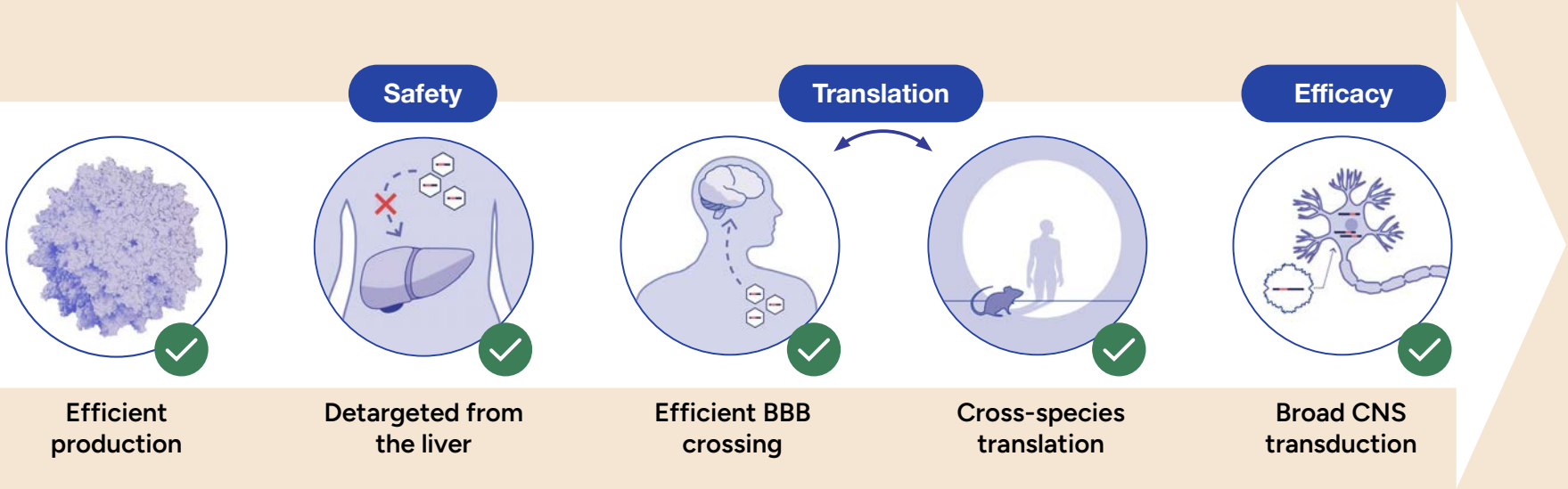
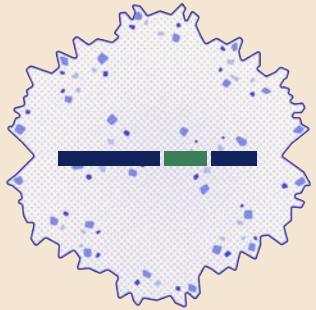
Dyno-9zh achieves broad CNS transduction and improved cross-species tropism upon IV delivery

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



Dyno-9zh is broadly compatible with AAV9-based production systems



Dyno-9zh capsid packaging CAG-H3F3-HA genome with ssAAV ITRs

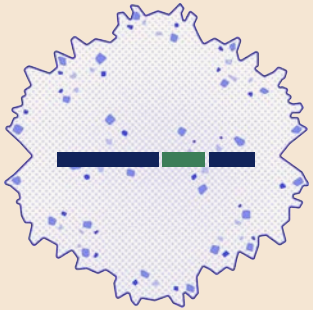
Upstream Production:

- Suspension production from 2L shake flask showed a crude yield **71% of AAV9**
- Material for the NHP study was produced in a 25L bioreactor production

Downstream Purification (Affinity Chromatography)**:**

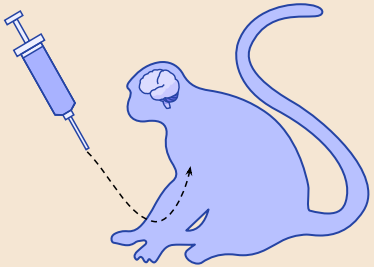
- *Resin choice:* POROS CaptureSelect AAV9 resin.
- *Elution:* Dyno-9zh is compatible with 100 mM citric acid (pH 3). With no optimization we see **68% step recovery**.

We compared Dyno-9zh head-to-head with the published ALPL-targeted capsid TTM-027



AAV capsid packaging
CAG-H3F3-HA genome
with ssAAV ITRs

Confirm engineered
binding to ALPL

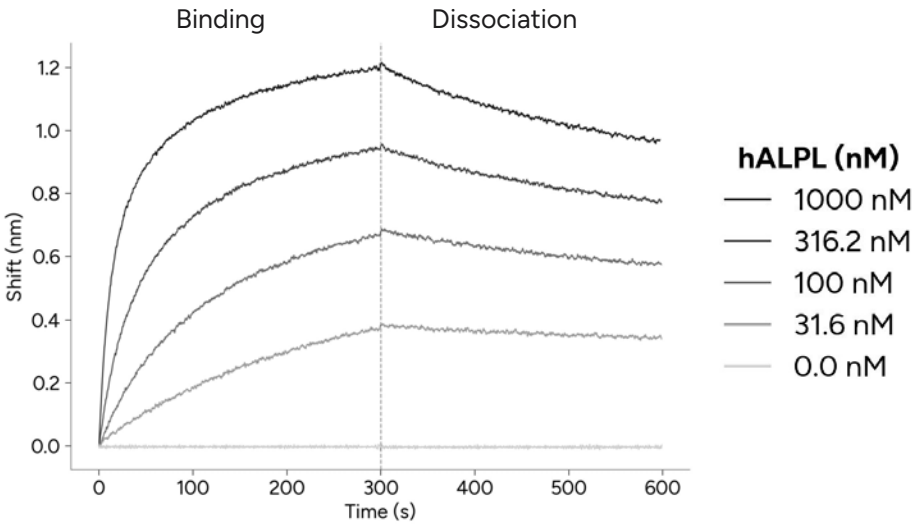


Adult Cyno NHPs
3e13 vg/kg, N=2
28 days in life

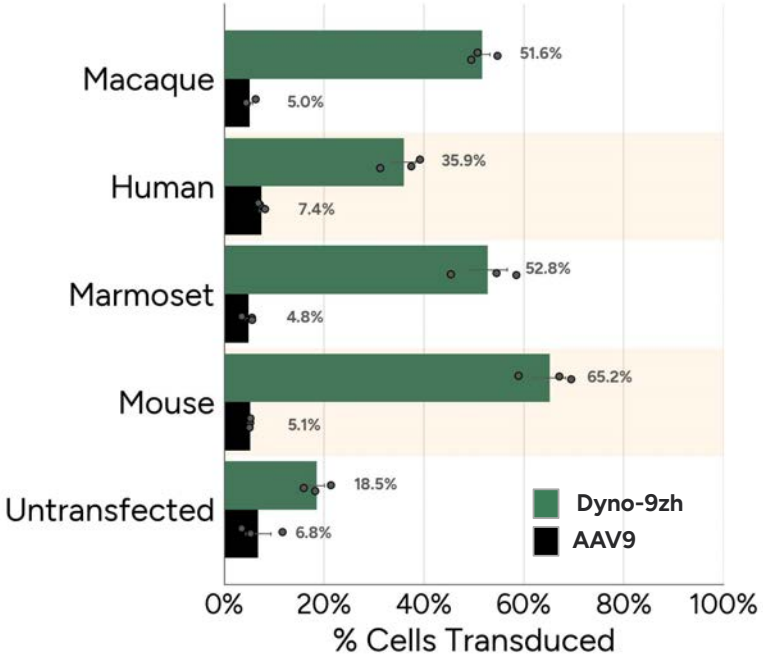
C57BL/6 Mice
1e13 vg/kg, N=3
21 days in life

Dyno-9zh binds human Alkaline Phosphatase (ALPL) receptor, increasing confidence in successful translation to humans

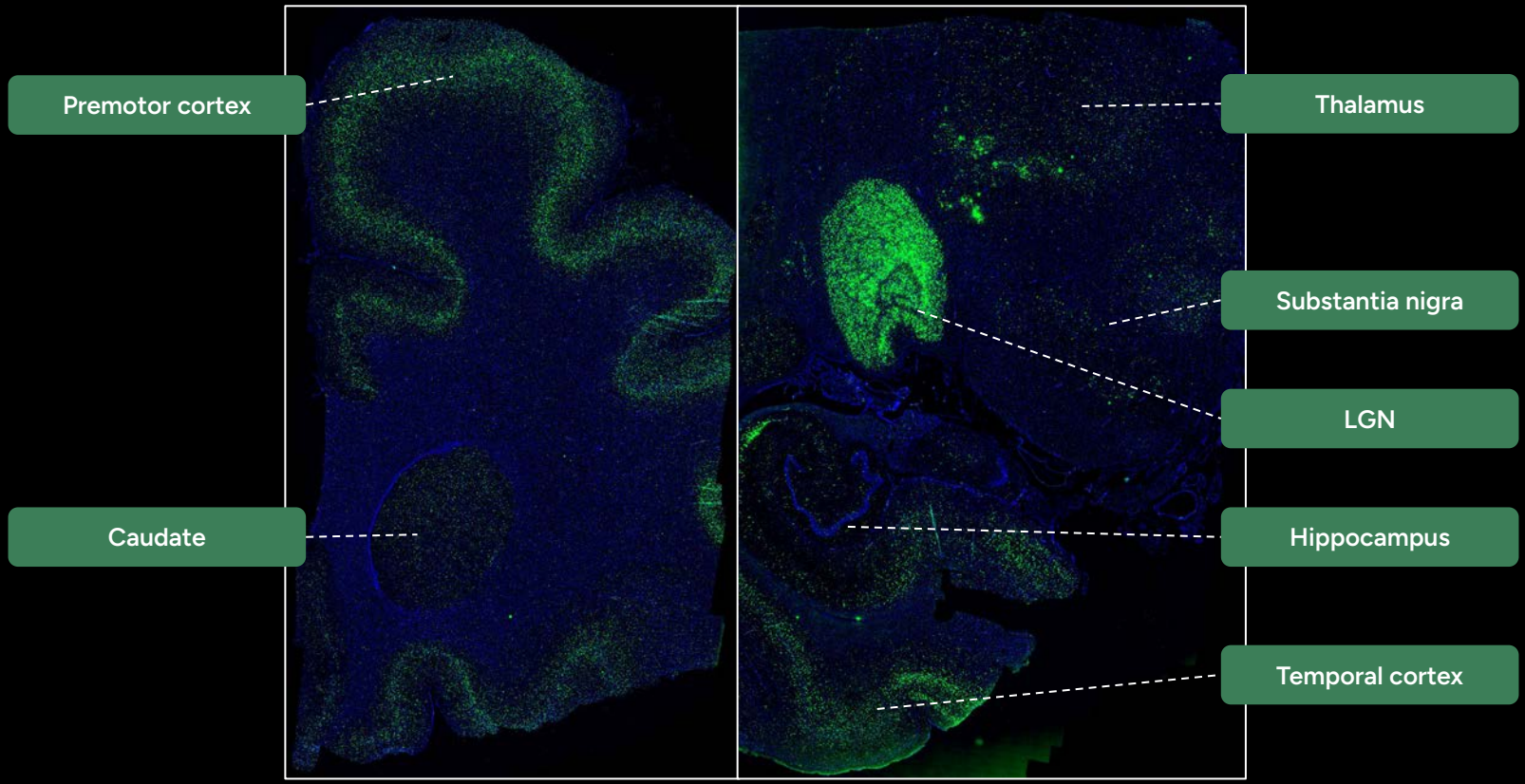
Dyno-9zh binds to human ALPL



Dyno-9zh efficiently transduces HEK cells overexpressing ALPL orthologs

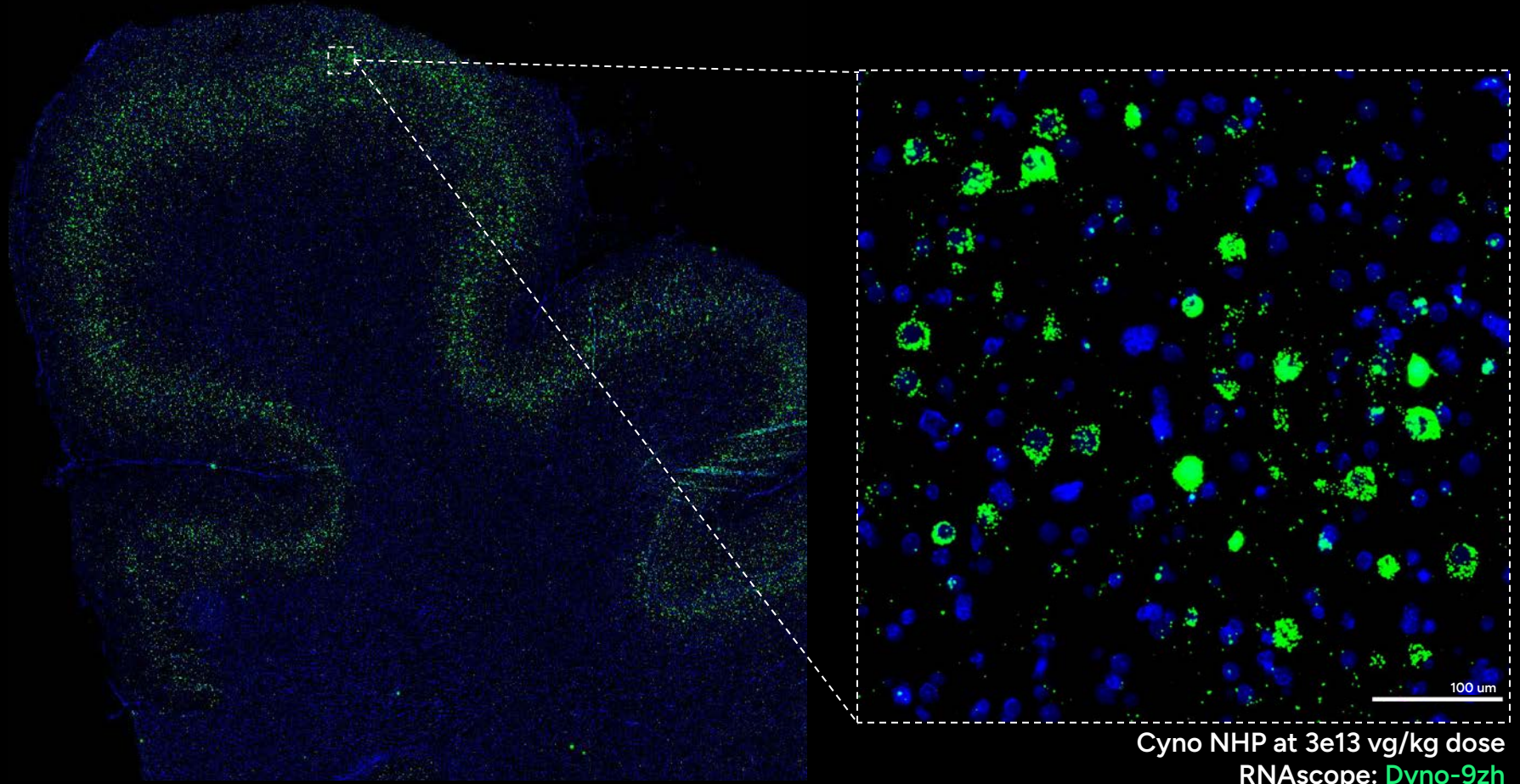


Dyno-9zh achieves widespread transduction across the NHP brain



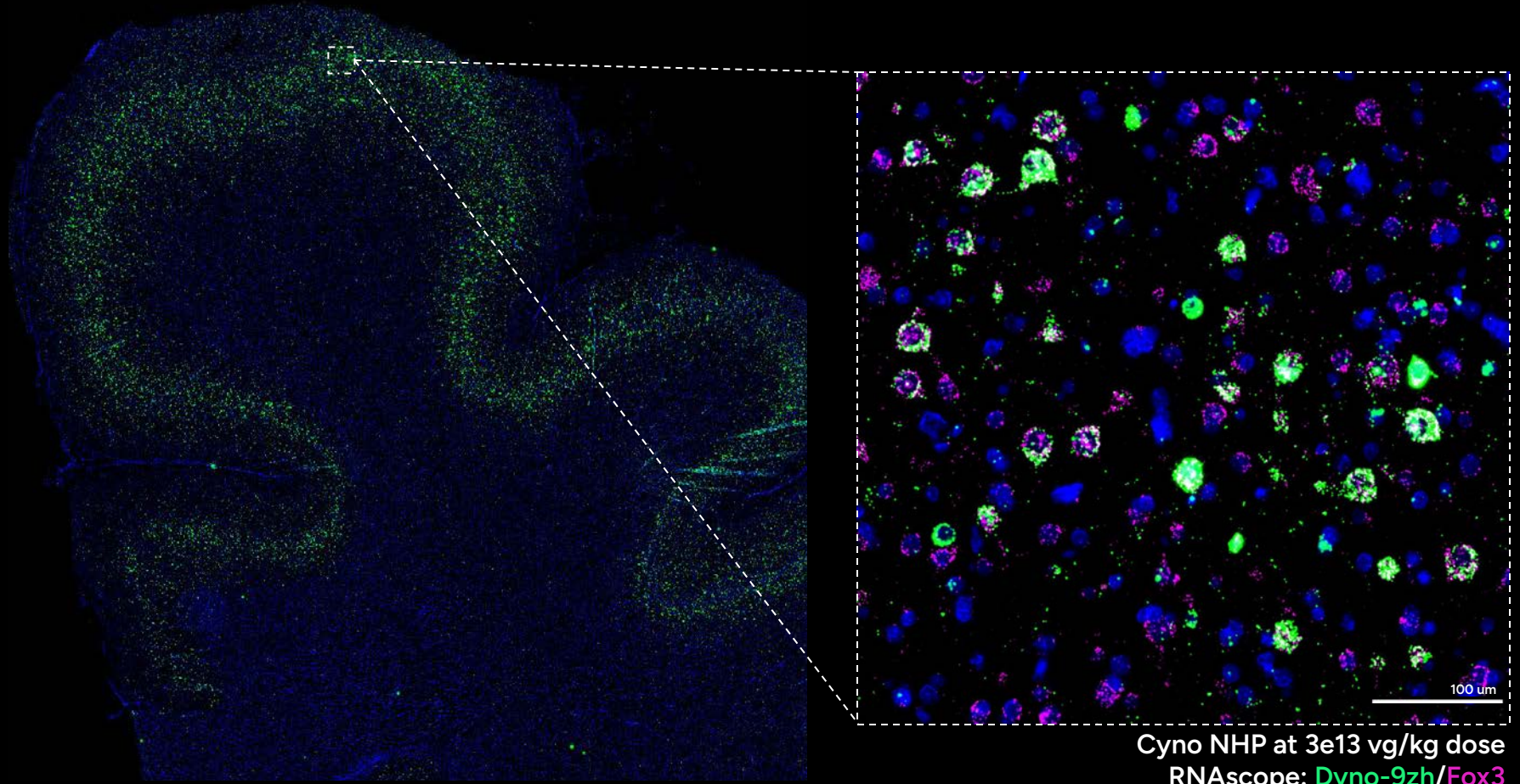
Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh

Dyno-9zh transduces up to 46% of cells in Premotor cortex



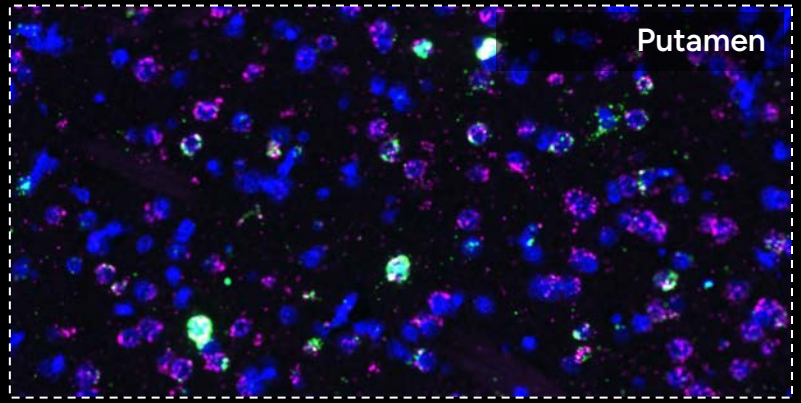
Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh

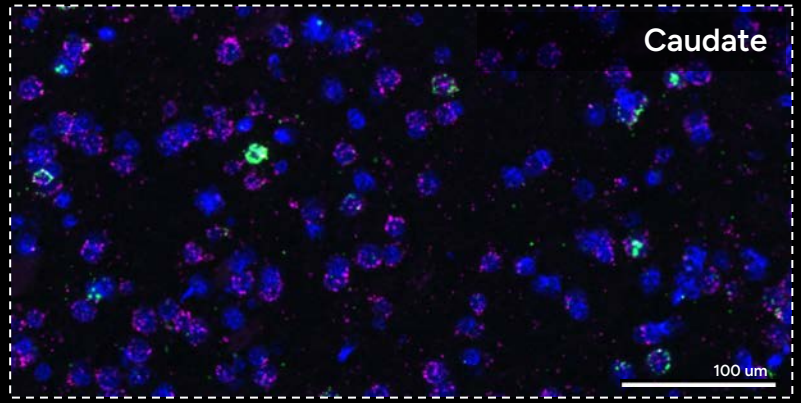
Dyno-9zh transduces up to 50% of neurons in Premotor cortex

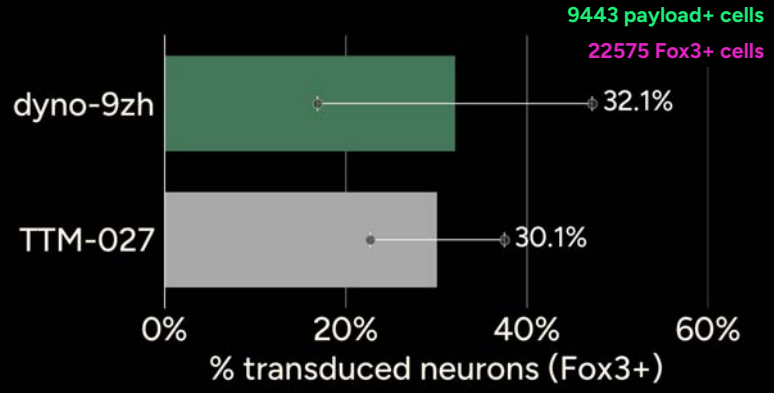


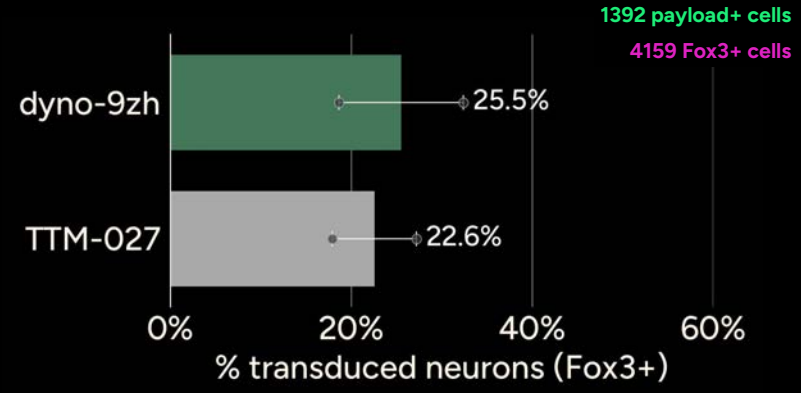
Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh/Fox3

Dyno-9zh transduces up to 47% neurons in striatum



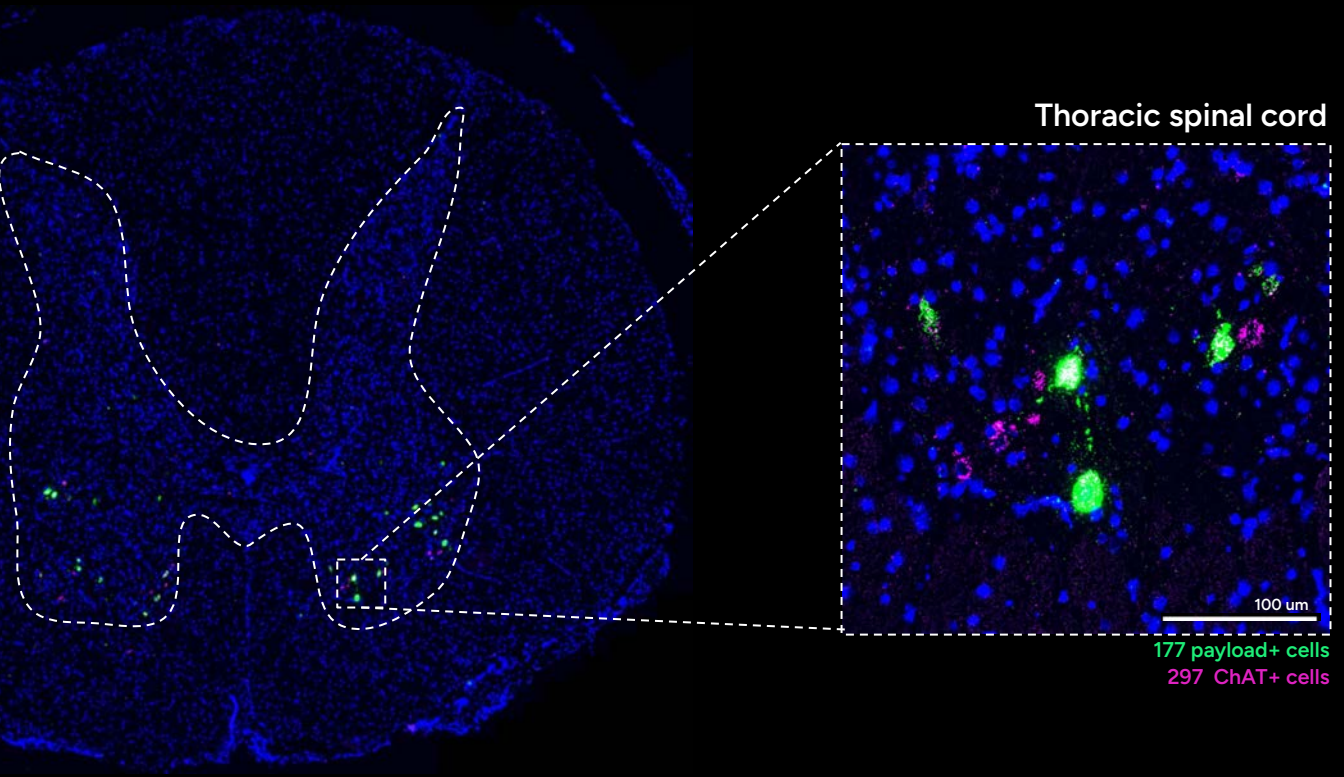


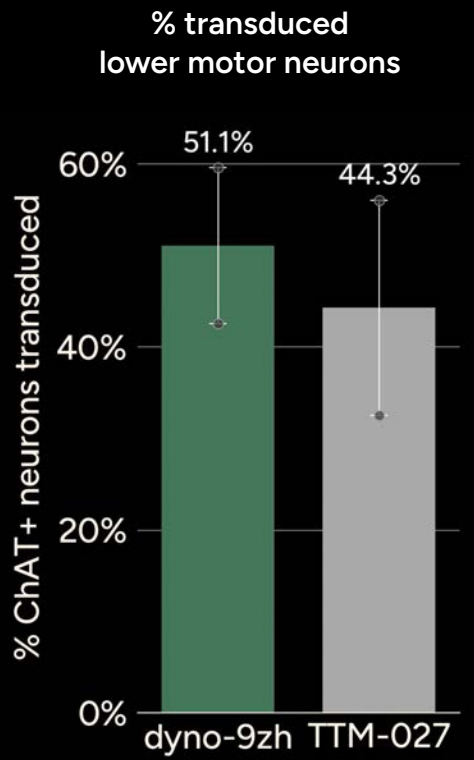




Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh/Fox3

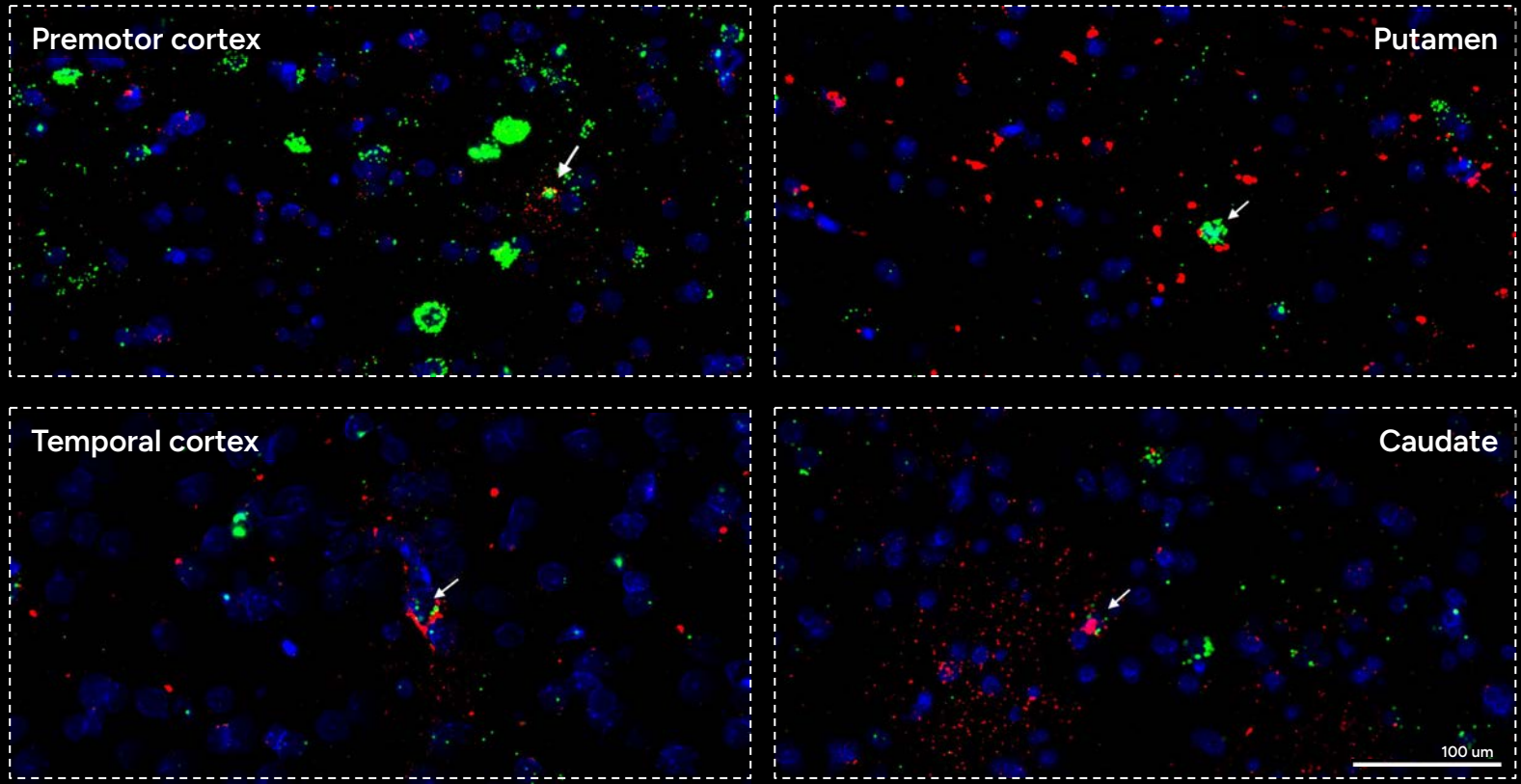
Dyno-9zh transduces up to 60% lower motor neurons





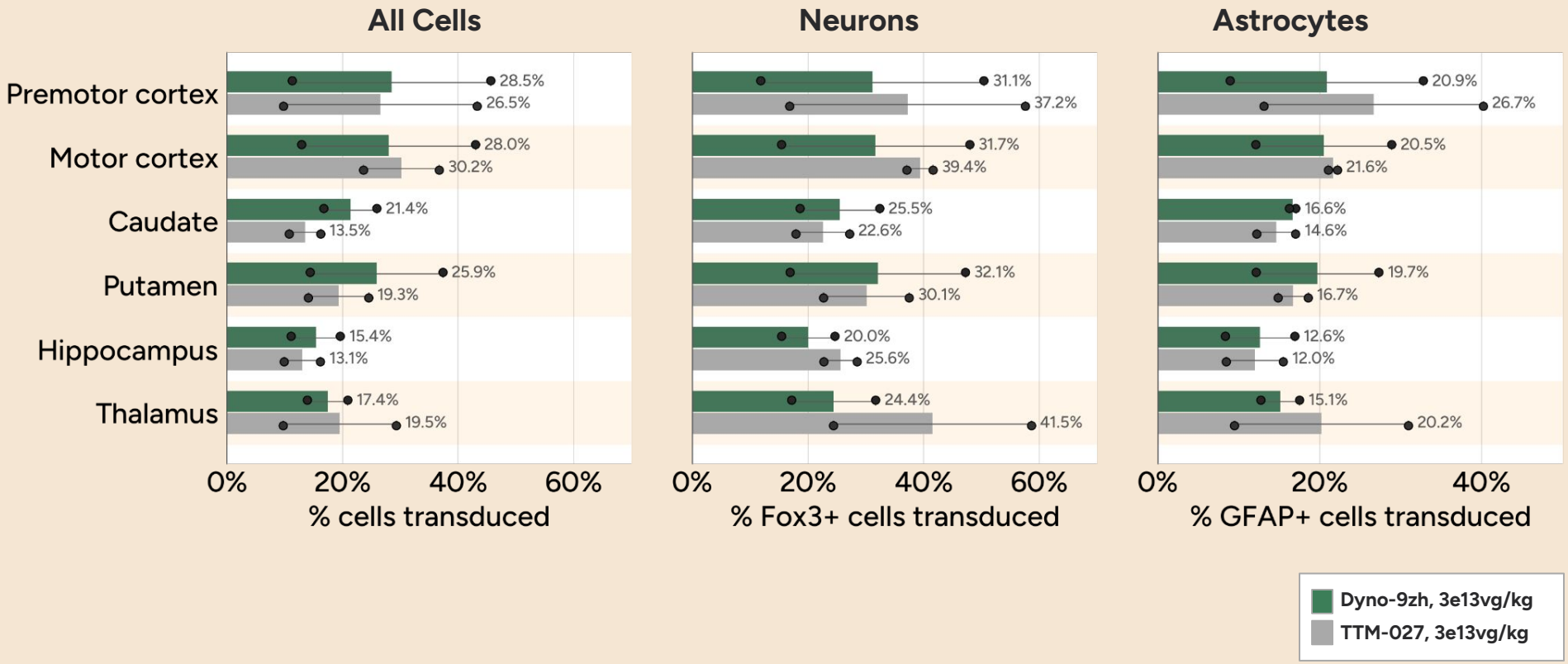
Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh/ChAT

Dyno-9zh transduces up to 32% of astrocytes in the CNS

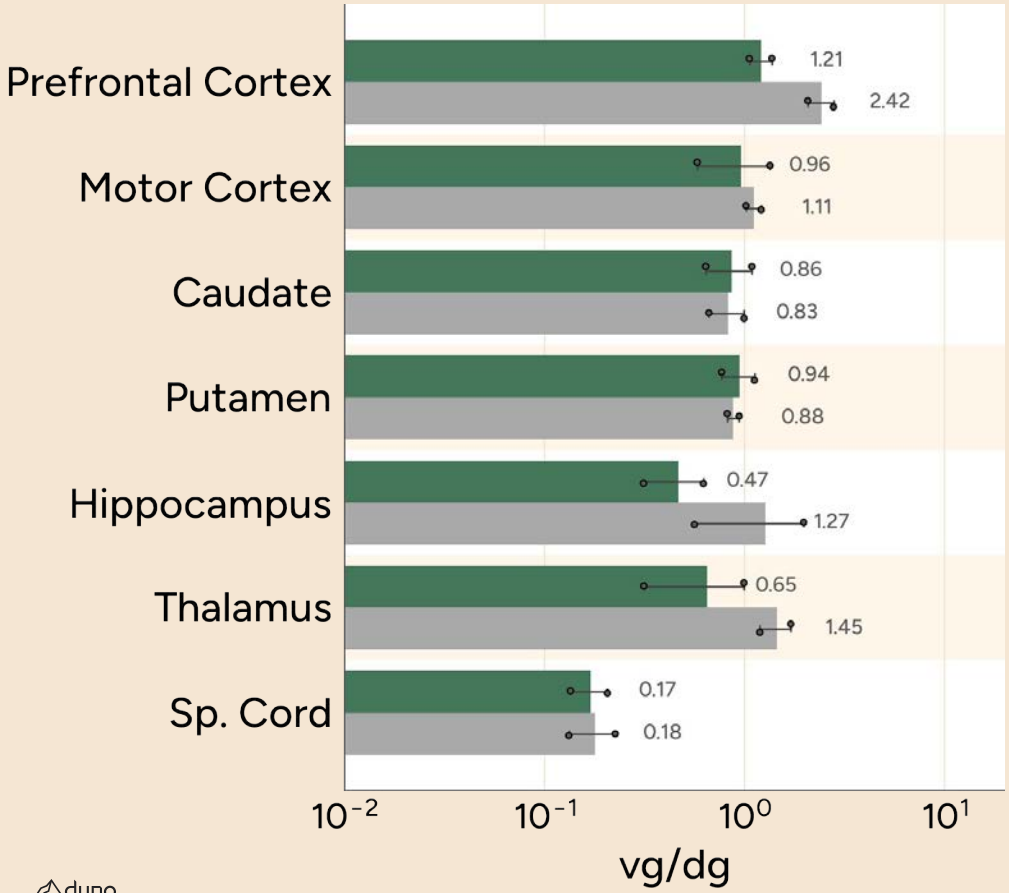


Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh/GFAP

Dyno-9zh shows broad CNS transduction matching the performance of TTM-027



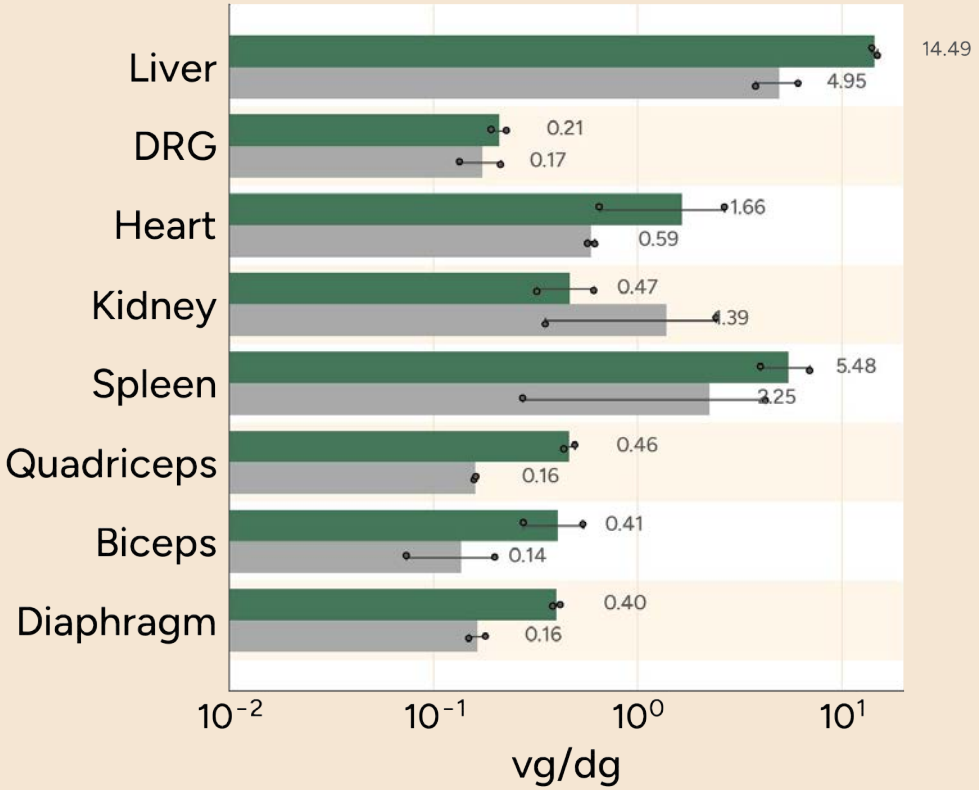
Dyno-9zh shows widespread CNS biodistribution



Dyno-9zh shows comparable biodistribution to TTM-027 across cortex and basal ganglia.

Dyno-9zh, 3e13vg/kg
TTM-027, 3e13vg/kg

Dyno-9zh shows minimal biodistribution to off-target organs



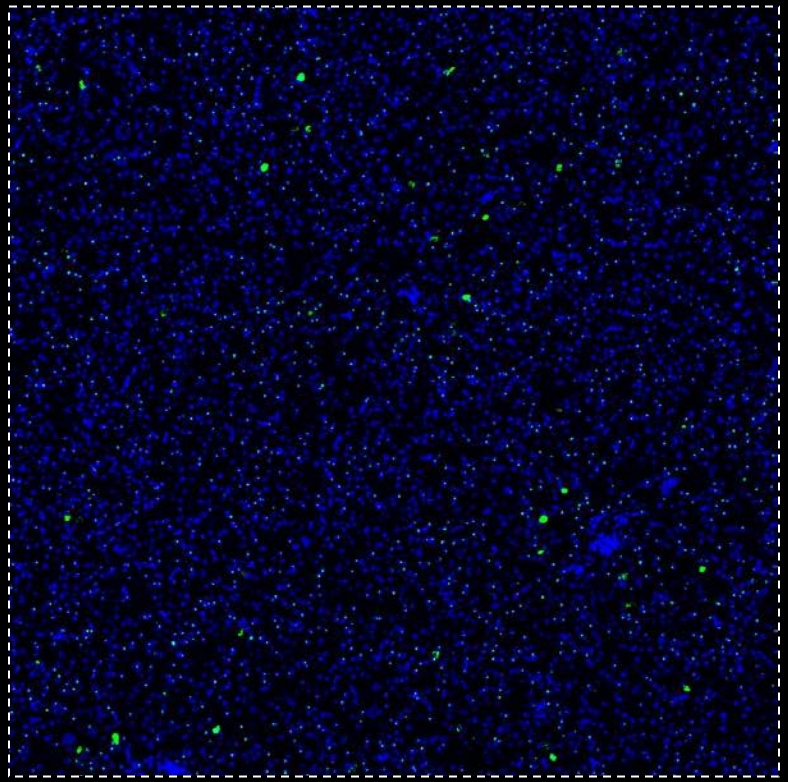
Dyno-9zh demonstrates a >10-fold reduction in liver exposure compared to AAV9.

AAV9, 1e13 vg/kg → **170 vg/dg**

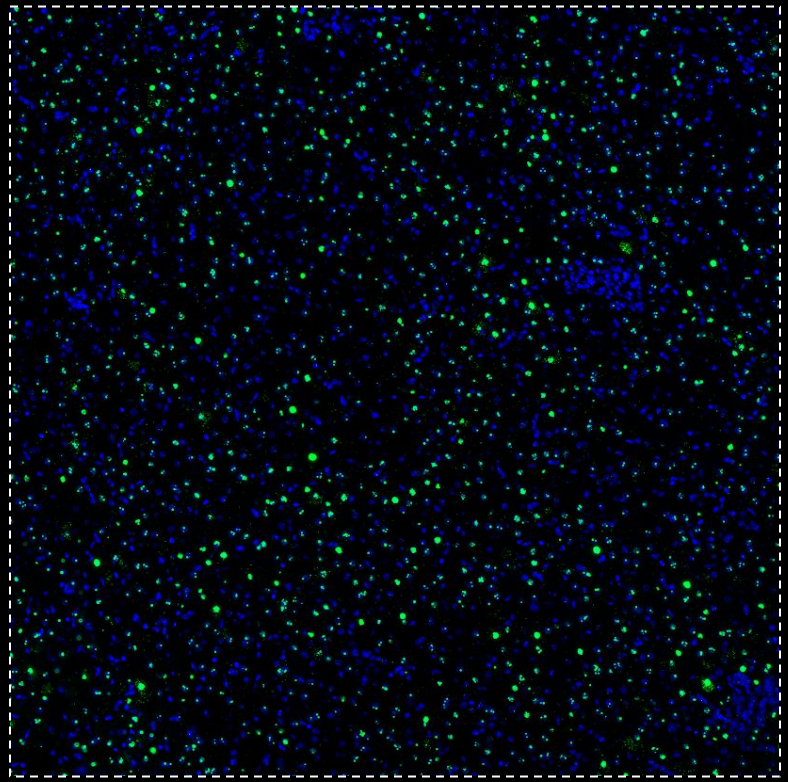
Dyno-9zh, 3e13 vg/kg → **14.5 vg/dg**

Dyno-9zh, 3e13vg/kg
TTM-027, 3e13vg/kg

Dyno-9zh shows excellent liver detargeting vs AAV9

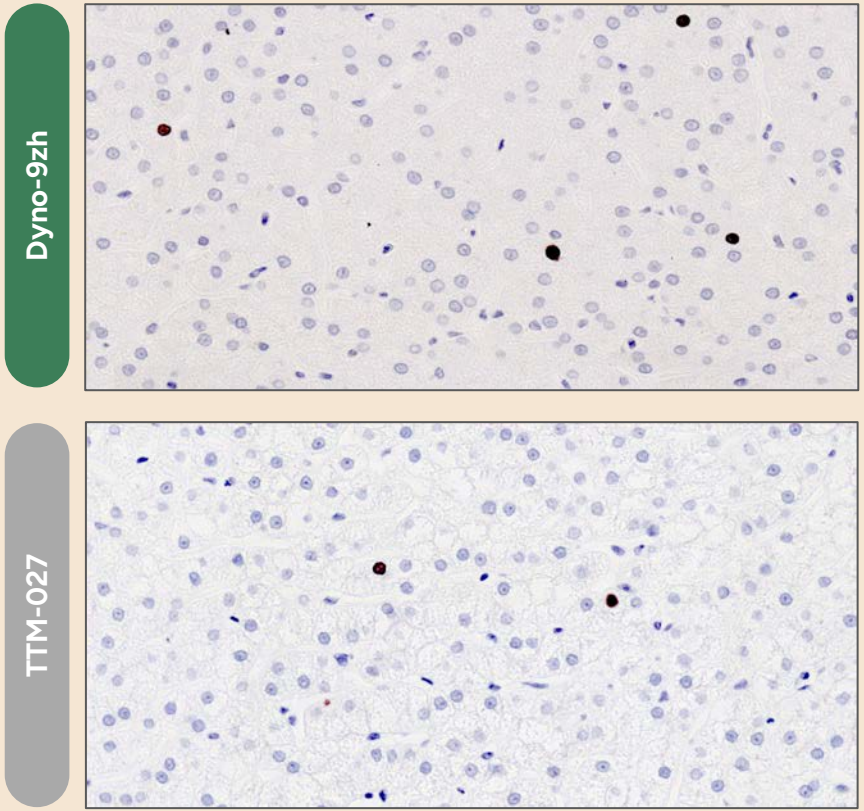


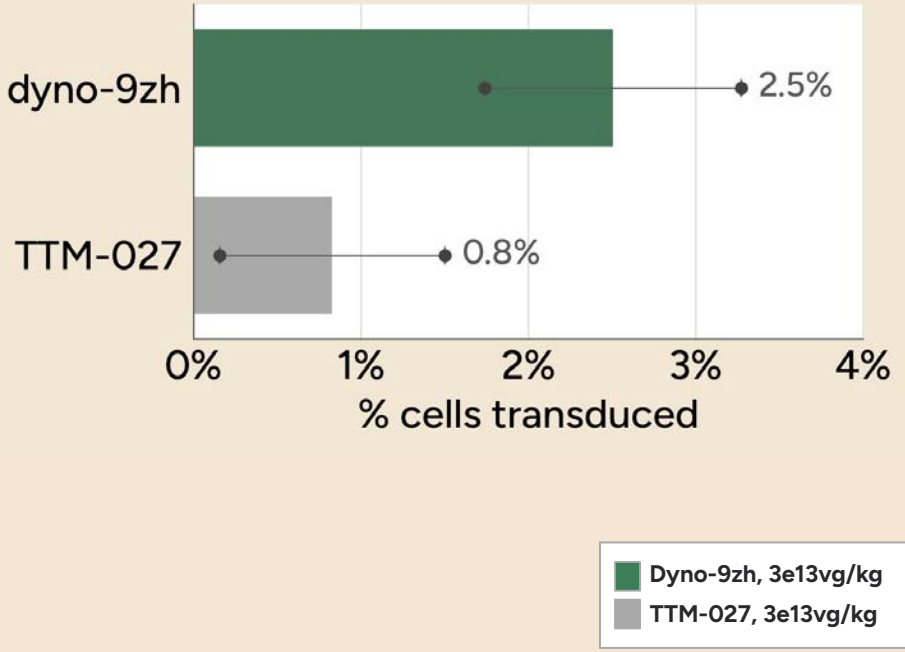
Cyno NHP at 3e13 vg/kg dose
RNAscope: Dyno-9zh



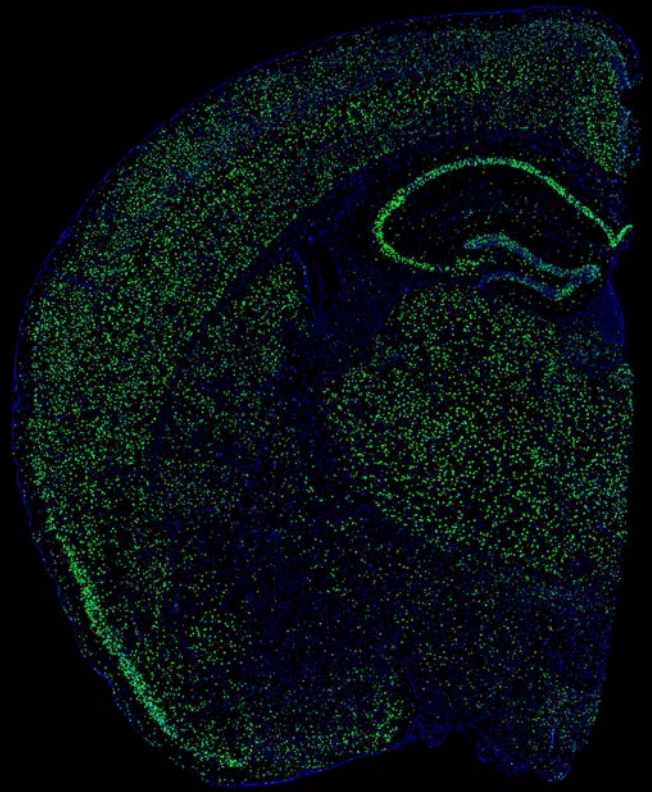
Cyno NHP at 1e13 vg/kg dose
RNAscope: AAV9

Dyno-9zh shows minimal payload expression in the liver, comparable to TTM-027

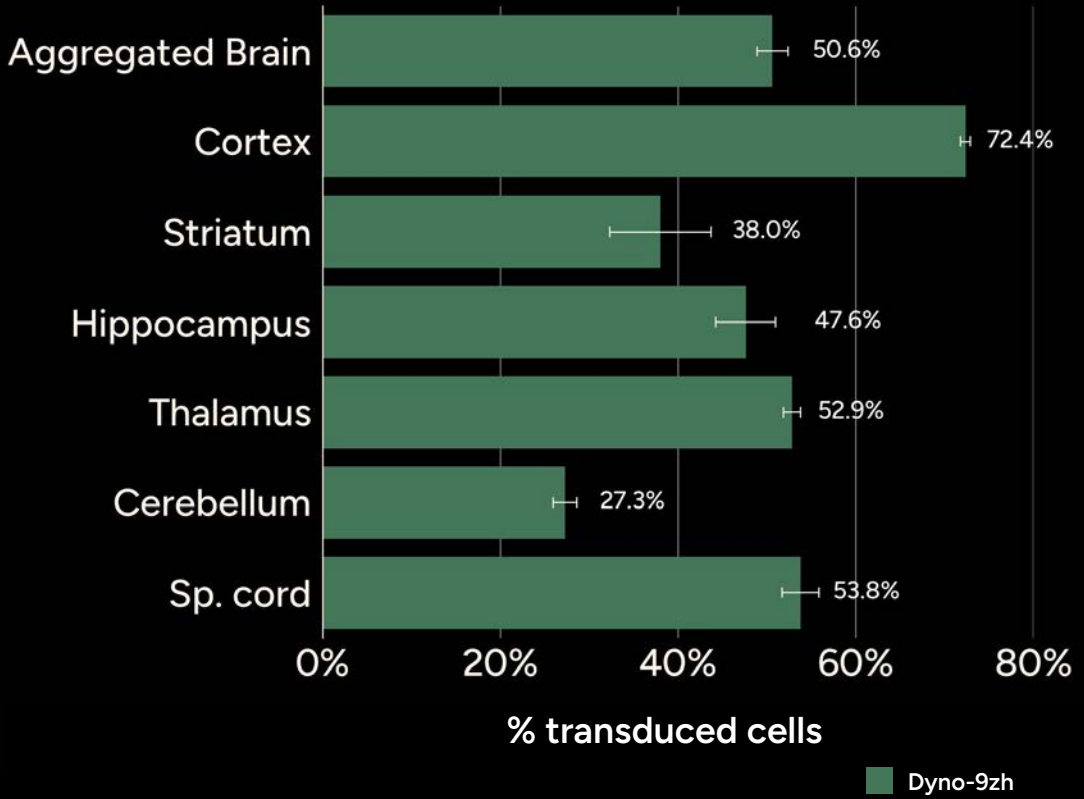




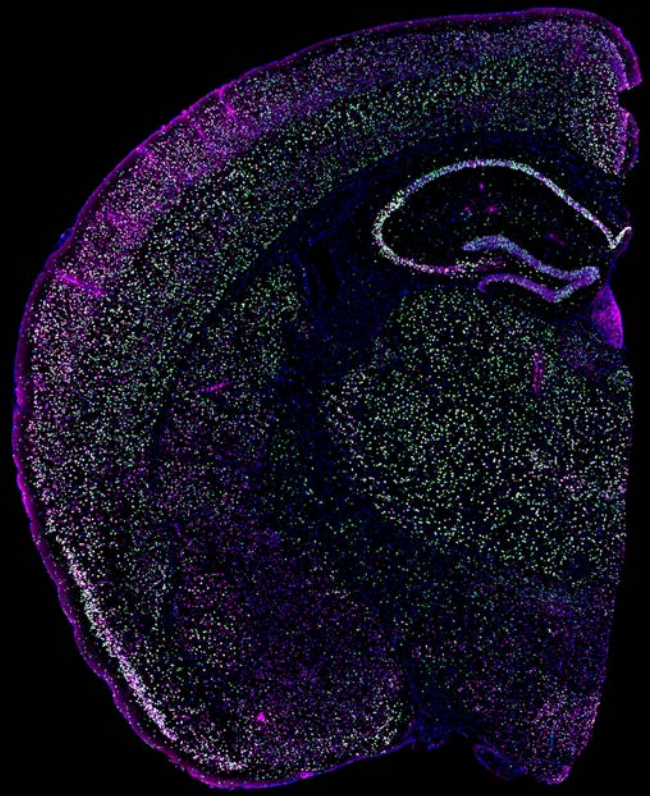
Dyno-9zh demonstrates robust mouse CNS transduction



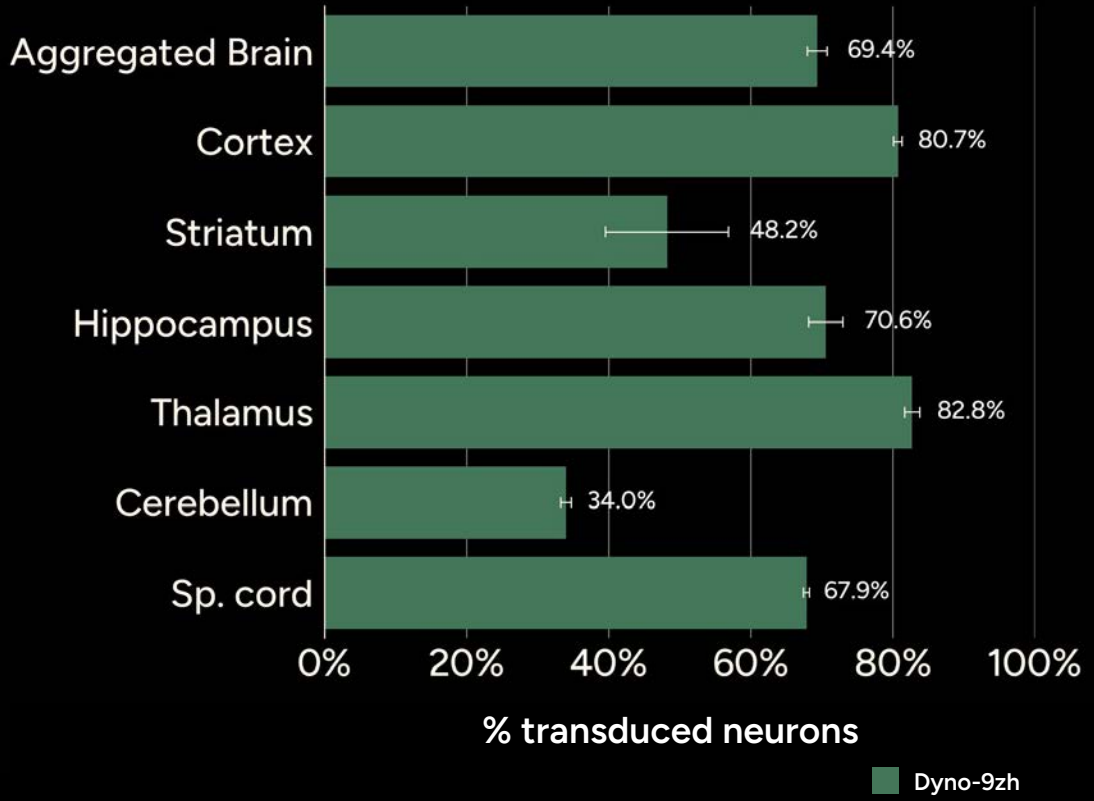
Dyno-9zh 1e13 vg/kg
C57BL/6 mice



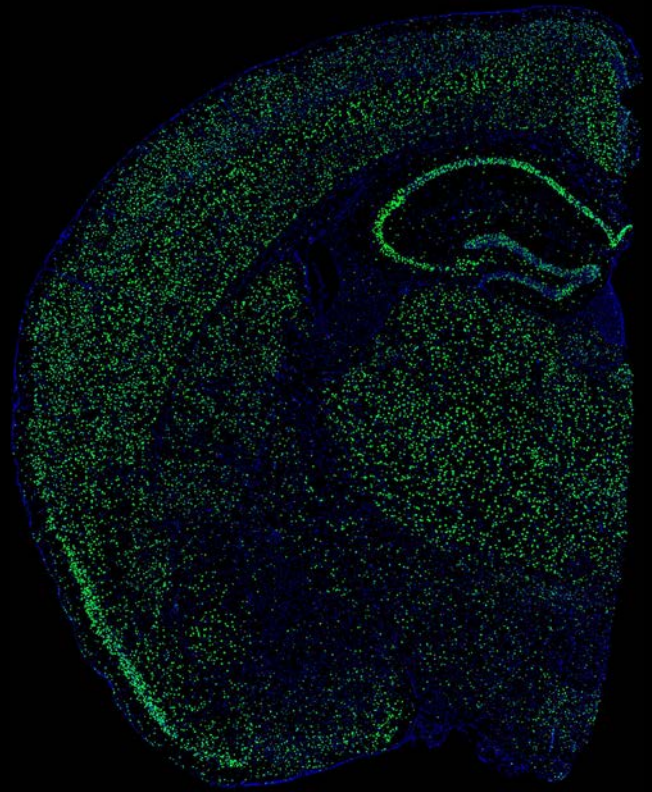
Dyno-9zh demonstrates robust mouse CNS transduction



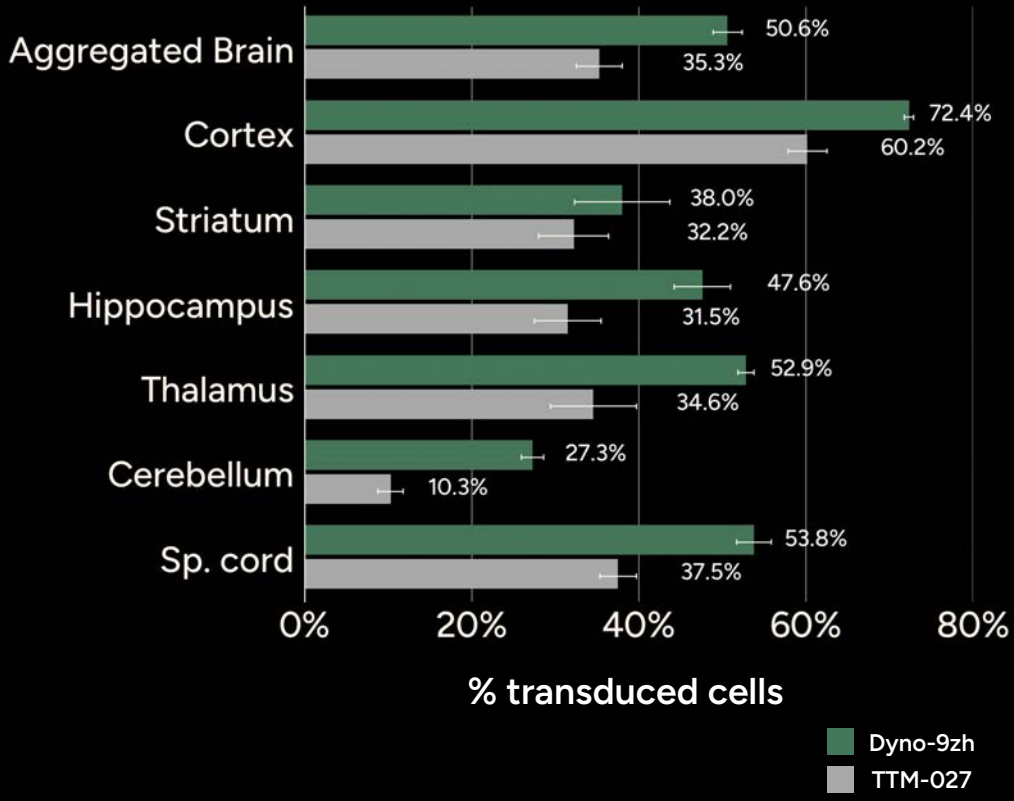
Dyno-9zh 1e13 vg/kg
C57BL/6 mice



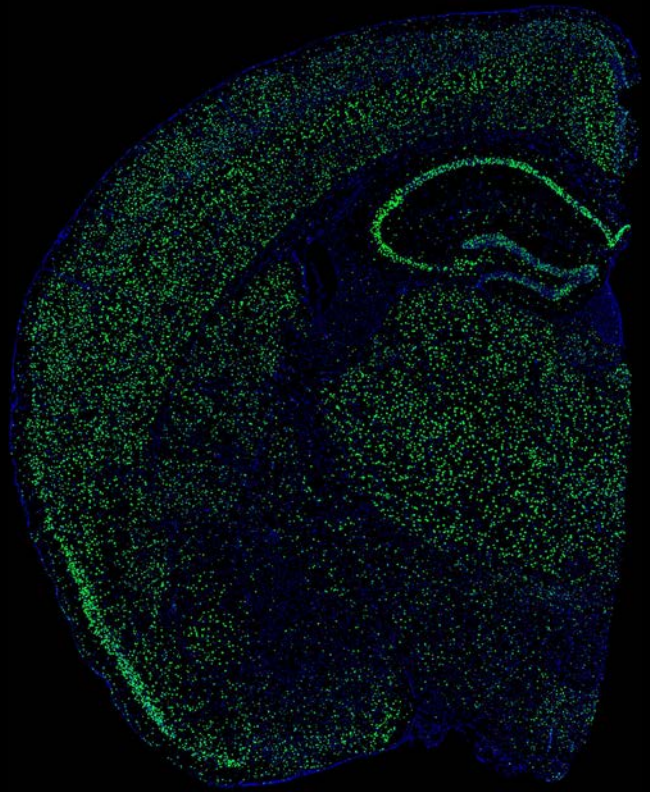
Dyno-9zh outperforms TTM-027 in mouse CNS transduction



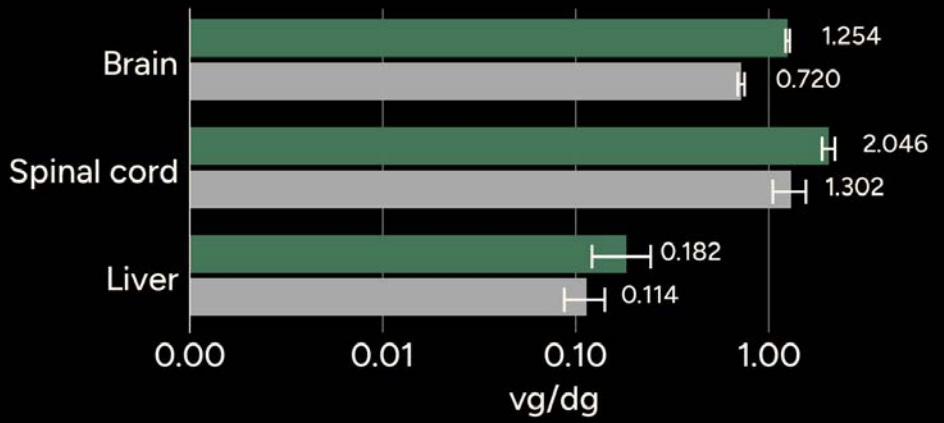
Dyno-9zh 1e13 vg/kg
C57BL/6 mice



Dyno-9zh outperforms TTM-027 in mouse CNS biodistribution

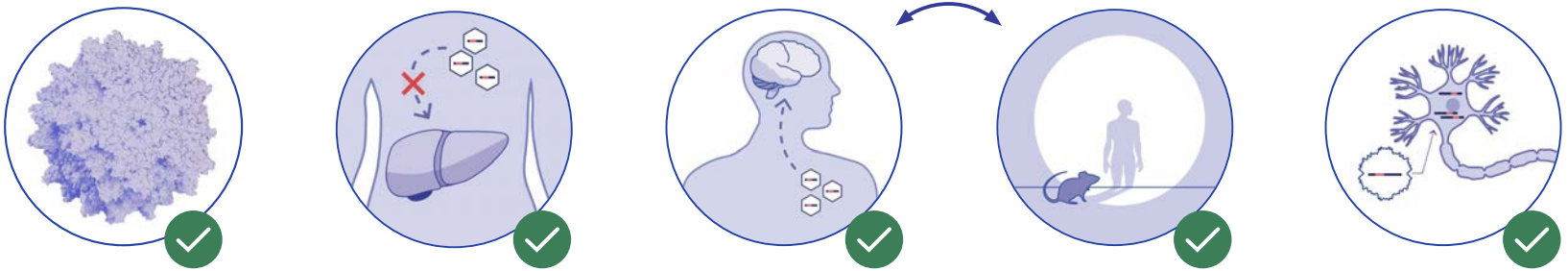


Dyno-9zh 1e13 vg/kg
C57BL/6 mice



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

dyno

DYNO FRONTIERS NETWORK

Access Dyno capsids.

EASY.