

# CynAxis

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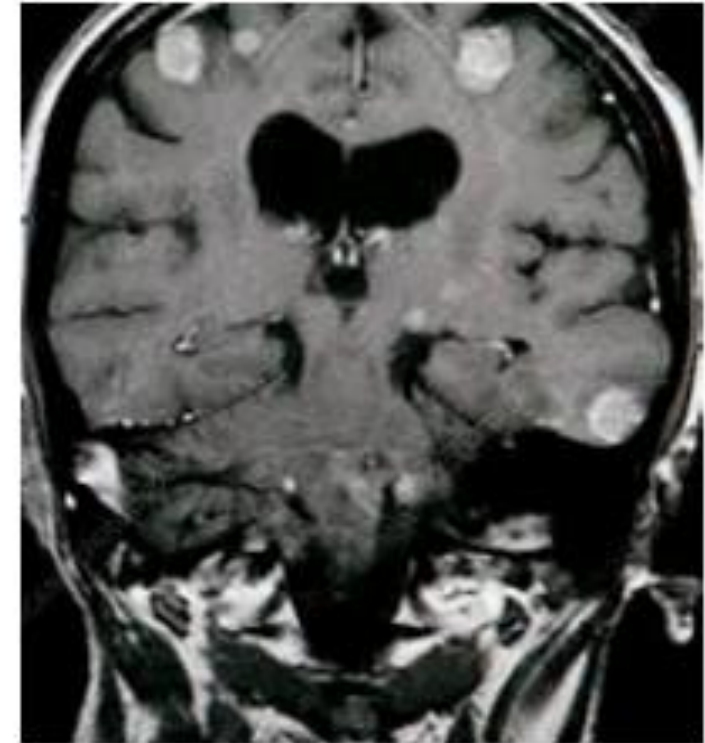
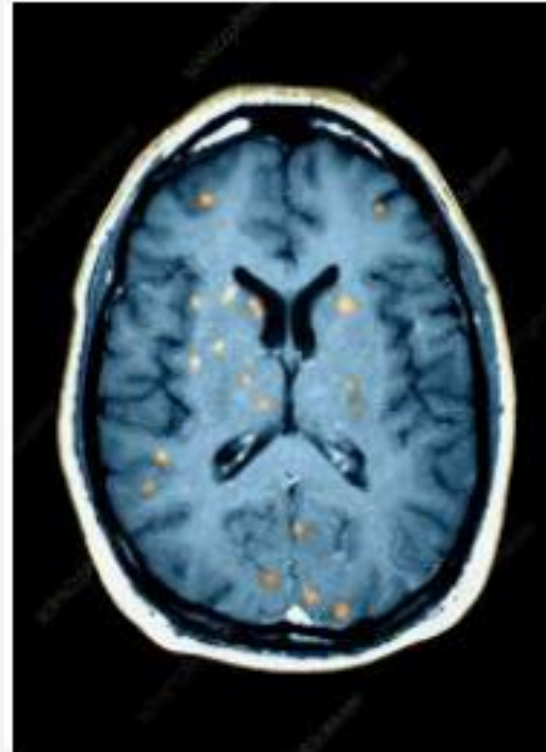
Traversing the Blood Brain Barrier

# Many Effective Therapies Cannot Cross the Blood Brain Barrier (BBB)

Cancer Type	Incident Proportion of Brain Metastasis by Cancer Type
Lung	20%
Breast	5%
Melanoma	7%
Renal	7%
Colorectal	2%

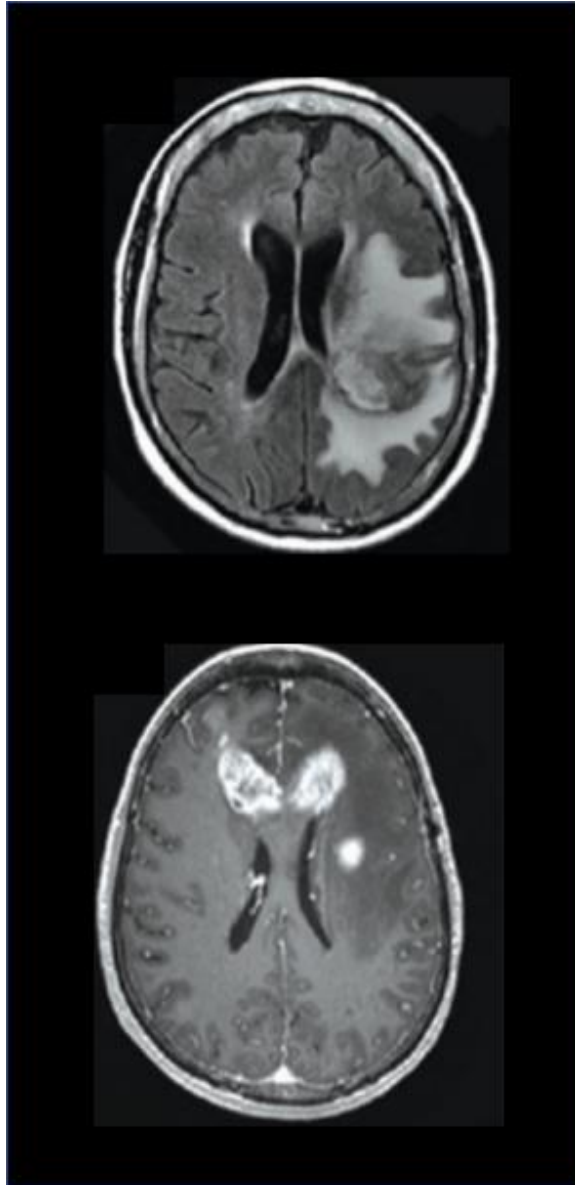
- 10-20% of all patients develop brain metastasis
- Brain metastasis portends high mortality
  - 8.1% survival rate at 2 year
  - 2.4% survival rate at 5 year
- Neurosurgical excision and radiotherapy not possible or sustainable for some patients

J Clin Oncol. 2004 Jul 15;22(14):2865-72.



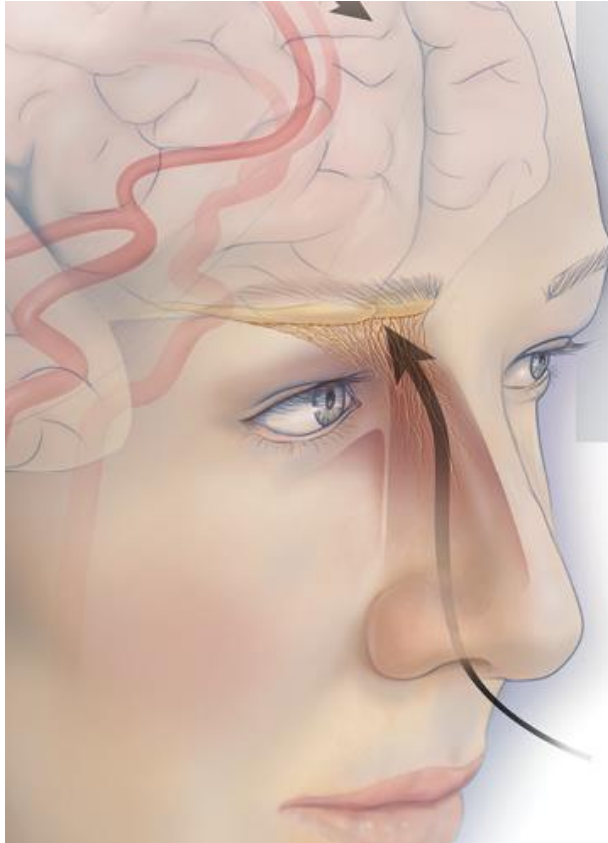
**Brain Metastases are difficult to treat because either effective therapies cannot cross the BBB or cannot reach adequate concentrations in the microtumor environment.**

# Glioblastoma Remains Largely Incurable



- Gliomas Grade 1-4 includes astrocytic tumors oligodendrogliomas ependymomas, and mixed glioma
- Glioblastoma multiforme (GBM) IV is malignant
- Accounts for 50% of all gliomas in all age groups; 60% of all brain tumors in adults
- Poor prognosis; 14-15 month survival after diagnosis
- Main challenges in therapy of GBM are related with the location of the disease and its complex and heterogeneous biology

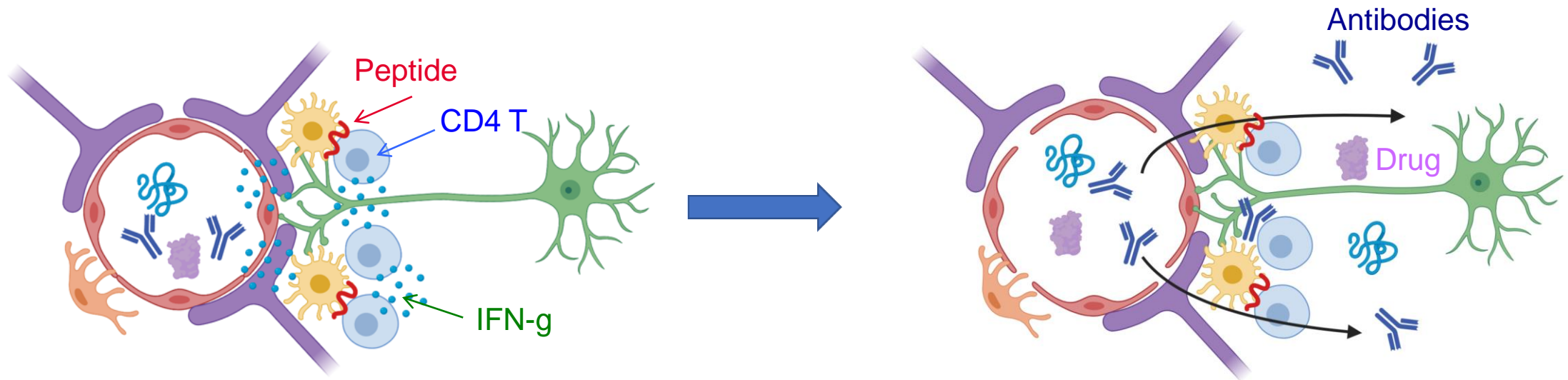
# CynAxis can solve the problem



2017, LISA CLARK, The Scientist Magazine

- CynAxis can engineer patient specific peptides to activate an adaptive immune response
- This enables transient and defined access of drugs and biologics to the CNS
- This technology can allow delivery any drugs or biologics to the CNS.

# CNS antigen-specific CD4<sup>+</sup> T Cells Could Mediate BBB opening



## Step 1

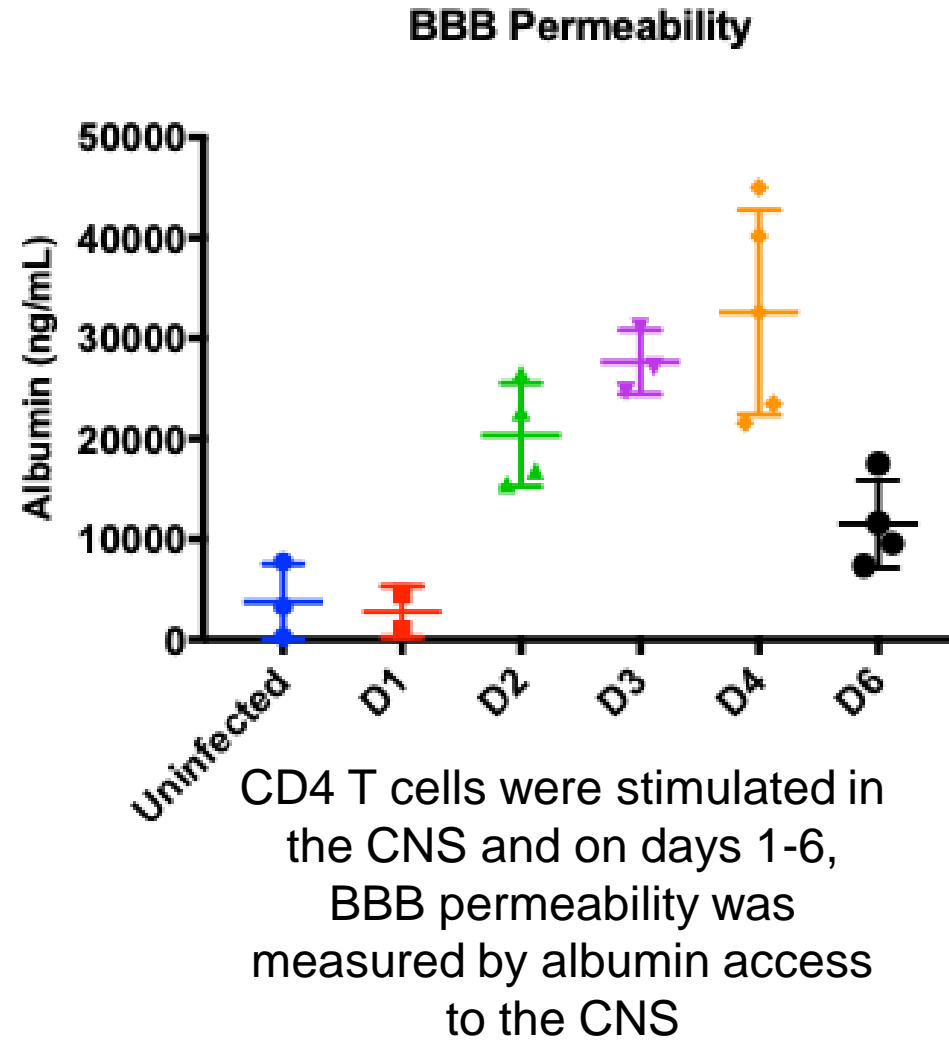
Stimulate CD4 T cells with specific peptides delivered to intranasally to the CNS.

## Step 2

Interferon gamma secreted by CD4 T cells enable transient permeability of the BBB, enabling drugs and biologics to access the CNS parenchyma.

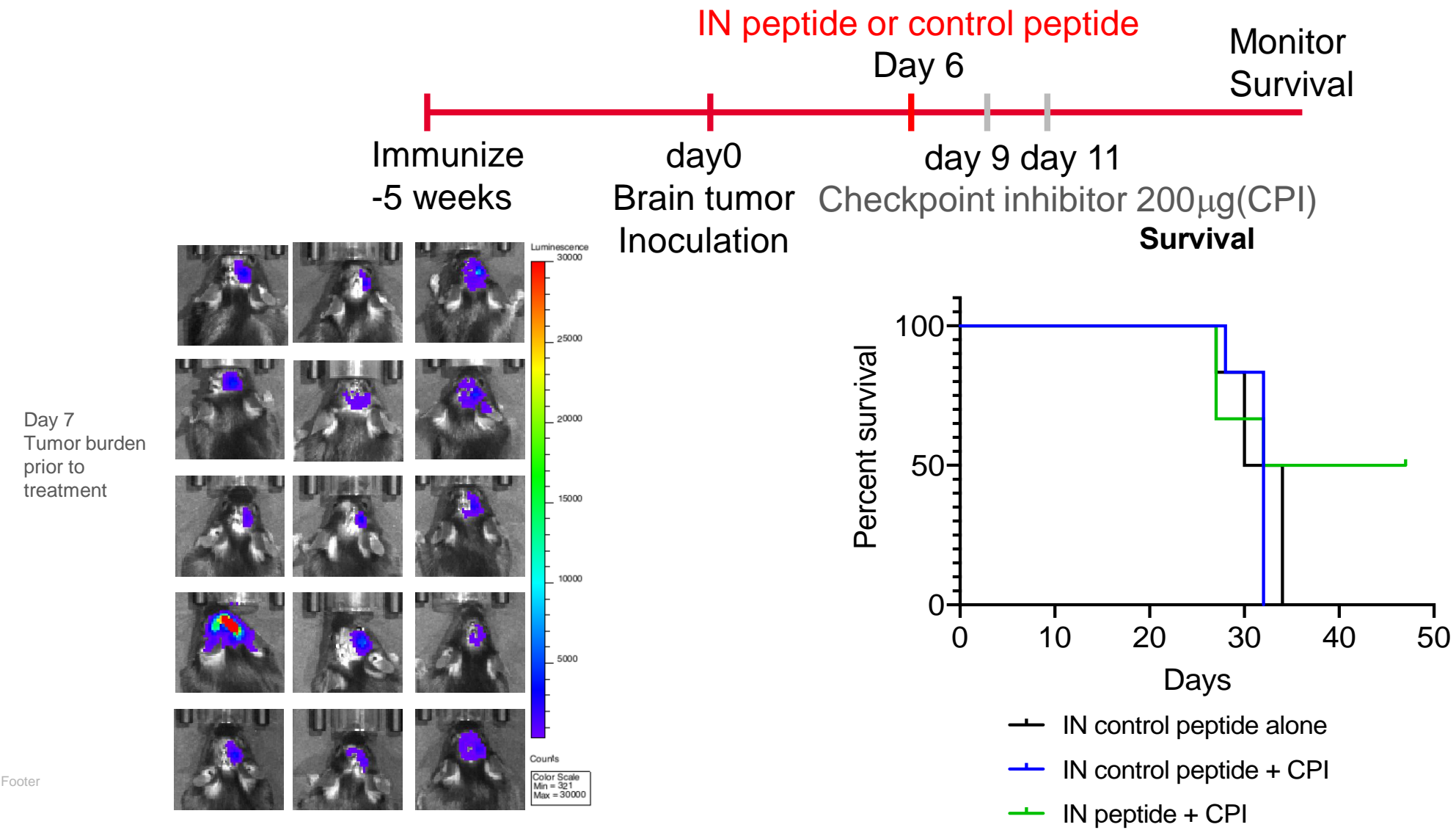


# CynAxis Intranasally Delivers MHC Class II Peptides to Open Up BBB



- MHC class II peptide will be delivered intranasally using a spray.
- Peptide will follow olfactory nerves to enter the CNS to stimulate CD4 T cells.
- CD4 T cells produce interferon gamma to open up the BBB for a few days.

# Stimulation of T cells by Intranasal Peptide (IN) Enables Checkpoint Inhibitor Biologics to Access Brain Tissue and Treat Tumor



# Competitive Landscape

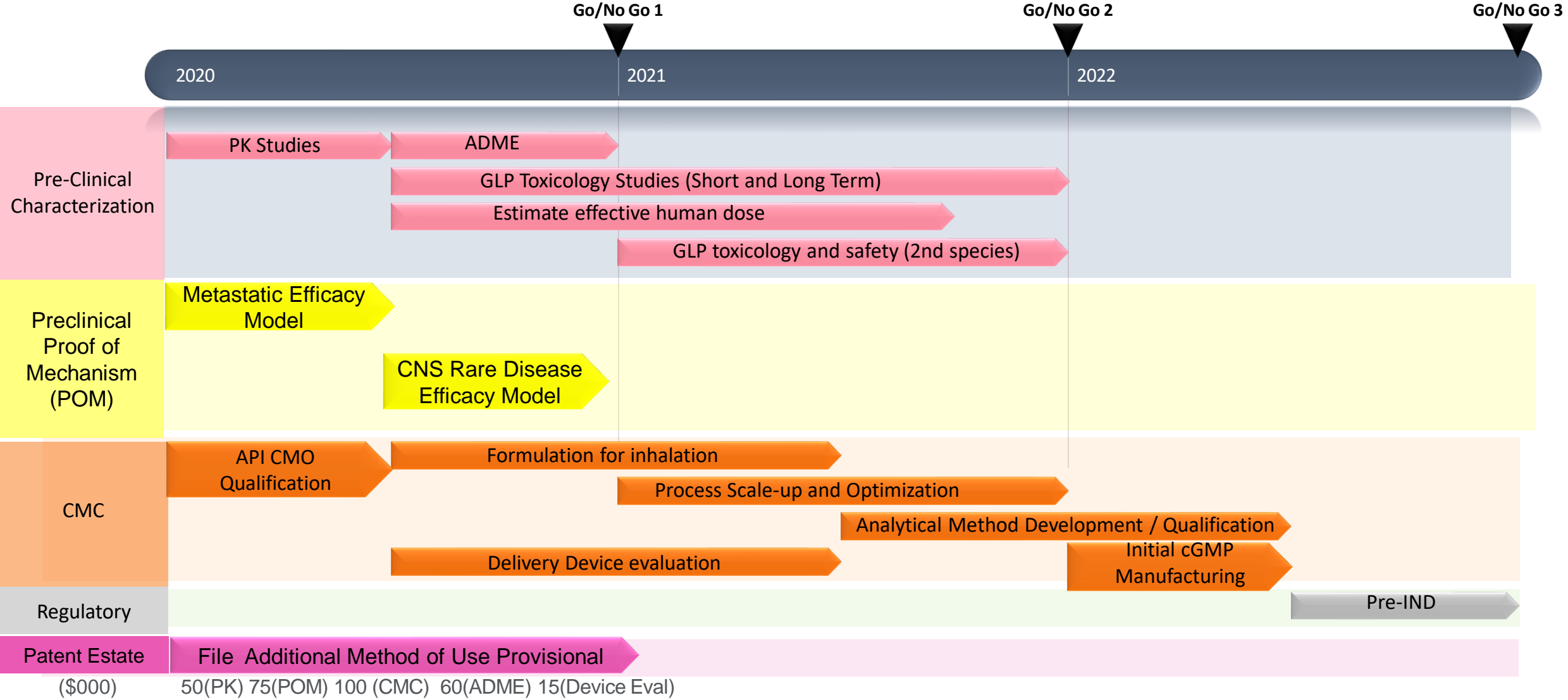
Intervention	Technology	Limitations
<b>Convection-enhanced delivery</b>  <b>Nanoparticles</b>	Catheters placed to infuse into a specified area of the brain  Various classes of particles types engineered to enhance delivery across BBB	<ul style="list-style-type: none"> <li>• Larger molecules have low Vd, hence limited efficacy</li> <li>• Relies on endocytosis so trafficking drug of interest to correct cellular compartments challenging</li> <li>• Rapid particle clearance in systemic circulation</li> </ul>
<b>Focused Ultrasound and Microbubbles</b>	Microbubbles are injected peripherally and ultrasound causes the bubbles to swell and contract.	<ul style="list-style-type: none"> <li>• Effects on endothelial tissue integrity unknown and may increase risk of leaky endothelium,</li> <li>• Increased risk thrombosis, infection</li> </ul>
<b>Chemical Disruption</b>	Non-Ionic Amphiphilic compounds can traverse BBB via endothelial cells.	<ul style="list-style-type: none"> <li>• Clinical trials to date have shown no efficacy</li> </ul>
<b>Utilizing specific receptors or transporters</b>	Leverage a specific receptor or transporter that gates BBB access.	<ul style="list-style-type: none"> <li>• Achieving sufficient concentrations in CNS via transport mechanism variable and unpredictable</li> </ul>
<b>Osmotic diuretics</b>	Temporary dehydration of BBB endothelial cells, grants small and large molecules indiscriminate access to the brain for limited time	<ul style="list-style-type: none"> <li>• Technology developed in 1970s</li> <li>• Osmotic BBB disruption results in transient cerebral edema</li> </ul>



# CynAxis IP Estate

Patent Title	Country	Application Type	Status	Application No.	Patent No.	Expiration Date
Composition and Methods	US		Issued			2036
Utility and Formulation	US		Issued			2038

# Cynaxis Timeline and Use of Proceeds



*Budget reflects development costs only and excludes personnel, G&A*