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# MOLECULAR TARGETS AND CANCER THERAPEUTICS

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## The IRAK4 inhibitor CA-4948 demonstrates antitumor activity in a preclinical model of CNS lymphoma

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Speaker: Christina von Roemeling

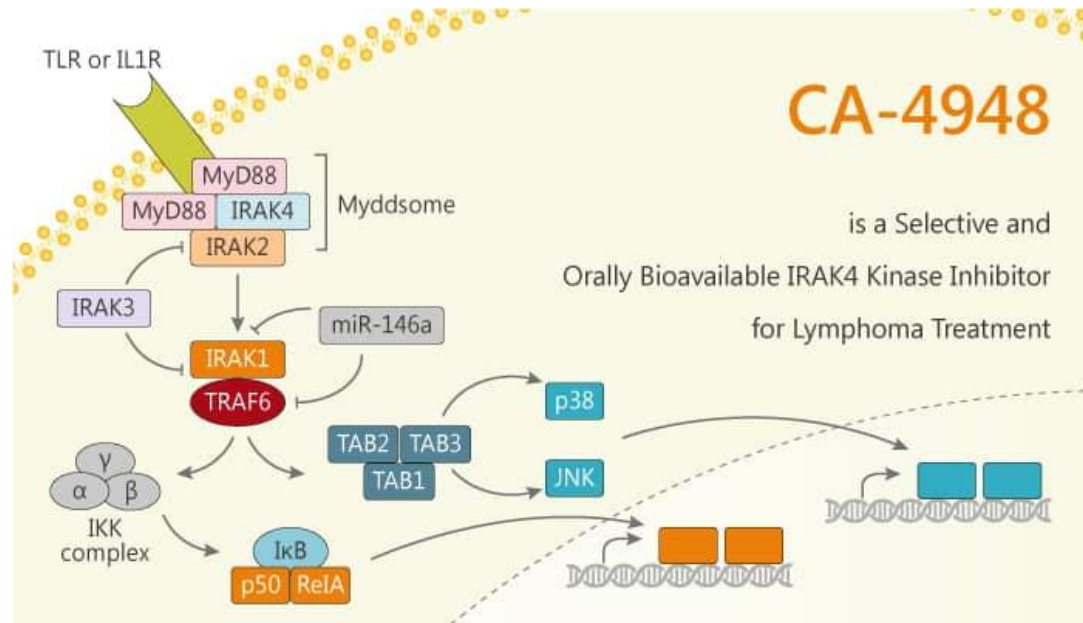
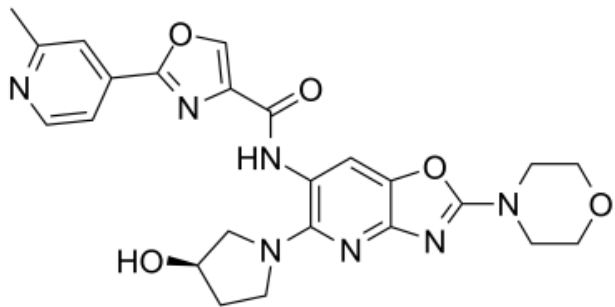
Duane Mitchell received institutional funds from Curis, Inc.

Reinhard von Roemeling, Elizabeth Martinez, and Raul Soikes are employees of Curis, Inc.



# CA-4948 is a novel small molecule inhibitor of IRAK4

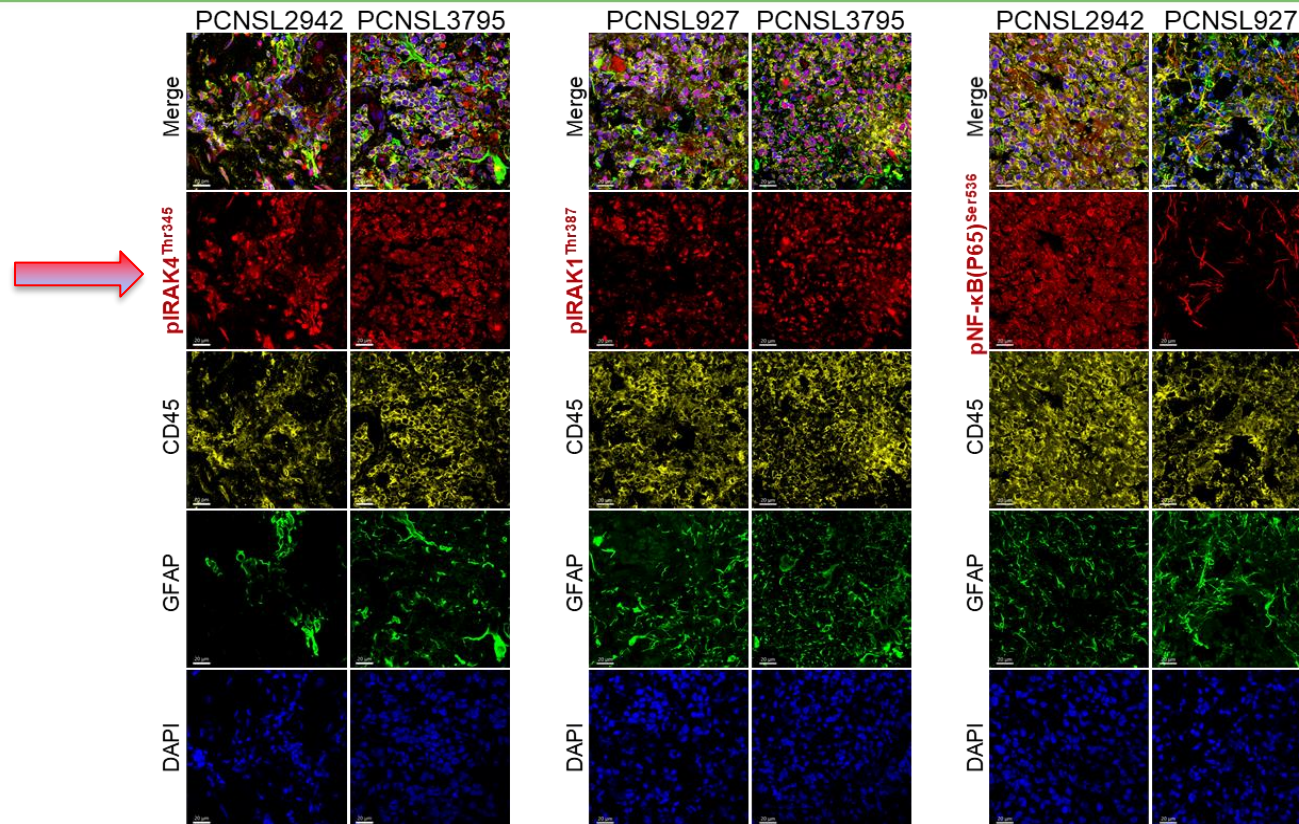
## CA-4948



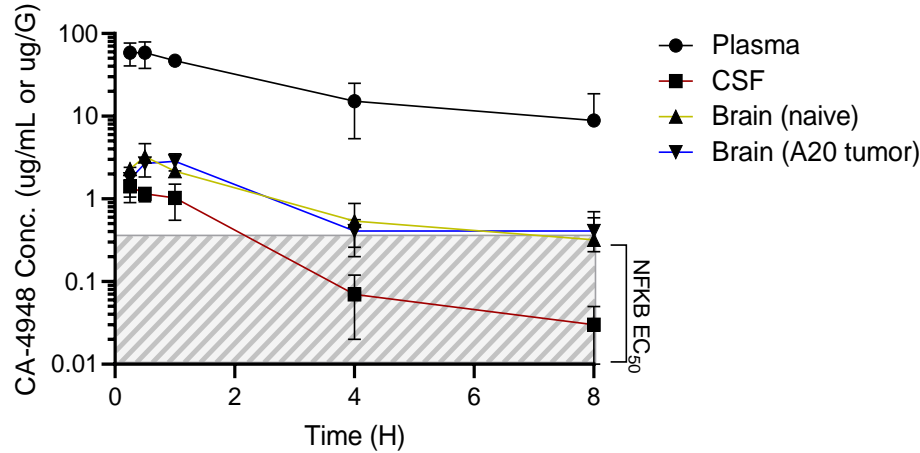
Adapted from Booher, et al. AACR Annual Meeting (2017)



# IRAK signaling is activated in PCNSL



# CA-4948 can cross the blood brain barrier

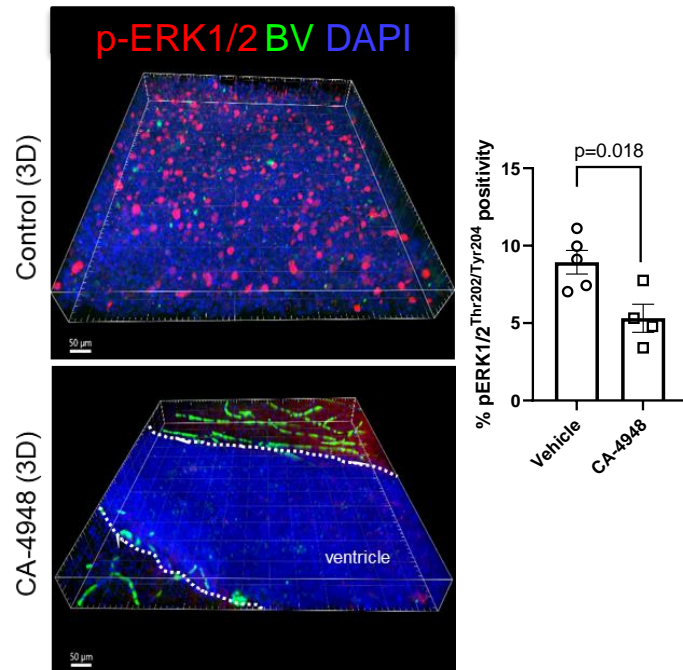
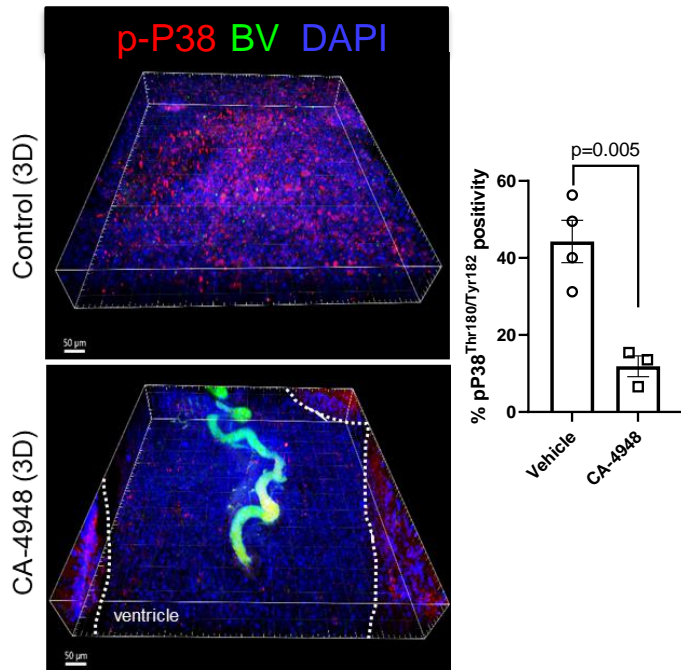


| Parameter             | Units             | Plasma       | CSF (Naïve) | Brain (Naïve) | Brain (A20 Tumor) |
|-----------------------|-------------------|--------------|-------------|---------------|-------------------|
| $C_{max}$             | ug/mL or ug/g     | 60.3 ± 19.26 | 1.42±0.52   | 3.25±1.41     | 3.22±0.18         |
| $T_{max}$             | h                 | 0.38 ± 0.14  | 0.25        | 0.5           | 0.83±0.29         |
| $T_{1/2}$             | h                 | 2.73         | 1.33        | 1.39          | 1.19              |
| $AUC_{0-8 h}$         | h*ug/mL or h*ug/g | 189.51       | 2.91        | 8.09          | 8.68              |
| $AUC_{0-\infty}$      | h*ug/mL or h*ug/g | 224.46       | 2.96        | 8.72          | 9.39              |
| Brain to plasma ratio | %                 |              | 1.53        | 4.26          | 4.95              |

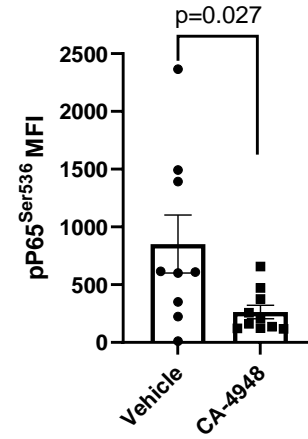
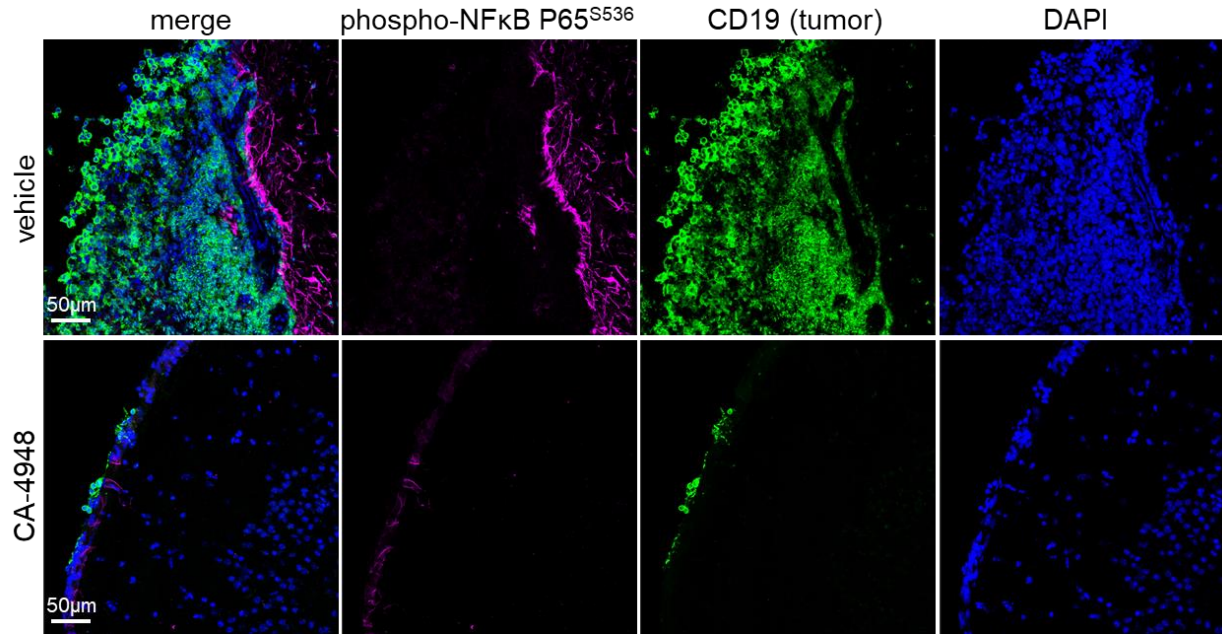




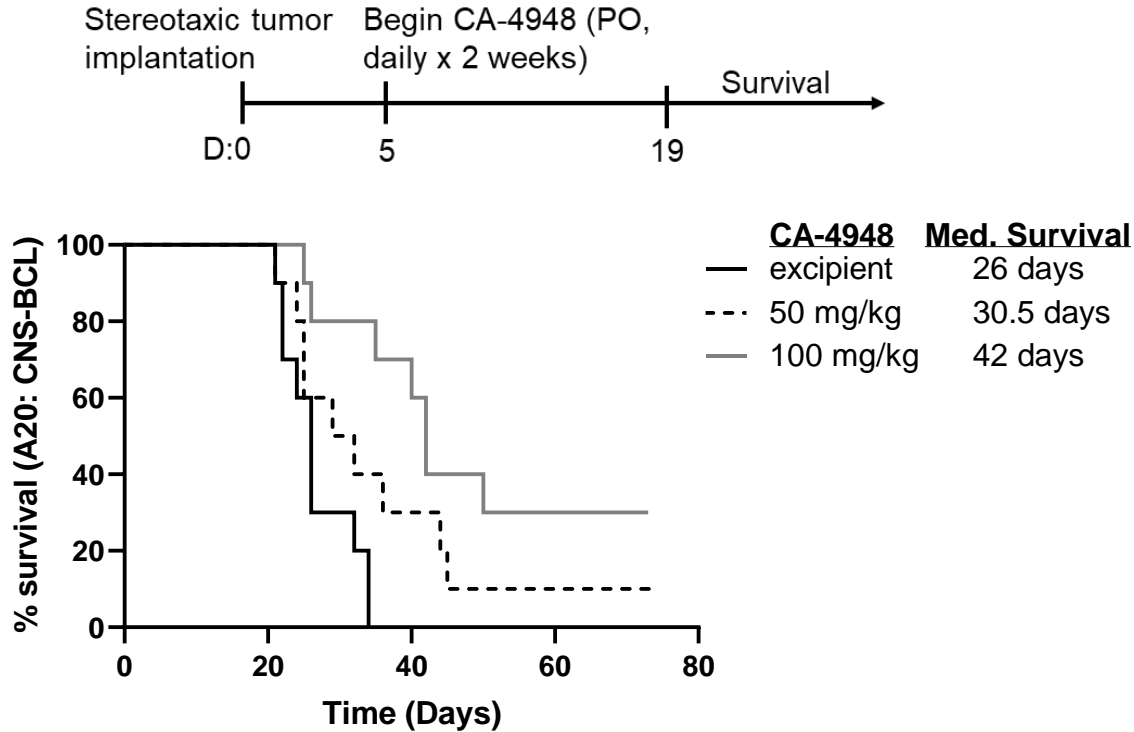
# CA-4948 reduces MAPK expression in preclinical PCNSL



# CA-4948 reduces NF- $\kappa$ B expression in preclinical PCNSL



# CA-4948 improves survival in preclinical PCNSL





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