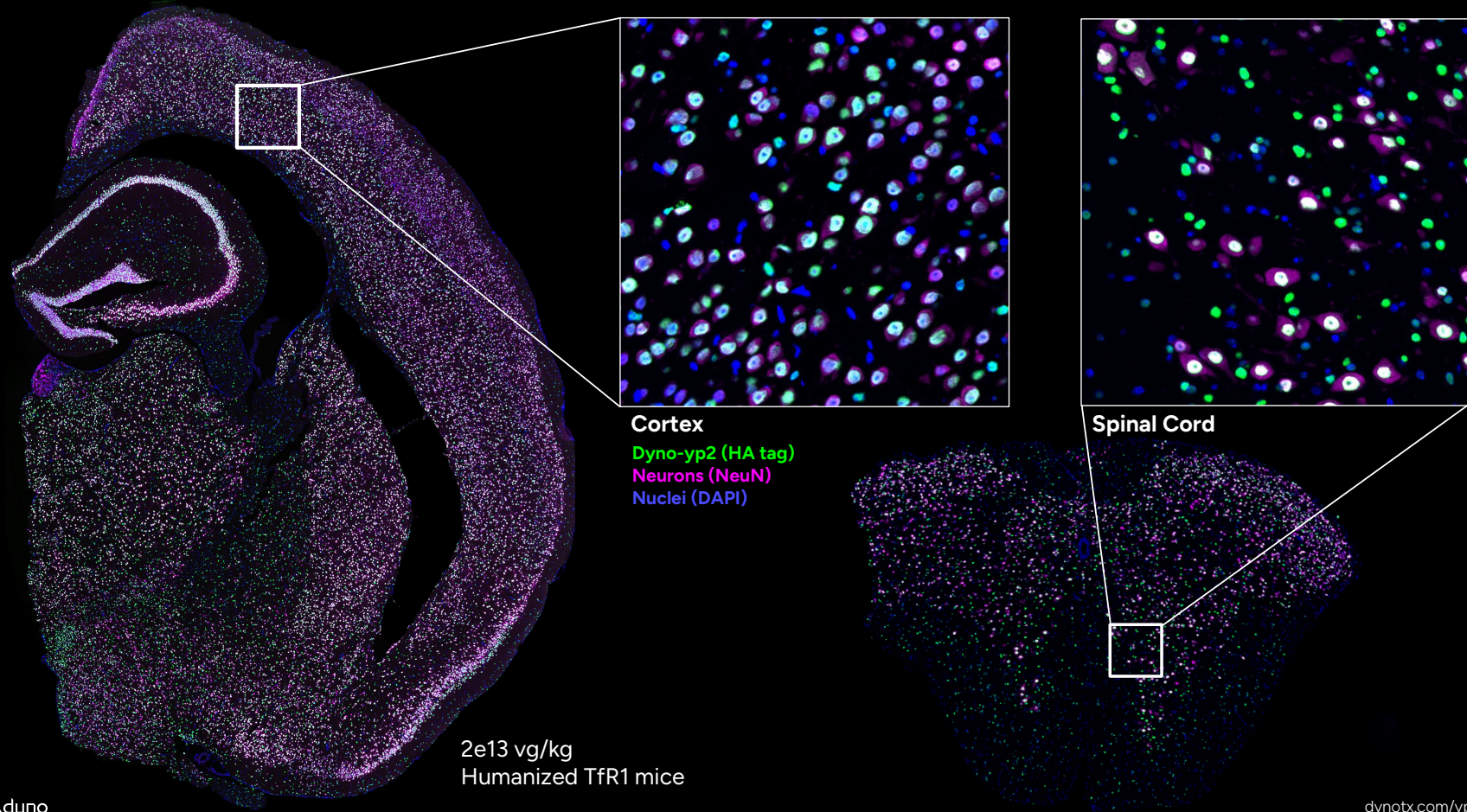


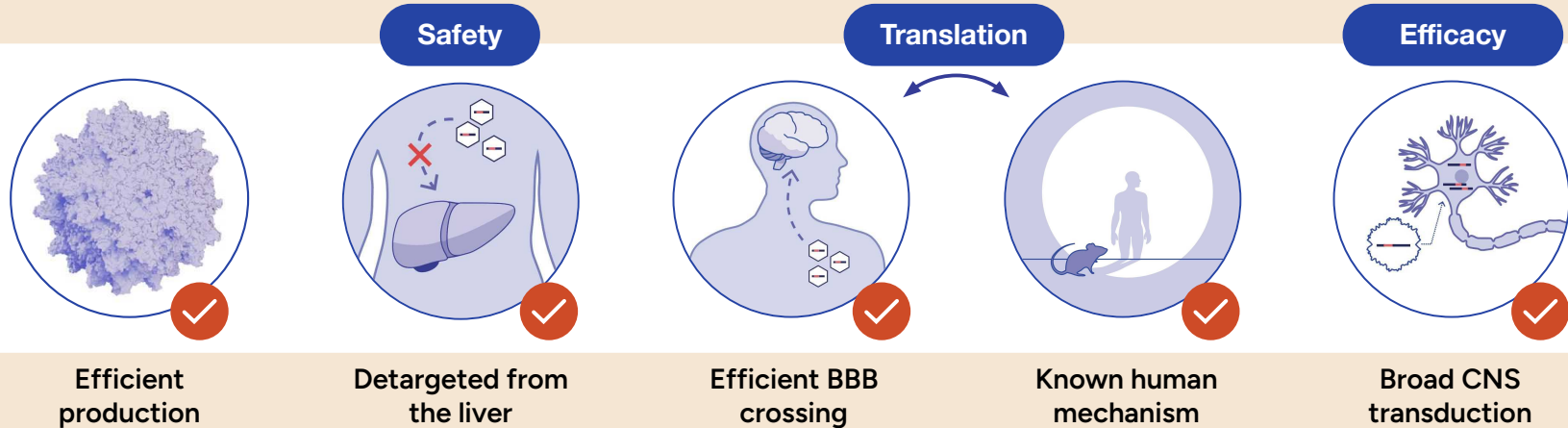


Dyno-yp2: A novel hTfR1-targeted capsid enabling robust brain transduction and liver detargeting

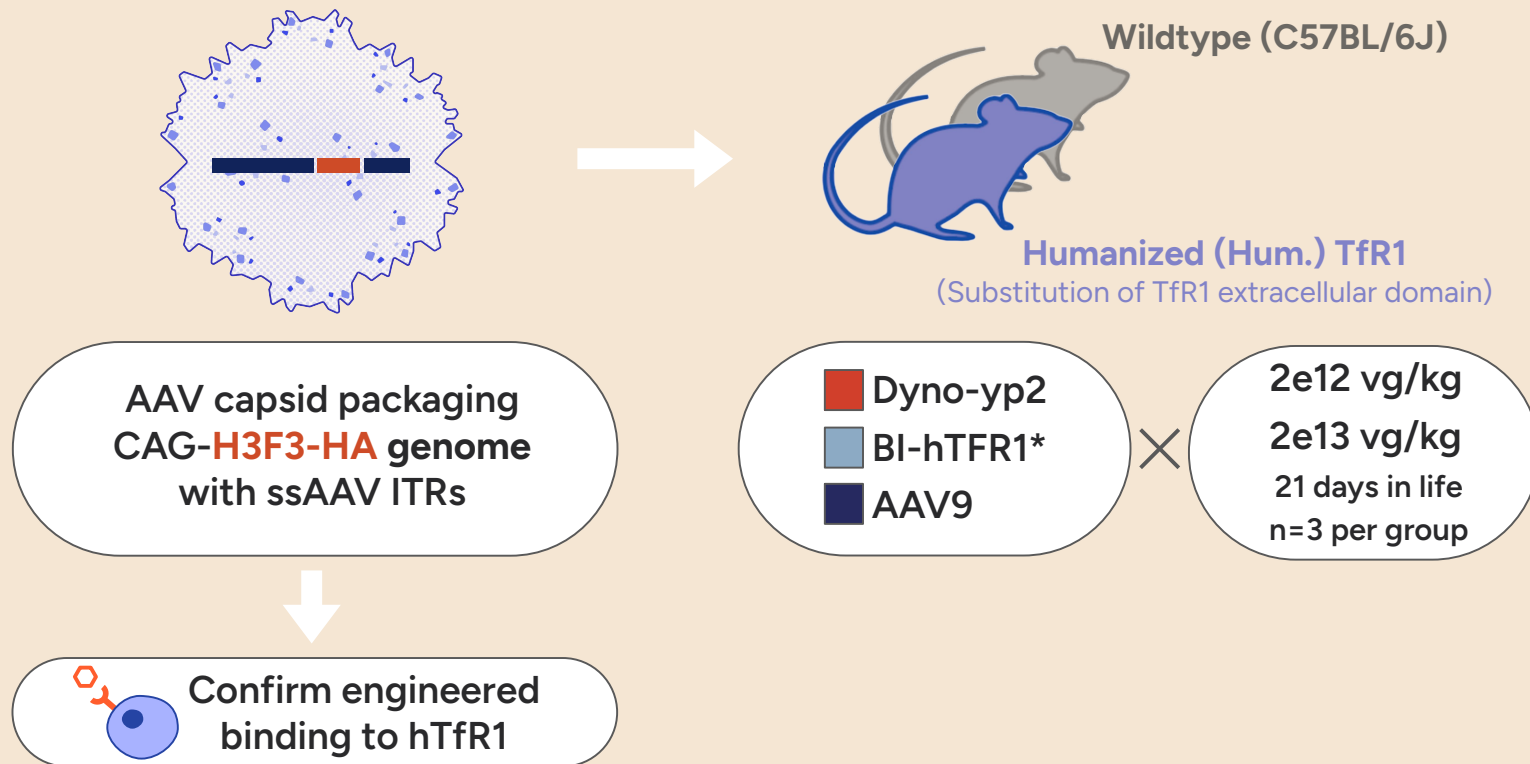
Dyno-yp2 transduces 94% of neurons in humanized TfR1 mice



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

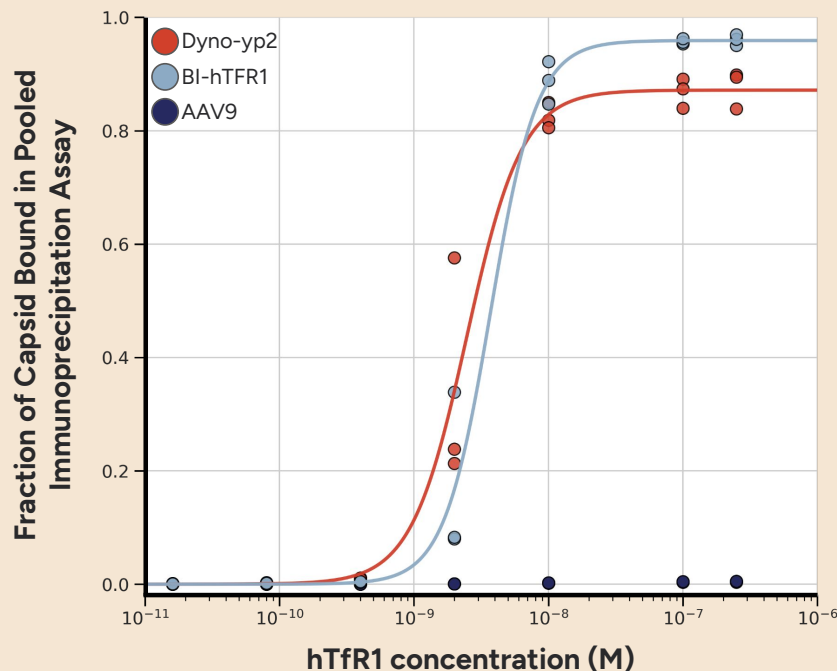


We compared **Dyno-yp2** head-to-head in humanized TfR1 mice with the published capsid BI-hTFR1

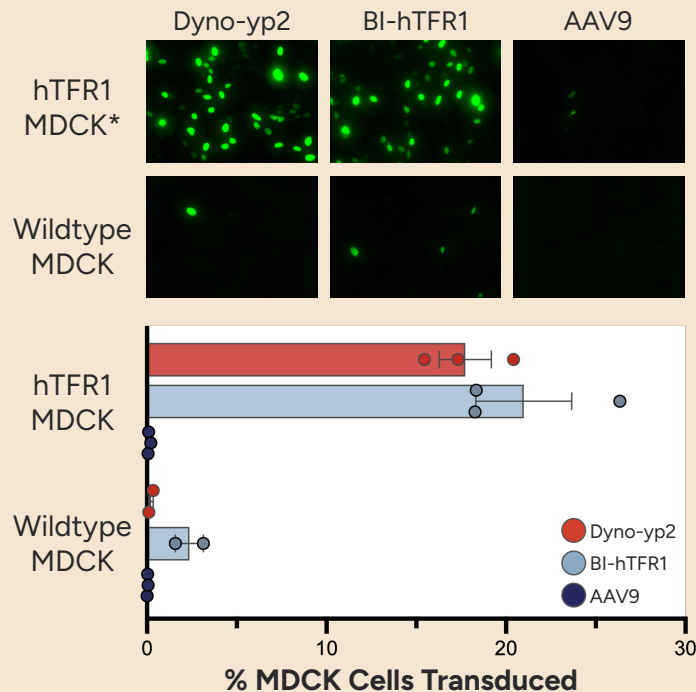


Dyno-yp2 binds the human TfR1 receptor, increasing confidence in successful translation to humans

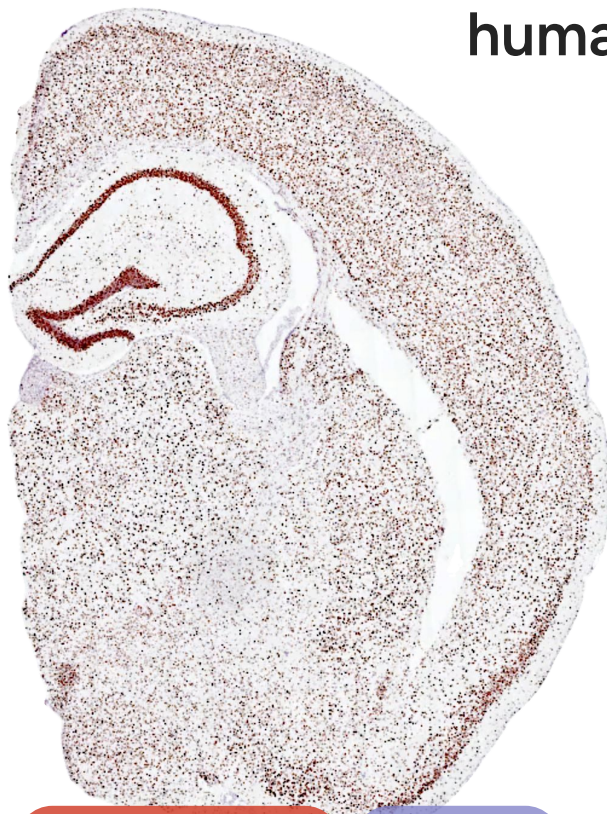
Dyno-yp2 binds to human TfR1



Dyno-yp2 specifically transduces cells expressing human TfR1

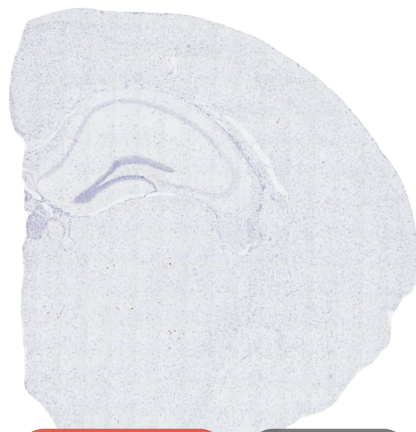


Dyno-yp2 transduction in the CNS is dependent on human TfR1 expression



Dyno-yp2
2e13 vg/kg

Hum. TfR



 **Dyno-yp2**

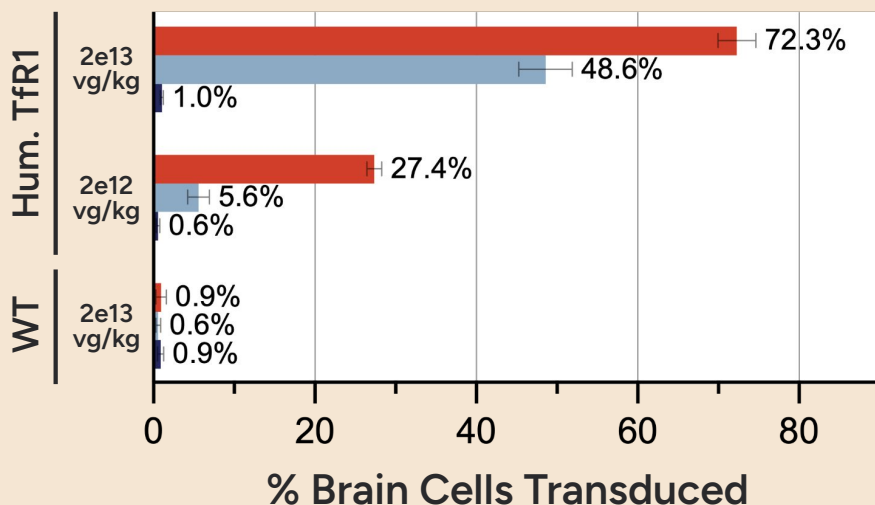
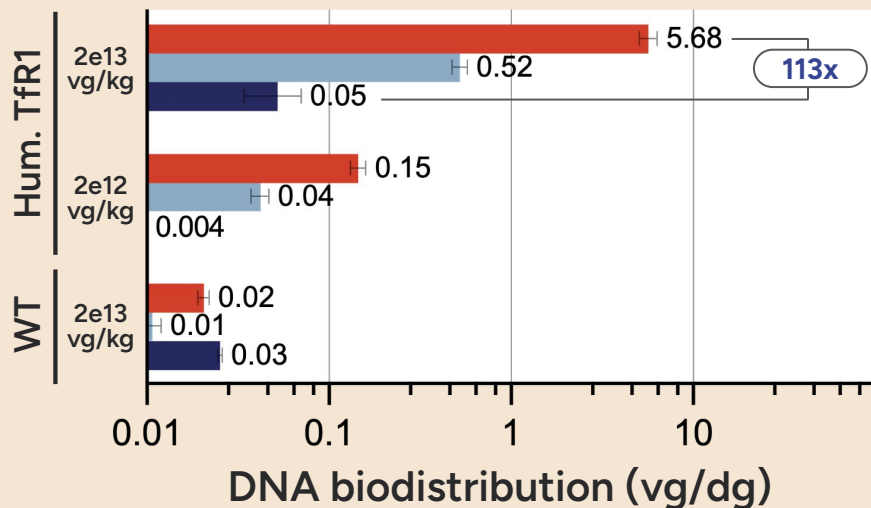
Wildtype



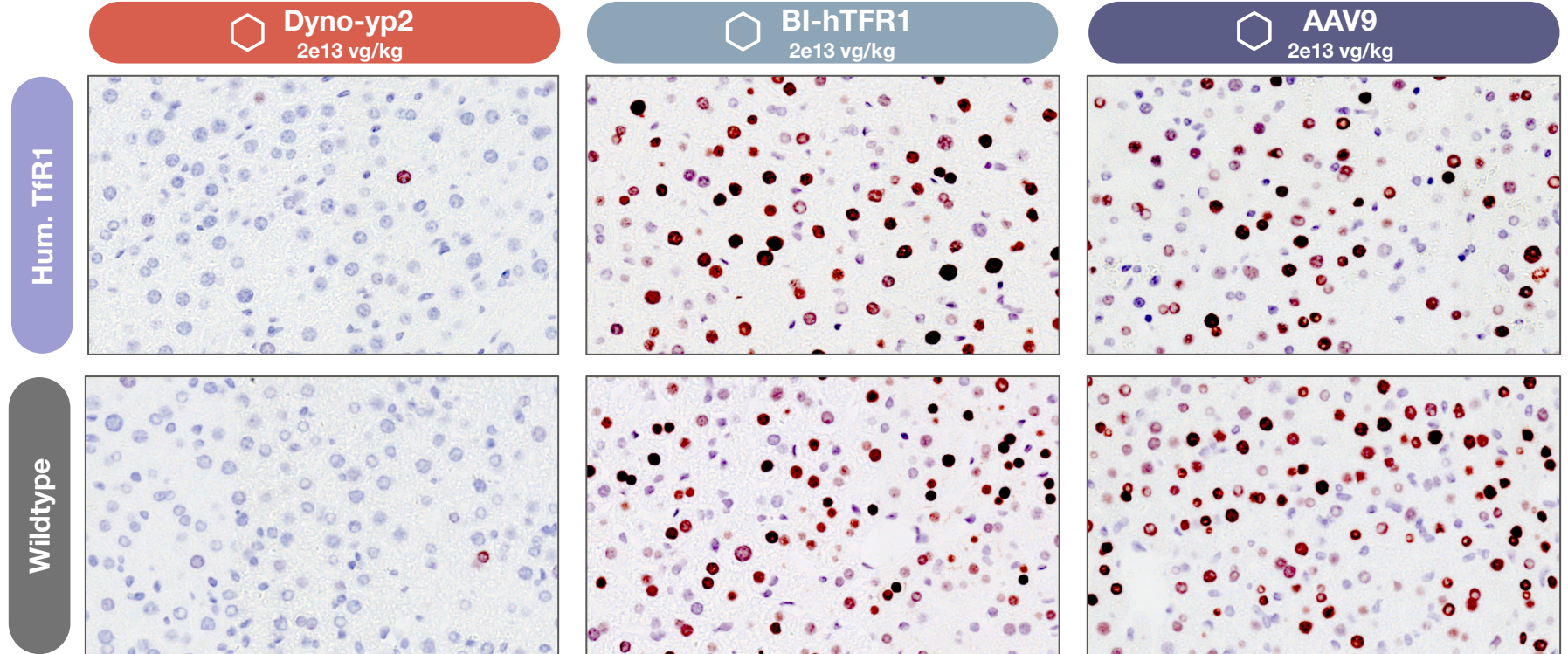
 **AAV9**

Hum. TfR

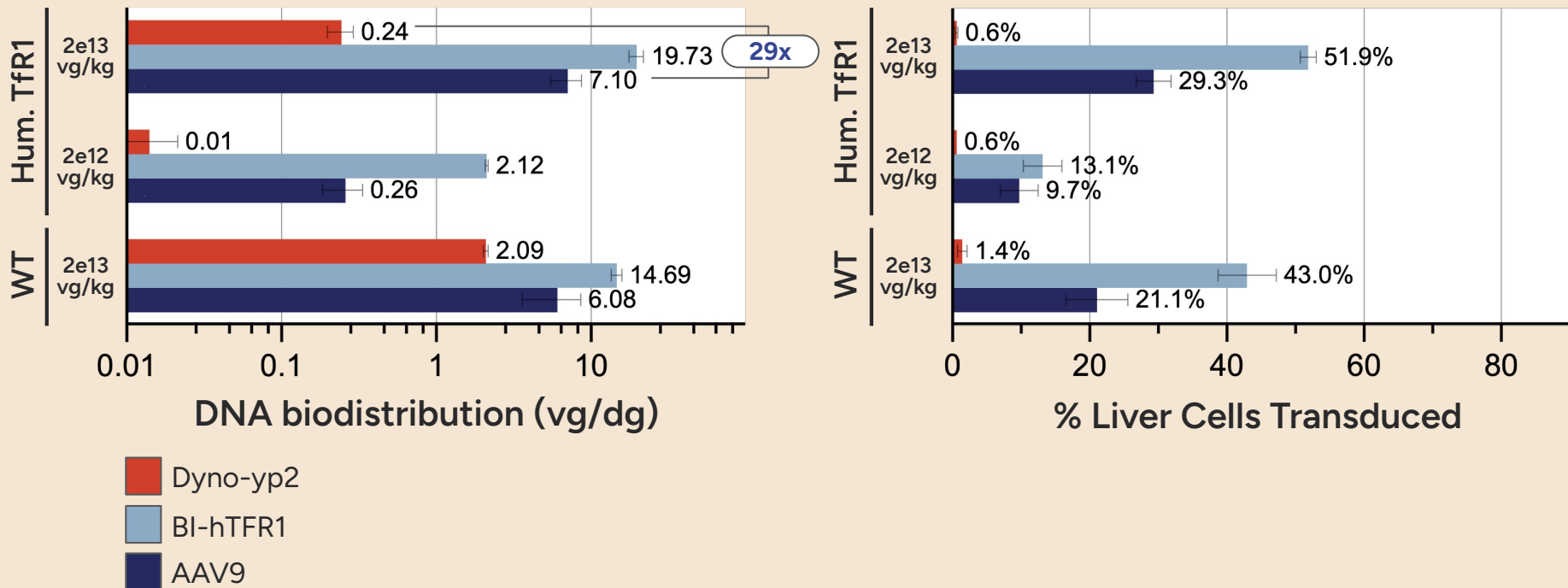
Dyno-yp2 brain biodistribution is 113x higher than AAV9 at 2e13 vg/kg in humanized TfR1 mice



Dyno-yp2 combines CNS tropism with excellent liver detargeting



Dyno-yp2 detargets the liver with 29x lower biodistribution compared to AAV9 at 2e13 vg/kg in humanized TfR1 mice



Dyno-yp2 liver detargeting is conserved across species

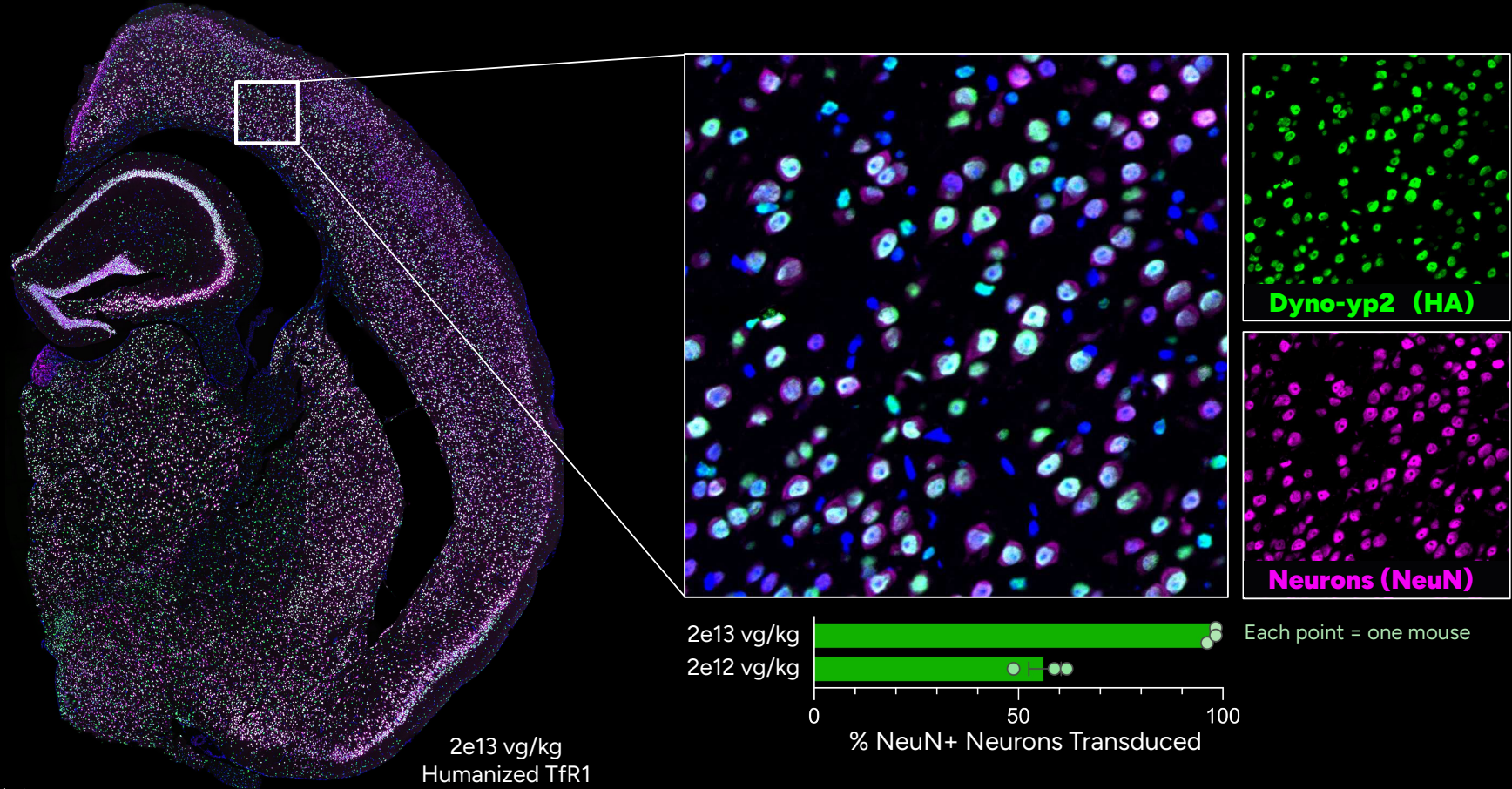
Liver detargeting in a pooled library (fold change over AAV9)

	Dyno-yp2	BI-hTFR1
Humanized TfR1 mice	12 x	1.3 x*
Wildtype mice	7 x	1.3 x
Cynomolgus macaque	6.1 x	1.6 x

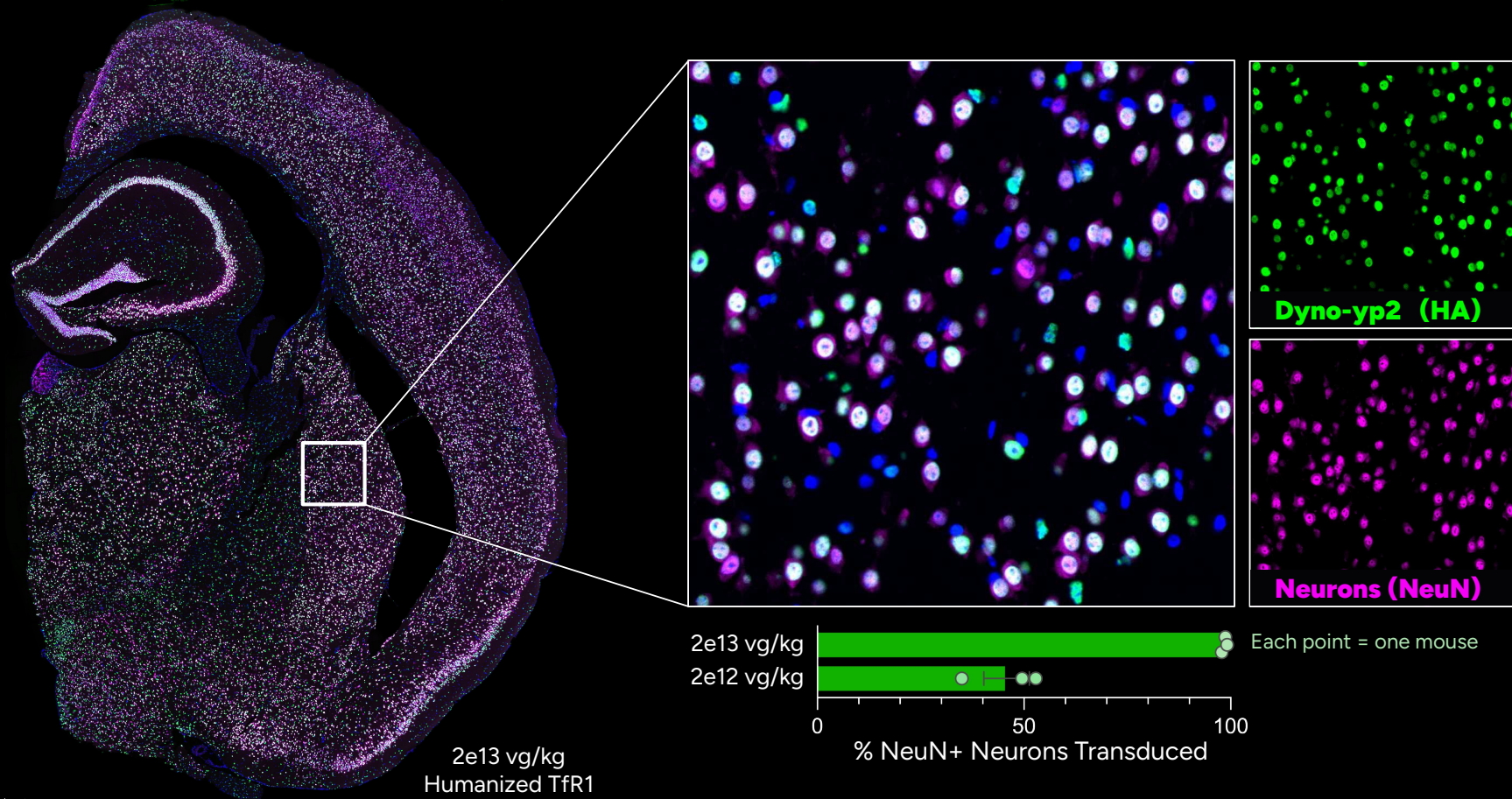
*Lack of liver detargeting for BI-hTFR1 was recapitulated in single capsid study.

- In a pooled capsid library, Dyno-yp2 de-targets the liver in **humanized TfR1** and **wildtype** mice as well as **cynomolgus macaques**.
- Although Dyno-yp2 does not bind to the cynomolgus macaque TfR1 receptor, **liver detargeting is conserved in both NHPs and mice** as measured in a pooled assay.
- These findings support that Dyno-yp2's excellent liver detargeting may be **translatable to humans**, improving the safety profile of this capsid compared to others.

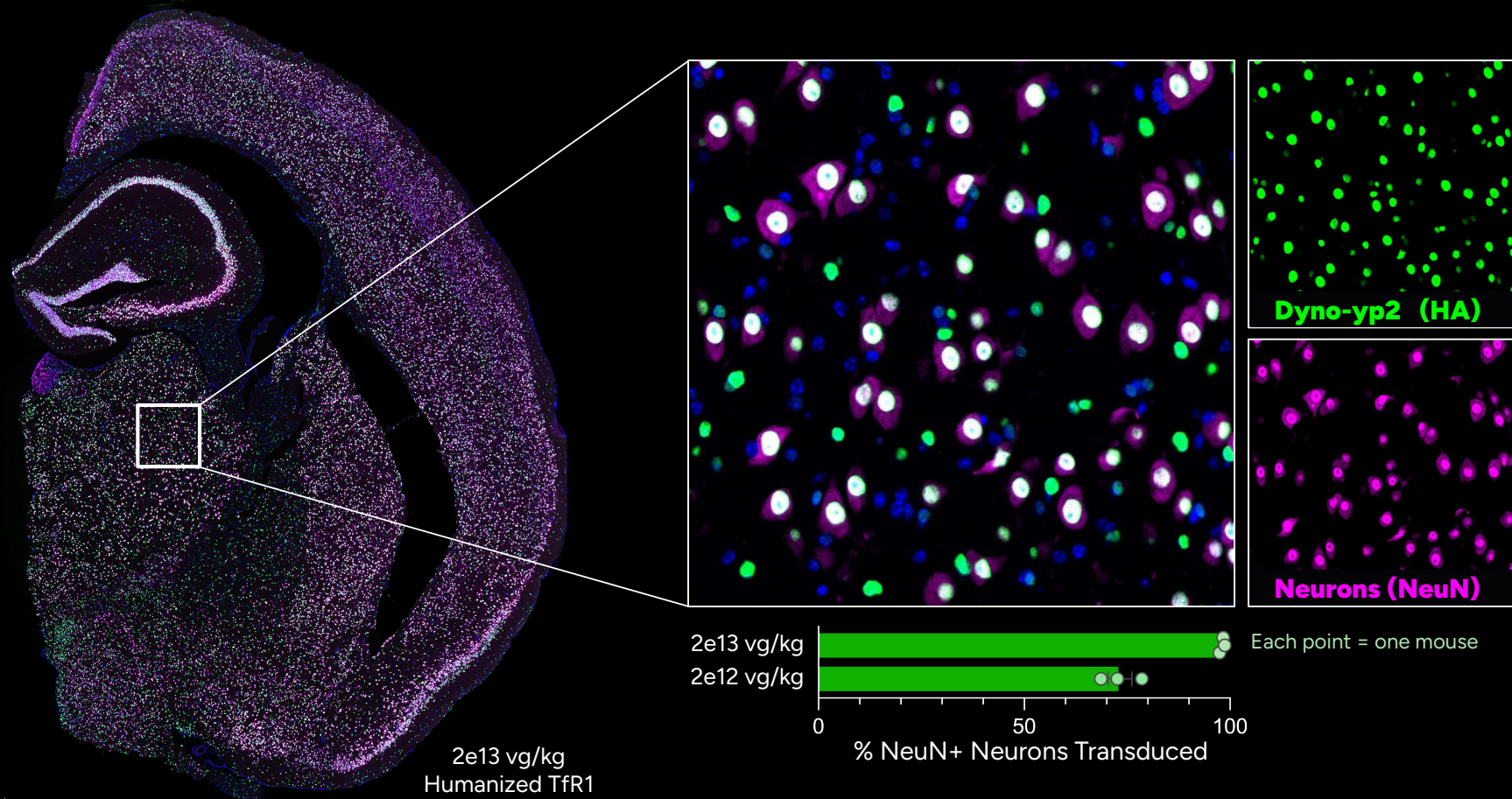
Dyno-yp2 transduces 98% of NeuN+ neurons in the cortex



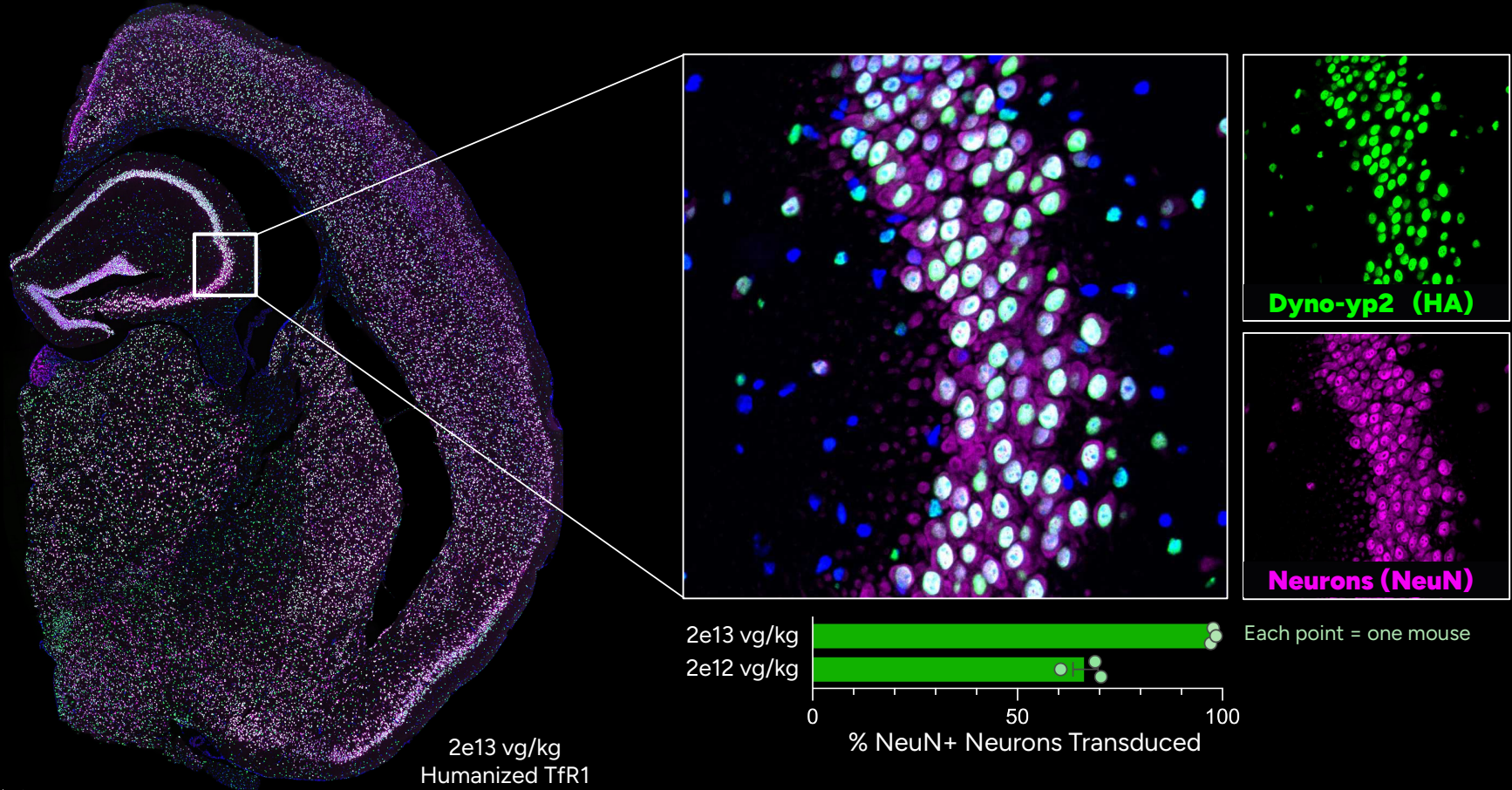
Dyno-yp2 transduces 99% of NeuN+ neurons in the striatum



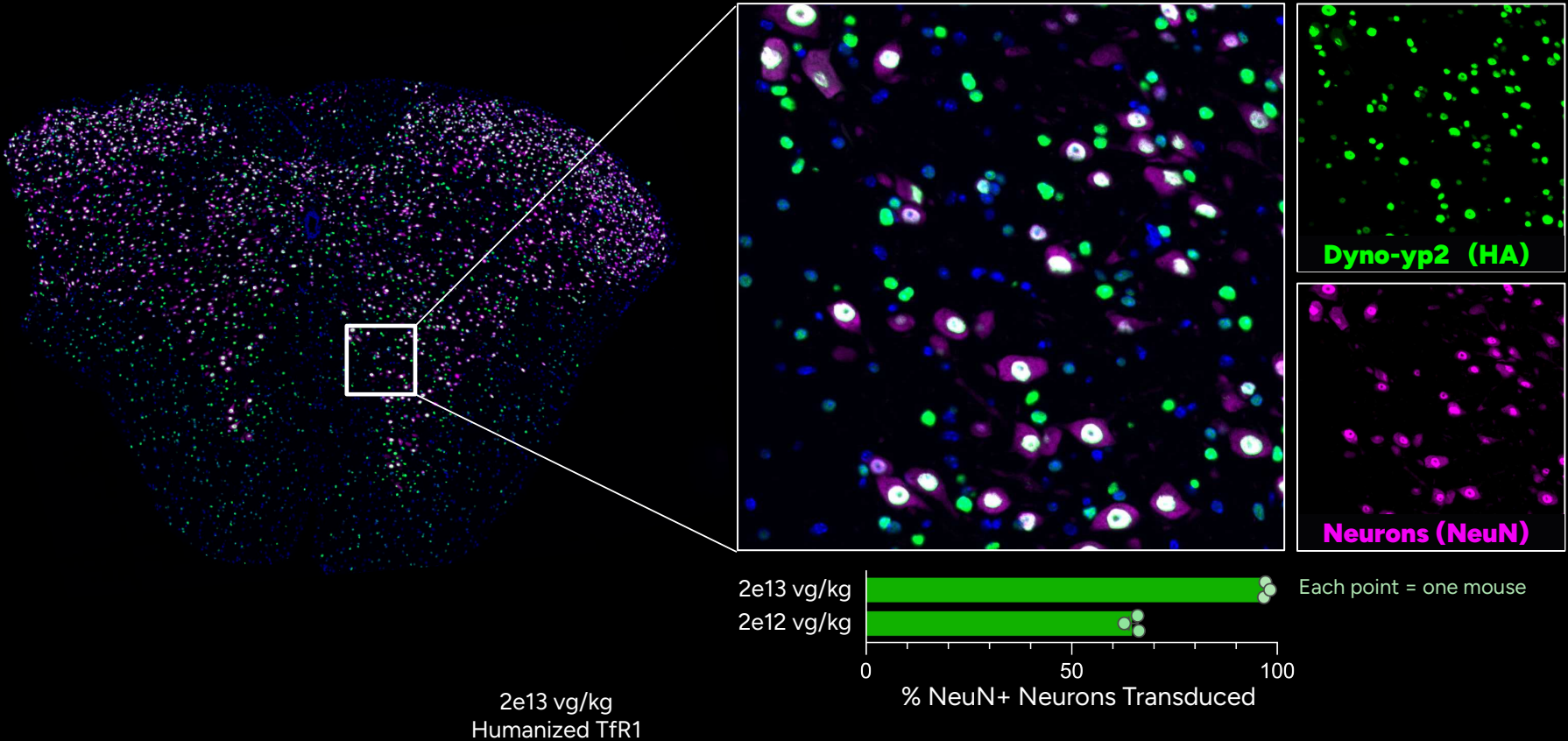
Dyno-yp2 transduces 98% of NeuN+ neurons in the thalamus



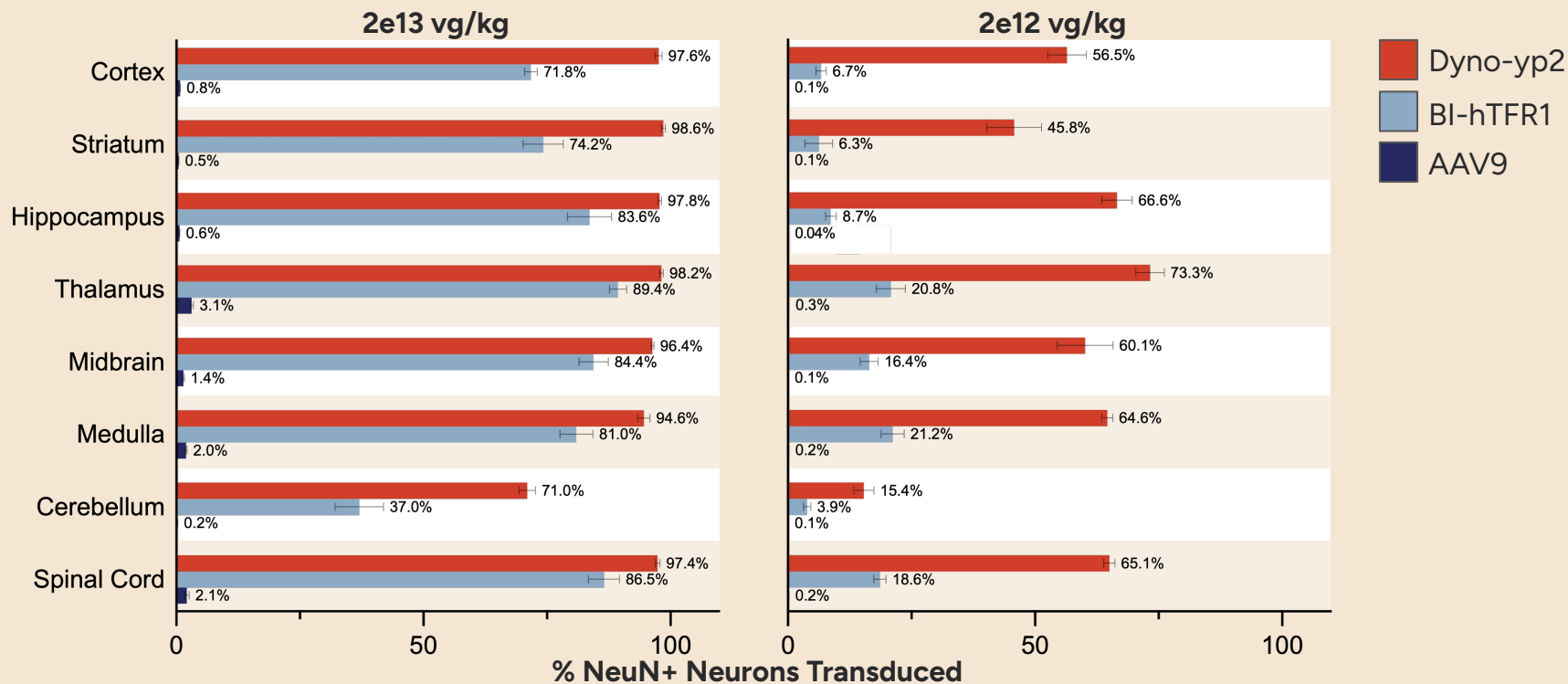
Dyno-yp2 transduces 98% of NeuN+ neurons in the hippocampus



Dyno-yp2 transduces 97% of NeuN+ neurons in the spinal cord

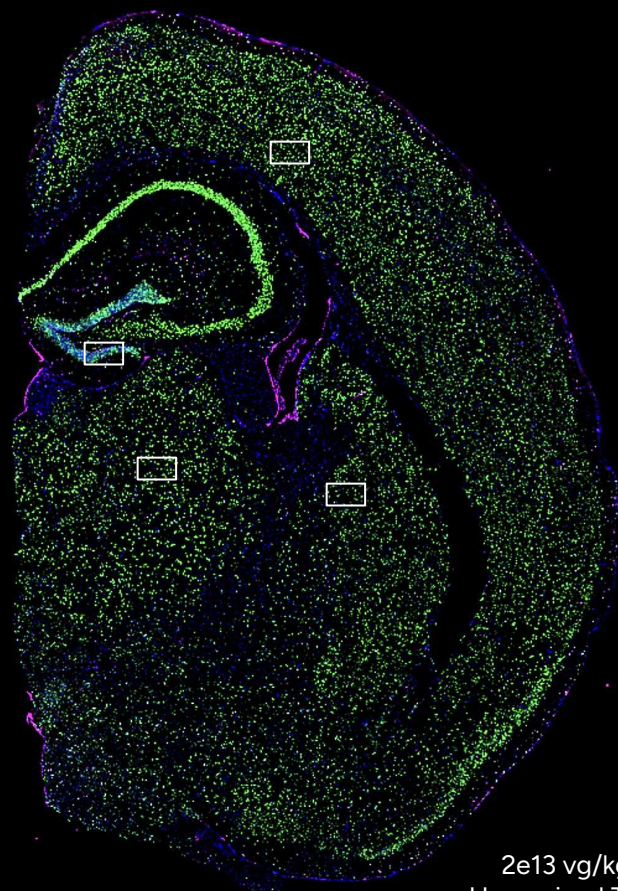


Dyno-yp2 achieves exceptional pan-brain neuronal transduction in humanized TfR1 mice

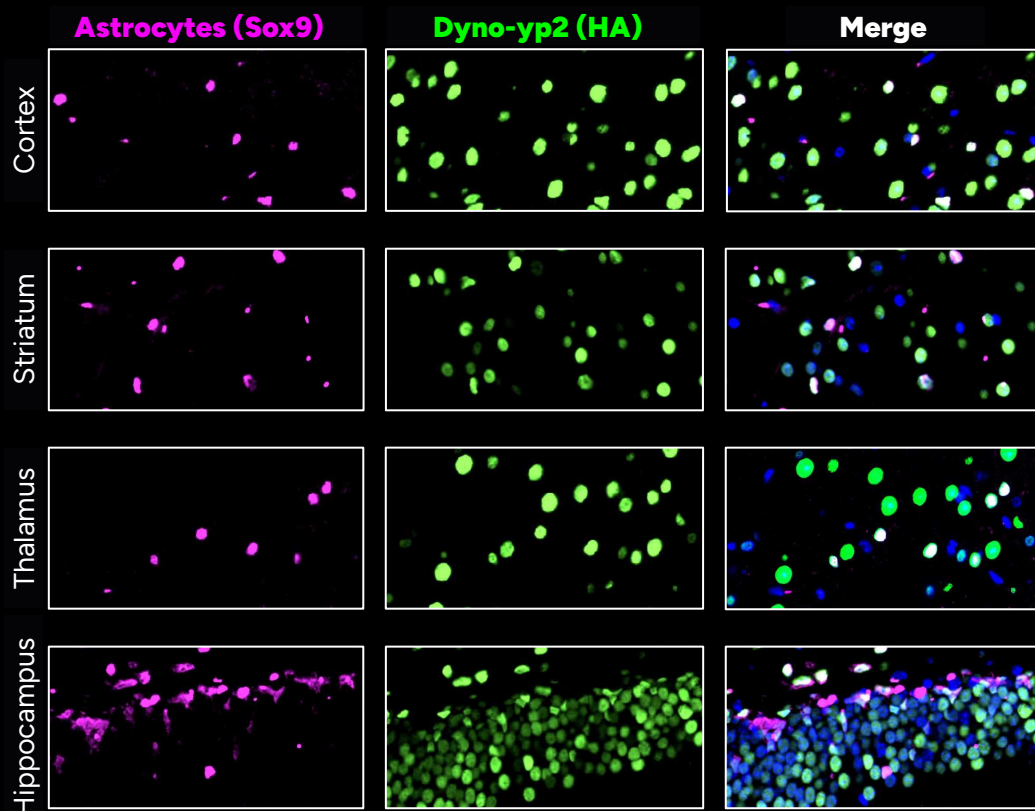


Dyno-yp2 outperforms BI-hTfR1 in every brain region at both doses

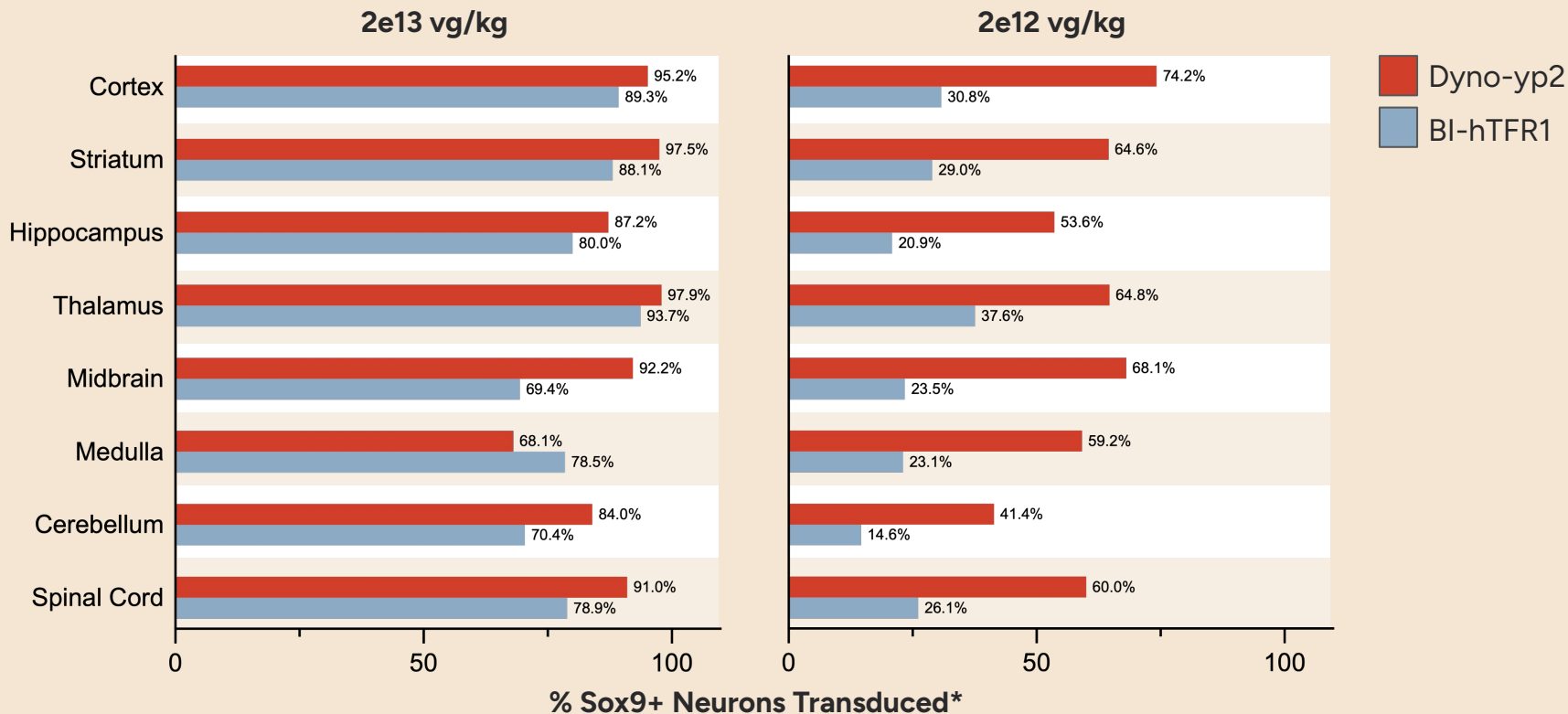
Dyno-yp2 transduces 89% of Sox9+ astrocytes in the brain



2e13 vg/kg
Humanized TfR1



Dyno-yp2 transduces Sox9+ astrocytes throughout the CNS in humanized TfR1 mice



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

