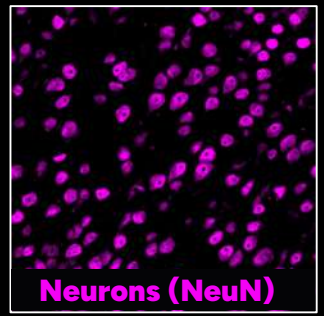
Dyno-yp2 transduces 98% of NeuN+ neurons in the cortex

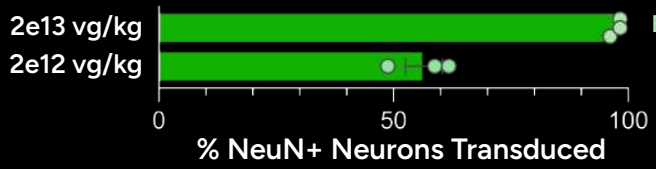


2e13 vg/kg
Humanized TfR1 mice



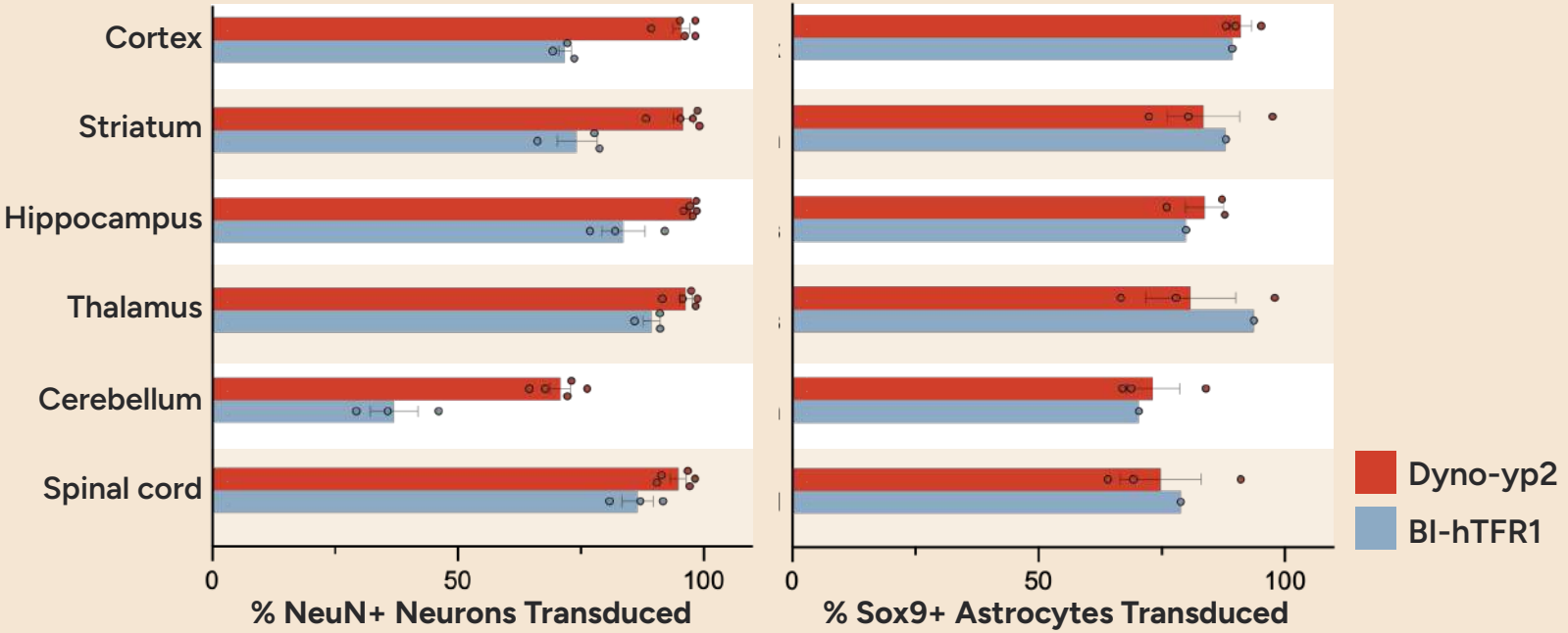






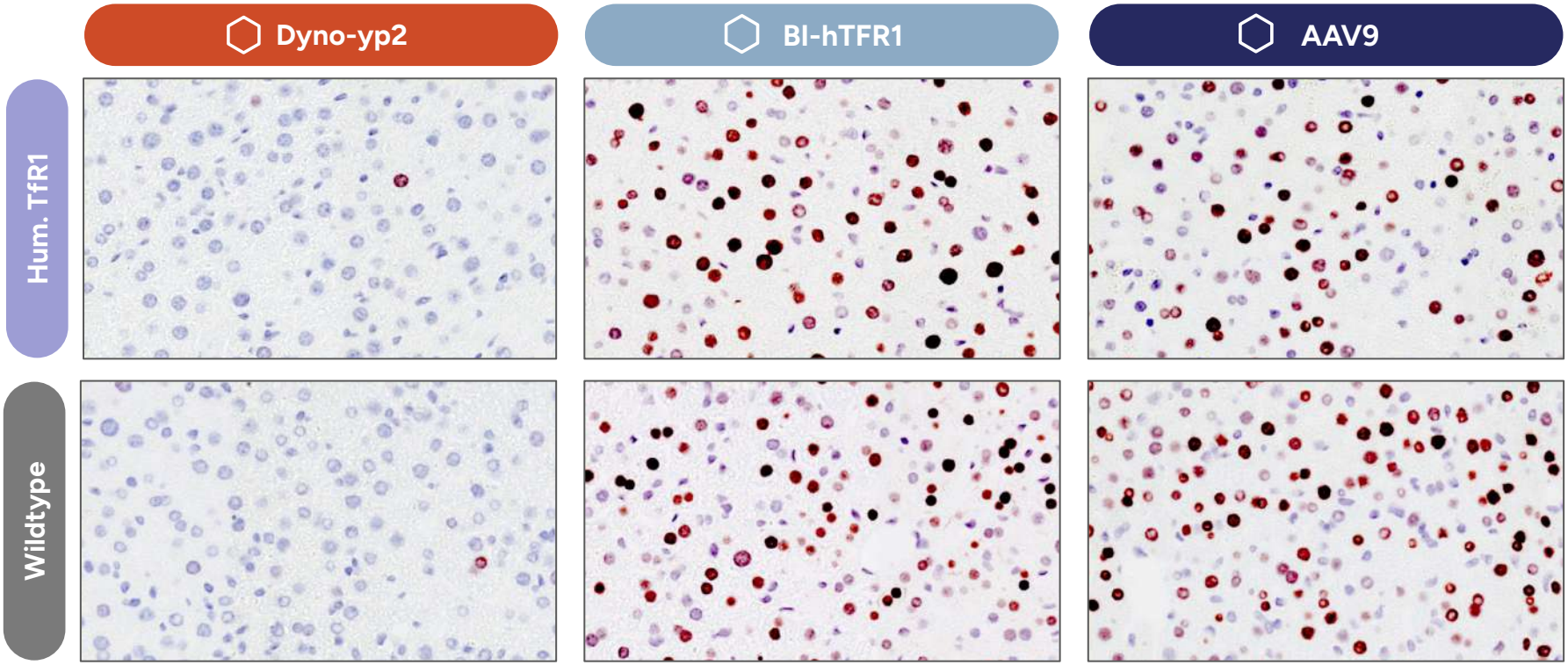
Each point = one mouse

Dyno-yp2 achieves exceptional pan-brain neuronal and astrocyte transduction in humanized TfR1 mice at 2e13 vg/kg



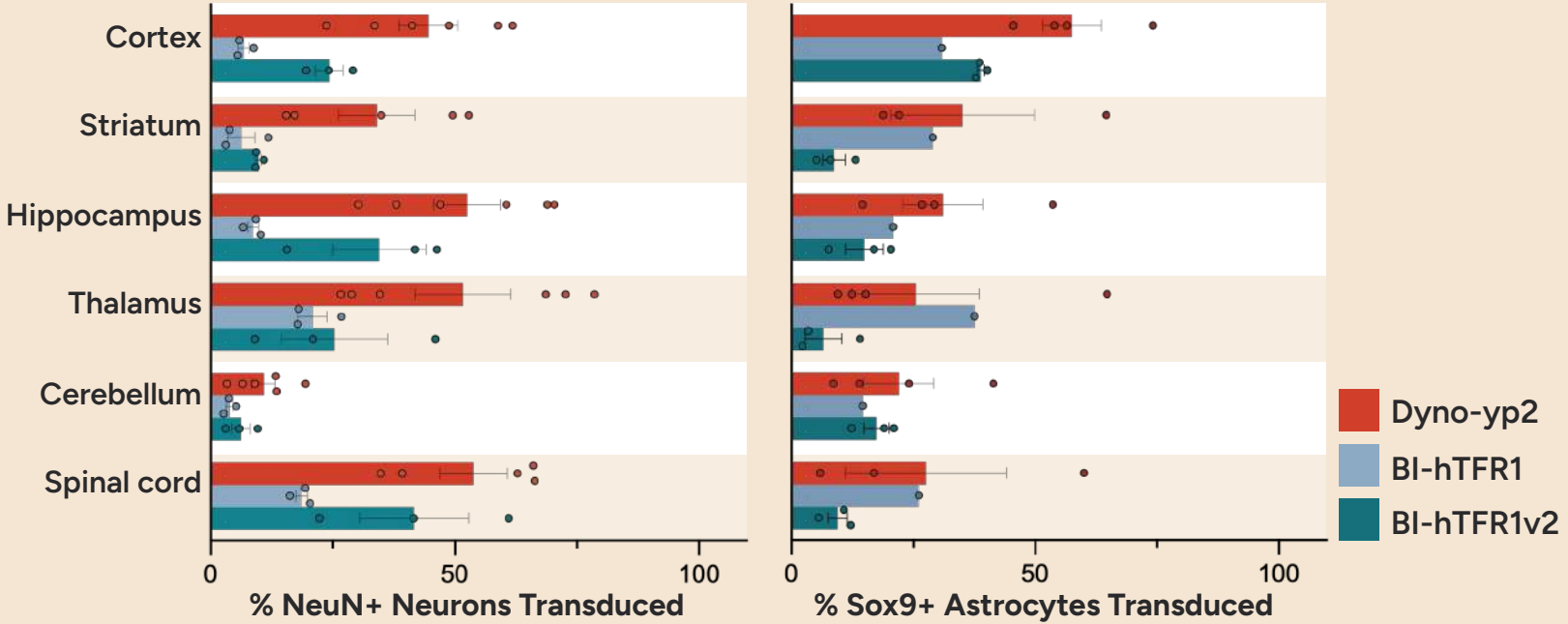
Dyno-yp2 outperforms BI-hTfR1 in every brain region

Dyno-yp2 combines CNS tropism with excellent liver detargeting



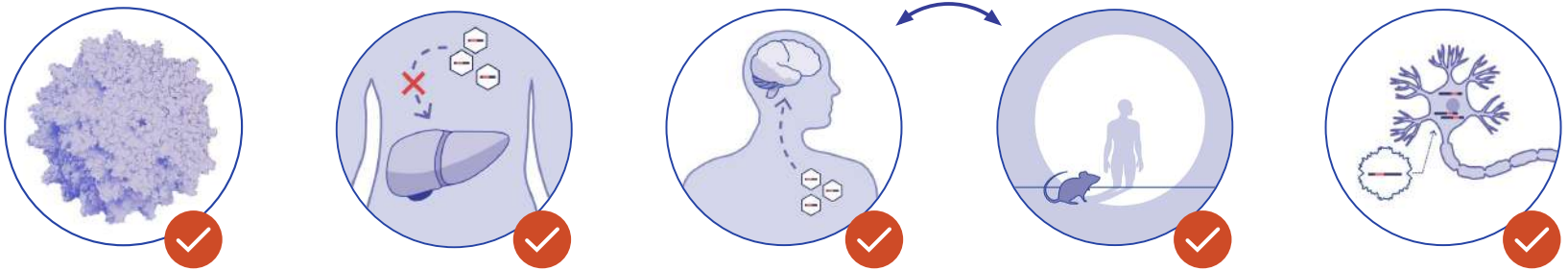
2e13 vg/kg dose

Dyno-yp2 outperforms BI-hTFR1 and BI-hTFRv2 capsids in neuronal and astrocytic delivery at 2e12 vg/kg



Dyno-yp2 broadly and efficiently transduces the CNS through a human TfR1-mediated mechanism

Safety | **Translation** | **Efficacy**



Efficient production

Detargeted from the liver

Efficient BBB crossing

Known human mechanism

Broad CNS transduction

Compatible with AAV9-based purification systems

29x liver detargeting compared to AAV9

Engineered for binding human TfR1; known mechanism translatable to humans

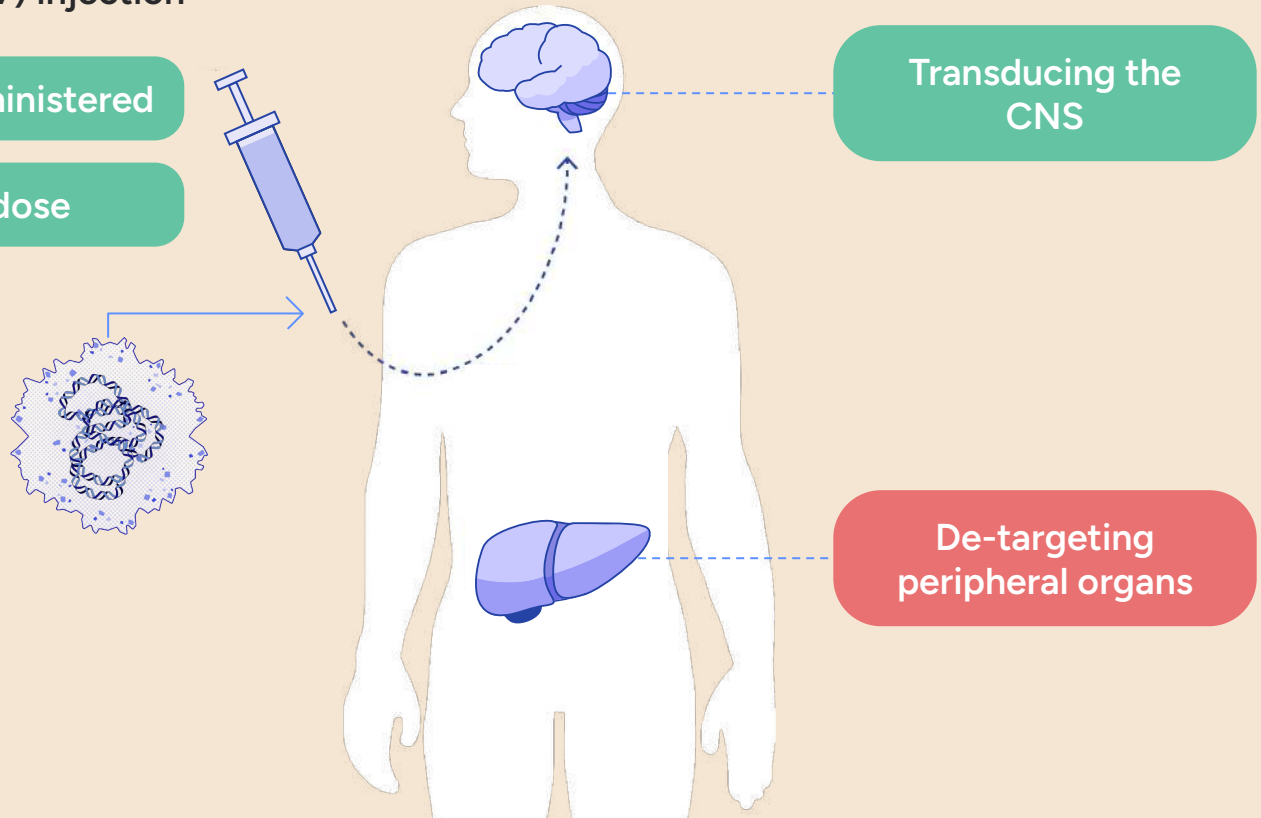
- 72% pan-brain cells
- 94% NeuN+ neurons
  - 98% thalamic neurons
  - 98% cortical neurons
  - 97% spinal cord neurons
- 89% Sox9+ astrocytes

Challenge: safe and effective cross-species IV gene delivery

Intravenous (IV) injection

Easily administered

Low dose



Transducing the CNS

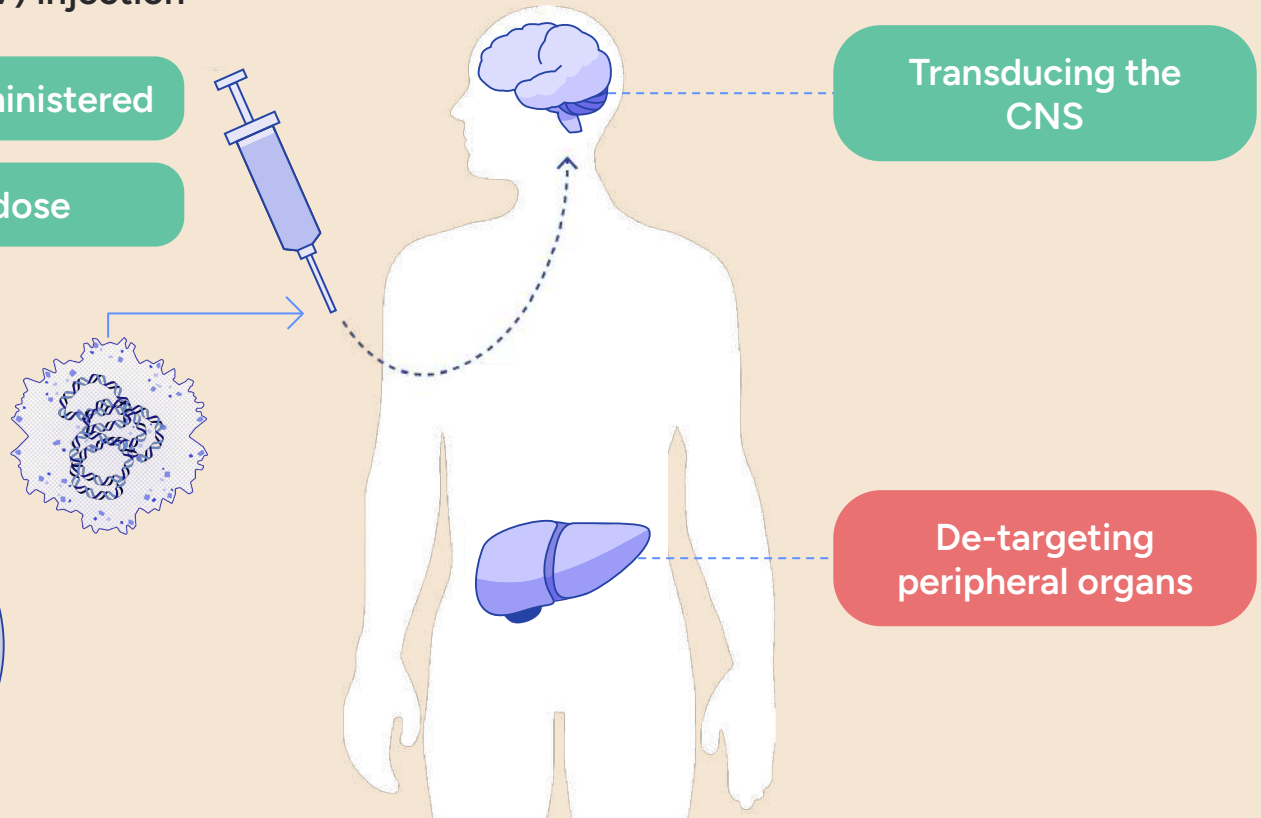
De-targeting peripheral organs

Challenge: safe and effective cross-species IV gene delivery

Intravenous (IV) injection

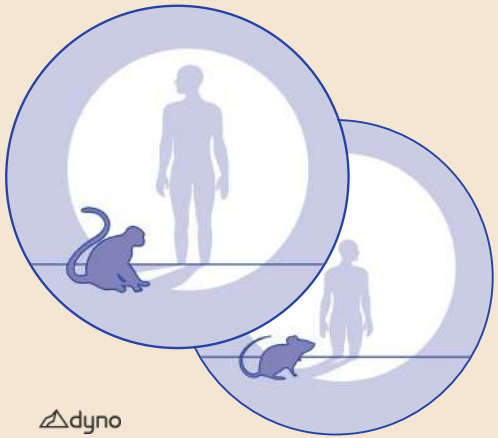
Easily administered

Low dose

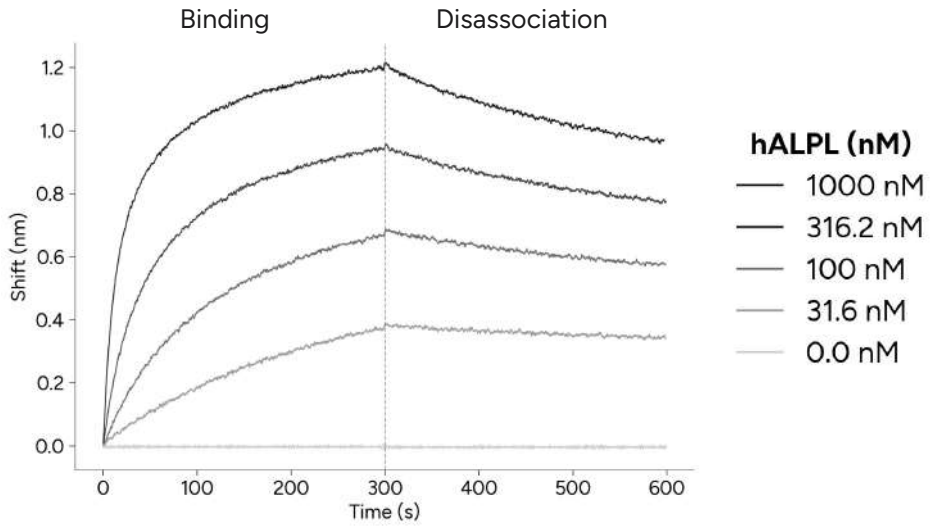


Transducing the CNS

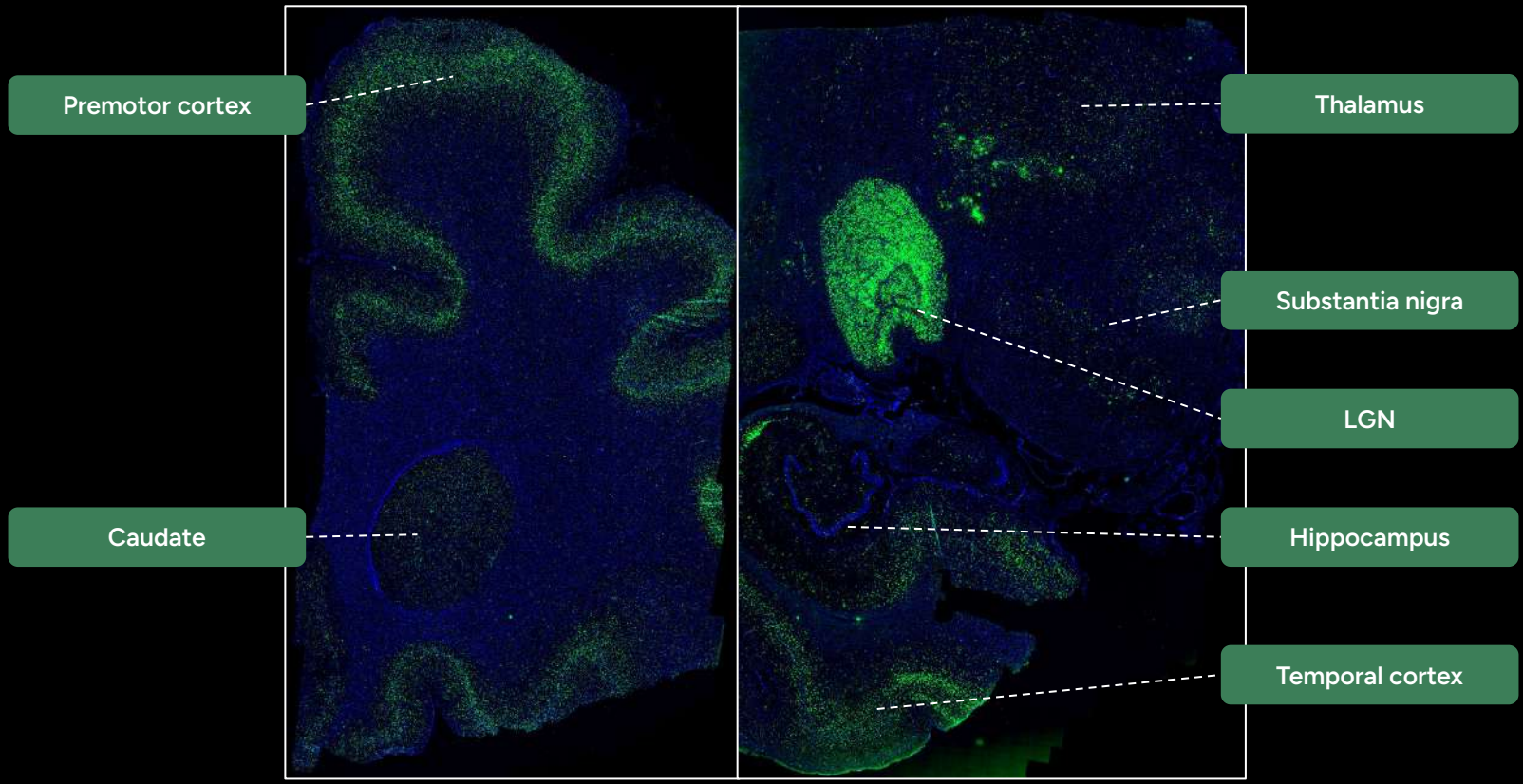
De-targeting peripheral organs



Dyno-9zh binds the human ALPL receptor

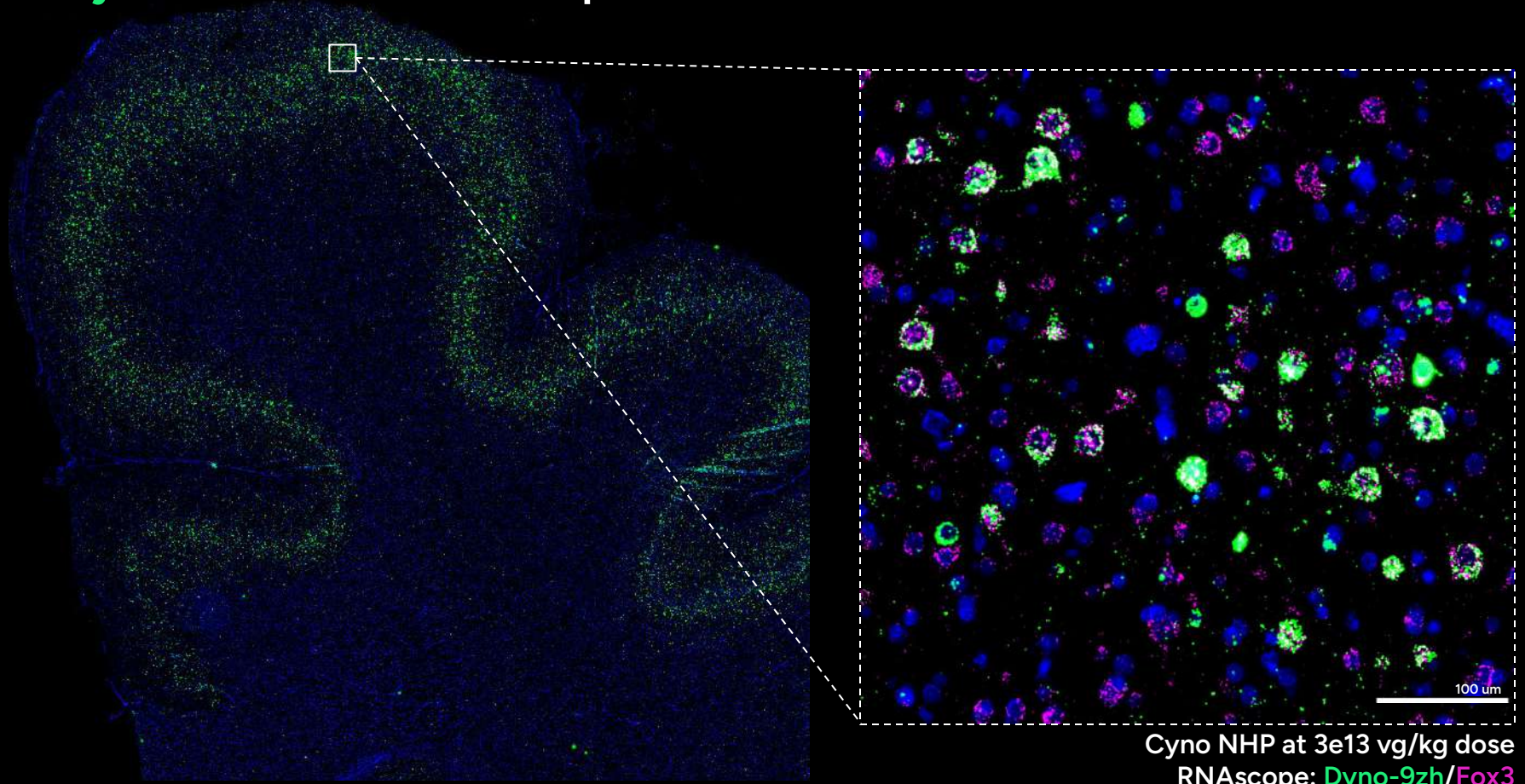


Dyno-9zh achieves widespread transduction across the NHP CNS



Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh

Dyno-9zh transduces up to 50% of neurons in Premotor cortex



Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh/Fox3

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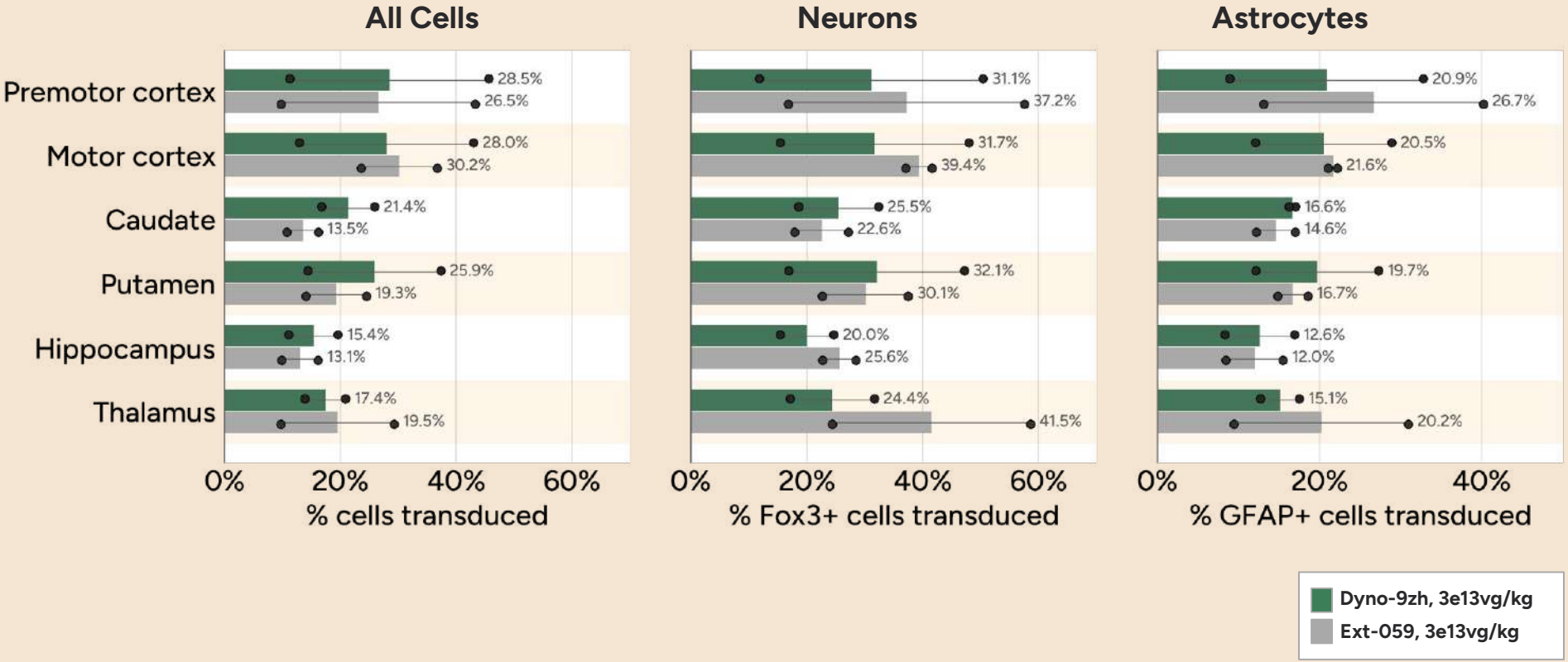
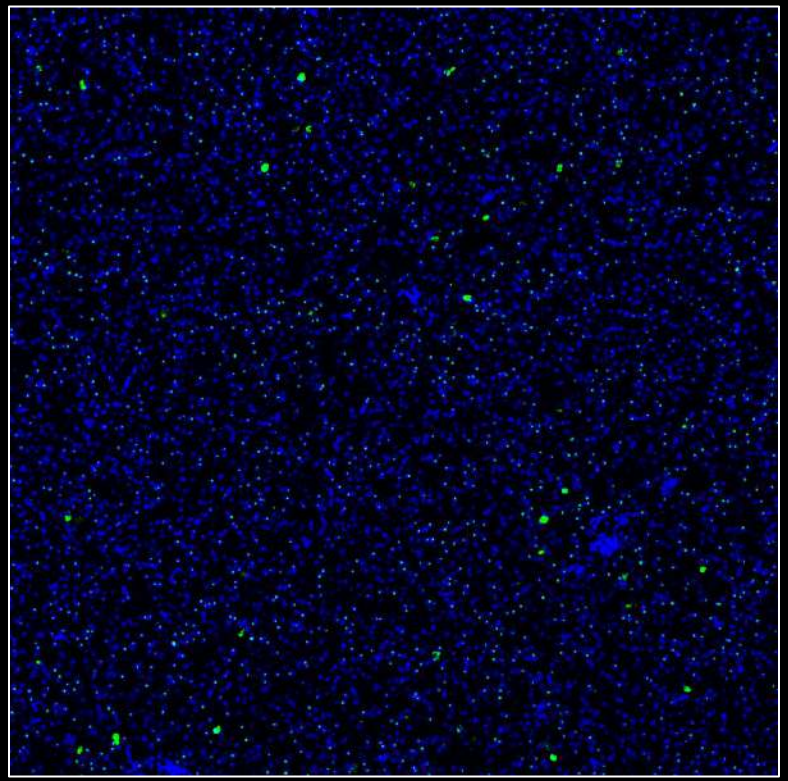
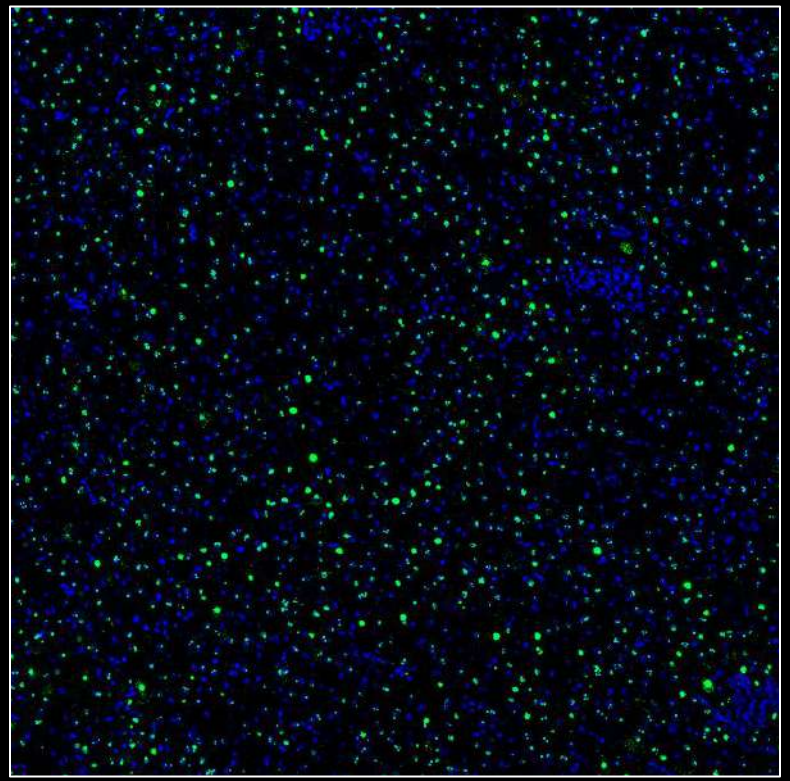
Dyno-9zh shows broad CNS transduction matching the performance of external capsid Ext-059



Dyno-9zh shows excellent liver detargeting vs AAV9

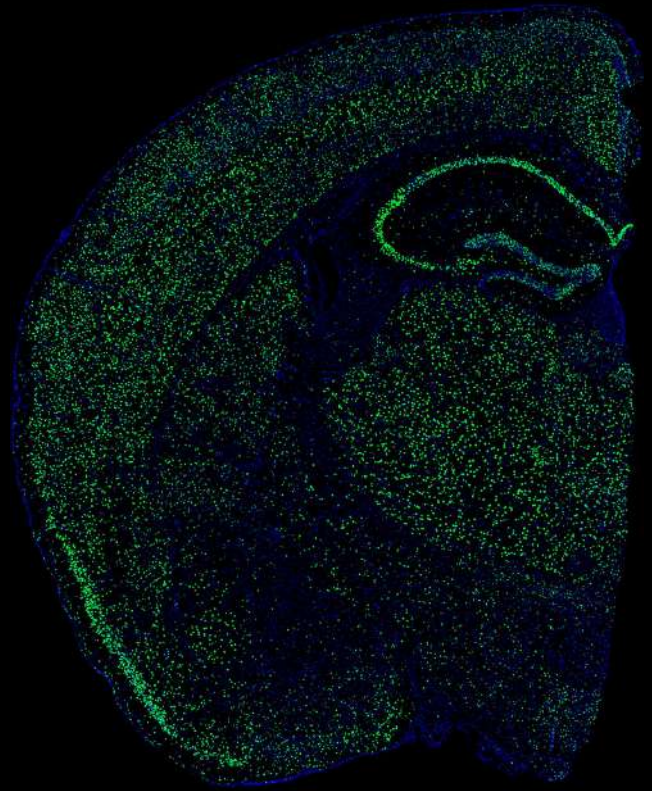


Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh

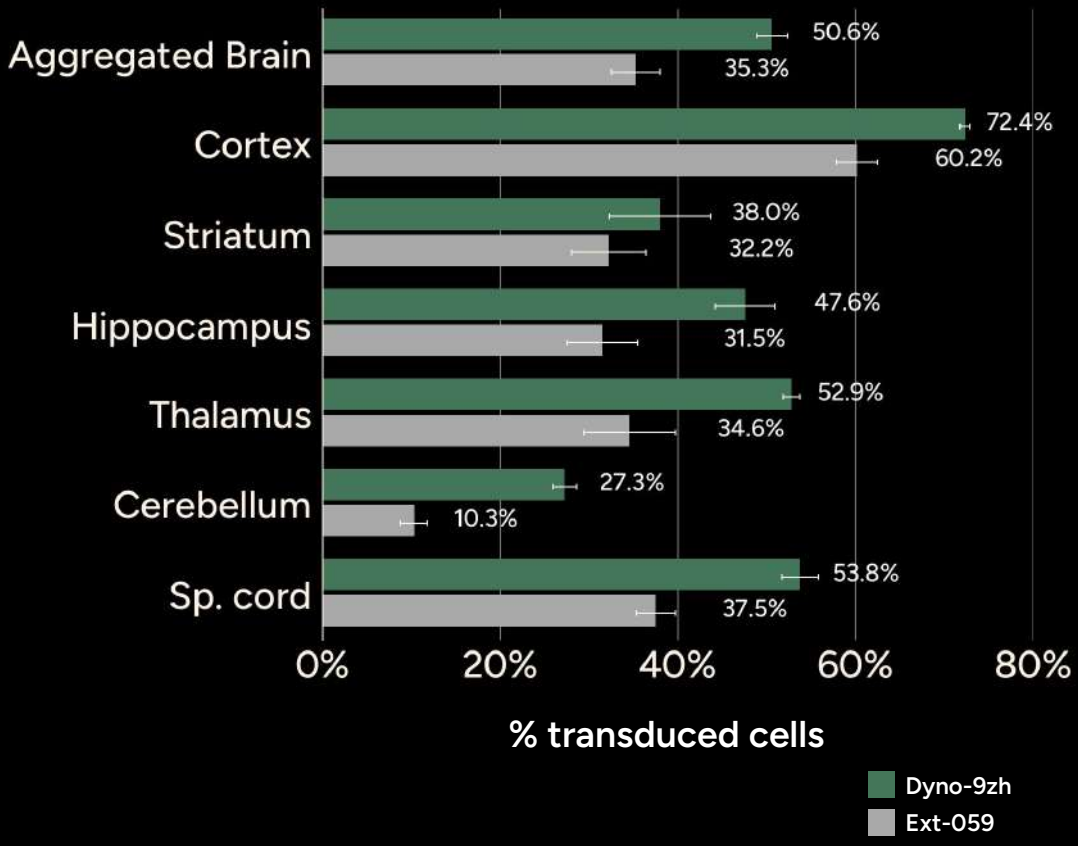


Cyno NHP at 1e13 vg/kg dose
RNAscope: AAV9

Dyno-9zh outperforms Ext-059 in mouse CNS transduction

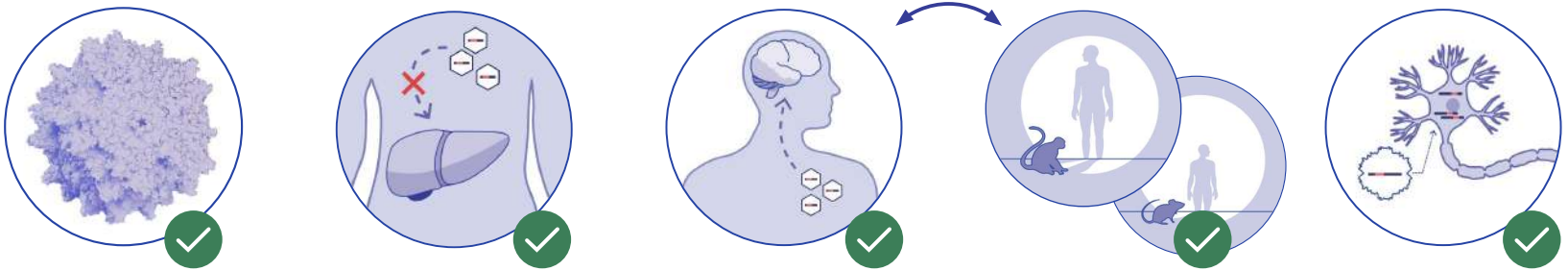


Dyno-9zh 1e13 vg/kg
C57BL/6 mice



Dyno-9zh broadly and efficiently transduces the CNS through a human ALPL-mediated mechanism

Safety | **Translation** | **Efficacy**



Efficient production

Compatible with AAV9-based purification systems

Detargeted from the liver

>10x liver detargeting compared to AAV9

Efficient BBB crossing

Engineered for binding ALPL; a mechanism with cross-species translation potential

Cross-species translation

In NHPs:
- Up to 50% cortical neurons
- Up to 47% striatal neurons
- Up to 60% lower motor neurons

In WT mice:
- Up to 80% cortical neurons

Broad CNS transduction

Learn more

Today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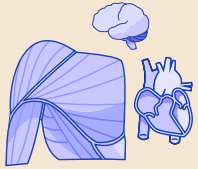
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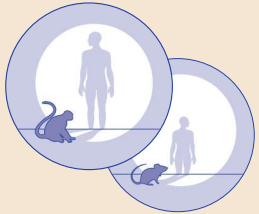
dynotx.com/9zh


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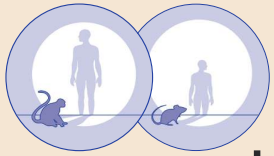
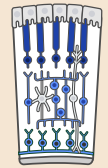

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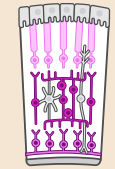


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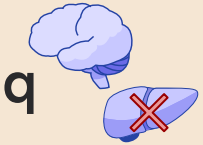

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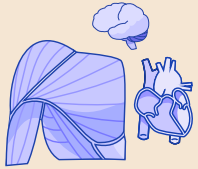
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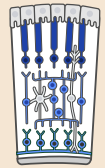
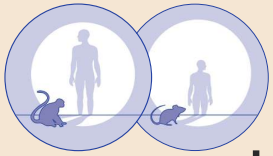
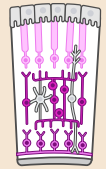
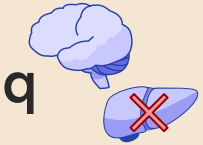
Prior

dynotx.com/4z2 


dynotx.com/86m 

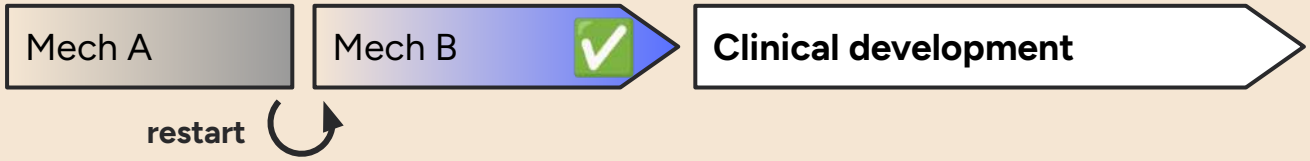

dynotx.com/ahq 

We've designed leading capsids for every promising BBB-crossing mechanism

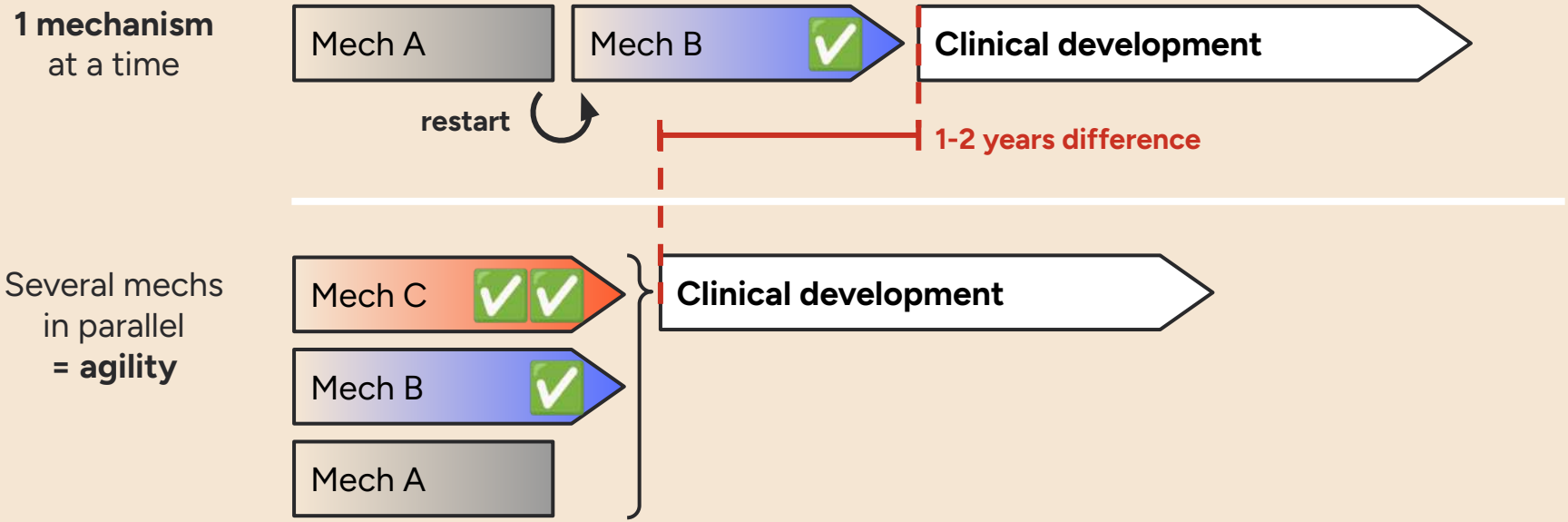
Novel primate-conserved BBB-crossing mechanisms	**Dyno Receptor 1** Dyno-ahq	**Dyno Receptor 2**
Known BBB-crossing mechanisms	**Alkaline Phosphatase (ALPL)** Dyno-9zh	**Transferrin Receptor 1 (TfR1)** Dyno-yp2

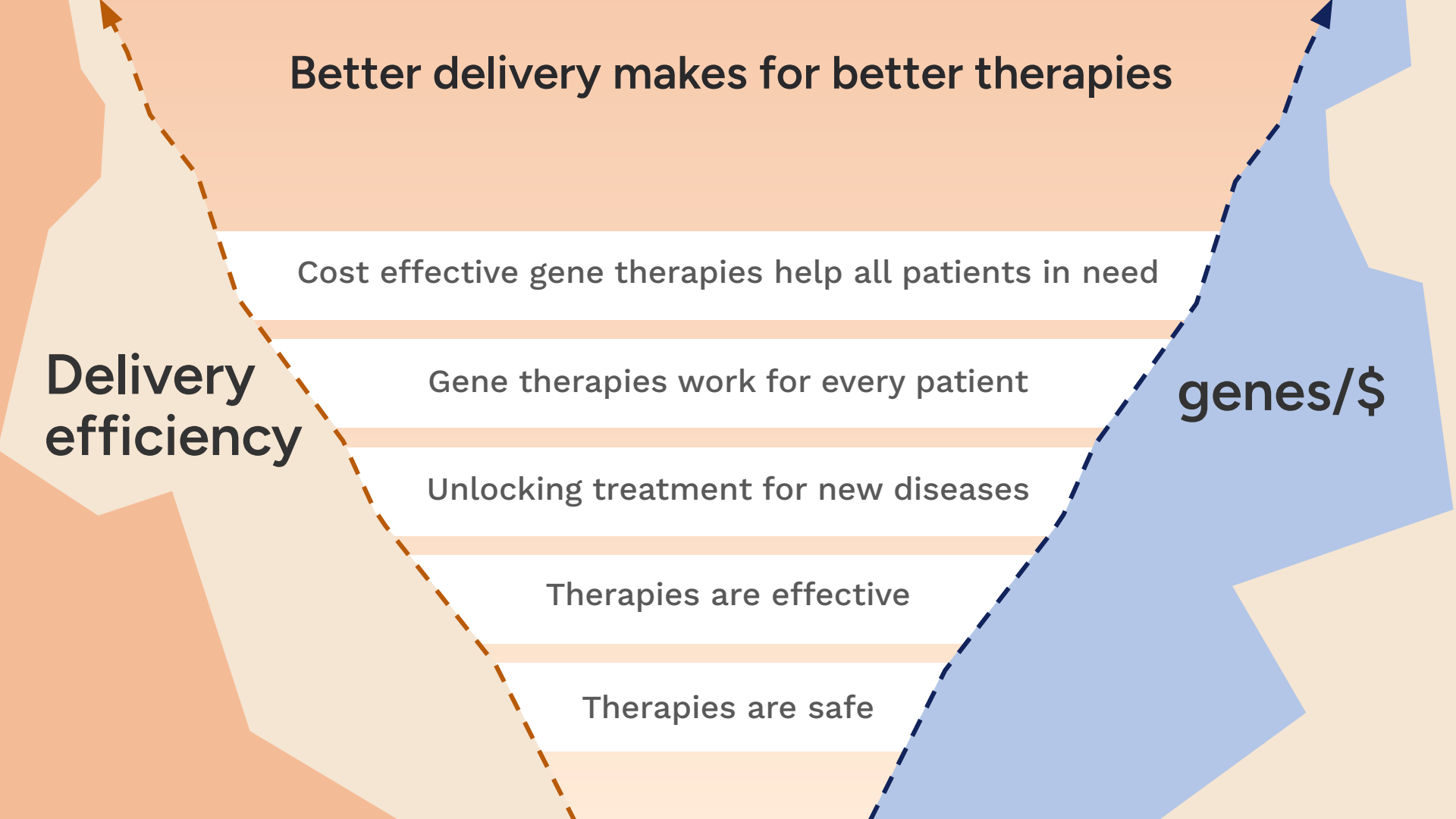
Strategic delivery agility enables gene therapy developers to move fast with confidence

1 mechanism at a time



Strategic delivery agility enables gene therapy developers to move fast with confidence



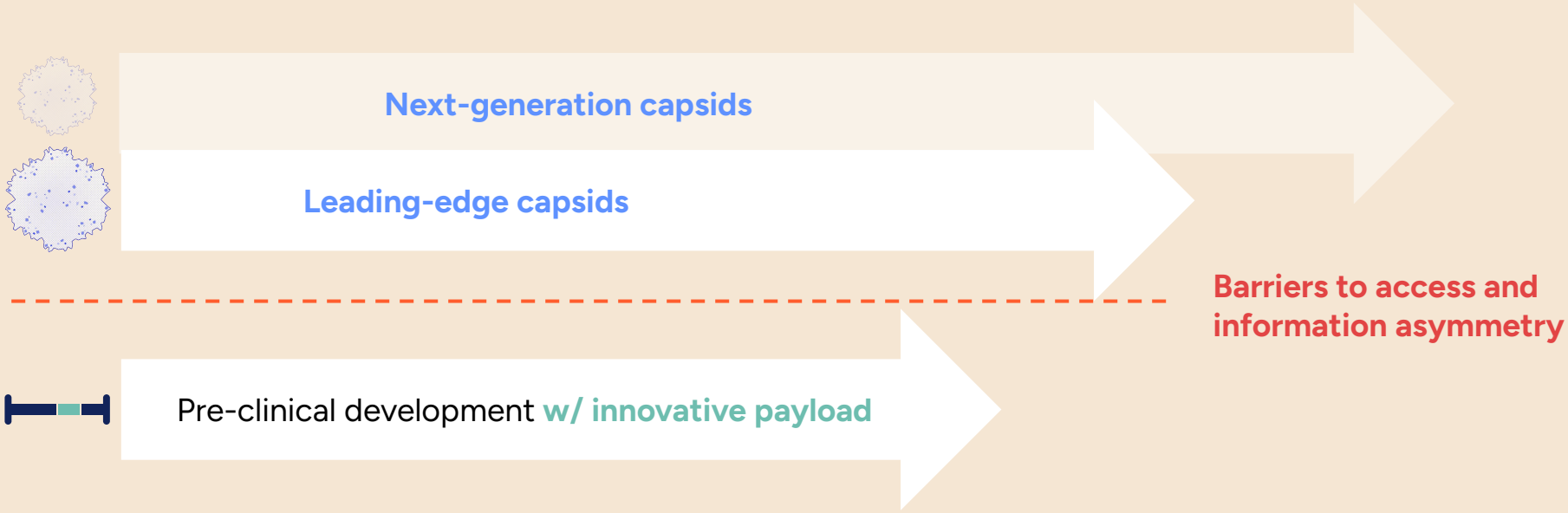

Better delivery makes for better therapies
Cost effective gene therapies help all patients in need
Gene therapies work for every patient
Unlocking treatment for new diseases
Therapies are effective
Therapies are safe
Delivery efficiency
genes/$

Why partner with Dyno?

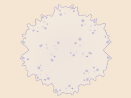


- **High-performance** - safe, effective and competitive - our platform focus
- **Flexibility** for multiple targets/indications - in support of your strategy
- **Future access** to improved capsids - due to Dyno's Platform committment
- **Support** of partnership success - due to our aligned interests

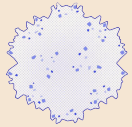
Problem: Without effective delivery, it is difficult to demonstrate payload effectiveness



Solution: Combine leading-edge delivery with innovative genetic payloads to demonstrate therapeutic potential



Next-generation capsids



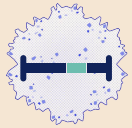
Leading-edge capsids

+



Pre-clinical development **w/ innovative payload**

=



More transformative therapies

dyno

Developers in Dyno Frontiers



Gain access to Dyno's delivery technology to demonstrate the *in vivo* effectiveness of innovative clinic-ready genetic payloads

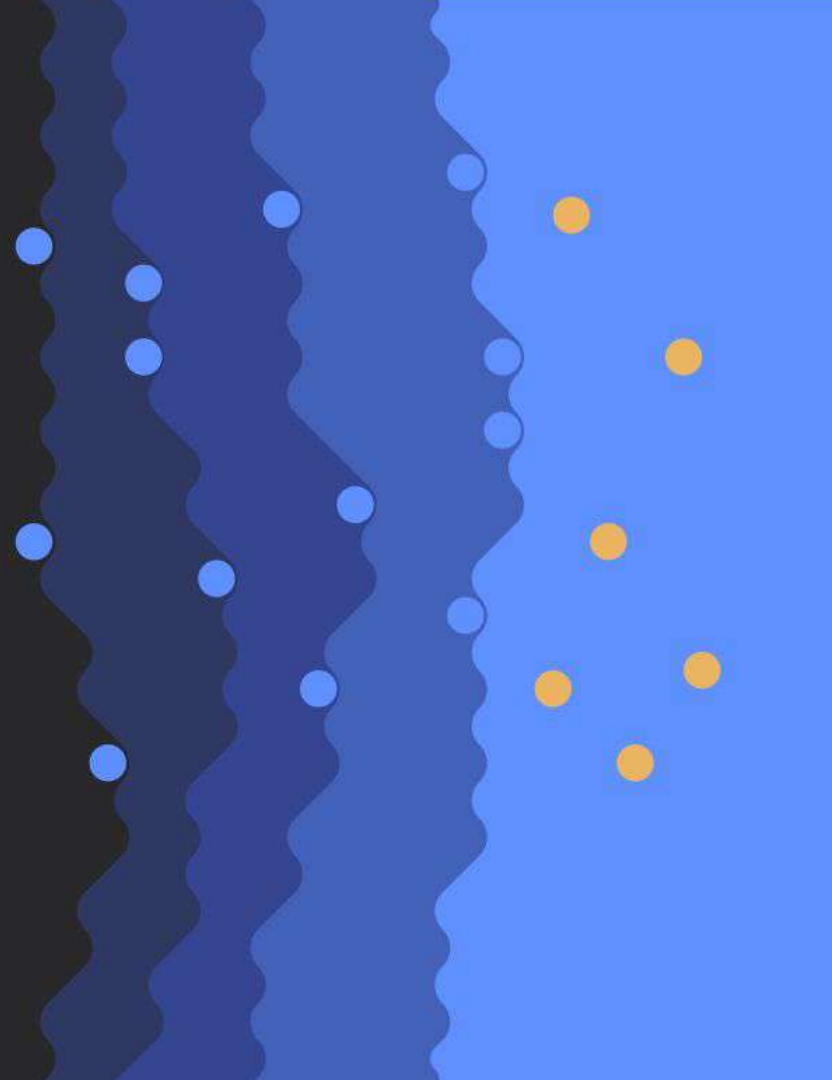


Receive scientific advice from Dyno on capsid selection, NHP study design and vector manufacturing



Collaborate with Dyno to accurately quantify capsid performance

Dyno Frontiers



ASGCT 2025: 0

End of 2025: 5

Today: 15

Announcing

Dyno Frontiers is now a Network



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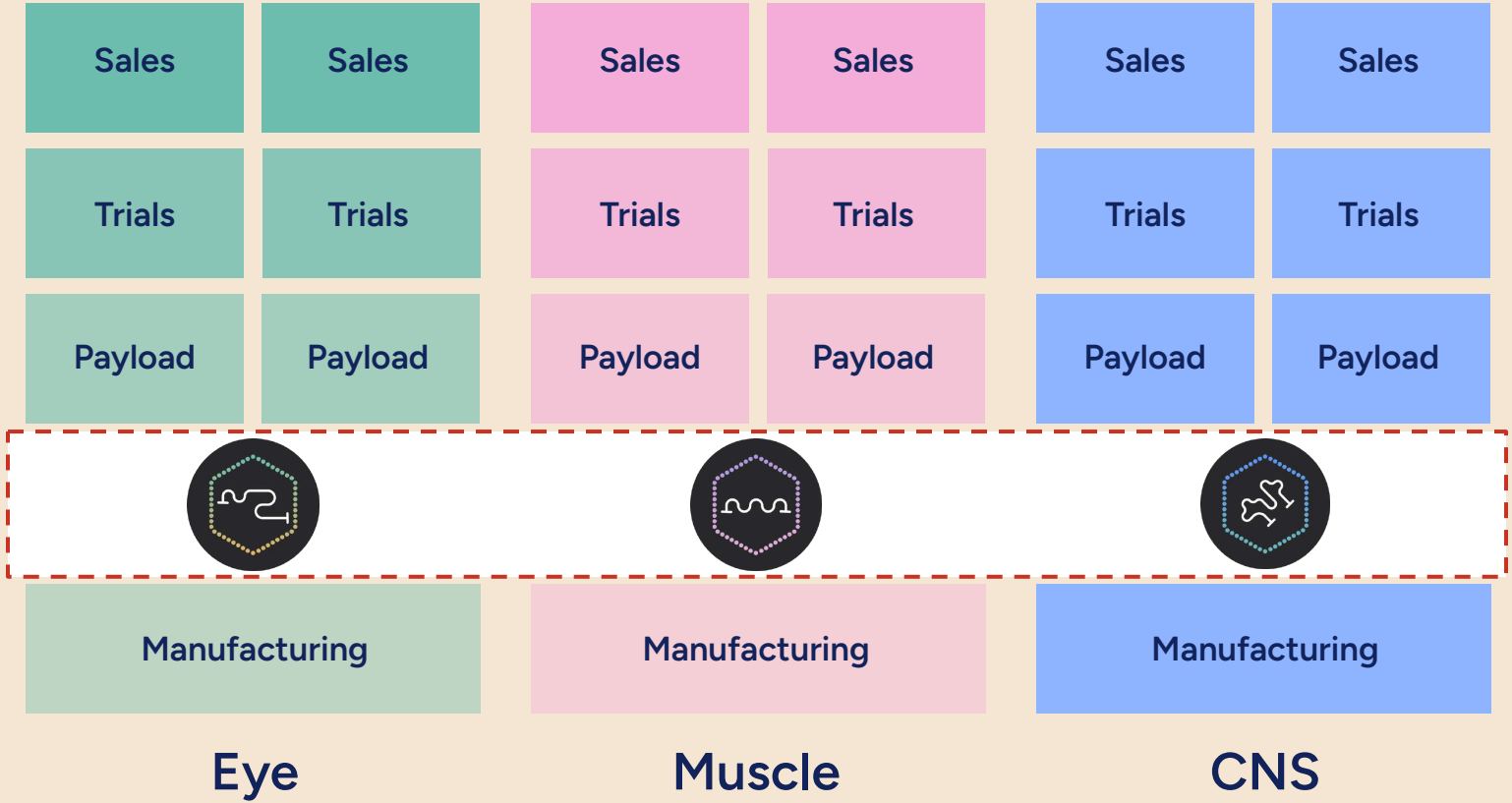
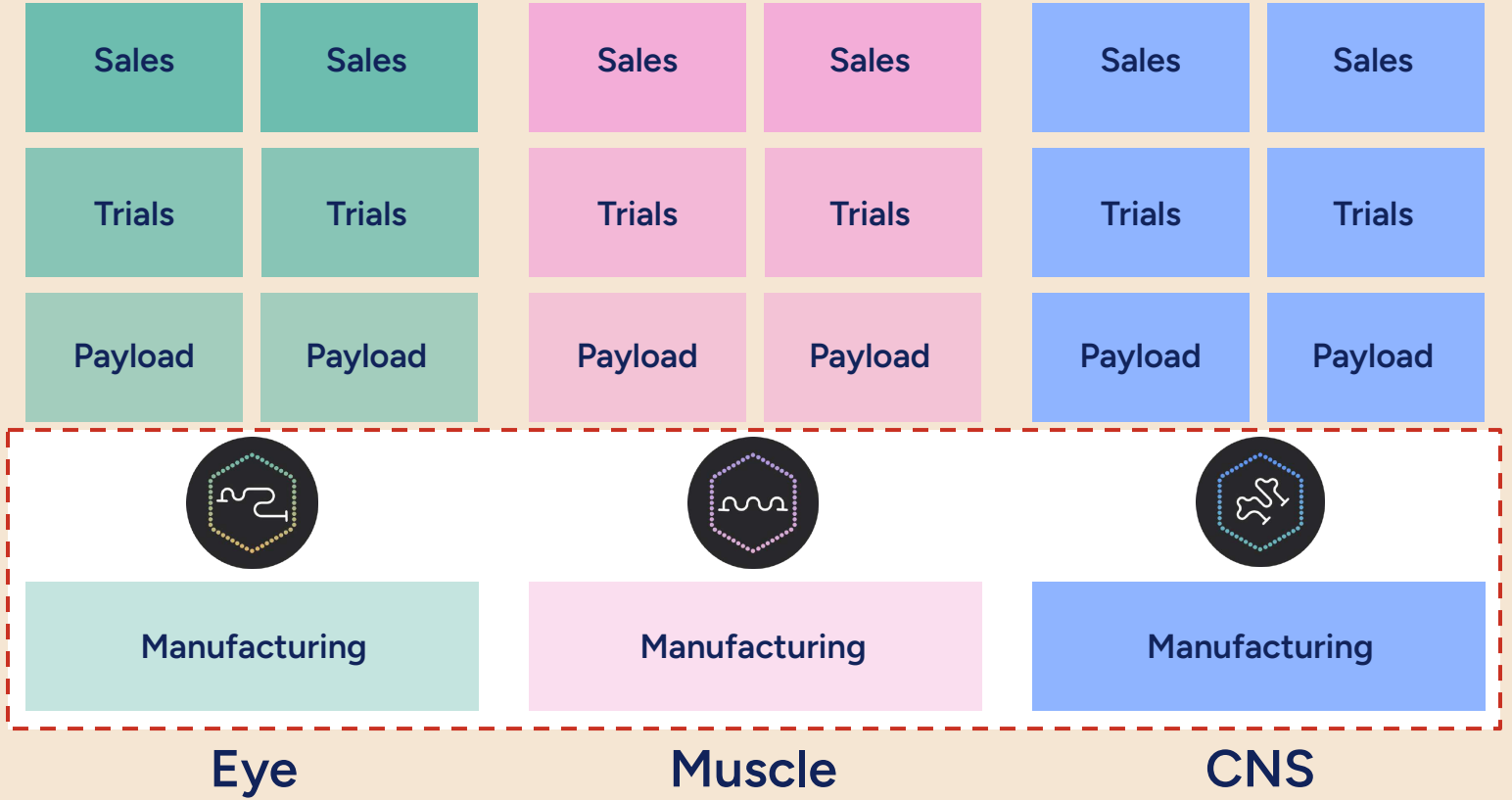
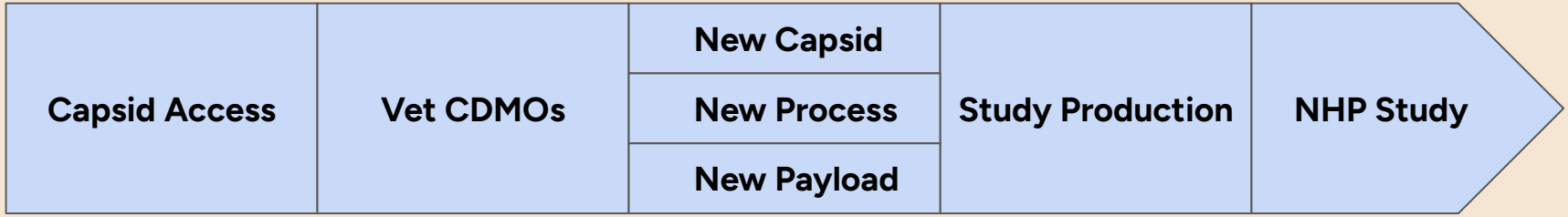
An ecosystem that supports developers and works for patients



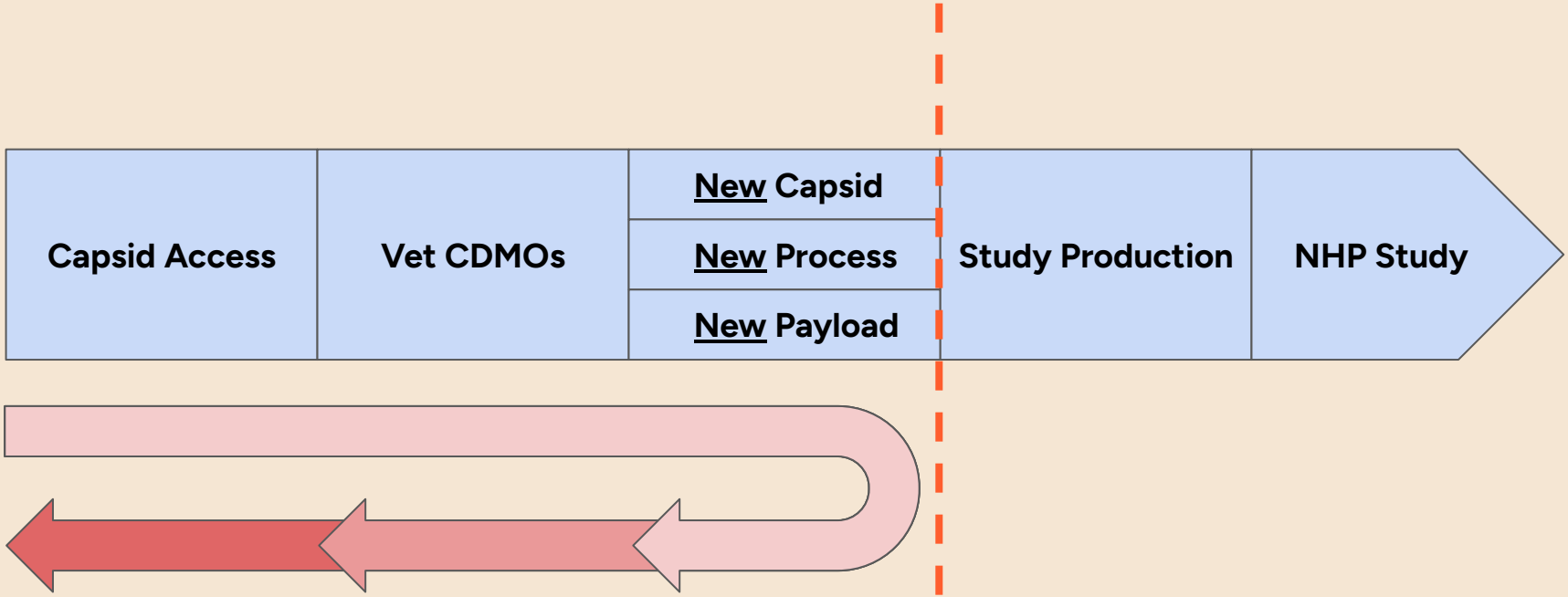
An ecosystem that supports developers and works for patients



Manufacturing introduces challenges for Developers

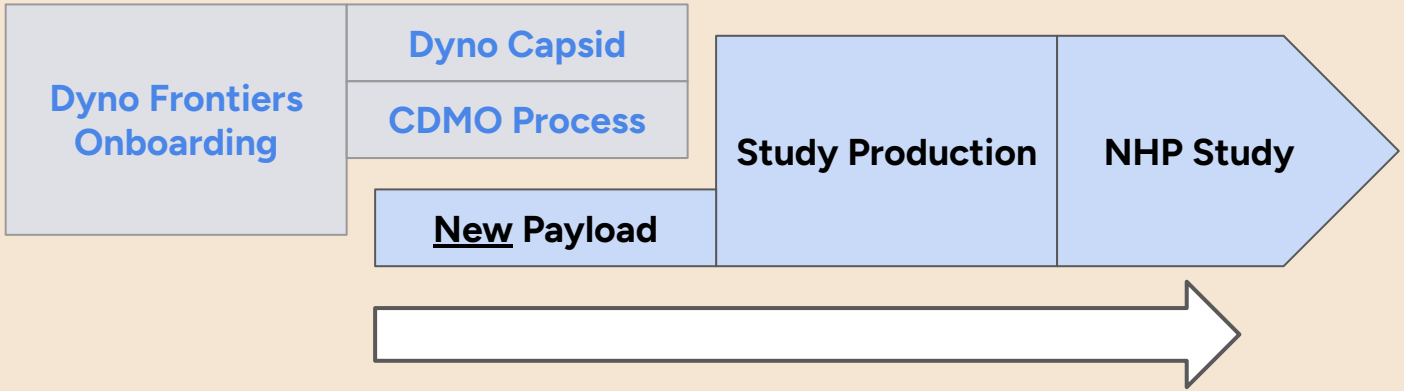


Manufacturing introduces challenges for Developers



Solving manufacturing challenges through Dyno Frontiers Manufacturing Partners

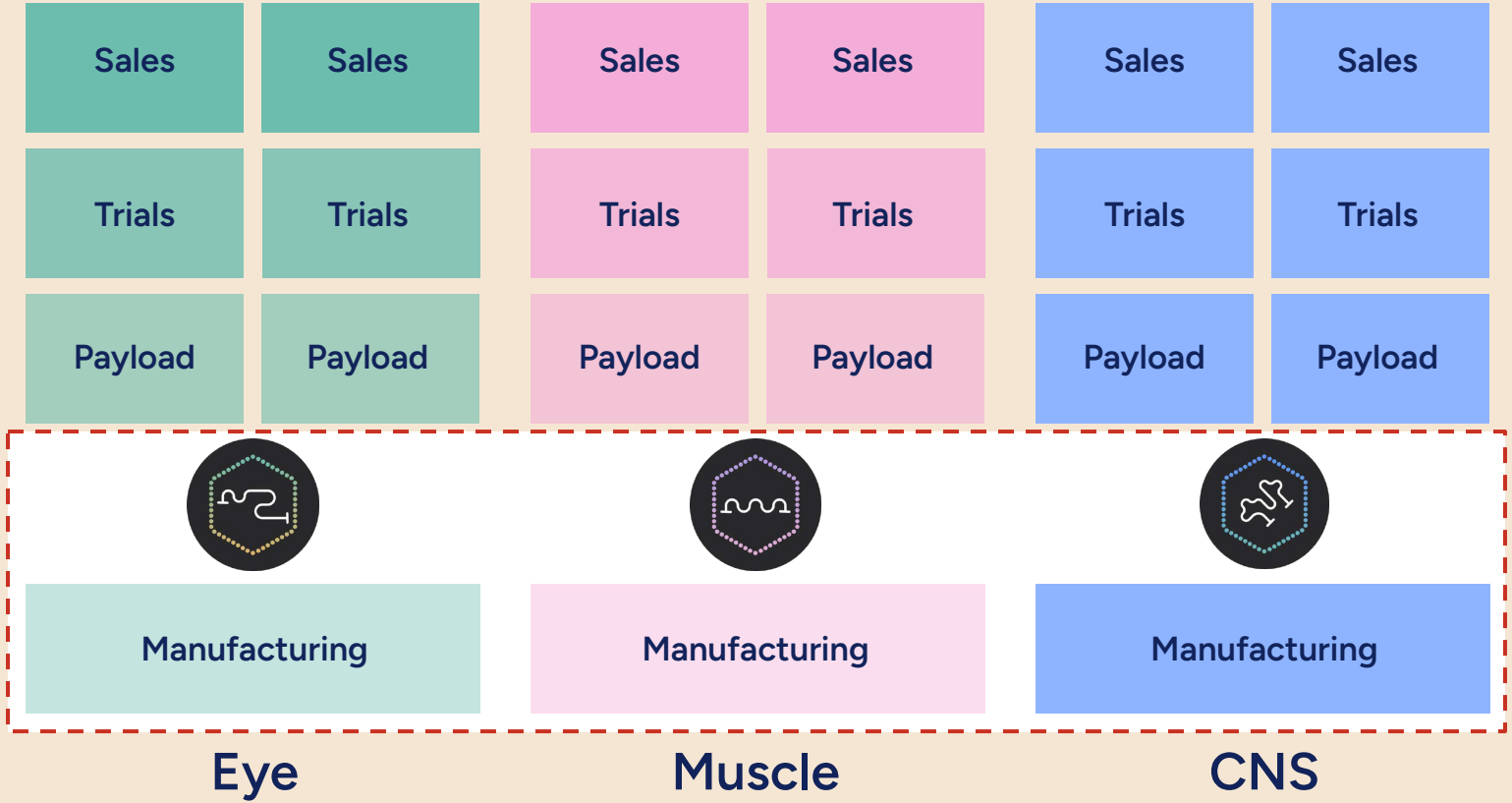
Trisk



Dyno Frontiers now includes manufacturing partners



An ecosystem that supports developers and works for patients



An ecosystem that supports developers and works for patients



Dyno Frontiers now includes service providers















An ecosystem that supports developers and works for patients



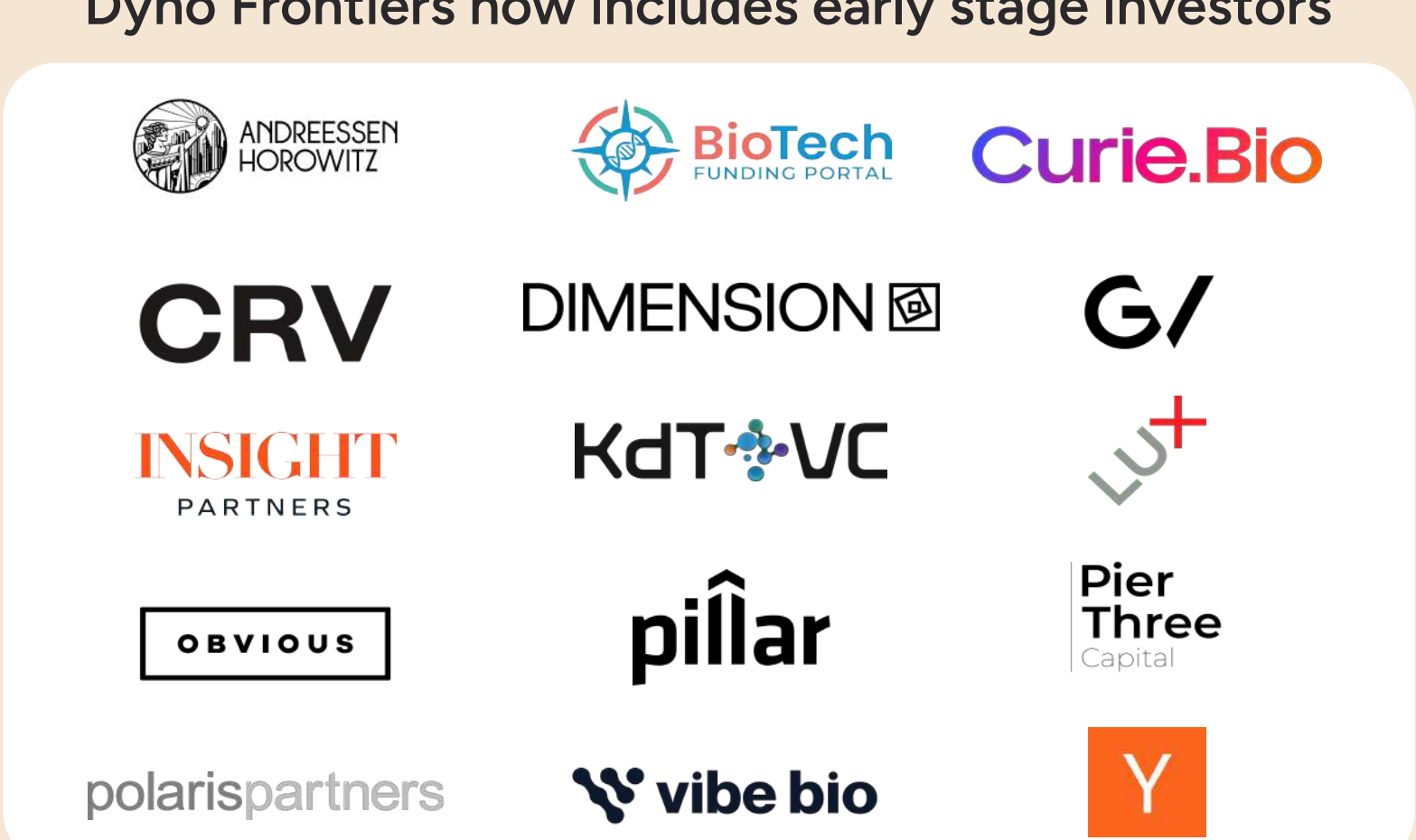
An ecosystem that supports developers and works for patients

Eye	Muscle	CNS
Sales	Sales	Sales
Trials	Trials	Trials
Payload	Payload	Payload
Manufacturing	Manufacturing	Manufacturing

Capital



Dyno Frontiers now includes early stage investors



An ecosystem that supports developers and works for patients



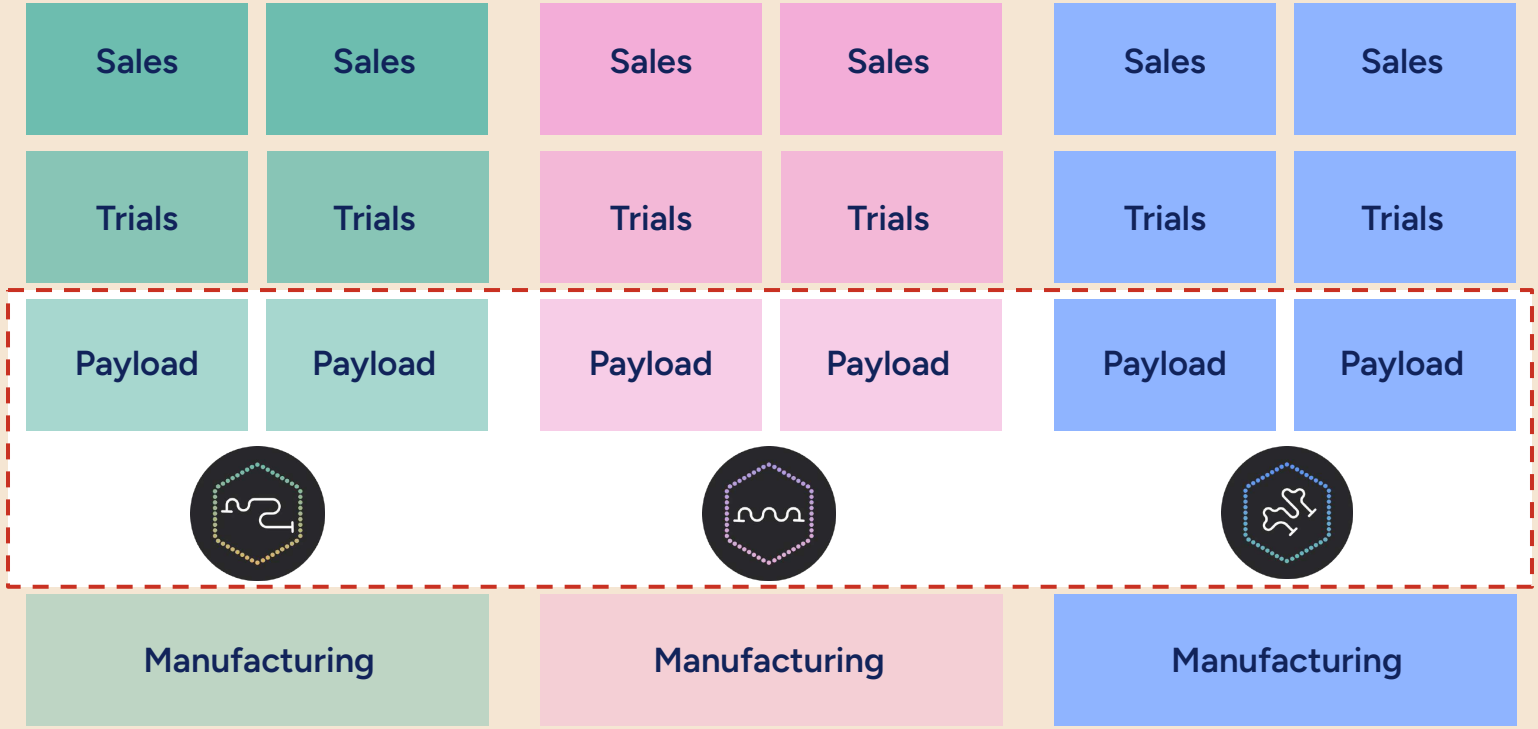
dynotx.com/frontiers-network

Frontier AI:

Building a better future



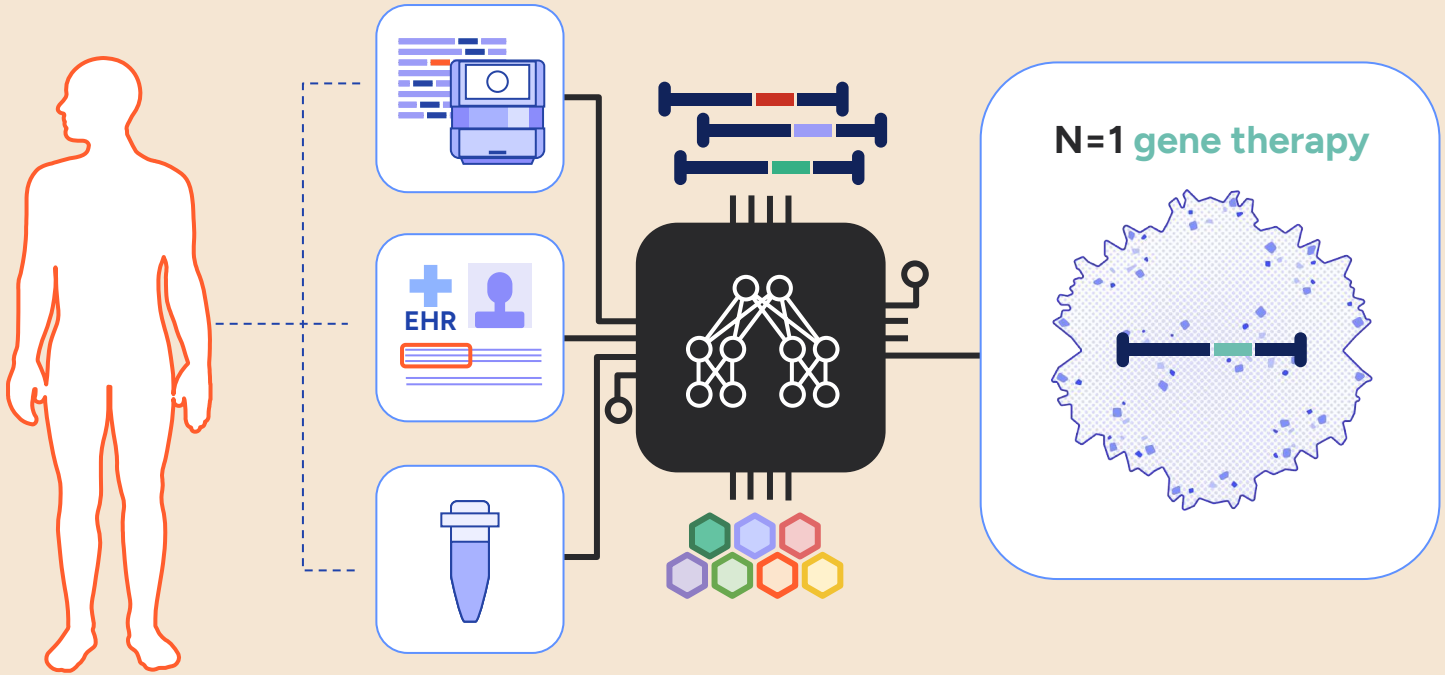
Solving therapeutic developers' grand challenges



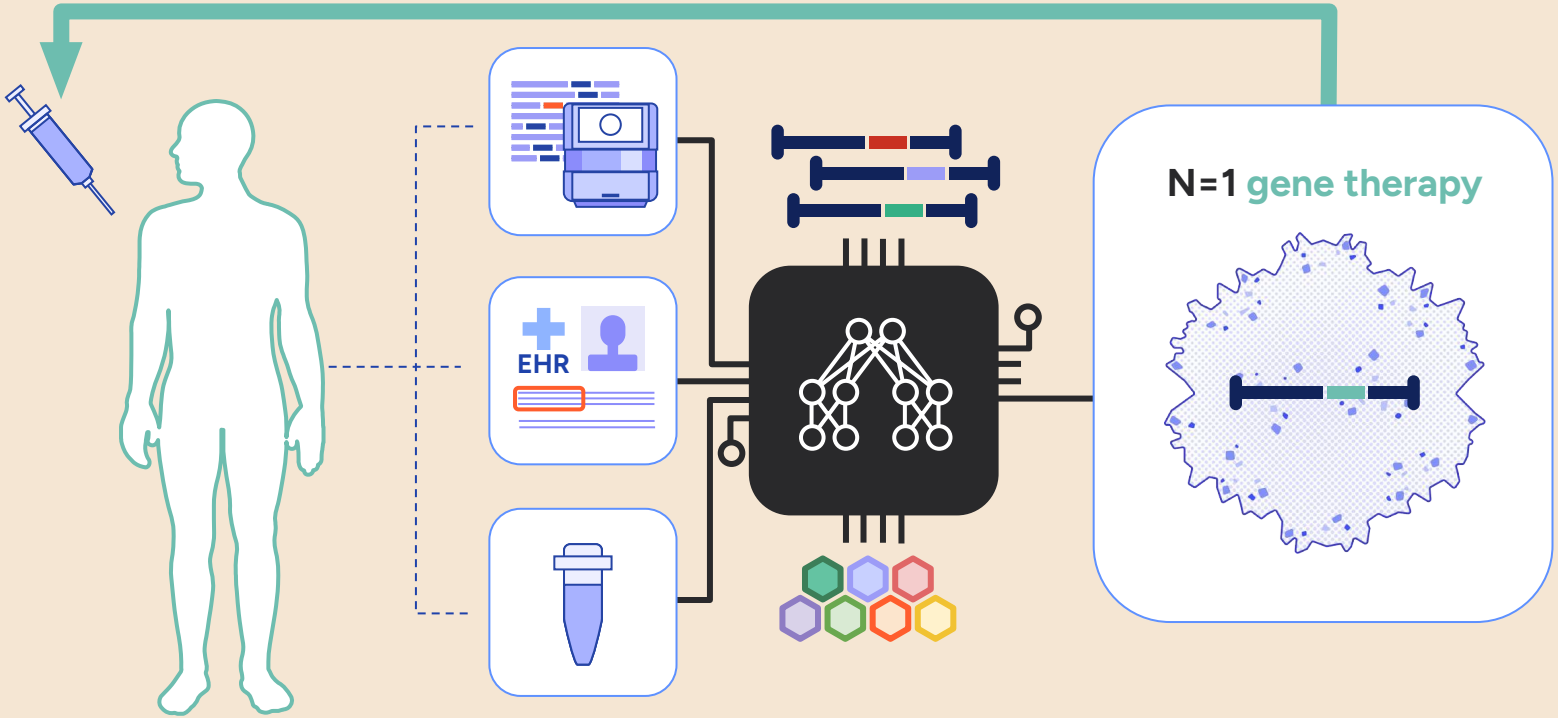
Grand challenges in payload design



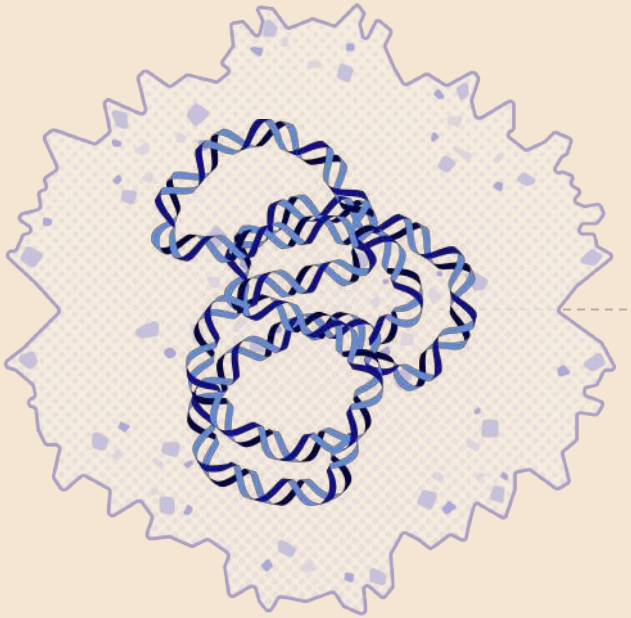
AI for empowering all patients with genetic agency



AI for empowering all patients with genetic agency



AAV payload: a ~4700 nucleotide sequence design problem



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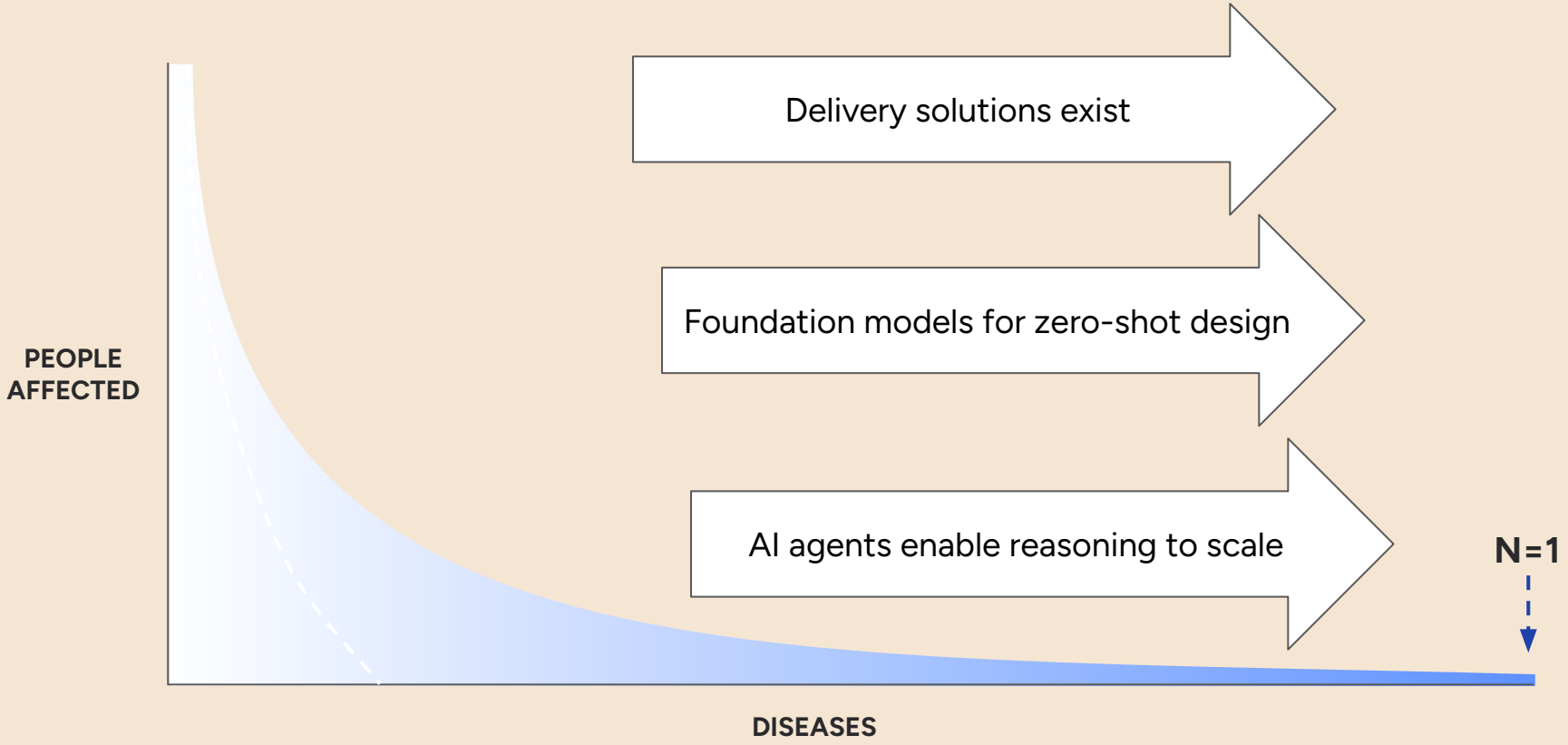
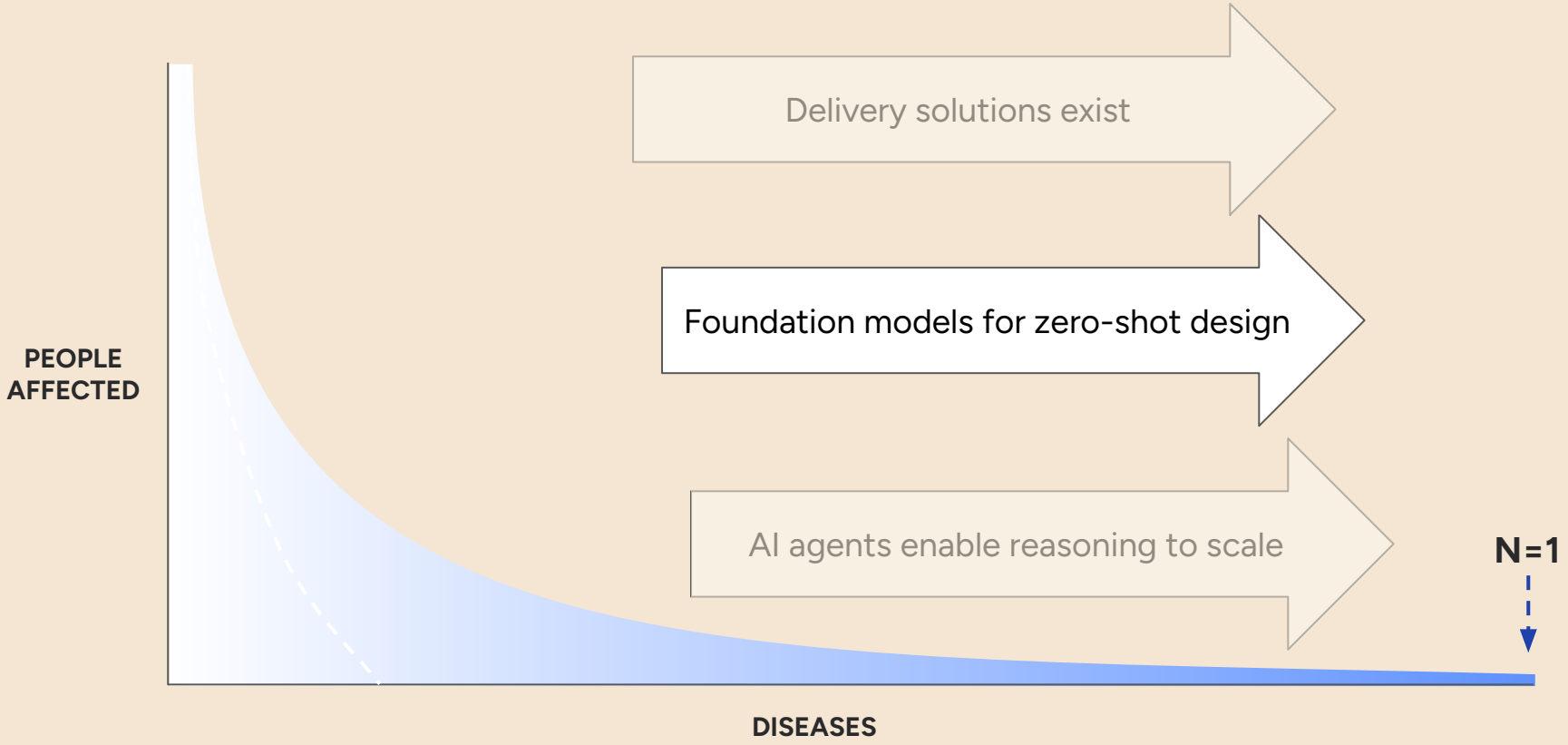
N=1 design: Why now?



N=1 design: Why now?

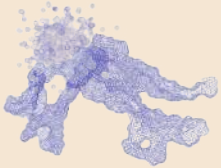


Dyno Psi-1: Controllable protein design for genetic medicines



Binding site specification

Control what you bind, where you bind it, and what not to bind.



Sequence re-design

Surgically replace parts of your protein while leaving other functionality intact.



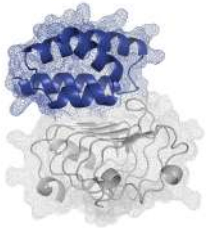
Cross-species targeting

Optimize for multiple related targets at the same time with the same binding interface.

Dyno Psi-1



Dyno Psi-1, an open-weights model with exceptional in-vitro design performance



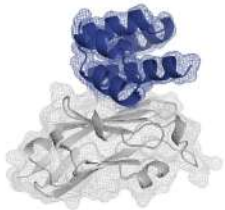
Insulin Receptor	
Expressed	50/50
Binders	27/50
Best K_D	19 nM



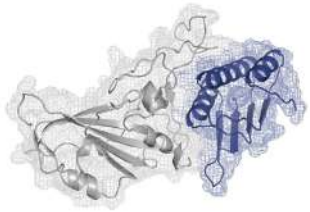
IL-7RA	
Expressed	50/50
Binders	22/50
Best K_D	2.1 nM



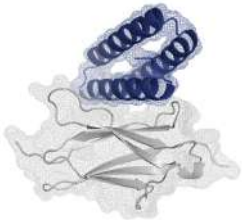
VEGF-A	
Expressed	50/50
Binders	29/50
Best K_D	0.48 nM



PD-L1	
Expressed	49/50
Binders	3/50
Best K_D	100 nM

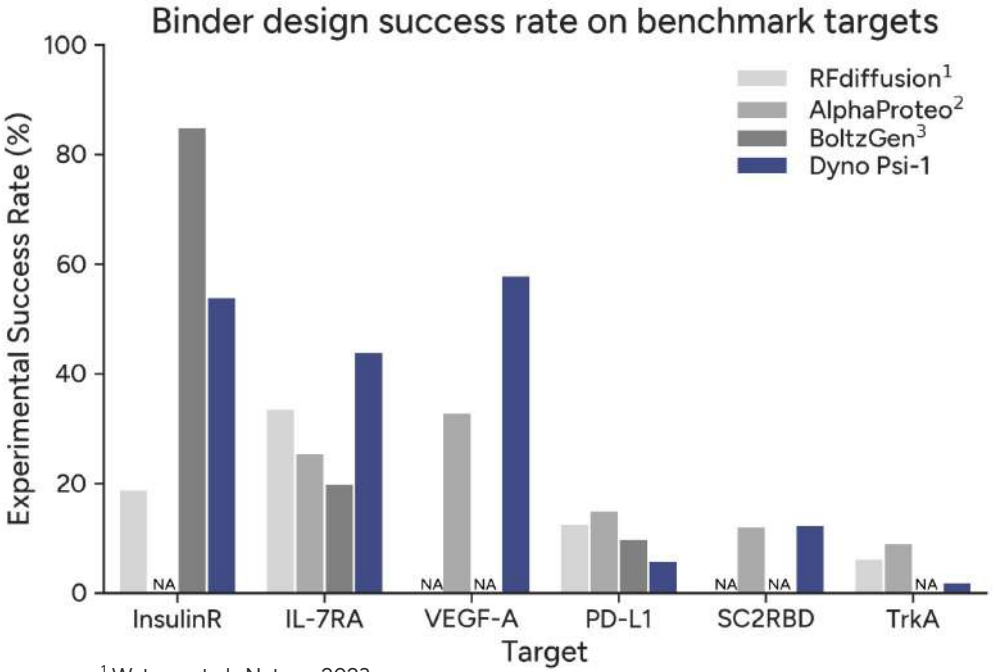


SARS-CoV-2 RBD	
Expressed	7/8
Binders	1/8
Best K_D	420 nM



TrkA	
Expressed	50/50
Binders	1/50
Best K_D	1000 nM

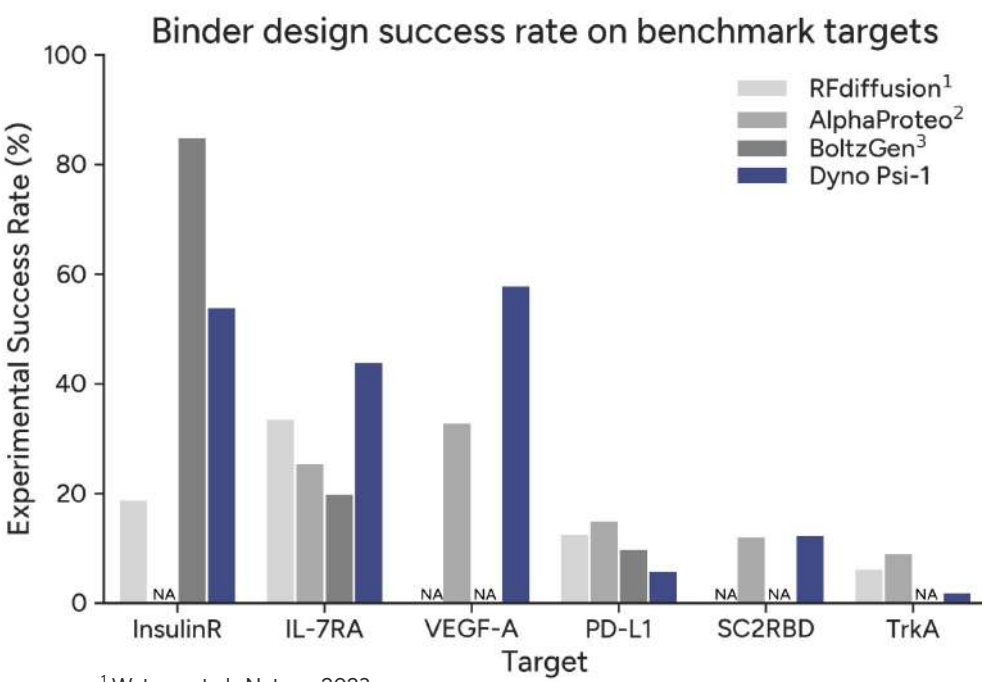
Dyno Psi-1, an open-weights model with exceptional in-vitro design performance

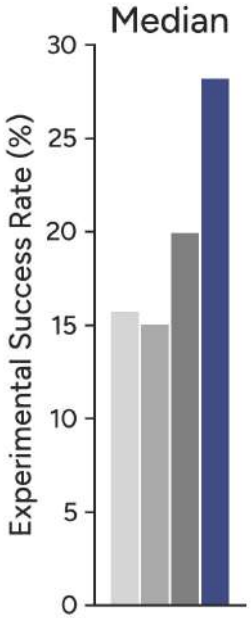


[1] Watson et al., Nature, 2023
[2] Zambaldi et al., arXiv, 2024
[3] Stark et al., bioRxiv, 2025

- Leads on 3/6 targets with available comparator data, while producing experimentally validated binders across all six targets tested

Dyno Psi-1, an open-weights model with exceptional in-vitro design performance



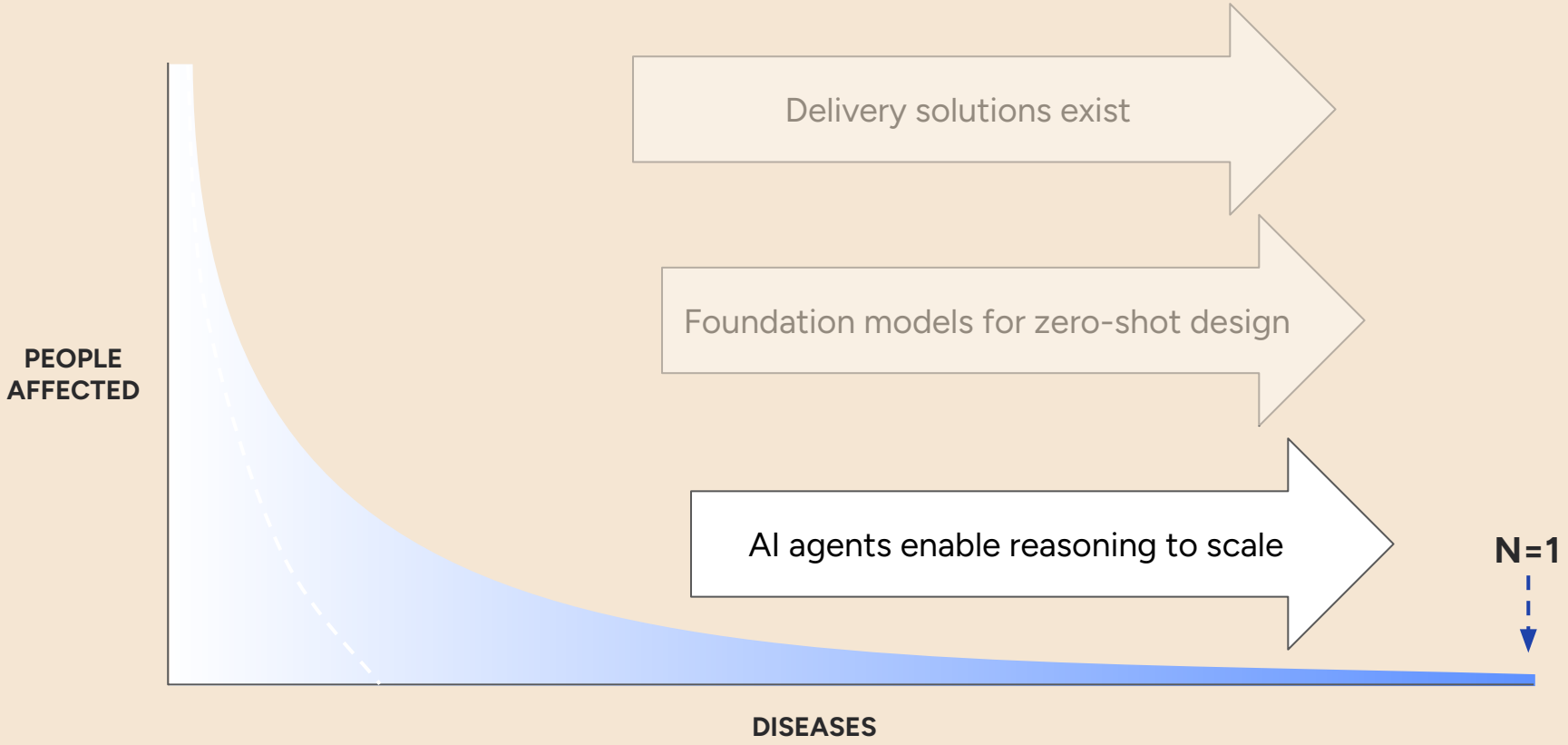


- Matches or exceeds experimental success rates for other open models across diverse binder design benchmarks

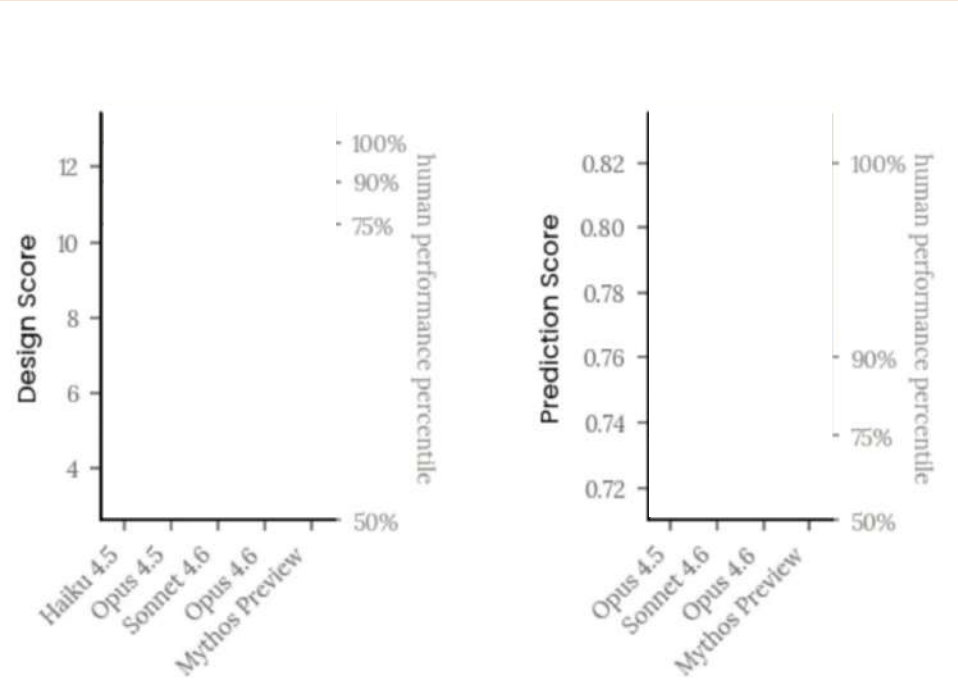
[1] Watson et al., Nature, 2023
[2] Zambaldi et al., arXiv, 2024
[3] Stark et al., bioRxiv, 2025

https://dynotx.substack.com/p/dyno-psi-phi-shaping-new-futures

N=1 design: Why now?

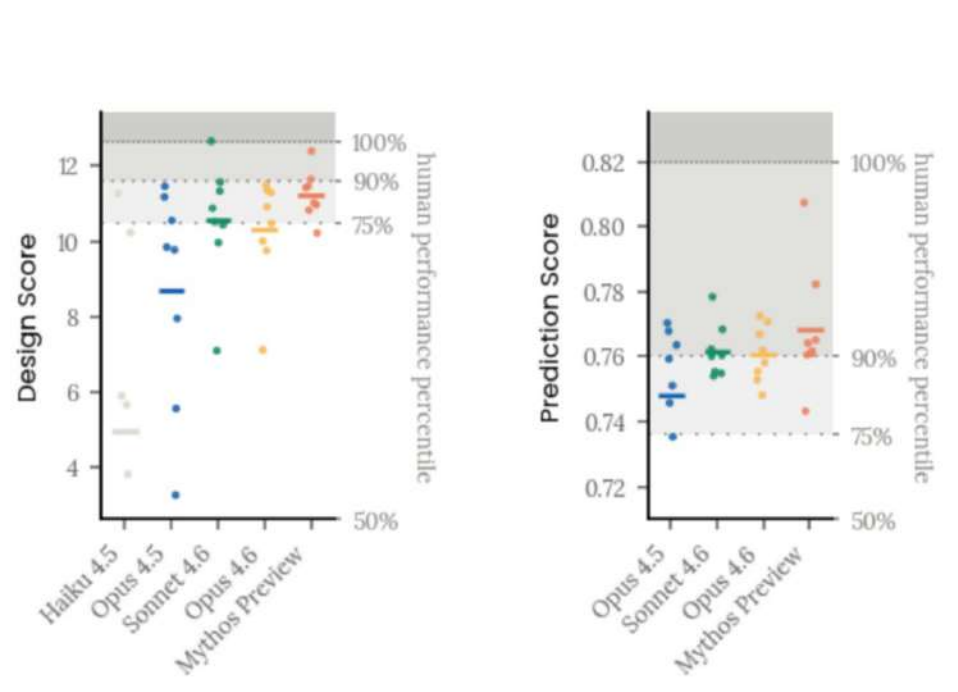


AI reasoning is now quite good for short time horizon tasks



ANTHROP\C

AI reasoning is now quite good for short time horizon tasks



ANTHROP\C

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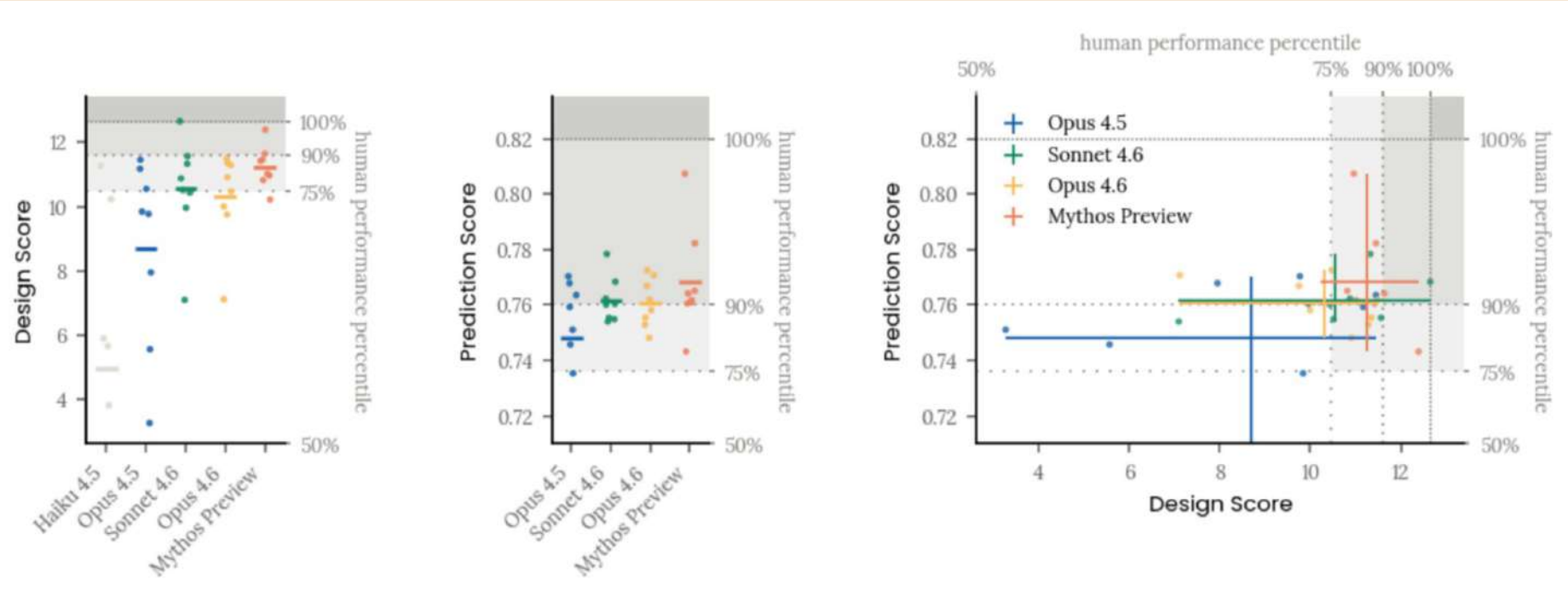


ANTHROP\C

*also collaborating w/ OpenAI using GPT-Rosalind: “best-of-ten model submissions ranked above the 95th percentile of human experts on the prediction task and around the 84th percentile of human experts on the sequence generation task.”

Connecting frontier AI to patients

Dyno Psi-Phi foundation models and APIs



Andreas Borg

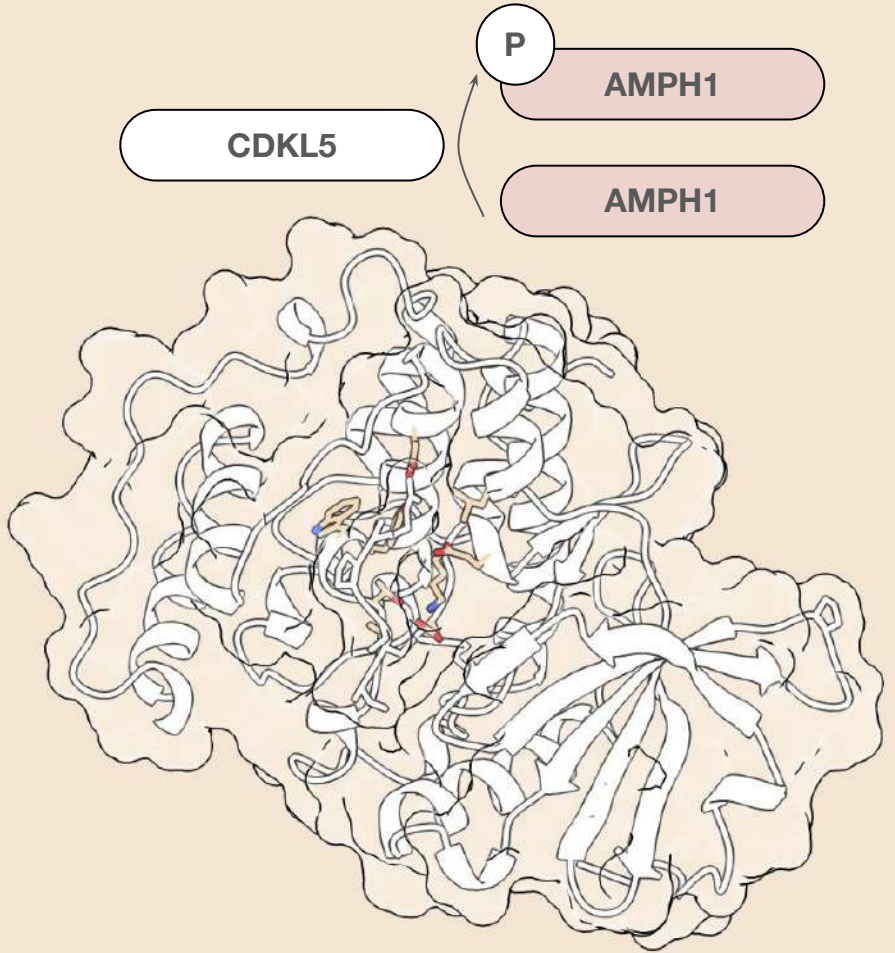
Founder at CURE5 Foundation and Full Stack Engineer at Jimini Health

Co-founded CURE5 Foundation after his daughter was diagnosed with CDKL5 Deficiency Disorder, and is applying his software engineering background to build AI tools that help families make decisions and accelerate therapeutic development.

Connecting frontier AI to patients

Opening Dyno Psi-Phi foundation models and APIs to patient advocacy orgs and rare disease communities

Classification	Biology	Analysis	Development
Which mechanism or modality?	Is the protein stable? Can it bind substrates?	Coordinating computational and wet-lab validation	Advancing therapeutics into clinical trials



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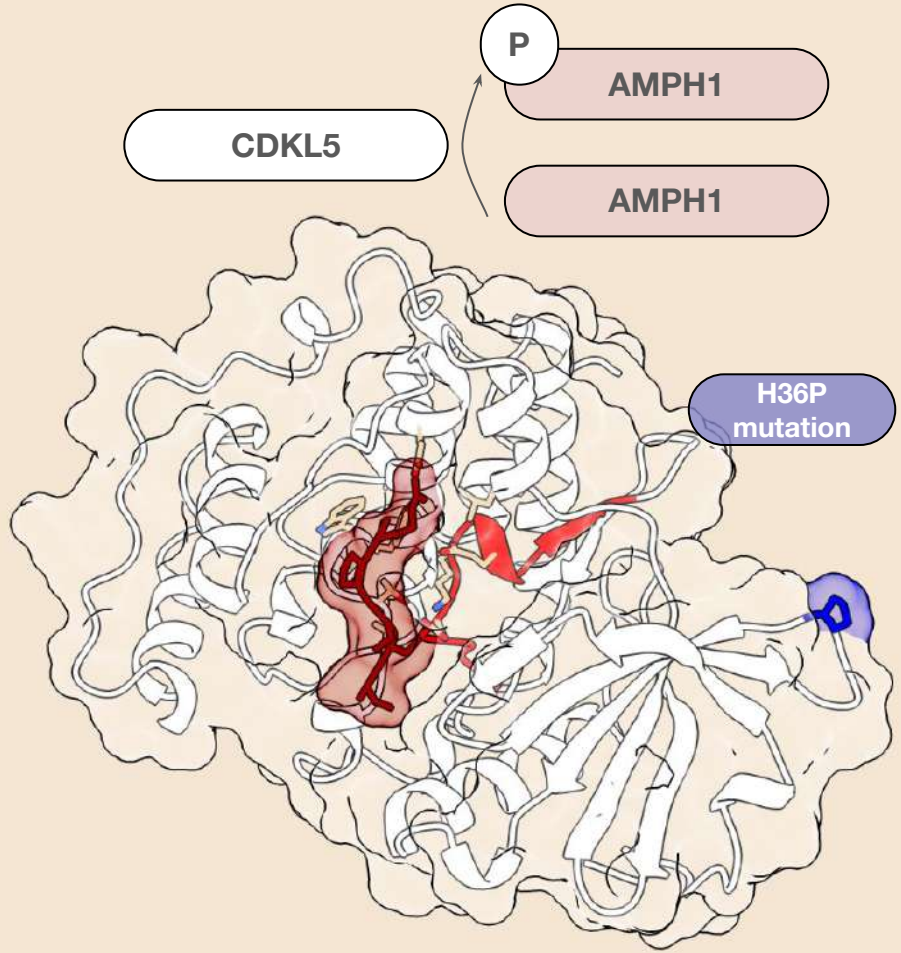
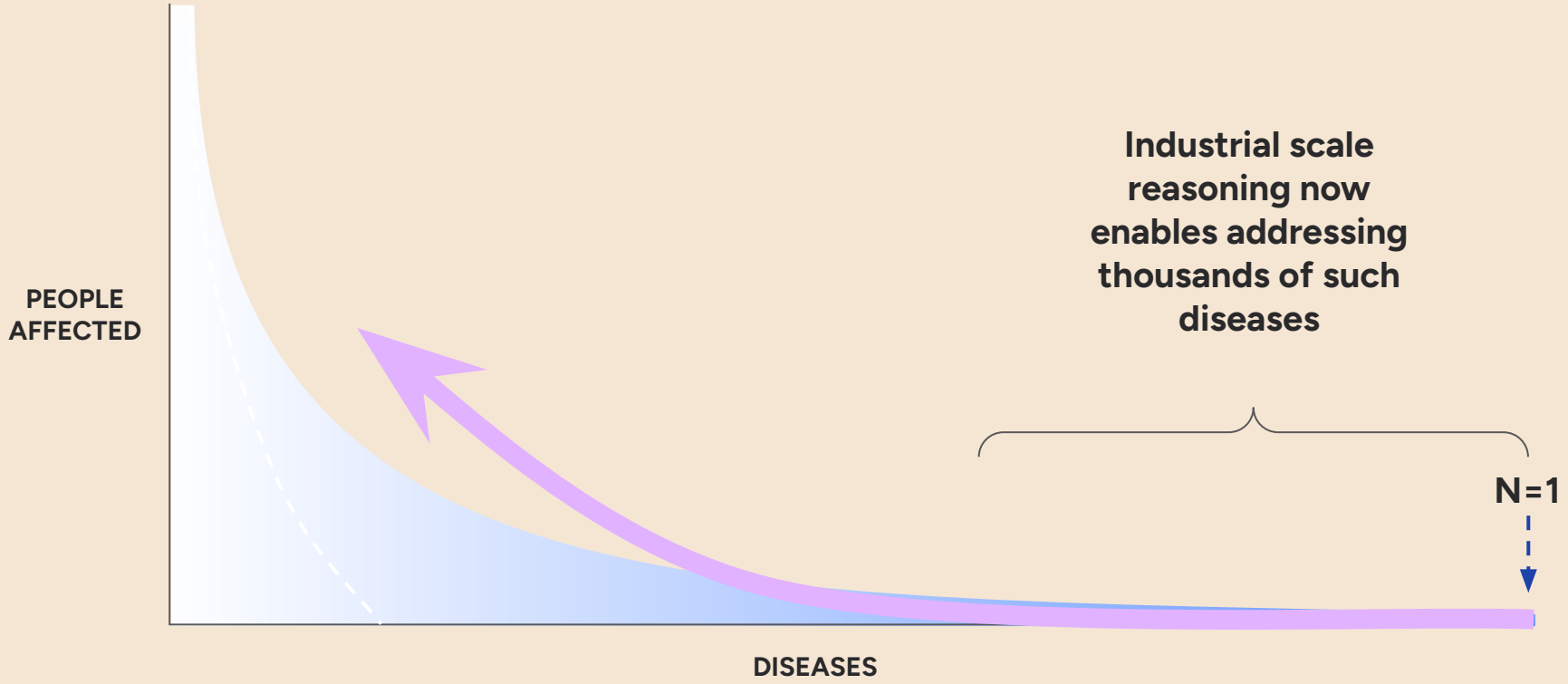


Dyno Phi APIs: **design.dynotx.com**

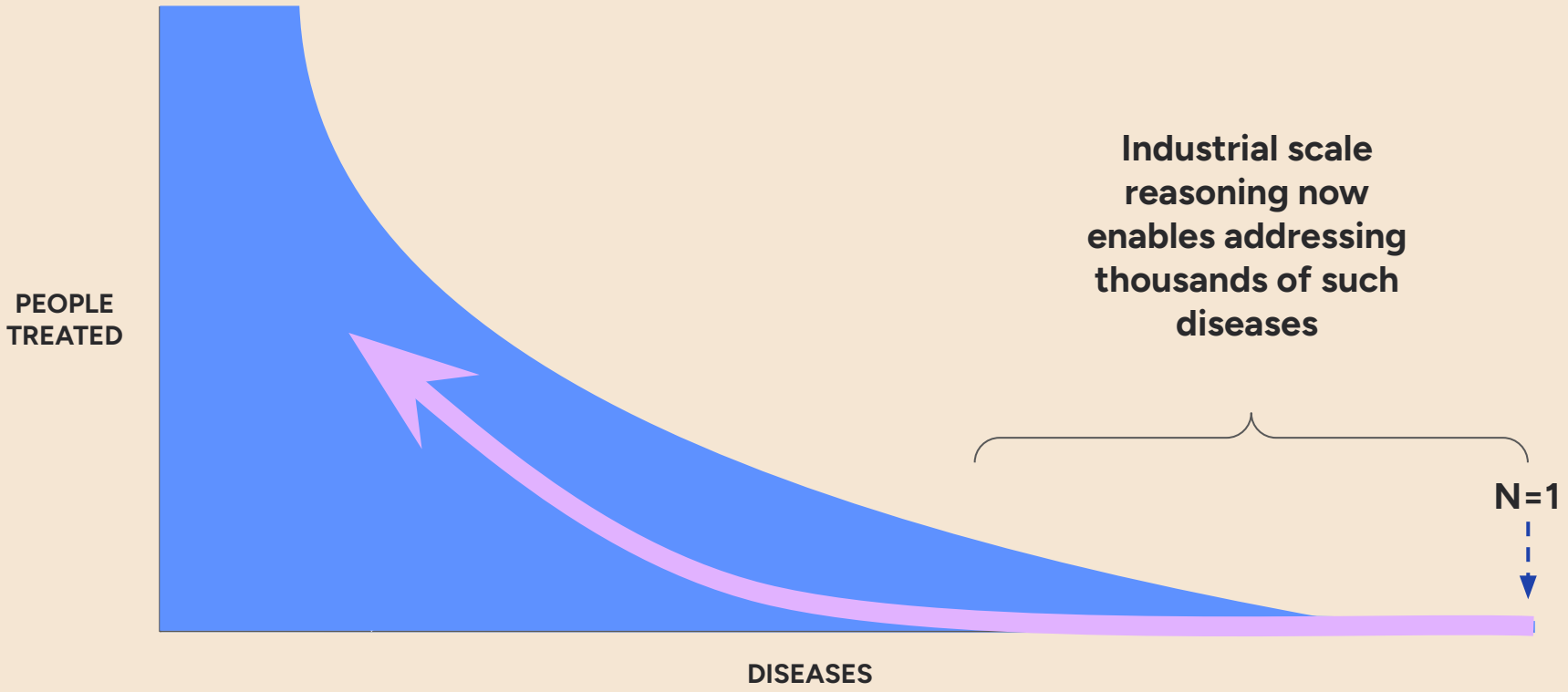
Email **partnerwith@dynotx.com** with an idea for how Dyno can help

dyno

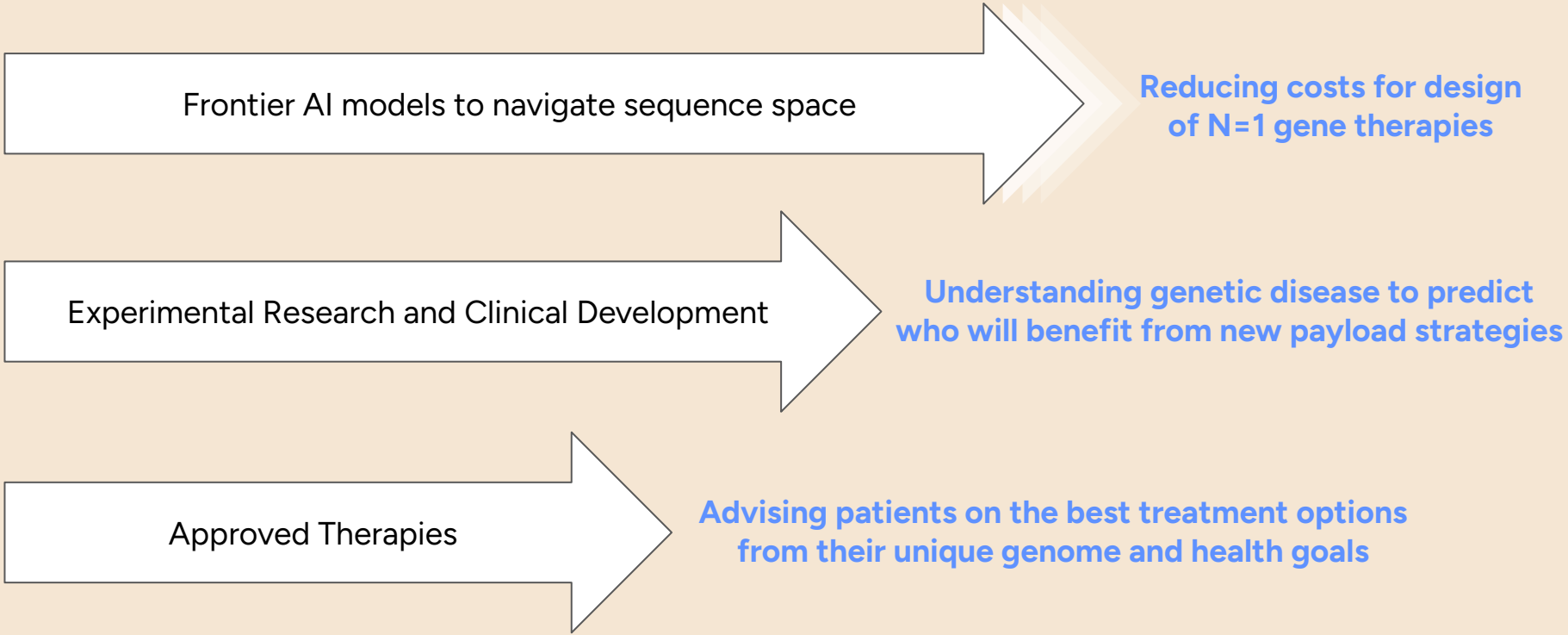
From N=1 to everyone



From N=1 to everyone



AI for advancing the genetic medicine frontiers, in the near future:



We have never had more opportunities and challenges ahead



dyno

GATC

Genetic Agency

TECHNOLOGY CONFERENCE 2025







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GATC

Genetic Agency

TECHNOLOGY CONFERENCE 2025















Come to co-create the future of genetic medicine

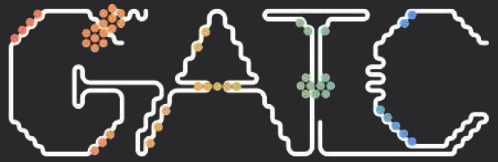
Hear from patients directly as co-creators shaping the next generation of genetic technologies

Meet your next collaborator and build lasting relationships across the gene therapy ecosystem, united by a shared commitment to genetic agency

Step into the future with sessions that reveal the technological trends shaping what's next

Leave with optimism and the conviction to act to build a future with genetic agency

dyno



Genetic Agency

TECHNOLOGY CONFERENCE

SAVE THE DATE

November 18th, 2026 | SF

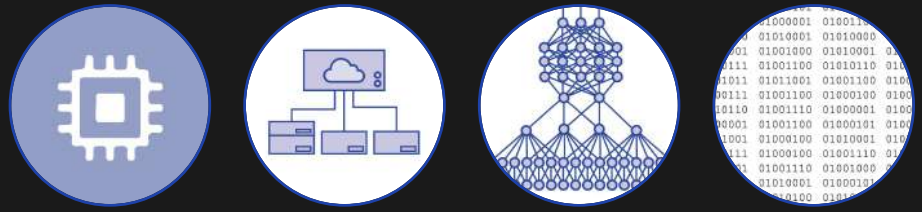
Apply to attend: dynotx.com/gatc2026



Reaching greater heights together

Partnerships are Dyno's business.

We give our partners a competitive edge with high-performance solutions for gene delivery and sequence design.



It’s time to build a future with genetic agency

