



**NTHI**

**NEONC**

TECHNOLOGIES HOLDINGS, INC. 

*Removing Barriers to Effective Neuro-Drug Delivery*

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# The Problem:

## Recurrent Brain Tumors Are Untreatable

### **Relapse is inevitable**

90% of high-grade glioma patients recur within 6–9 months despite maximal therapy

### **Clinical focus at recurrence is overall survival, not partial response**

In recurrent disease, relapse is expected; objective responses rarely translate into durable benefit

### **Standard-of-care breaks down at recurrence**

Surgery is non-curative and often not repeatable; temozolomide and alternatives face rapid resistance and cumulative toxicity

### **Drug delivery to the brain is fundamentally constrained**

The blood–brain barrier prevents most oncology drugs from achieving therapeutic CNS exposure

### **Recurrent tumors are biologically more aggressive**

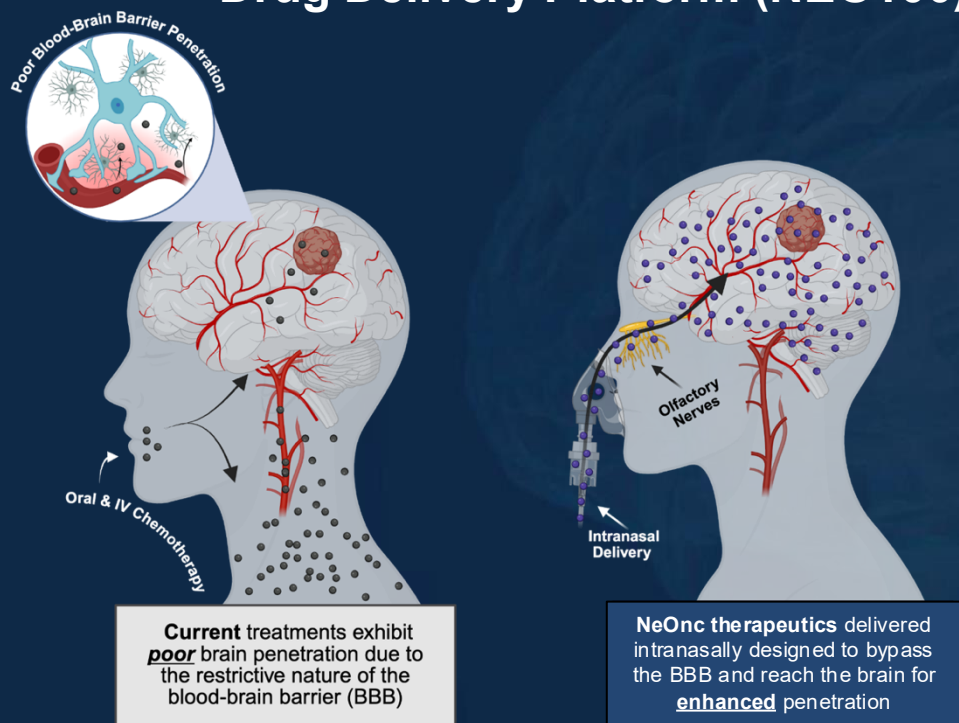
Therapy-driven evolution produces invasive, stem-like, treatment-resistant disease in an immunosuppressive CNS niche

### **Outcomes remain dismal**

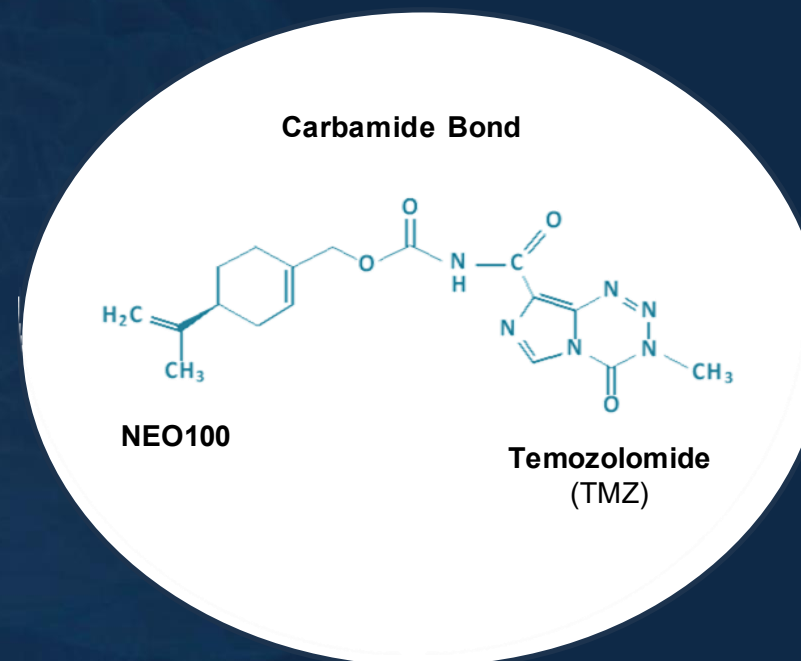
Median survival after recurrence is ~6–9 months with no FDA-approved therapy that meaningfully extends life

# A Next-Generation Neuro-Oncology Company Built on Two Proprietary Platforms

## Drug Delivery Platform (NEO100)



## Drug Conjugation Platform (NEO212)







- Direct, non-invasive CNS delivery powered by patented technology
- Clinically practical, patient-friendly dosing suitable for chronic use
- Patented platform drives efficient, brain-targeted pharmacokinetics

- Patented platform enables targeted, non-invasive CNS Delivery
- Chemistry and mass spectrometry confirm brain exposure
- Addresses BBB penetration, drug resistance and system toxicity

# Phase 2 Development & Clinical Pipeline

Important Disclaimer: This development & clinical pipeline is subject to regulatory approval, risk and uncertainties, as well as potential changes to the pipeline and other factors that are beyond our control.

| Drug Candidate | Application   | Indication   | Preclinical | IND Enabling* | FDA Authorized Clinical Trials |          |           | Commercialization |
|----------------|---|--|-------------|---------------|--------------------------------|----------|-----------|-------------------|
|                |   |  |             |               | Phase I                        | Phase II | Phase III |                   |
| NEO100-01      |  Intranasal NEO100 | Recurrent Grade III & Grade IV Astrocytoma Brain Cancer w/ IDH1 Mutation |             |               | Registrational Trial Phase 2a  |          |           |                   |
| NEO100-02      |  Intranasal NEO100 | Meningioma Brain Tumors  |             |               | Phase 2                        |          |           |                   |
| NEO100-03      |  Intranasal NEO100 | Pediatric Brain Tumors   |             | Phase 1**     |                                |          |           |                   |
| NEO212         |  Oral NEO212     | All Brain Tumors   |             |               | Phase 2                        |          |           |                   |

\*\*IND Enabling: Research to establish whether a compound is reasonably safe for initial use in humans and exhibits pharmacological activity that justifies commercial development.

**Our Clinical Pipeline Continues to Expand to Include Other Applications of NEO100 & NEO212**



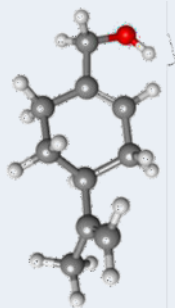
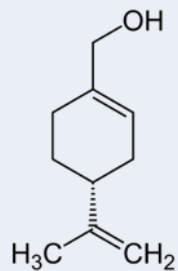
**NEO100**

# NEO100: Foundation of a Next-Generation Drug Delivery and Tumor-Treating Platform

**Proprietary Chemistry:** NEO100 is a patented, ultra-pure pharmaceutical compound derived from Perillyl Alcohol (POH), a natural substance found in citrus and peppermint oils.

**Innovative Synthesis:** Using a proprietary crystalline intermediate, we produce NEO100 through a patented process designed to ensure pharmaceutical-grade purity.

**Patented** NEO100 is designed to facilitate targeted drug delivery to the brain, potentially unlocking new treatments for CNS disorders.



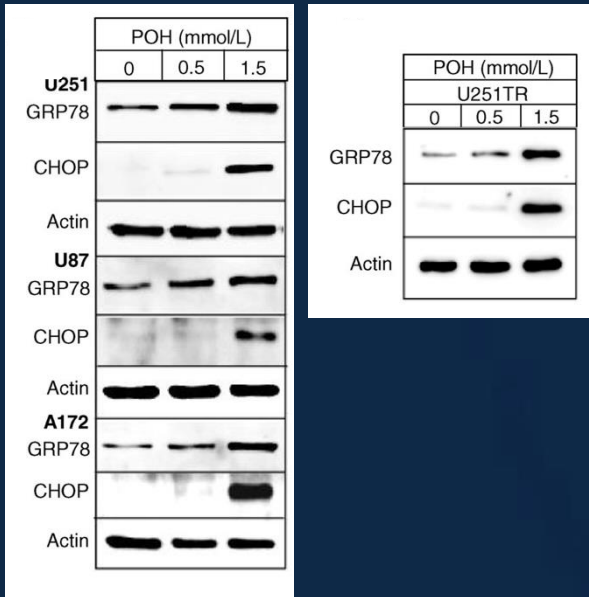
**NEO100** – Our proprietary synthesis of Perillyl Alcohol (POH)



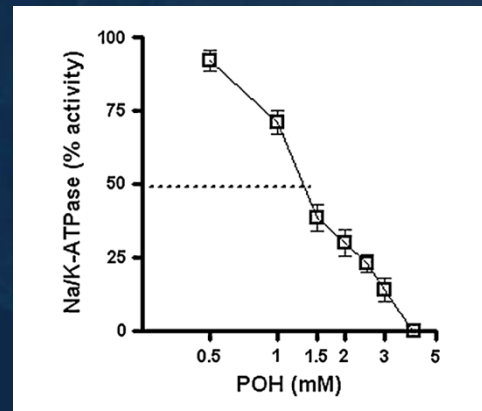
# NEO100 (POH) Efficacy in Temozolomide-Resistant Gliomas

**Mechanism-Driven Second-Line Opportunity:** NEO100 induces ER stress in TMZ-resistant brain tumors while inhibiting  $\text{Na}^+/\text{K}^+$ -ATPase and downregulating RAS—supporting its clinical development as a second-line therapy for HGG patients progressing on TMZ.

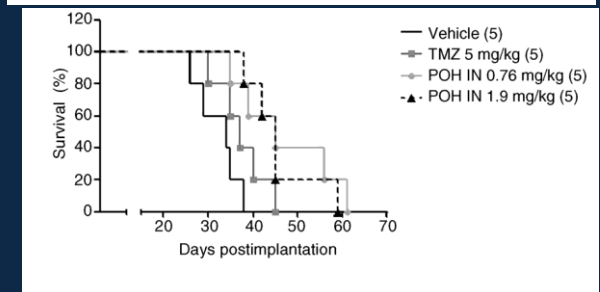
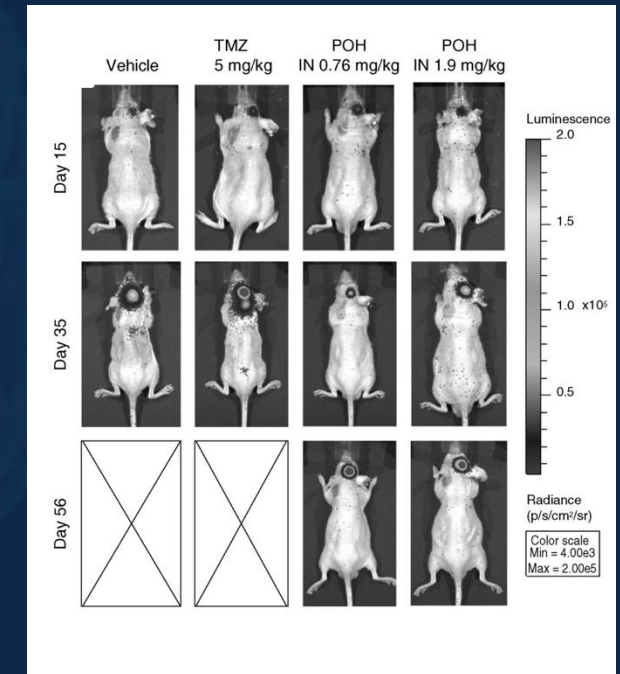
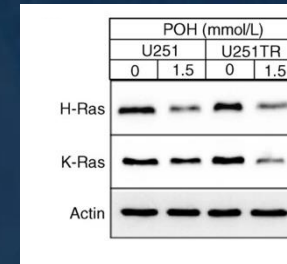
## ER Stress Induction



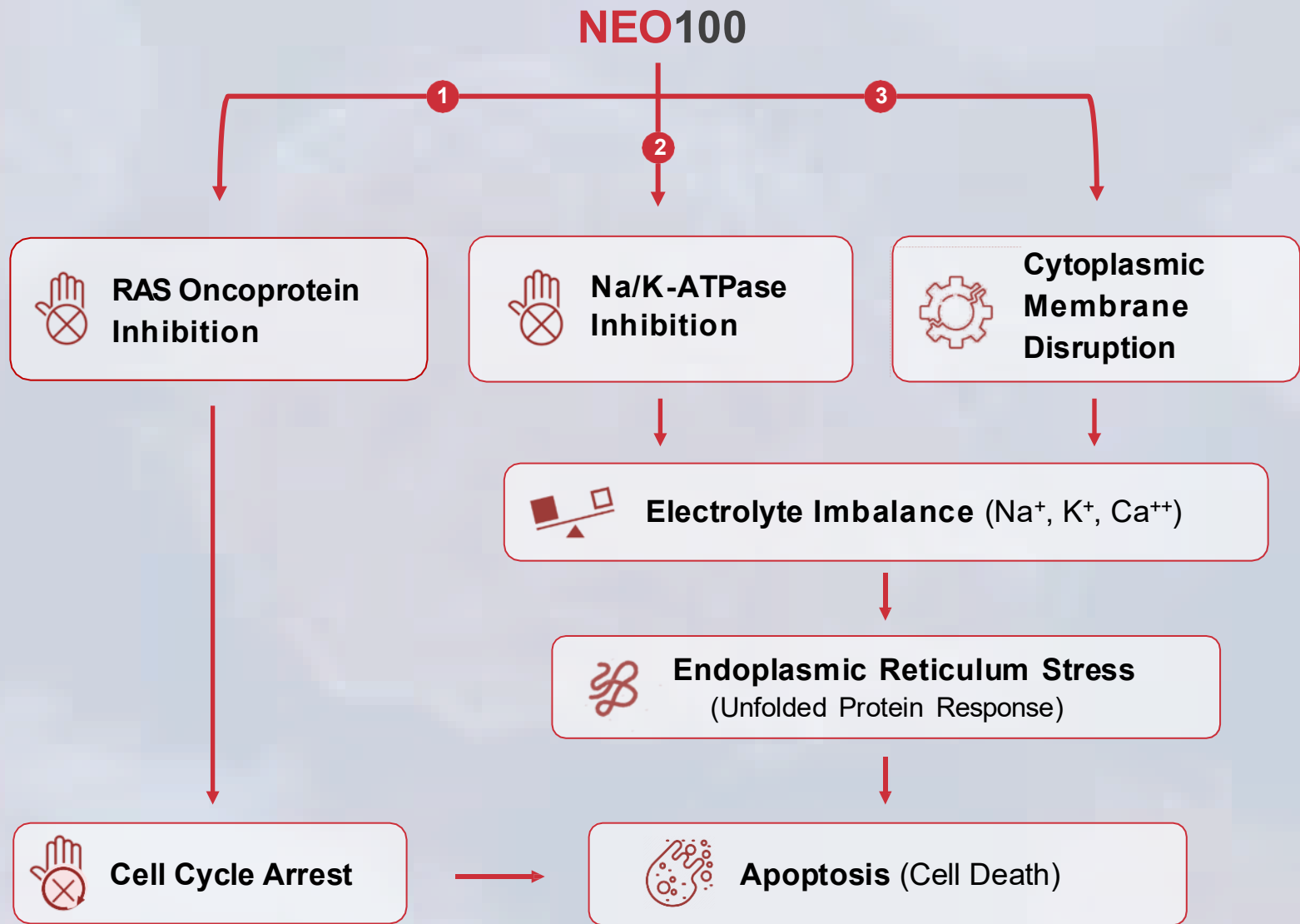
## Na/K -ATPase Inhibition



## RAS Inhibition



# With three mechanisms of action, NEO100 is designed to corner and combat tumors from all sides.



Garcia DG et al. Mol Cell Biochem 2010  
Cho HY et al, Mol Cancer Ther. 2012  
Marín-Ramos NI et al. Neurosurg. 2019  
Wang W et al. Neuro Oncol. 2021  
Schönthal AH et al., Neurooncol Adv. 2021

# IDH1-Mutant Grade 3 & 4 Astrocytomas: Critical Unmet Need

## Meaningful patient population with advanced disease

Approximately **15,000–18,000 patients with IDH1-mutant glioma** across the U.S. and EU; an estimated **~35–45%** present with or progress to **Grade 3 or Grade 4** disease over time

## Current treatment paradigm is not curative

SOC has remained consistent over decades with includes **maximal surgical resection followed by radiation with or without TMZ**

## Disease progression remains common

Despite standard therapy, many patients experience **tumor progression or malignant transformation**, particularly at higher grades

## Post-radiation and post-temozolomide settings are underserved

Therapeutic options following radiation and/or temozolomide exposure are limited, and treatment decisions often rely on off-label use or clinical trials

## Survival outcomes vary by grade and recurrence

Grade 3 IDH1-mutant glioma: reported median overall survival of **~3–6 years**, with risk of progression

Grade 4 IDH1-mutant glioma: reported median overall survival of **~2–3 years**; outcomes after recurrence are substantially shorter

## First-generation IDH inhibitors show defined clinical scope

Clinical activity reported primarily in **lower-grade, non-enhancing tumors**, with limited evidence of benefit refractory Gr3/4 disease

## Unmet need persists with limited approval options in recurrent and transformed disease

There are **no FDA-approved targeted therapies specifically indicated for advanced or recurrent IDH1-mutant astrocytomas**

Treatment of **recurrent or malignant-transformed IDH1-mutant glioma** remains an area of ongoing clinical investigation

# NEO100 Phase I Clinical Trial Results

**Unmet Need:** Recurrent GBM after radiation + temozolomide; historical median OS ~6–9 months

**Trial Design:** multi-center U.S. study (n=12), continuous intranasal dosing until progression

**Dosing:** 384–1,152 mg/day, 4× daily; non-invasive CNS-targeted delivery

**Safety:** Well tolerated at all doses; **no severe or dose-limiting toxicities**

**Efficacy Signal:** PFS-6 ~30–33%, OS-12 ~55%, median OS 15 months

**Durability:** ~33% survived >24 months; **complete remission at 2 years** in one patient

**Long-Term Survival:** Patient on continued NEO100 therapy **alive at 3 years**

**Biomarker Insight:** All long-term survivors were **IDH1-mutant**, supporting biologic enrichment

**Differentiation:** Intranasal delivery bypasses BBB, avoids systemic chemo toxicity

**Strategic Implication:** De-risked safety + survival signal supports advancement and lifecycle expansion

# NEO100 Phase I Survival Data

## NEO100 OVERALL SURVIVAL RATES

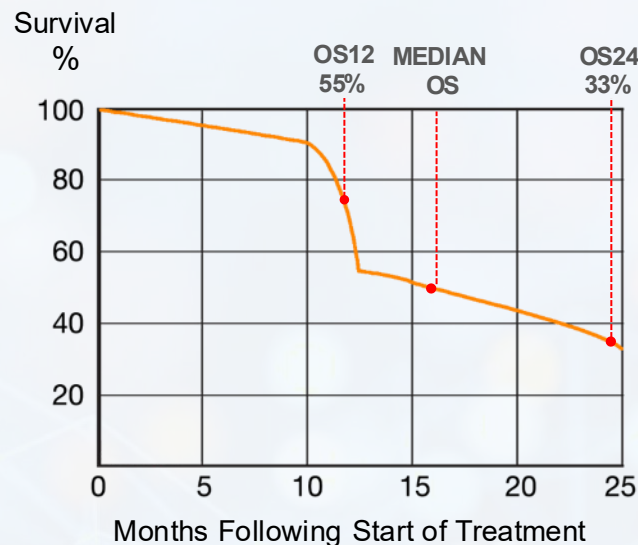


Chart shows the survival rate of all patients within first 24 months of the trial.

Shows specific highlights of survival at 12 months (OS-12) and 24 months (OS-24) vs. Median Overall Survival (OS) rate at 15 months.

## NEO100 TREATMENT CYCLE SURVIVAL RATES

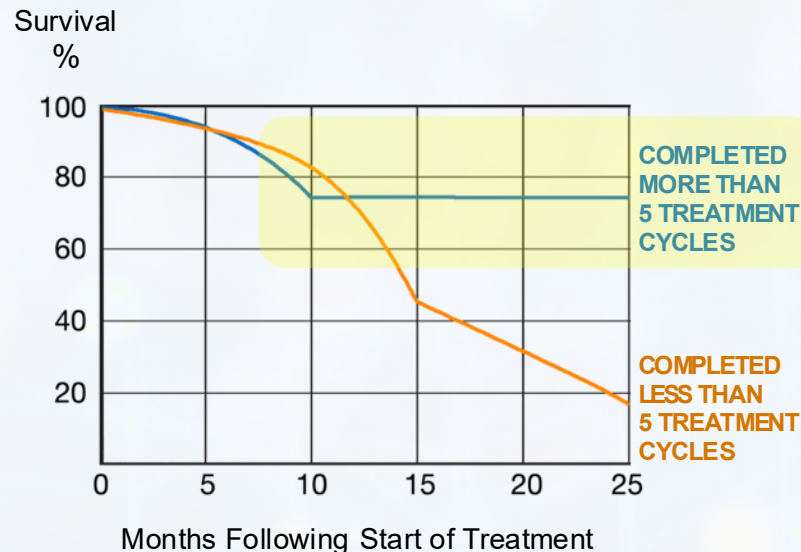


Chart shows survival rate of all patients in first 24 months based on number of treatment cycles.

**Patients who completed more than 5 cycles of NEO100 treatment demonstrated higher survival rate.**

## NEO100 TREATMENT OF PATIENTS WITH IDH1 MARKER

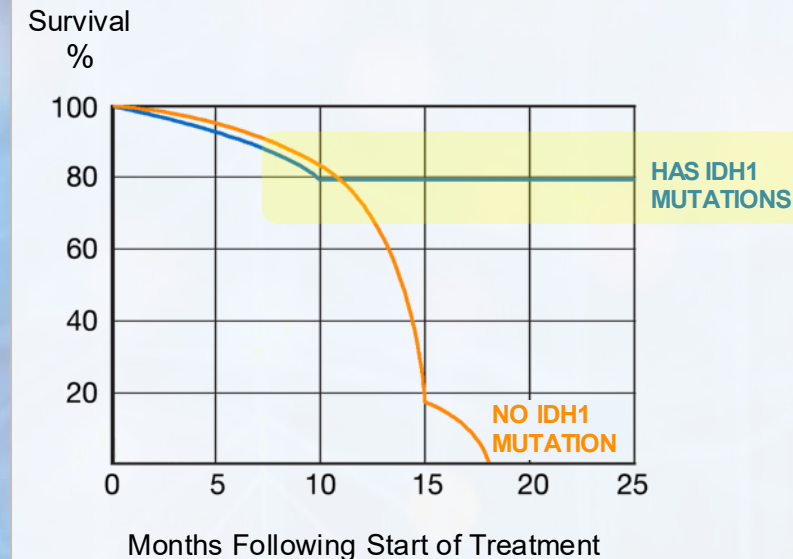
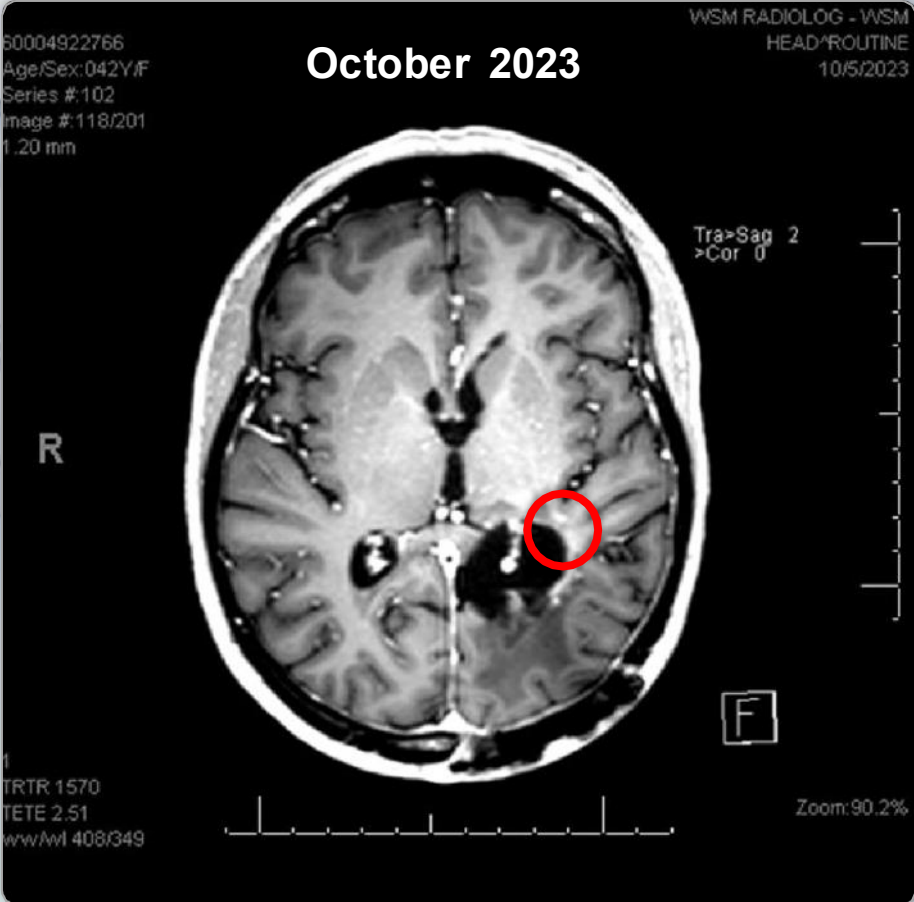


Chart shows survival rate of patients based on indication of **IDH1 biomarker** in patient profile.

**Studies demonstrate that patients with IDH1 do better with disease resistance.**

**Results Demonstrate Greater Survival Rates with NEO100, Particularly for Patients Receiving Additional Treatments Cycles and Those with IDH1 Marker**

# Before & After NEO100 Treatment



**Brain Scan Shows Significant Tumor Reduction at Nine Months Following Treatment with NEO100**

# NEO100 vs. 2nd-Line Recurrent Brain Tumor Benchmarks

NEO100 demonstrates survival outcomes that exceed historical second-line recurrent GBM benchmarks—highlighting a potentially differentiated therapy in a setting with limited effective options and historically low survival rates.

| Therapy (Setting)   | OS-12      | OS-24        | PFS-6                         | Median OS    |
|---|------------|--------------|-------------------------------|--------------|
| <b>NEO100 (intranasal POH) – Phase I (n=12)</b>                 | <b>55%</b> | <b>33%**</b> | <b>33%</b>                    | <b>15 mo</b> |
| Lomustine (CCNU) – control arm benchmark (REGOMA lomustine arm) | 15%        | NR           | 8%                            | 5.6 mo       |
| Regorafenib (Stivarga) – REGOMA                                 | 39%        | NR           | 17%                           | 7.4 mo       |
| TTFields (monotherapy) – EF-11 (recurrent GBM)                  | ~20%       | ~9%          | Reported as endpoint (varies) | 6.6 mo       |
| Bev + Lomustine – EORTC 26101 (progressive GBM)                 | NR         | NR           | PFS improved                  | 9.1 mo*      |
| HDAC inhibitor (Vorinostat) – recurrent GBM Phase II            | NR         | NR           | 15%                           | 5.7 mo       |

NR = not routinely reported as a fixed landmark endpoint in the cited source/trial.

\*No OS gain vs lomustine

\*\*IDH1m population

# NEO100 Phase II — Registrational Path in IDH1-Mutant Glioma



**Objective:** Generate confirmatory efficacy and durability data to advance **NEO100** toward **commercialization**

**Design:** Phase II, biomarker-enriched (IDH1-mutant), building directly on Phase I signal

**Enrollment:** **25 patients** with recurrent **IDH1-mutant Grade III–IV glioma**

**Sites:** Targeting **~12 U.S. affinity centers** with neuro-oncology expertise

**Dose & Delivery:** **1,152 mg/day** NEO100 via **intranasal inhalation (288 mg QID)**

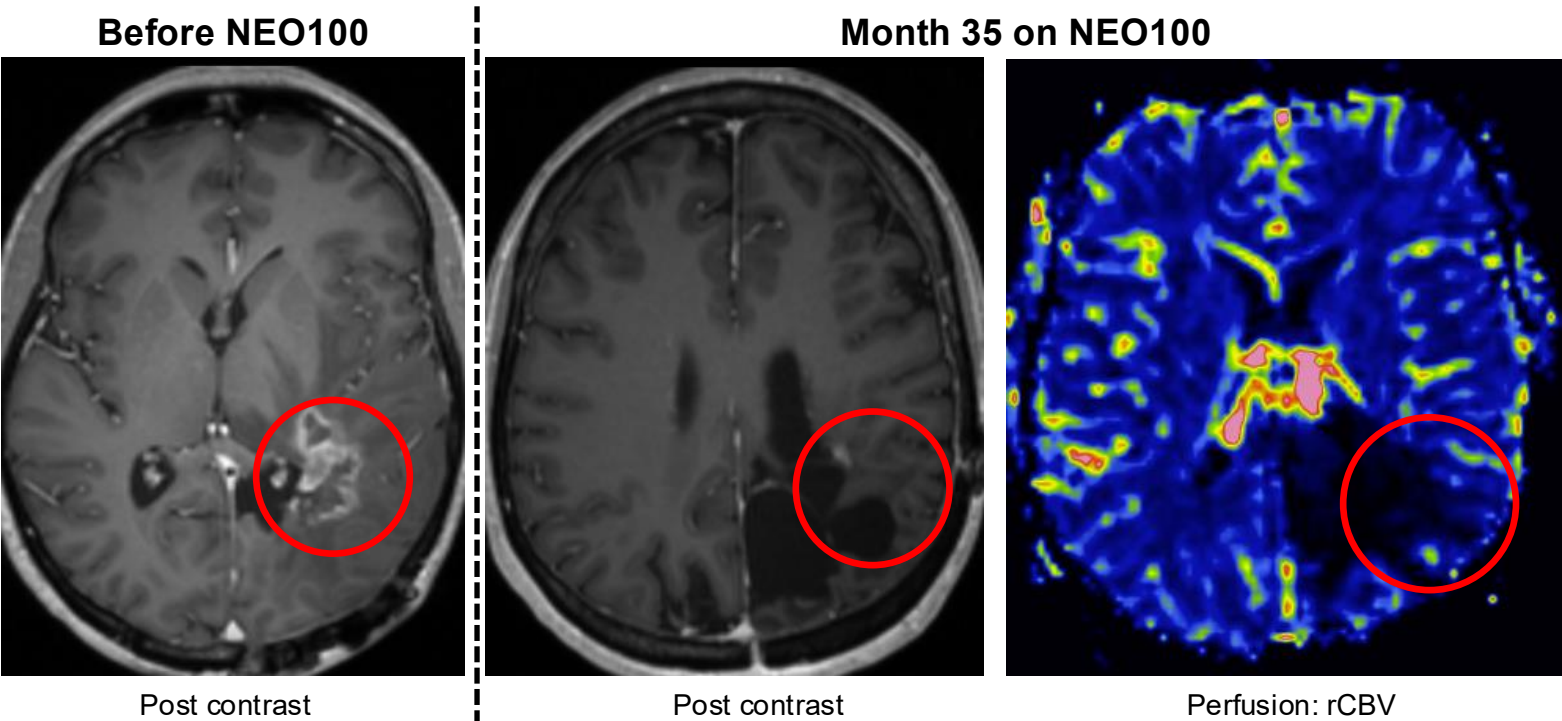
**Rationale:** Phase I showed **exceptional long-term survival** exclusively in IDH1-mutant patients—many **>3 years post-diagnosis**, far exceeding recurrence benchmarks

**Differentiation:** No other recurrent GBM program has demonstrated comparable **durable survival with minimal toxicity**

**Regulatory Strategy:** Leverages **modest historical GBM approval thresholds** (e.g., **~3-month OS benefit** accepted in prior approvals)

# NEO100 Phase 2a Demonstrates PFS-6 Above Historical IDH1-Mutant Benchmarks

| Metric                             | NEO100-01  | Historical IDH1 mut recurrent HGG <sup>1,2</sup>   |
|------------------------------------|--|--|
| 6 months Progression Free Survival | 44% (8/18)<br>≥6-month follow-up prior to data cutoff. | 21-31%<br>References:<br><sup>1</sup> Fanucci et al., 2023<br><sup>2</sup> Walbert et al. 2010 |



**CR: 17% 3/18**  
**PR/stable: 28% (5/18)**  
**Progression: 50% (9/18)**

# Takeaways from Phase I & II of NEO100

- 6 of 25 (24%) patients achieved significant radiographic remission. This response rate exceeds the <8% typically observed with salvage therapies for recurrent gliomas.
- 9 of 25 (36%) patients are long-term survivors, surviving  $\geq 18$  months following initiation of NEO100, with a **median overall survival of 88 months**
- No major toxicity reported across cohort; chronic intranasal dosing well tolerated
- Adverse events predominantly low-grade; safety consistent with prolonged exposure

| Subject Number | Phase | Diagnosis              | Survival following initiation of NEO100 (Months) | Overall Survival (Months) |
|----------------|-------|------------------------|--|---------------------------|
| 04-302         | 1     | Astrocytoma IDH-mt IV  | 89+  | 133+                      |
| 01-301         | 1     | Astrocytoma IDH-mt IV  | 58+  | 101+                      |
| 04-202         | 1     | Astrocytoma IDH-mt IV  | 52   | 140                       |
| APR            | CC    | Astrocytoma IDH-mt III | 35+  | 45+                       |
| 01-506         | 2     | Astrocytoma, IDH-mt IV | 29   | 139                       |
| 01-508         | 2     | Astrocytoma, IDH-mt IV | 27   | 41                        |
| 01-507         | 2     | Astrocytoma, IDH-mt IV | 27   | 53                        |
| 11-501         | 2     | Astrocytoma IDH-mt III | 20+  | 75+                       |
| 12-501         | 2     | Astrocytoma IDH-mt IV  | 15+  | 198+                      |
| 01-511         | 2     | Astrocytoma IDH-mt III | 15+  | 19+                       |
| 01-512         | 2     | Astrocytoma IDH-mt IV  | 15+  | 19+                       |
| 07-501         | 2     | Astrocytoma IDH-mt IV  | 12   | 31                        |
| 10-501         | 2     | Astrocytoma IDH-mt IV  | 12+  | 30+                       |
| 08-501         | 2     | Astrocytoma, IDH-mt IV | 10   | 12                        |
| 04-510         | 2     | Astrocytoma IDH-mt III | 9  | 24                        |
| 04-511         | 2     | Astrocytoma IDH-mt IV  | 8  | 21                        |
| 09-504         | 2     | Astrocytoma IDH-mt IV  | 8+   | 11                        |
| 01-514         | 2     | Astrocytoma IDH-mt IV  | 7+   | 7                         |
| 11-502         | 2     | Astrocytoma IDH-mt III | 7+   | 84+                       |
| 01-513         | 2     | Astrocytoma IDH-mt IV  | 5  | 9                         |
| 09-502         | 2     | Astrocytoma, IDH-mt IV | 3  | 91                        |
| 01-106         | 1     | Astrocytoma, IDH-mt IV | 2  | 50                        |
| 04-105         | 1     | Astrocytoma, IDH-mt IV | 2  | 16                        |

+ Subject alive

# NEO100-02 — Intranasal Therapy for Meningioma



**Large Market:** Meningioma is the most common primary brain tumor (~35% of all primary CNS tumors)

**Prevalence:** ~170,000+ patients living with meningioma in the U.S.; 30–35% recur after surgery ± radiation

**Unmet Need:** No FDA-approved systemic therapies for recurrent or radiation-refractory meningioma

**Current Paradigm:** Surgery and radiation dominate; repeat surgery is often infeasible and medical options lack durability

**NEO100 Fit:** Non-invasive intranasal delivery enables direct CNS access without surgery or catheters

**Safety Advantage:** Well-tolerated profile supports chronic dosing in slow-growing, recurrent disease

**Phase II Design (NEO100-02):** Recurrent meningioma treated with continuous intranasal NEO100

**Primary Objective:** PFS-6

**Strategic Goal:** Establish NEO100 as a first-in-class medical therapy in a large market with no standard systemic option

# NEO100-03 — Pediatric High-Grade Glioma (pHGG) | Rare Pediatric Disease Opportunity

**Rare & Lethal:** Pediatric HGGs (incl. H3-altered/DIPG) represent ~15–20% of pediatric brain tumors with median OS <12 months

**Prevalence Threshold Met:** ~1,500–2,000 new cases/year worldwide, consistent with Rare Pediatric Disease designation criteria

**Extreme Unmet Need:** No FDA-approved effective systemic therapies for recurrent or progressive pHGG

**Current Paradigm:** Surgery (often infeasible) + radiation; chemotherapy offers minimal survival benefit

**NEO100 Fit:** Non-invasive intranasal CNS delivery avoids systemic toxicity and invasive procedures in children







**Safety Rationale:** Favorable tolerability profile supports pediatric development and chronic dosing

**Regulatory Strategy:** Development aligned with Rare Pediatric Disease designation and eligibility for a Priority Review Voucher (PRV) from the FDA

**Strategic Upside:** First-in-class pediatric CNS therapy with potential PRV.

# What Sets Us Apart

## NEO100 vs. Current Standard of Care for Recurrent High-Grade Gliomas

|  |                                       | vs. Current Standard of Care for Recurrent High-Grade Gliomas |                |                       |          |             |                |   |
|--|---------------------------------------|---|----------------|-----------------------|----------|-------------|----------------|---|
|  |                                       | Repeat Surgery  | Oral Lomustine | Bevacizumab (Avastin) | Novocure | Gamma Tiles | Gliadel Wafers |   |
|    | No Surgery Required <sup>1</sup>      | NEONC TECHNOLOGIES, INC.                                      | ✓              | -                     | ✓        | ✓           | -              | - |
|    | Bone Marrow Unaffected                | NEONC TECHNOLOGIES, INC.                                      | ✓              | -                     | -        | ✓           | ✓              | ✓ |
|    | Normal Wound Healing                  | NEONC TECHNOLOGIES, INC.                                      | ✓              | -                     | -        | ✓           | -              | - |
|    | Radiation Not Required                | NEONC TECHNOLOGIES, INC.                                      | ✓              | ✓                     | ✓        | ✓           | -              | ✓ |
|  | No Systemic Side-effects <sup>2</sup> | NEONC TECHNOLOGIES, INC.                                      | ✓              | -                     | -        | ✓           | ✓              | ✓ |
|  | Easy to Administer Treatment          | NEONC TECHNOLOGIES, INC.                                      | -              | ✓                     | -        | -           | -              | - |

***NEO100 has the Potential to Outperform the Current Standard of Care Across These Key Treatment Factors***

1) Drug dosage does not require surgery. 2) No significant systemic side-effects reported in our NEO100 Phase I clinical trial.

# NEO100 — Key Upcoming Milestones & Next Steps



**NEO100-01 (IDH1-Mutant Glioma):** Phase II clinical data expected 2H 2026

**Regulatory Engagement:** Planned interactions with the FDA to define next development steps based on Phase II results

**Registrational Strategy:** Preparation for a **registrational Phase III pathway** contingent on Phase II outcomes

**NEO100-02 (Meningioma):** Phase II study ongoing; clinical results expected in 2027

**NEO100-03 (Pediatric pHGG):** Enrollment expected to begin Q1 2026



**NEO212**

# GBM & Temozolomide (TMZ): Fundamental Limitations

- **Foundational standard of care since ~2005**, used with surgery and radiation; provides modest median OS benefit (~14-16 months), **~70–80% of patients experience tumor progression within 12 months**
- **Widespread global adoption**, with peak sales estimated at ~\$3–4B, despite known limitations in the durability of response
- **MGMT promoter methylation (~35–45% of patients)** is associated with increased TMZ sensitivity
- **Broad real-world use regardless of MGMT status**, including in unmethylated tumors with reduced expected benefit
- **Systemic exposure to active metabolite (AIC)** is associated with hematologic toxicity, including bone marrow suppression
- **Treatment-limiting myelosuppression** may reduce dose intensity or duration, independent of tumor response
- **Median frontline PFS ~6–7 months, with progression observed in both methylated and unmethylated disease**
- **Limited options post-progression**, with salvage therapies providing variable benefit and **a median survival of ~6–9 months following recurrence**

## 2nd-Line Recurrent Brain Tumor Benchmarks

| Therapy                     | Median OS (mo) | OS-12 (%) | Key Trial Context                    |
|-----------------------------|----------------|-----------|--------------------------------------|
| CCNU (lomustine) alone      | 5.6–8.6        | ~20–35%   | REGOMA (~20%); EORTC 26101 (~30–35%) |
| Bevacizumab (Avastin) alone | ~9.2           | ~38–43%   | BRAIN Trial                          |
| CCNU + Bevacizumab*         | ~9.1           | ~35–40%   | EORTC 26101                          |
| TTFields alone              | ~6.6           | ~20–25%   | EF-11                                |

*Bottom line: Temozolomide validated market demand in GBM; its clinical limitations inform the development rationale for NEO212*

# NEO212: Brain-Optimized Temozolomide Bioconjugate Designed to Enhance Brain Tumor Targeting

**Novel bioconjugate** combining NEO100 with temozolomide (TMZ).

Builds on TMZ, the established GBM standard of care, with the goal of **improving brain delivery and durability of response**.

Designed to **achieve BBB penetration** targeting brain tumors more effectively than TMZ

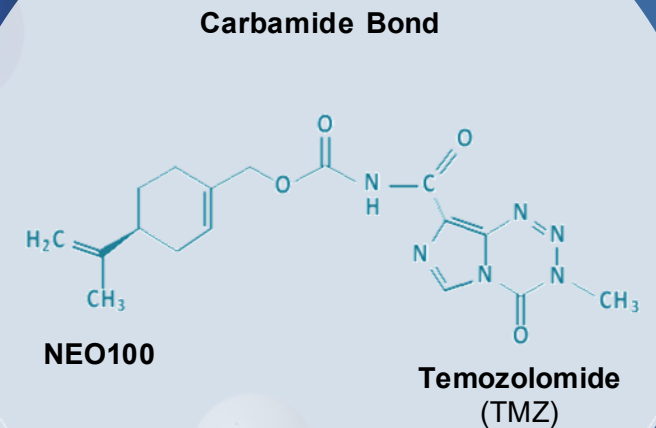
**Dual-mechanism:** Complementary activity from NEO100 and TMZ in one molecule.

**Bioconjugation** designed to optimize PK and CNS exposure

**Clinically ready** for studies in primary and secondary malignant brain cancers, including GBM and brain metastases.

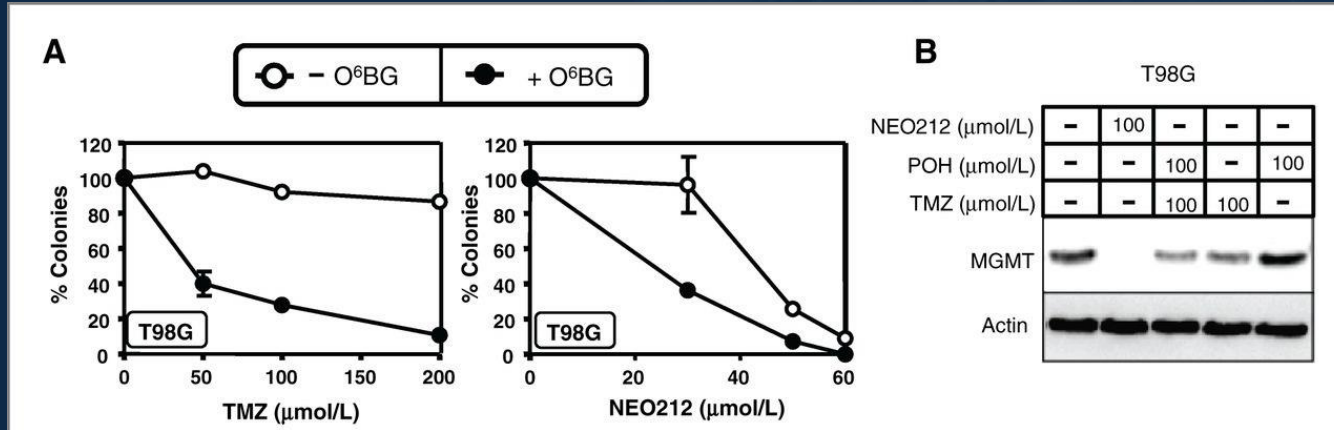
**Multiple delivery routes** planned, with evaluation of both oral and intranasal administration.

## NEO212 Bioconjugated Molecule

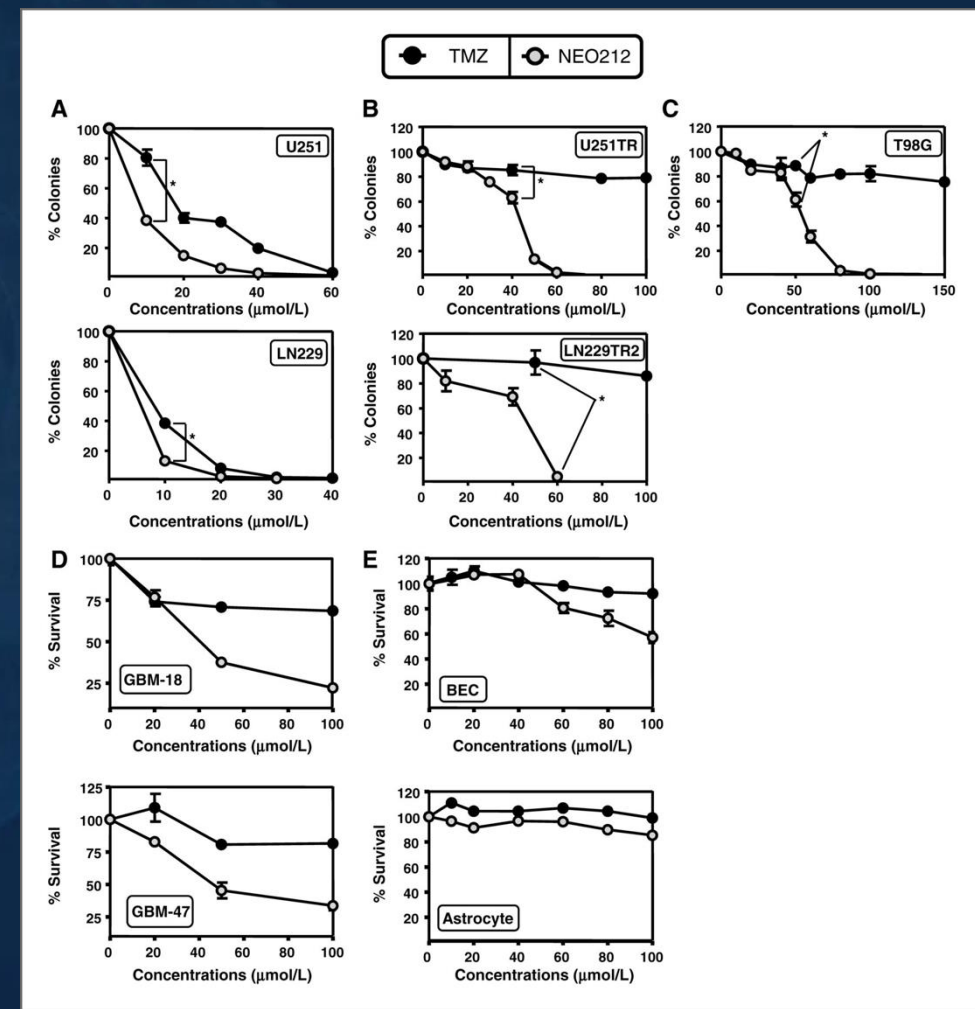


# NEO212 Degrades MGMT and Overcomes TMZ Resistance in GBM

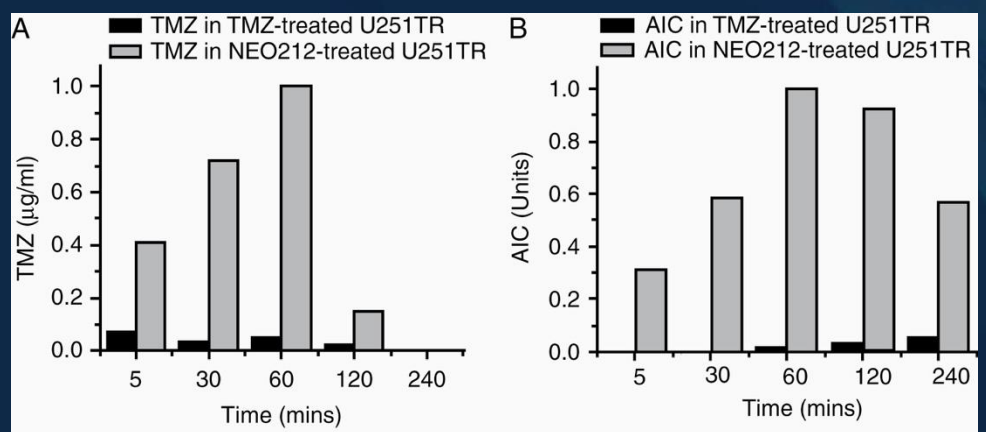
NEO212 degrades MGMT and Kills TMZ-Resistant GBM Without the Need for MGMT Inhibitor O<sup>6</sup>BG



NEO212 Demonstrates Greater Cytotoxicity Than Temozolomide in Human GBM Cell Lines



NEO212 Achieves Higher Intratumoral TMZ/AIC Exposure in TMZ-Resistant GBM

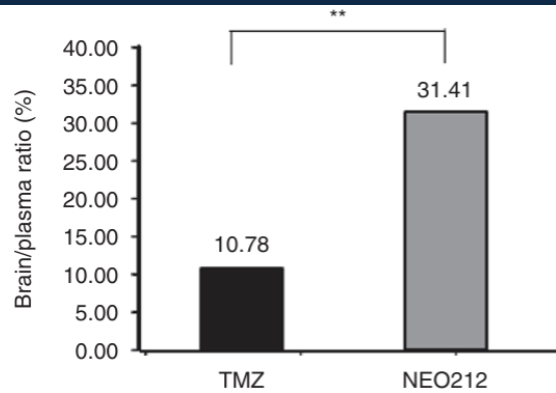


Chen TC et al. Cancer Lett. 2015 Mar 28;358(2):144-151.  
 Cho HY et al. Neurooncol Adv. 2020 Nov 20;2(1):vdaa160.  
 Cho HY et al Mol Cancer Ther. 2014 Aug;13(8):2004-17.

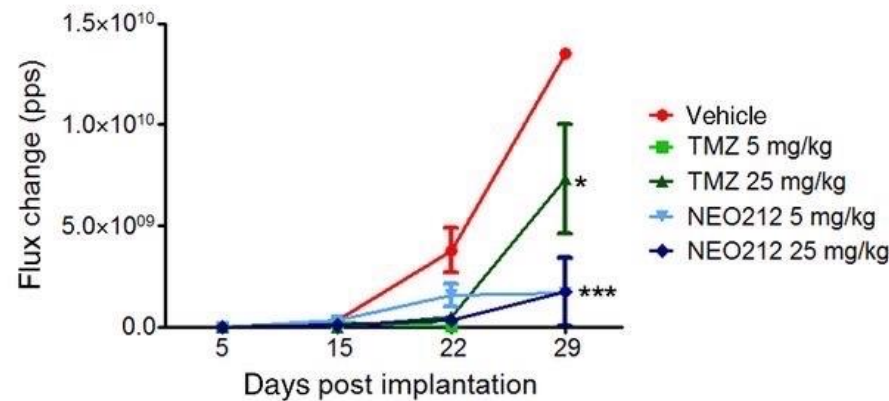
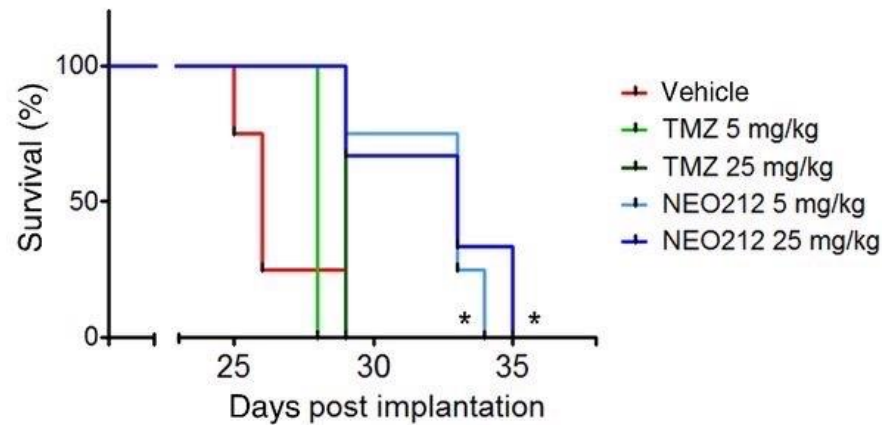
# NEO212 Demonstrates Enhanced Brain Delivery and Antitumor Activity in TMZ-Resistant GBM

*BBB penetration* ↑ | *Overall survival* ↑ | *Tumor size* ↓

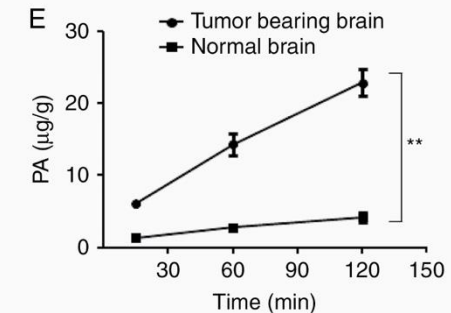
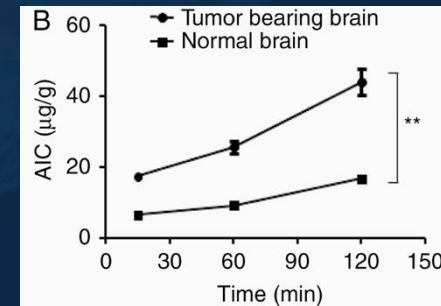
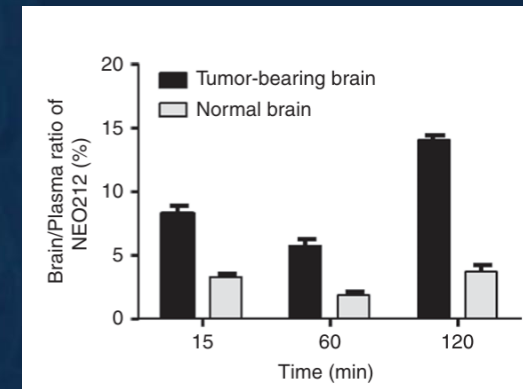
≈3× Higher Brain-to-Serum Ratio Observed for NEO212 vs Temozolomide



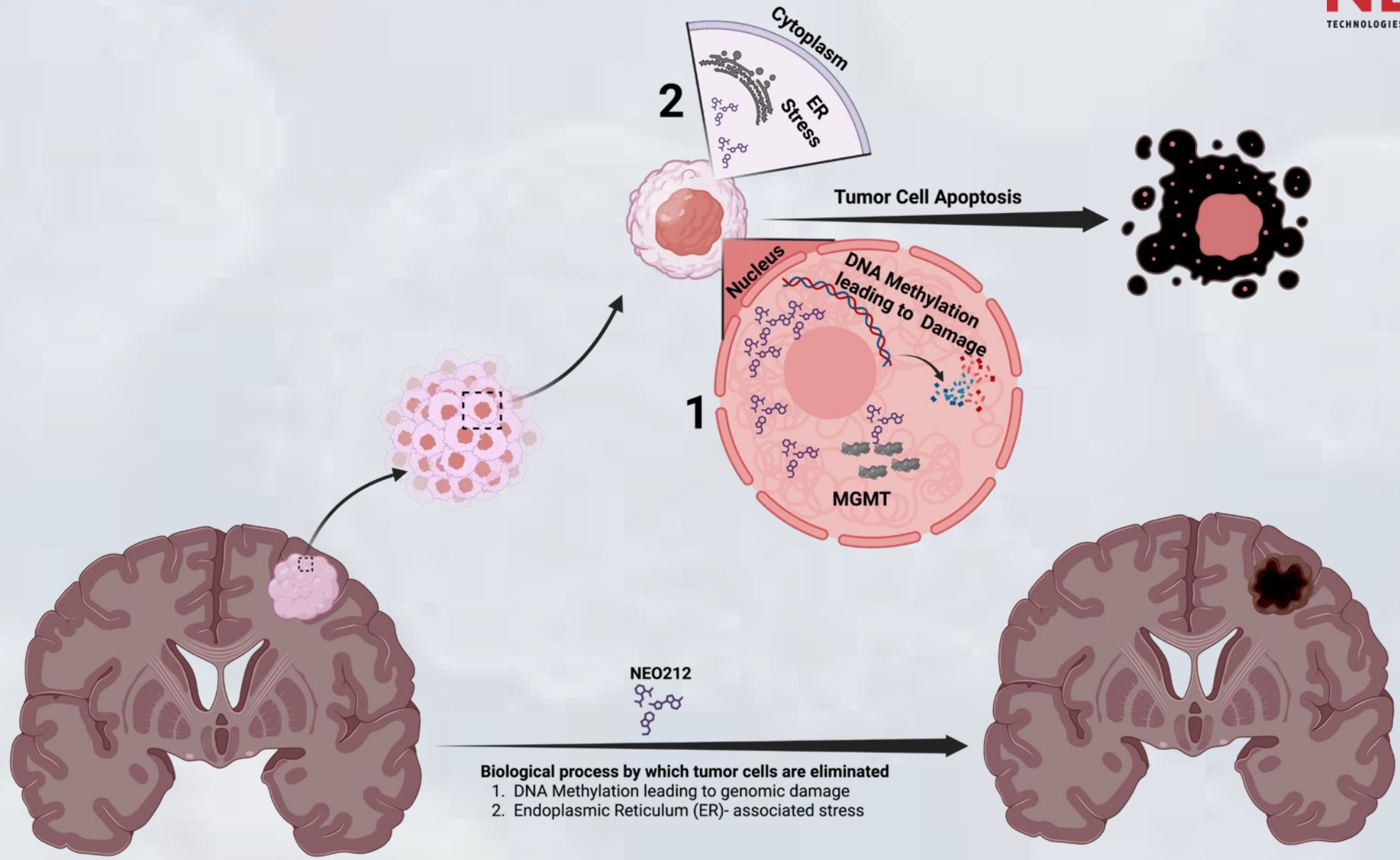
Intracranial Xenograft Model  
Patient-derived USC-02 MGMT<sup>+</sup> GBM



Increasing NEO212 Levels Observed in Tumor Tissue Along with Its Metabolites PA and AIC



# NEO212 Mechanism of Action



**Biological process by which tumor cells are eliminated**  
1. DNA Methylation leading to genomic damage  
2. Endoplasmic Reticulum (ER)- associated stress

# NEO212: Novel Alkylating Therapy with Preclinical Evidence of MGMT Inactivation and Brain Penetration in Clinical Development for Brain Tumors

**Broad Scope:** Primary brain tumors and **brain metastases** as monotherapy and in combination with SOC

**Differentiation vs TMZ:** Up to 10× greater preclinical efficacy, including **MGMT-positive (TMZ-resistant) tumors** with **NEO212-Mediated MGMT Inactivation**

**Safety Advantage:** Lower systemic toxicity and myelosuppression vs TMZ

**Brain Delivery:** 3× higher BBB penetration (brain: serum ratio) vs TMZ

**Phase I (completed):** Assessing **safety, tolerability, and preliminary efficacy** in primary brain tumors and solid-tumor brain metastases

**Strategic Opportunity:** Designed to **replace or augment TMZ** across primary and metastatic brain cancer indications

# Phase 1: Safety and Efficacy of NEO212 in Patients With Astrocytoma IDH-mutant, Glioblastoma IDH-wildtype or Brain Metastasis



## Phase 1: (dose escalation) Primary Objectives:

- Assess the safety and tolerability of increasing dose levels of orally administered NEO212 alone in patients with Astrocytoma IDH-mutant, Glioblastoma IDH-wildtype or patients with select solid tumors with uncontrolled metastases to the brain.
- Identify the maximum tolerated dose (MTD) of NEO212.
- Determine the recommended Phase 2 dose (RP2D) of NEO212.

## Secondary Objectives:

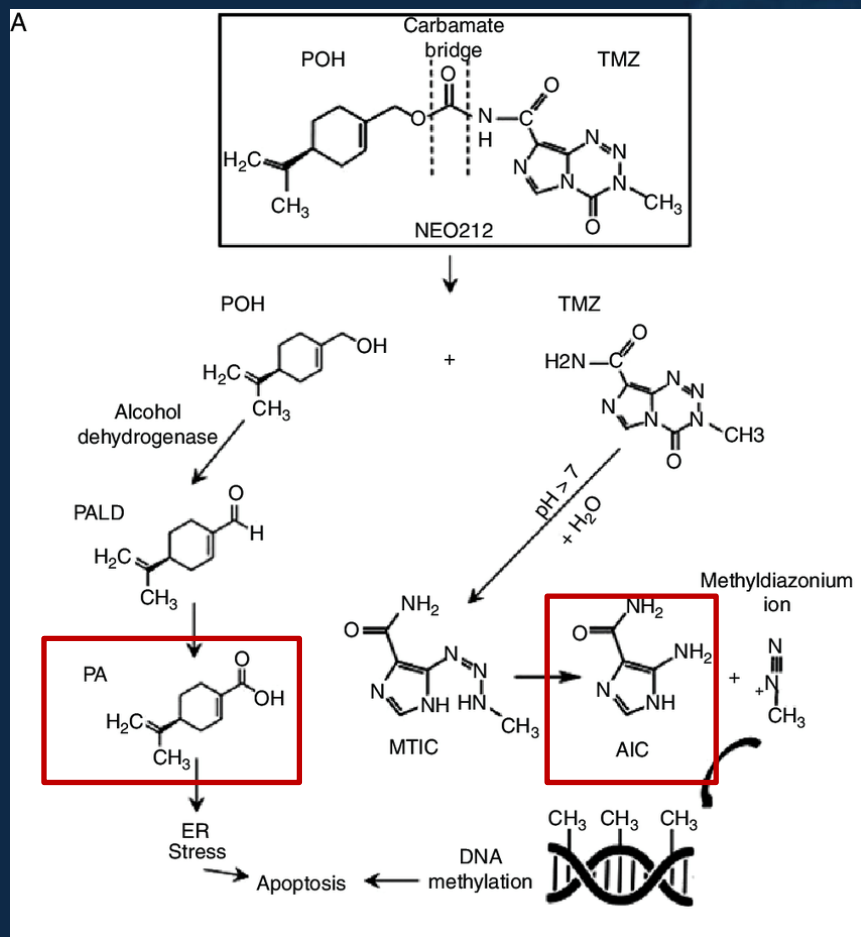
- Characterize the pharmacokinetics (PK) of NEO212.
- Evaluate anti-tumor activity of NEO212 in patients with Astrocytoma IDH-mutant, Glioblastoma IDH-wildtype and patients with select solid tumors with uncontrolled metastases to the brain.

**NEO212 Phase 1 – Patient Distribution by Cohort**

|                                | Tumor Type                                | MGMT Status                                      | Total Subjects |
|--------------------------------|---|--|----------------|
| <b>Cohort 1</b><br>(170mg/day) | Squamous NSCLC-to-Brain Metastasis        | N=1, Not applicable                              | 3              |
|                                | GBM <i>IDH1</i> -wildtype                 | N=2 Methylated                                   |                |
| <b>Cohort 2</b><br>(220mg/day) | GBM <i>IDH1</i> -wildtype                 | N=2 Methylated, N=1 Unmethylated                 | 3              |
| <b>Cohort 3</b><br>(400mg/day) | Esthesioneuroblastoma-to-Brain Metastasis | N=1, Not applicable                              | 3              |
|                                | Breast-to-Brain Metastasis                | N=1, Not applicable                              |                |
|                                | GBM <i>IDH1</i> -wildtype                 | N=1, Methylated                                  |                |
| <b>Cohort 4</b><br>(610mg/day) | GBM <i>IDH1</i> -wildtype                 | N=1 Equivocal1, N=1 Unmethylated, N=1 Methylated | 3              |
| <b>Cohort 5</b><br>(810mg/day) | GBM <i>IDH1</i> -wildtype                 | N=2 Methylated                                   | 2              |

*Subjects received NEO212 orally once daily on Days 1 through 5 of each 28-day treatment cycle.*

# Low Peripheral Blood Detection of NEO212 Metabolites (AIC and PA) in Phase 1 PK Samples, Consistent with Preclinical Observations of Tumor Uptake and Intratumoral Metabolism



|                              | Cohort 1<br>(170 mg/QD) | Cohort 2<br>(220 mg/QD) | Cohort 3<br>(400 mg/QD) | Cohort 4<br>(610 mg/QD) | Cohort 5<br>(810 mg/QD) |
|------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| <b>N (evaluable)</b>         | 3                       | 3                       | 3                       | 3                       | 2                       |
| <b>Mean Peak AIC (ng/mL)</b> | 1.94                    | 2.52                    | 12.19                   | 16.8                    | 3.25                    |
| <b>AIC Range (ng/mL)</b>     | 0–49.6                  | 0–47.0                  | 0–117.0                 | 0–120.0                 | 0–36.0                  |
| <b>Mean Peak PA (ng/mL)</b>  | 0.17                    | 0.07                    | 2.04                    | 13.83                   | 6.96                    |
| <b>PA Range (ng/mL)</b>      | 0–27.7                  | 0–12.5                  | 0–21.2                  | 0–80.2                  | 0–43.6                  |

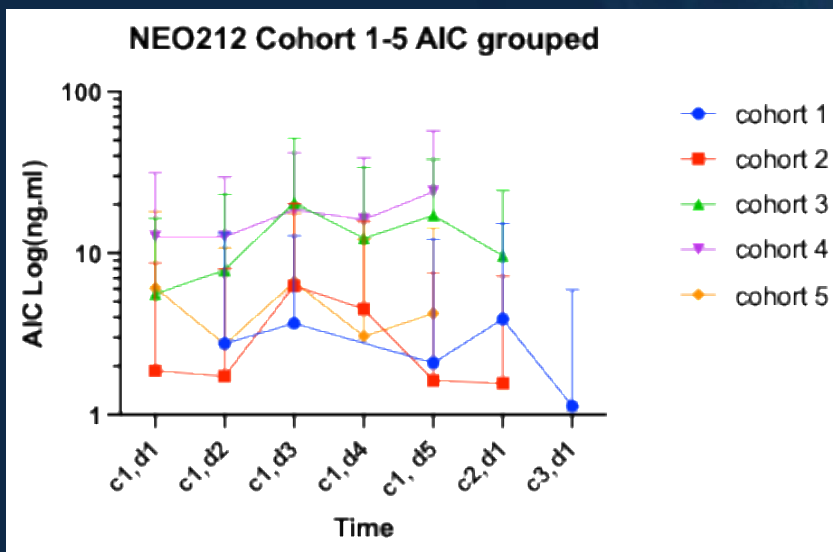
**These findings suggest reduced systemic metabolite exposure and potential enhanced tumor targeting, which may be associated with lower systemic toxicity compared with temozolomide.**

# 39× Lower AIC Levels Observed with NEO212 vs Temozolomide, Reflecting Reduced Systemic Metabolite Levels and Potentially Supporting an Improved Hematologic Safety Profile

## Adjusted for Body Weight, NEO212 Achieves Higher CNS Delivery vs. TMZ

| Brain-adjusted exposure NEO212 vs TMZ 200 mg/m <sup>2</sup> (Cycle 2+) |                               |  |                            |                                   |  |
|--|-------------------------------|--|----------------------------|-----------------------------------|--|
| NEO212 (mg/day)  | NEO212 total over 5 days (mg) | NEO212 total 5-day dose (TMZ-equivalent, mg; conversion ratio = 0.521) | TMZ total over 5 days (mg) | Relative Exposure compared to TMZ | Brain-adjusted relative (3x BBB-permeable) |
| Cohort 1   | 170                           | 443  | 1800                       | 0.25                              | 0.73                                       |
| Cohort 2   | 220                           | 573  | 1800                       | 0.32                              | 0.93                                       |
| Cohort 3   | 400                           | 1,042  | 1800                       | 0.58                              | 1.69                                       |
| Cohort 4   | 610                           | 1,589  | 1800                       | 0.88                              | 2.56                                       |
| Cohort 5   | 810                           | 2,110  | 1800                       | 1.17                              | 3.40                                       |

### NEO212



|                      | cohort 1 | cohort 2 | cohort 3 | cohort 4 | cohort 5 |
|----------------------|----------|----------|----------|----------|----------|
| Cmax (ng/ml)         | 3.91     | 6.29     | 20.54    | 24.01    | 6.62     |
| Mean (ng/ml)         | 1.94     | 2.52     | 12.19    | 16.78    | 3.25     |
| Std. Deviation       | 1.62     | 2.13     | 5.71     | 4.76     | 2.64     |
| Std. Error of Mean   | 0.61     | 0.81     | 2.33     | 2.13     | 1.00     |
| Lower 95% CI of mean | 0.44     | 0.54     | 6.20     | 10.87    | 0.81     |
| Upper 95% CI of mean | 3.44     | 4.49     | 18.18    | 22.69    | 5.69     |

### TMZ

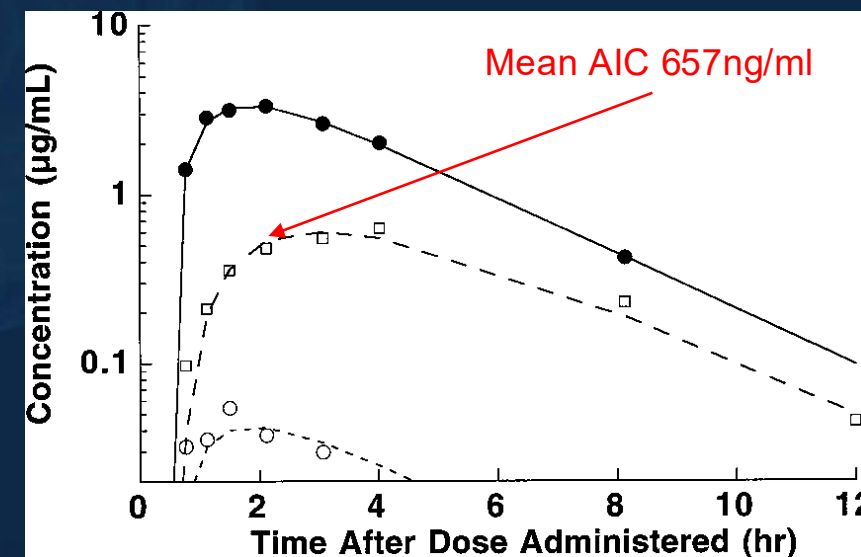
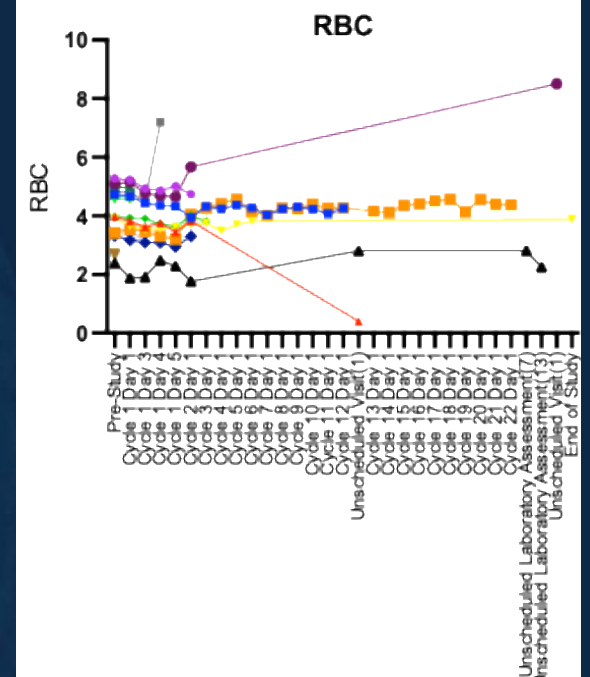
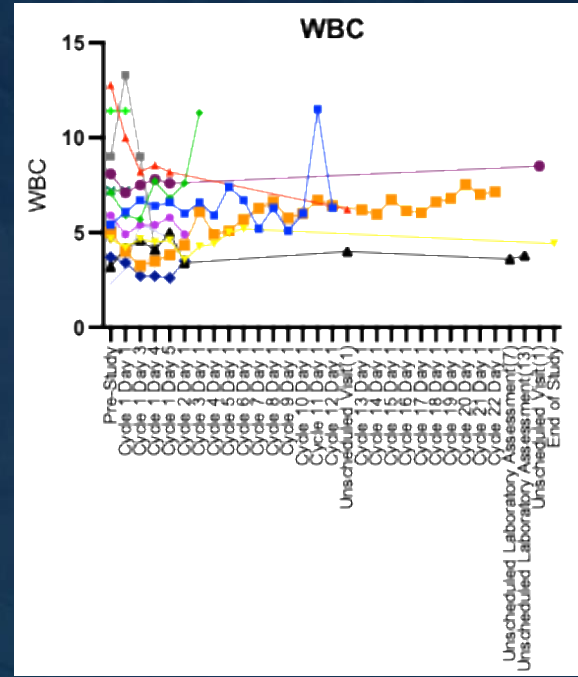
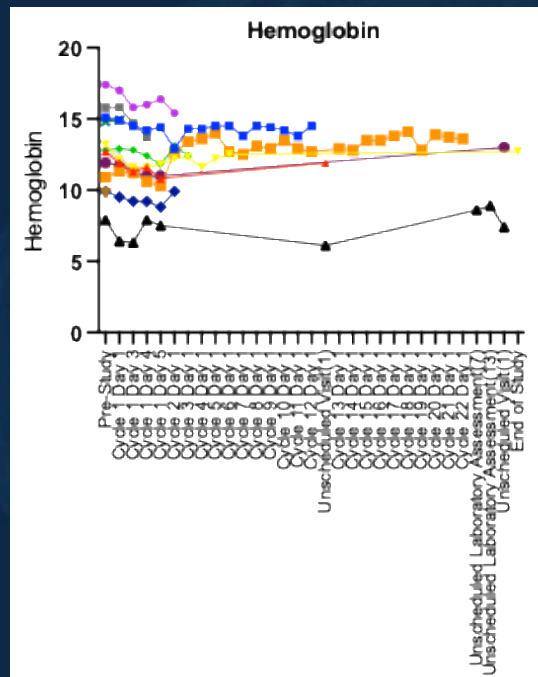
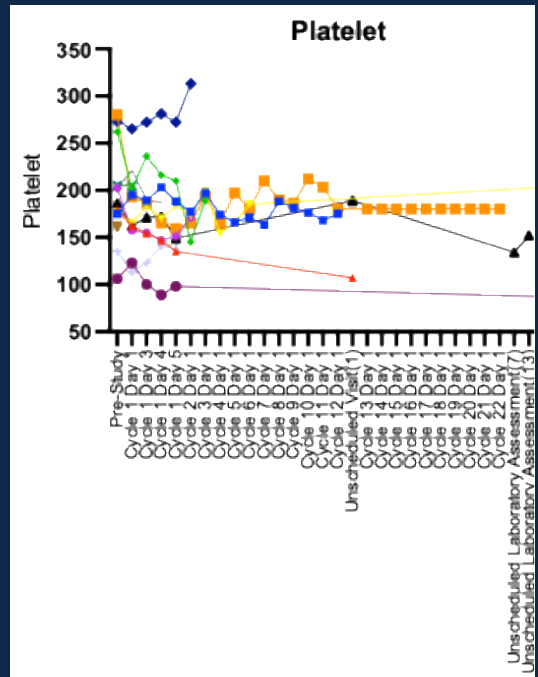


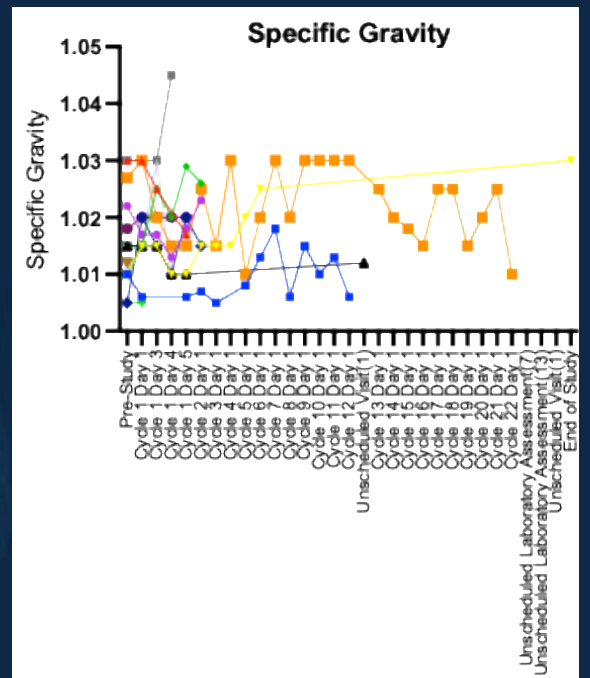
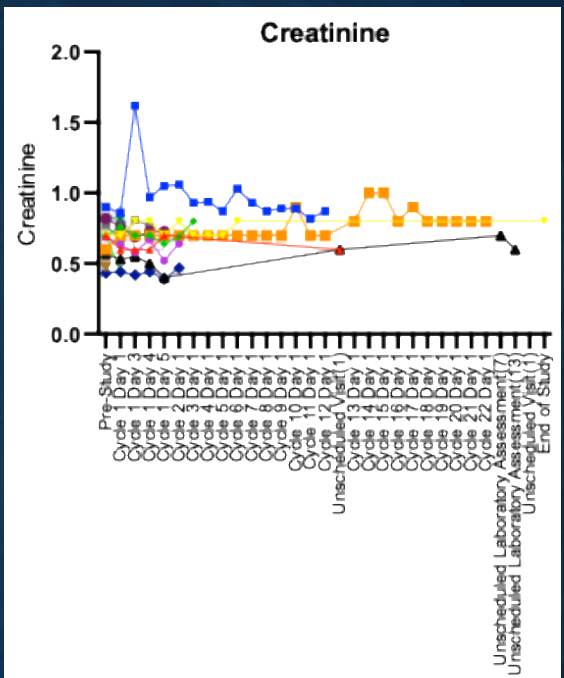
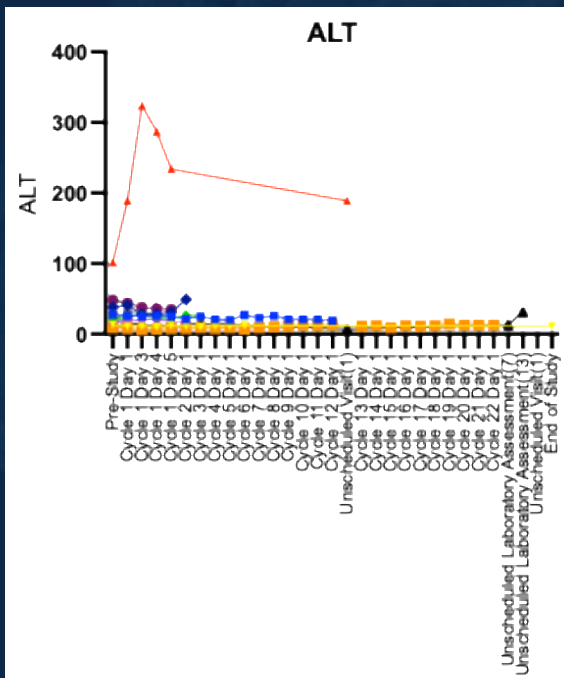
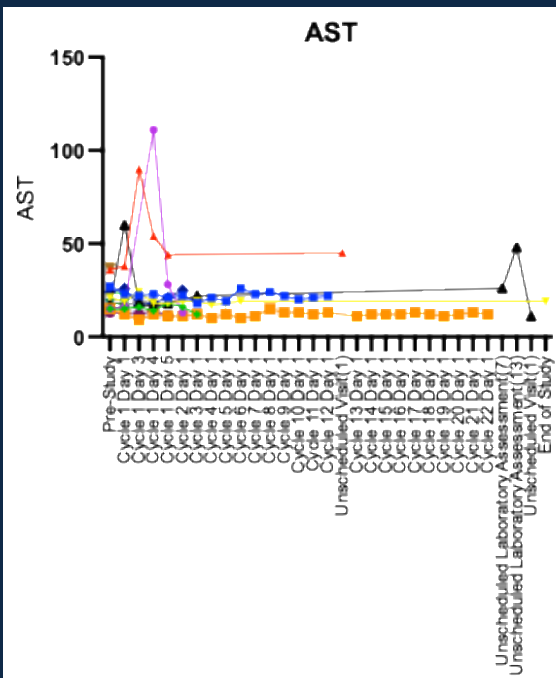
Fig. 4 Representative TMZ (F), MTIC (E), and AIC (□) concentration-time profiles from a patient who received 200 mg of TMZ. Solid and dashed lines, best-fit curves from the model-estimated parameters.

# NEO212 PK: No Clinically Meaningful Myelosuppression Detected



| Cohort 1 |        | Cohort 2 |        |
|----------|--------|----------|--------|
| 01-101   | 01-201 | 01-201   | 01-203 |
| 02-101   | 01-203 | 02-102   | 02-201 |
| 02-102   | 02-201 | Cohort 3 |        |
| Cohort 3 |        | Cohort 4 |        |
| 01-301   | 01-401 | 01-302   | 04-401 |
| 01-302   | 04-401 | 01-303   | 04-403 |
| 01-303   | 04-403 | Cohort 5 |        |
| Cohort 5 |        | 02-502   | 05-502 |
| 02-502   | 05-502 |          |        |

# NEO212 PK: No Clinically Meaningful Hepatic or Renal/Urinary Toxicity Observed



| Cohort 1 |        | Cohort 2 |        |
|----------|--------|----------|--------|
| 01-101   | 01-201 | 02-101   | 01-203 |
| 02-102   | 02-201 |          |        |
| Cohort 3 |        | Cohort 4 |        |
| 01-301   | 01-401 | 01-302   | 04-401 |
| 01-303   | 04-403 |          |        |
| Cohort 5 |        |          |        |
| 02-502   |        | 05-502   |        |

# MTD Cohort 5 (810 mg QD) – Key Learnings

Observed SAEs were consistent with complications commonly seen in advanced recurrent GBM and during temozolomide- Phase 1 dose escalation studies.

| Brain-adjusted exposure NEO212 vs TMZ 200 mg/m <sup>2</sup> (Cycle 2+) |                               |  |                            |                                   |  |      |
|--|-------------------------------|--|----------------------------|-----------------------------------|--|------|
| NEO212 (mg/day)  | NEO212 total over 5 days (mg) | NEO212 total 5-day dose (TMZ-equivalent, mg; conversion ratio = 0.521) | TMZ total over 5 days (mg) | Relative Exposure compared to TMZ | Brain-adjusted relative (3x BBB-permeable) |      |
| Cohort 1   | 170                           | 850  | 443                        | 1800                              | 0.25                                       | 0.73 |
| Cohort 2   | 220                           | 1,100  | 573                        | 1800                              | 0.32                                       | 0.93 |
| Cohort 3   | 400                           | 2,000  | 1,042                      | 1800                              | 0.58                                       | 1.69 |
| Cohort 4   | 610                           | 3,050  | 1,589                      | 1800                              | 0.88                                       | 2.56 |
| Cohort 5   | 810                           | 4,050  | 2,110                      | 1800                              | 1.17                                       | 3.40 |

Importantly, across Phase 1:

- **No signal of clinically meaningful myelosuppression**
- **No hepatic or renal toxicity signal**

This differentiates systemic safety profile from traditional TMZ-associated hematologic suppression.



# **NEO212 measurable anti-tumor activity in Phase 1**

# Partial Response Observed in Recurrent IDH1 Wild-Type, MGMT-Methylated GBM – Patient Remains Stable 21 Months Post-Recurrence

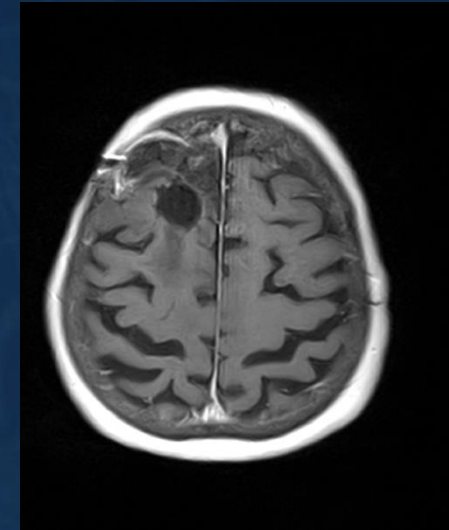
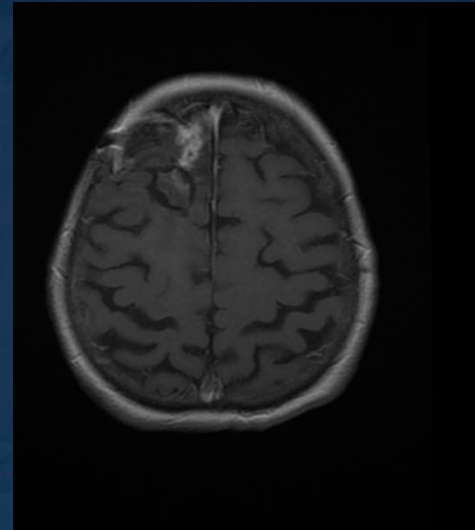
Primary Diagnosis: 8/25/2023  
Prior Tx: XRT+TMZ (10/23-4/24)  
Progressed on TMZ After 6 Cycles

NEO212 C1D1: 6/10/2024  
Currently on Cycle 22 of NEO212

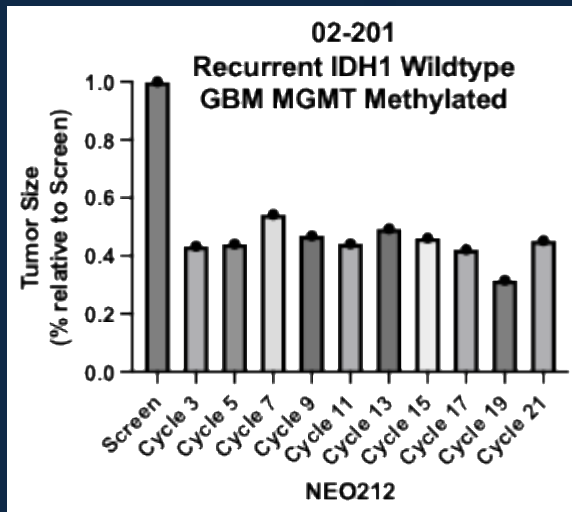
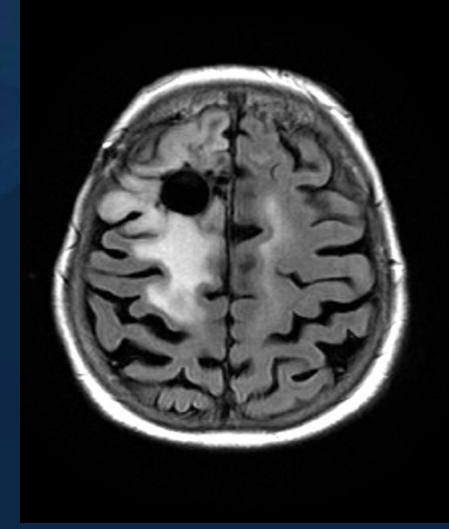
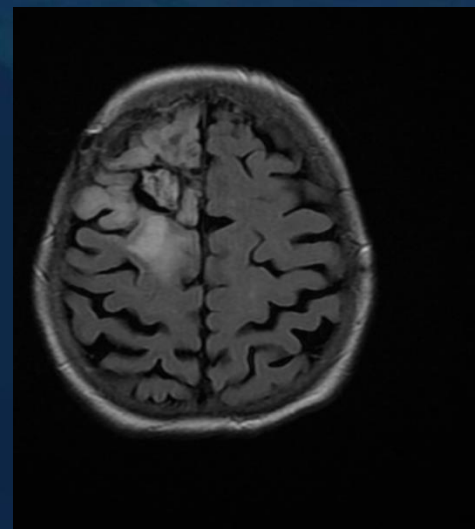
Screen

Cycle 21

Contrast



FLAIR



# Lung-to-Brain Metastasis | 55 Months Since Diagnosis | Last 16 Months on NEO212

*Brain Met Diagnosis: Squamous NSCLC (7/20/2021)*

*Prior Tx: Taxol/Carboplatin (7/2018); Keytruda, Alimta (5/2020)*

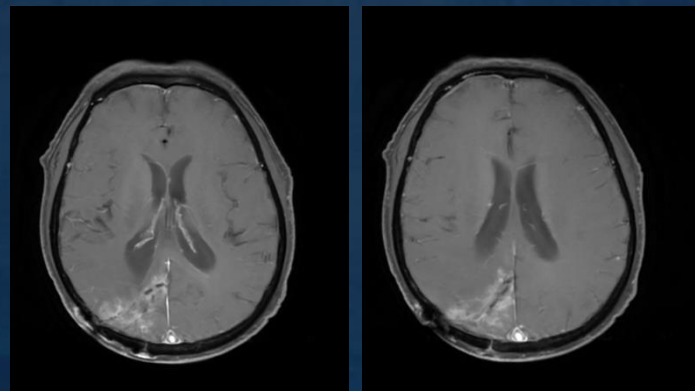
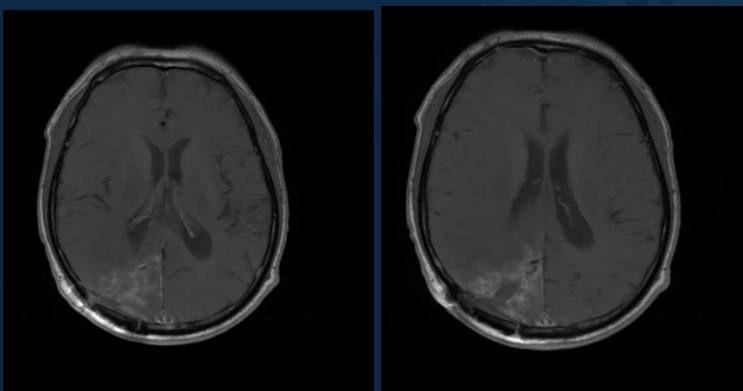
*NEO212 C1D1: 3/25/2024*

*Currently on Cycle 16*

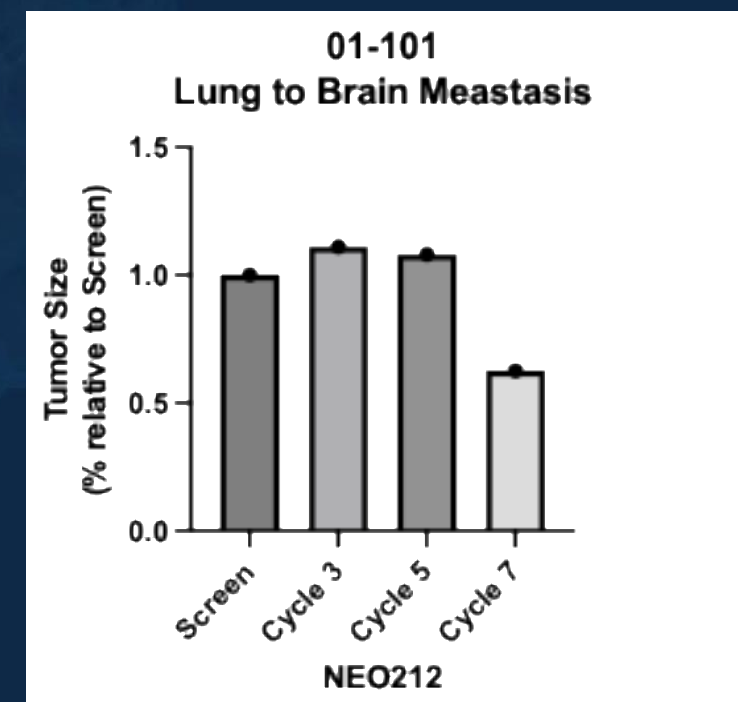
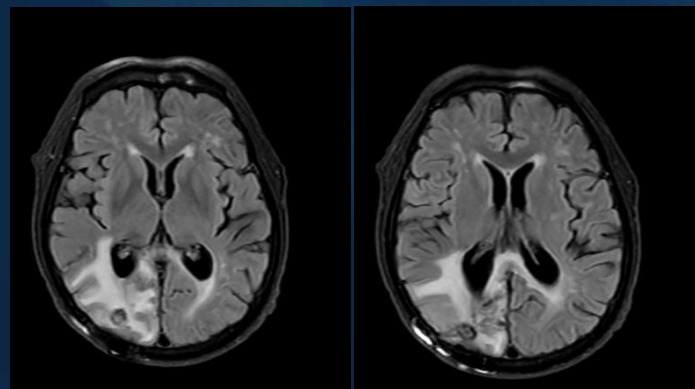
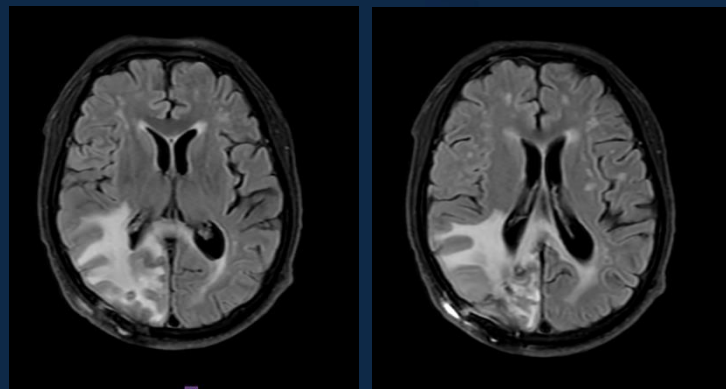
Screen

Cycle 7

Contrast



FLAIR



# NEO212 — Next Potential Steps & Accelerated Regulatory Approval

**Phase I Readout:** Initial safety, PK, and preliminary efficacy data

**Accelerated Approval Strategy:** Advancement into Two Phase II Clinical Trials

- Trial 1: Randomized evaluation of single-agent NEO212 in recurrent GBM versus standard-of-care therapy
- Trial 2: Randomized evaluation of NEO212 in combination with standard-of-care therapy versus standard-of-care therapy alone in patients with brain metastases

**Unmet Need (Brain Mets):** >30% of adult cancer patients develop brain metastases with **no durable systemic standard of care**

**TAM — Primary GBM:** ~\$3.0-4.0B estimated market opportunity

**TAM — Brain Metastases:** Approximately **10x** the size of the primary GBM market

# NEO212: Phase 1 Clinical Data Informing an Accelerated Phase 2 Development Strategy in TMZ-Resistant Glioblastoma and Brain Metastases



## 1. Safety Foundation Established

- Phase 1 demonstrated favorable systemic tolerability

**Why It Matters: Temozolomide's dose ceiling is bone marrow suppression. NEO212 may enable sustained alkylator therapy without the traditional hematologic limitation.**

## 2. Early Signals of Clinical Activity in Recurrent GBM

- Durable disease control observed in heavily pretreated patients
- Biological rationale supported by activity in TMZ-resistant, MGMT-high preclinical models
- Designed to enhance brain delivery while preserving cytotoxic potency

**Why It Matters: ~70–80% of GBM patients progress within 12 months of TMZ. NEO212 is positioned to retain activity where TMZ fails.**

## 3. Phase 2 Targets the Highest-Value Unmet Segment

- Focus on **MGMT-unmethylated** and **TMZ-refractory** patients
- Includes patients who discontinued TMZ due to hematologic toxicity
- Randomized vs SOC for clean efficacy signal
- ORR primary endpoint built for Accelerated Approval

**Why It Matters: Phase 2 directly tests NEO212 in the population most underserved by current standard therapy — resistance-driven and toxicity-limited patients.**

# NeOnc has the potential to become a leader in the refractory neuro-oncology market.

**First-Mover Advantage:** Pioneering non-invasive intranasal drug delivery for central nervous system (CNS) diseases

**Robust IP Protection:** Backed by a global portfolio of 179 patents

**Near-Term Milestones:** Several upcoming data readouts expected in 2026

**Global Expansion:** Active expansion into the Middle East market

**Superior Therapeutic Focus:** Demonstrated advantages in CNS drug delivery and tumor targeting

**Proven Leadership:** Seasoned management team and supported by leading medical and scientific KOLs

# Upcoming Milestones

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**2H 2026: NEO-100-03 in Pediatric pHGG –  
commence enrollment**

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**2H 2026: NEO100-01 – Phase II clinical data in IDH1-  
Mutant Glioma**

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**2027: NEO100-02 in Meningioma – Phase II clinical  
study results**

# Contact Us

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[www.neonc.com](http://www.neonc.com)

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[James@haydenir.com](mailto:James@haydenir.com)

646-755-7412



**NEONC**  
TECHNOLOGIES HOLDINGS, INC.

THE FUTURE OF DRUG DELIVERY



# Appendix

# Executive Summary



**Founded in 2023, NTHI is a clinical stage life sciences company.**

Focused on development & commercialization of central nervous system (CNS) therapeutics.



**Our platform is designed to enable the creation of breakthrough drug candidates and cutting-edge delivery technologies.**

Designed to address the persistent challenge in overcoming the blood-brain barrier (BBB).



**Robust IP Portfolio**

Holds 179 biotech-related patents developed at University of Southern California (USC).



**NTHI first mover advantage**

Innovative intranasal CNS drug delivery, reinforcing its focus on non-invasive therapies for brain tumors



**63 scientific published studies**

Highlight the potential of perillyl alcohol (POH) and its conjugates as efficient chemotherapeutic delivery platforms against brain tumors



**Advancing Pipeline**

Two drug candidates in FDA Phase II trials (NEO100-01, NEO100-02) and two in Phase I (NEO100-03, NEO212).



**Multi-billion-dollar, high-growth addressable markets.**

Great unmet need supports commercial launch.



**Experienced Leadership**

Proven track record in capital markets, medical, scientific, and biotech value creation.






# Board of Directors



**Amir F. Heshmatpour**  
CEO, Executive Chairman  
& President



**Thomas Chen, MD, PhD**  
Founder, CMO & CSO

| <br><b>Victoria Medvec, PhD</b><br><i>Compensation Committee Chair</i>   | <br><b>Bader Al Monawer</b><br><i>Audit Committee Chair</i>  | <br><b>Steven L Giannotta, MD</b>  | <br><b>Jim Delshad</b><br><i>Corporate Governance Chair</i>   | <br><b>Alan Chiang, MD, PhD, MBA, FICS</b>   |
|---|--|---|--|---|
| <p><b>20+ years as CEO of Medvec &amp; Associates, advisory firm servicing more than a third of Fortune 100.</b></p> <p>Advising on regulatory negotiations, partnerships and global market access. Clients have included <b>Amgen, Sanofi, Astra Zeneca, Bristol Myers Squibb, Pfizer and Gilead.</b></p> <p>Founding member of Extraordinary Women on Boards. Frequent speaker and author of best-selling book, <i>"Negotiate Without Fear."</i></p> <p>Accomplished public &amp; private board director, specializing in mergers and acquisitions, customer growth, revenue maximization, supply chain, human capital, and risk management. Applying expertise in negotiations and decision-making to drive revenue expansion.</p> | <p><b>More than a decade of experience in venture capital, investment banking, and business consulting and development.</b></p> <p>Currently serves as managing partner of Arabian Group, overseeing venture capital investments. Previously founded the VC fund, Oasis Capital, investing in numerous startups, many of which have grown into multibillion-dollar corporations.</p> <p>Extensive background in investment banking and consulting at <b>McKinsey &amp; Company, Citigroup's M&amp;A advisory, Wafra's</b> Alternative Investments Division, and the <b>World Bank.</b></p> <p>MBA, Massachusetts Institute of Technology (MIT); Master's degree in economics and financial policy, Cornell University.</p> | <p><b>Chair Emeritus of Neurological Surgery at USC.</b></p> <p>Research primarily centers around cerebral blood flow and protecting the brain from ischemia.</p> <p>Specializes in surgical strategies for cranial base lesions, including acoustic neuromas. Has surgically removed 400+ acoustic neuromas.</p> <p>Treated 1,000+ intracranial aneurysms and developed a comprehensive approach to cerebrovascular conditions, employing techniques such as microsurgical clip ligation, coil embolization, and stereotactic radiosurgery.</p> <p>Medical degree and residency at the University of Michigan.</p> | <p><b>Served two terms as Mayor of Beverly Hills, starting in 2007,</b> pioneering "Smart City" initiatives that transformed the city into a model of technological advancement and security. He holds the honorary title of "Goodwill Ambassador of Beverly Hills" in recognition of his contributions to the city.</p> <p>Served as former President and Chairman of Magbit Foundation</p> <p>Over the past two decades he has provided management consulting services, which includes strategic advisory services across private, public, and non-profit sectors.</p> | <p><b>Board-certified neurosurgeon.</b></p> <p>Focused on development of novel pharmacological and interventional treatments for cancer &amp; CNS disorders and biomechanical studies on spine surgery.</p> <p>Founder &amp; Chairman of NeuCen Biomedical and Orion Biotech.</p> <p>Associate Professor of Neurosurgery at Taiwan Adventist Hospital and Chung Shan Hospital.</p> <p>Expertise in brain tumor operation and minimally invasive spine surgery, and peer reviewer for several medical journals. Published 60+ articles in international peer-reviewed journals.</p> <p>International fellow of American Assoc. of Neurological Surgeons; member of N. American Spine Society; and International College of Surgery Fellow.</p> |

# Senior Management Team

Our management team possesses significant experience in capital markets, with a track record of building shareholder value in clinical biotech companies.



**Amir F. Heshmatpour**  
CEO,  
Executive Chairman & President

Mr. Heshmatpour served on NeOnc Technologies Holdings, Inc.'s board of directors since January 2023, President since April 2025 and CEO since November 2025. Mr. Heshmatpour founded AFH Holding and Advisory LLC ("AFH") in July 2005. Since July 2005, Mr. Heshmatpour has been the Managing Director of AFH. Mr. Heshmatpour, through AFH, his family office, has been involved in multiple biotech transactions from private to public. From 2018 to 2022, through a special purpose vehicle, Shuttle Pharmaceuticals Holdings Inc. ("SPH"), Mr. Heshmatpour restructured the board of directors, management, and recapitalized an IPO of a Georgetown phase II oncology asset. The SPV was created in 2018 and eventually was successfully listed on NASDAQ in 2022. Since then, he has been involved in NeOnc Technologies Inc., where he has provided strategic advisory services. Mr. Heshmatpour has a certification from the UCLA Anderson School of Business in corporate governance. He is also involved in the UCLA Anderson School of Business Management, Price Center, as a member of the Board of Advisors. In February 2024, Mr. Heshmatpour joined the Board of Directors of Make-A-Wish CVS in Los Angeles. We believe that Mr. Heshmatpour's extensive corporate and leadership experience qualifies him to serve on our Board of Directors.

**Thomas Chen, MD, Ph.D.**  
Founder, CMO & CSO

Dr. Chen has served as NeOnc Technologies Holdings, Inc.'s Chief Executive Officer since April 2023 through October 2025 and Chairman of the Board since its inception. Dr. Chen also serves as its Chief Medical Officer and Chief Scientific Officer. Since July 1997, Dr. Chen has worked as a Neurosurgeon at Keck Medicine of USC and a Professor Neurological Surgery at the University of Southern California Keck School of Medicine ("USC"). He has been the Director of Surgical Neuro-Oncology and Professor of Neurosurgery & Pathology. Dr. Chen's work is widely published, including 148+ peer-reviewed clinical studies. He maintains a clinical practice in both surgical neuro-oncology and spine surgery, as well as heads a research laboratory focused on glioma biology. He graduated summa cum laude from the University of Illinois at Urbana-Champaign with Bronze Tablet honors and Phi Beta Kappa. He graduated from University of California San Francisco with M.D. degree, and was in the top 10% of his class, awarded Alpha Omega Alpha. He earned his Ph.D. in pathology from University of Southern California where he wrote his thesis on the role of immunotherapy in malignant brain tumors. We believe that Dr. Chen's extensive knowledge of NeOnc's business and his extensive corporate and leadership experience as the founder of NeOnc and its Chief Executive Officer qualifies him to serve on our Board of Directors.

**Josh Neman, PhD**  
Chief Clinical Officer

Dr. Neman has served as Chief Clinical Officer of NeOnc Technologies Holdings, Inc. since June 2024, where he leads clinical strategy and translational development across the Company's neuro-oncology pipeline. Dr. Neman is an established cancer scientist and academic leader in brain tumor and brain metastasis research. Since July 2014, he has served as an Associate Professor of Neurological Surgery, Neuroscience, and Physiology at the Keck School of Medicine of the University of Southern California. His research program focuses on the biology of malignant brain tumors, brain metastases, tumor-microenvironment interactions, and mechanisms of therapeutic resistance, with an emphasis on translating laboratory discoveries into clinically actionable strategies. In addition to his faculty appointment, Dr. Neman has held multiple leadership roles at USC, including Program Chair of the Cancer Biology and Genomics Ph.D. Program since July 2019 and Scientific Director of the USC Brain Tumor Center since July 2021, where he has overseen interdisciplinary research initiatives spanning basic, translational, and clinical neuro-oncology. In January 2021, Dr. Neman co-founded Synaptical Inc., a digital health company focused on providing cancer patients with education, guidance, and care-navigation resources, and currently serves as its Chief Executive Officer. He also founded CNSMENDER Consulting LLC in January 2022, where he advises on clinical development and translational strategy in oncology and CNS disorders. Dr. Neman earned his Bachelor of Science and Doctor of Philosophy (Ph.D.) in Neurobiology from the University of California, Los Angeles.

**Keithly A. Garnett**  
Chief Financial Officer

Mr. Garnett has served as NeOnc Technologies Holdings, Inc.'s Chief Financial Officer since April 2023 and served as a director from January 2023 to March 2025. Mr. Garnett spent over 17 years with Ernst & Young LLP in their Transaction Advisory Services practice. During that time, he specialized in business valuation modelling and strategy. His services were provided in support of audit related work for financial reporting, tax planning and management planning. His client list included companies such as Amgen, Edwards Life Sciences, Medtronic, etc. In any given year, he led over 50 transaction analyses and/or review for publicly traded companies, in connection with their SEC financial reporting requirements. From March 2017 to January 2023, Mr. Garnett was a Director at Sycamore Valuation. Since January 2021, Mr. Garnett has worked as the Chief Financial Officer of AFH Holding & Advisory, a single member family office based in Malibu. From 2018 to 2022, he was involved with the Shuttle Pharmaceutical Holdings public offering, which was successfully listed on the Nasdaq in 2022. Mr. Garnett holds a Master's in Business Administration with a concentration in Corporate Financial Management, and a Bachelor of Science degree in Business Management. He also completed the Columbia University Executive Education program with a certificate from the Chief Financial Officer program.

**David Choi, CPA**  
Chief Accounting Officer

David Choi was appointed Chief Accounting Officer of NeOnc Technologies Holdings Inc. in 2026. In this role, he oversees the Company's accounting, financial reporting, internal controls, and corporate governance as NeOnc advances its clinical-stage biotechnology platform and expands globally. He focuses on strengthening financial reporting processes, building scalable accounting infrastructure, and supporting the Company's growth as a public company. Mr. Choi brings more than a decade of experience in accounting, financial reporting, and internal controls. Prior to joining NeOnc, he was a Director at Blythe Global Advisors, advising companies on technical accounting matters, SEC reporting, and SOX compliance, and leading projects involving financial reporting transformation and accounting for complex transactions. Earlier in his career, he held roles at Grant Thornton and Ernst & Young, providing audit and technical accounting advisory services. Mr. Choi is a Certified Public Accountant (CPA) and holds a Master of Professional Accountancy and a Bachelor of Arts in Business Economics with a minor in Accounting from the University of California, Irvine.

# Scientific Advisory Board

Our Scientific Advisory Board provides objective perspective and guidance in product development, clinical trials, regulatory compliance, and biotech commercialization strategies.



| <b>Henry S. Friedman, MD</b><br><i>Chair, SAB</i>  | <b>Axel H. Schönthal, PhD</b>  | <b>Alan Chiang, MD, PhD, MBA, FICS</b>  | <b>Steven L. Giannotta, MD</b>  | <b>Alexandra M. Miller, MD, PhD</b>  | <b>David M. Ashley, MBBS (Hons), FRACP, PhD</b>   |
|--|--|---|---|--|---|
| <p><b>Senior neuro-oncologist at Duke and deputy director of The Preston Robert Tisch Brain Tumor Center.</b></p> <p>Holds the James B. Powell, Jr. Distinguished Professorship in the Duke School of Medicine. Cares for adult and pediatric patients at the Duke Cancer Center's Brain Tumor Clinic.</p> <p>Internationally recognized authority in neuro-oncology with 500+ peer-reviewed works and decades of national and international presentations. Research focuses on clinical trials and translational work in high-grade glioma, medulloblastoma, and ependymoma. Helped shape treatment standards for challenging CNS tumors through sustained leadership and collaborative, multi-center research.</p> | <p><b>Associate Professor, Department of Molecular Microbiology &amp; Immunology at Keck School of Medicine at University of Southern California.</b></p> <p>Research focused on novel agents and delivery methods for improving cancer therapeutic regimens, particularly for brain cancers.</p> <p>Authored or coauthored 180 scholarly articles with an H-Index of 50.</p> <p>Over past 10 years, engaged in grant reviews for <b>The Qatar National Research Fund</b>. Includes applications for Undergraduate Research Experience Program that engages students in research projects under the guidance of academic and business mentors.</p> <p>PhD, University of Karlsruhe, Germany. Postdoc in molecular &amp; cellular cancer biology at USC, San Diego.</p> | <p><b>Board-certified neurosurgeon.</b></p> <p>Focused on development of novel pharmacological and interventional treatments for cancer &amp; CNS disorders and biomechanical studies on spine surgery.</p> <p>Founder &amp; Chairman of NeuCen Biomedical and Orion Biotech.</p> <p>Associate Professor of Neurosurgery at Taiwan Adventist Hospital and Chung Shan Hospital.</p> <p>Expertise in brain tumor operation and minimally invasive spine surgery, and peer reviewer for several medical journals. Published 60+ articles in international peer-reviewed journals.</p> <p>International fellow of American Assoc. of Neurological Surgeons; member of N. American Spine Society; and International College of Surgery Fellow.</p> | <p><b>Chair Emeritus of Neurological Surgery at USC.</b></p> <p>Research primarily centers around cerebral blood flow and protecting the brain from ischemia.</p> <p>Specializes in surgical strategies for cranial base lesions, including acoustic neuromas. Has surgically removed 400+ acoustic neuromas.</p> <p>Treated 1,000+ intracranial aneurysms and developed a comprehensive approach to cerebrovascular conditions, employing techniques such as microsurgical clip ligation, coil embolization, and stereotactic radiosurgery.</p> <p>Medical degree and residency at the University of Michigan.</p> | <p><b>Chief of the Division of Neuro-Oncology at NYU Langone's Perlmutter Cancer Center and Co-Director of the Brain &amp; Spine Tumor Center.</b></p> <p>Leads the Neuro-Oncology Program, with a clinical and research focus on primary brain tumors, particularly malignant gliomas.</p> <p>Oversees multidisciplinary care and strategic planning at a major NCI-designated cancer center. Holds clinical faculty appointments in Medicine and Neurology at NYU Grossman School of Medicine.</p> <p>Works at the intersection of neurology, oncology, and clinical trials.</p> <p>Recognized for leadership, invited talks, program development, and collaborative research in neuro-oncology.</p> | <p><b>Rory David Deutsch Distinguished Professor of Neuro-Oncology and Director of The Preston Robert Tisch Brain Tumor Center at Duke.</b></p> <p>Previously trained and led major neuro-oncology programs in Australia before joining Duke. Practices adult and pediatric neuro-oncology and oversees one of North America's largest dedicated brain tumor centers. Leads integrated efforts in clinical care, translational research, and education. Research focuses on CNS tumor biology, immuno-oncology, and clinical trials. Served as principal investigator on national and international studies shaping current practice. Internationally recognized for advancing patient-centered innovation in neuro-oncology.</p> |

## Middle East Expansion Plan

- Integrated GCC/MENA Platform – NuroMENA and NuroCure (controlled by NuroMENA) hold the exclusive sub-license for all 178 NTHI patents in the GCC and MENA. NTHI retains 20% non-dilutive equity and negative control rights over Corporate Board and management.
- Government Backing – Partnership with GCC government stakeholders, with access to sovereign wealth fund investments for capital depth and execution strength.
- 510M Population Access – Expanding CNS clinical trial enrollment across the GCC/MENA region to address urgent unmet medical needs and accelerate regulatory approvals.
- Global Expansion Platform – Partnerships with top oncology and neuro-oncology institutions create a scalable model for entry into other high-growth regions.
- Smart Capital & Sub-Licensing – Disciplined capital strategy and sublicensing generate recurring revenue and broaden NTHI's global reach while maximizing ROI.
- Long-Term Growth & Control – Government alignment, and NTHI innovation—combined with strategic governance rights—drive sustainable value for patients and shareholders.

# NeOnc's Game-Changing Acquisition from McMaster University & USC

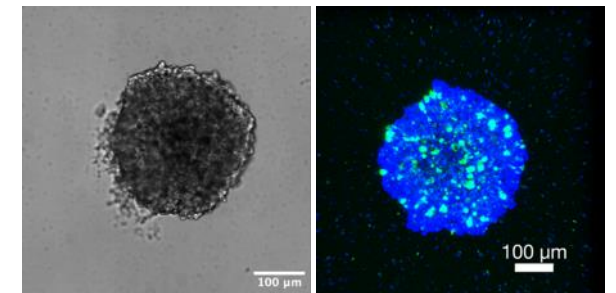


## Acquisition of SilicoVitro Technology

- **Strengthens NeOnc's leadership** in next-generation CNS cancer research with SilicoVitro's AI engine and patented 3D bioprinting platform (US Patent No. 11,788,057 B2)
- **Accelerates clinical programs**, expands R&D capabilities, and **enhances our IP portfolio** in high-growth therapeutic markets.

| AI Drug Modeling (USC)   | 3D Bioprinting (McMaster)  |
|--|--|
| <ul style="list-style-type: none"><li>➤ Simulates blood-brain barrier penetration and ROS generation</li><li>➤ Models tumor response to ultrasound</li><li>➤ Personalizes therapy for each patient</li><li>➤ Identifies optimal drug combinations for trials</li></ul> <p><b>Impact:</b> Enables in-silico testing to guide clinical decisions</p> | <ul style="list-style-type: none"><li>➤ Creates realistic human tumor organoids</li><li>➤ Models neurodegenerative diseases like Alzheimer's &amp; Parkinson's</li><li>➤ Produces organoids for liver, lung, and kidney</li><li>➤ Replaces animal models in preclinical testing</li></ul> <p><b>Impact:</b> Enhances accuracy and predictability of trial outcomes</p> |

Breast to Brain Metastasis  
3D-Printed Sphere



# Our Strategic Focus: Deliver Intranasal Chemotherapy to Bypass the Blood-Brain Barrier and Directly Target Brain Tumors

## •Direct Brain Access:

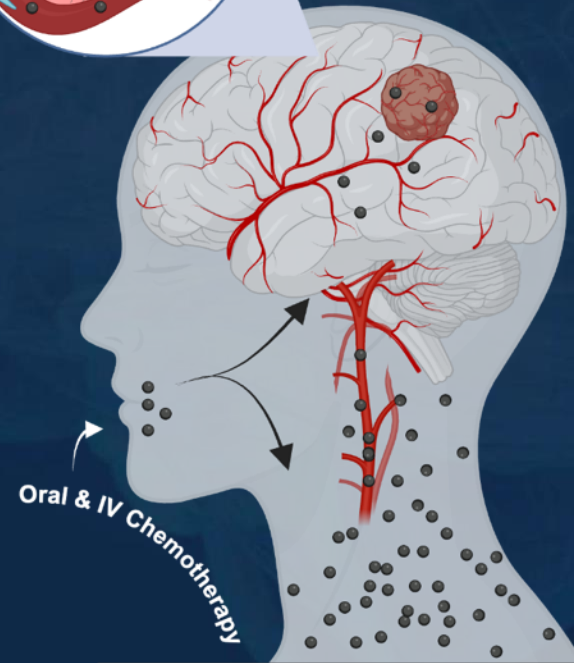
Intranasal delivery is designed to enable small-molecule therapeutics to bypass the BBB via the olfactory and trigeminal nerves, reaching the brain through the CSF.

## •Non-Invasive & Patient-Friendly:

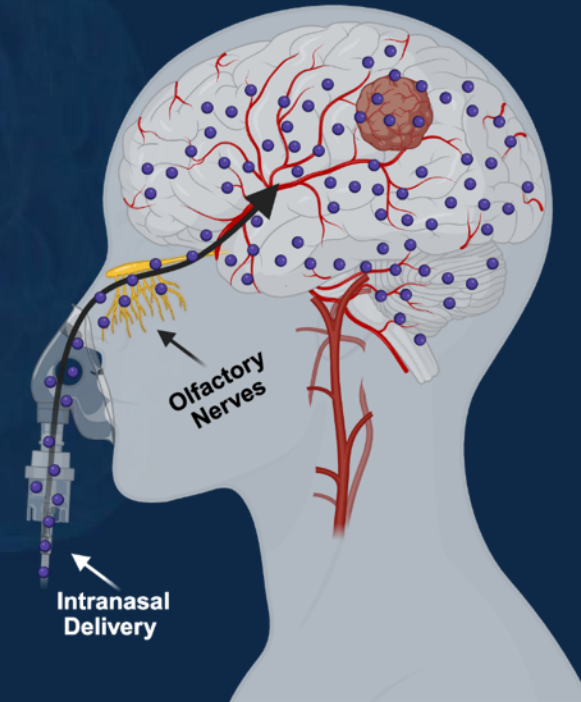
Administered with a nasal mask and nebulizer, this method is designed to be simple, non-invasive, and suitable for self-use—potentially reducing costs and improving adherence.

## •Enhanced Efficiency:

Intranasal delivery designed to avoid first-pass metabolism, allow rapid onset, and enable targeted drug delivery to brain tumors such as GBM.



Current treatments exhibit **poor** brain penetration due to the restrictive nature of the blood-brain barrier (BBB)



NeOnc therapeutics delivered intranasally bypass the BBB and reach the brain for **enhanced** penetration

# The Need

**1 Million**

American Adults are  
Living with a Primary  
Brain Tumor

**13,657** are Children

**29%**

of Brain Tumors are  
Malignant (Cancerous)

**#1**

Brain Tumors are the  
Leading Cause Of Cancer-  
Related Death Among  
Children

**94,390**

New Primary Brain Tumors  
Diagnosed This Year

**3,920** in Children

**18,990**

Patients Expected to Lose  
Their Life Due to Malignant  
Brain Tumors This Year

**1-in-143**

Your Odds of Developing Brain  
Cancer if You're Male

**1-in-188** if Female

## The Need

#1

Brain Tumors are the Leading Cause of Cancer-Related Death Among Children.

4,170

Primary Pediatric Brain Tumors Diagnosed Last Year

40%

**Pediatric High-Grade Gliomas (pHGGS)** are responsible for 40% of all child brain tumor deaths and is the most common solid brain tumor.

## The Challenge

Radiation & chemotherapy for children with high-grade gliomas are:

Complex

Time consuming

Prognosis remains poor

These challenges underscore the importance of developing effective therapies that are:

Less invasive

More tolerant for such populations

## Our Solution

- **NEO100**: our first therapeutic being developed for pediatric patients diagnosed with **pHGGS**.
- We believe our novel **intranasal delivery** makes a study in a pediatric population **easier** than other methods.
- In consultation with the FDA under **Orphan Drug & Fast-Track** status, we expect to collect data from clinical trials that demonstrates the **important therapeutic value of NEO100 for pHGGS**.

# The Challenge



While the FDA has approved many drugs for treating Malignant Glioblastomas (GBM), **survival rates remain low with no significant improvement in prognosis over past 50 years.**

## Lack of Progress Primarily Due to Natural Resistance Mechanisms that Limit Efficacy of GBM Treatments



**Therapeutics cannot enter** Central Nervous System (CNS) due to blood-brain barrier (BBB).



**Heterogeneity** of GBMs contributes to therapeutic resistance by preventing adequate control of the entire tumor mass by a single drug.



**Natural brain responses (i.e. tumor microenvironment)** counteract tumor-targeting medications.



**Stem cell-like characteristics** of GBMs have resistance to current standard treatment options:

| Treatment            | Resistance Mechanism  |
|----------------------|---|
| <b>Chemotherapy</b>  | Upregulation of Efflux Transporters                                   |
| <b>Radiation</b>     | Promotion of Glioblastoma Stem Cell Proliferation In Neurogenic Zones |
| <b>Immunotherapy</b> | Immune Suppression  |



**Metabolic cascades** in GBMs prevent effective treatments through:

- Optimization of glucose use.
- Alternative nutrient precursors for energy production.
- Induction of hypoxia to enhance tumor growth.

# NEO100 Offers Broad Potential for Clinical Benefit and Commercial Application



**Designed to act as a regulator**  
for neurologic pathways associated with tumor cell growth.



**When delivered intranasally,** its small molecular size is designed to allow it to bypass the Blood Brain Barrier (BBB).



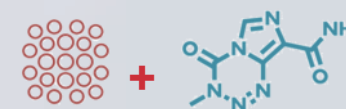
**When delivered intra-arterially,** it may create a temporary opening in the BBB, allowing larger molecule therapeutics to pass through.



**In high concentrations** may act as a therapeutic for brain cancers.



**In low concentrations** to act as solvent for traditional large molecule therapeutics, which may enable them to bypass the BBB.



**Conjugate with other CNS therapeutics** to create compound formulations that may be capable of BBB penetration & greater therapeutic effect.

# NEO100: Impact & Significance



- **First-of-its-kind signal for durable response:** MRI-confirmed significant response in setting rarely seen
- **Potential paradigm shift with multi-year survival:** CNS-penetrant metabolic therapy
- **Differentiation:** Minimal toxicity vs. standard salvage therapies
- **Translational momentum:** Supports Phase 2b/3 and global trials (e.g., Cleveland Clinic, UAE, M42/IROS)

# Clinical Trial Sites



## Sites in pre-activation phase

- Tufts Medicine
- Penn State
- Washington University
- Johns Hopkins
- Harvard/ Mass General Hospital
- New York University
- Tampa General
- University of South Carolina
- Washington University
- Northwestern University
- Beverly Hills Cancer Center
- Pacific Neuroscience Institute
- Sutter Health
- City of Hope
- University of Vermont
- Westchester Medical Center
- Michigan University
- PNOG

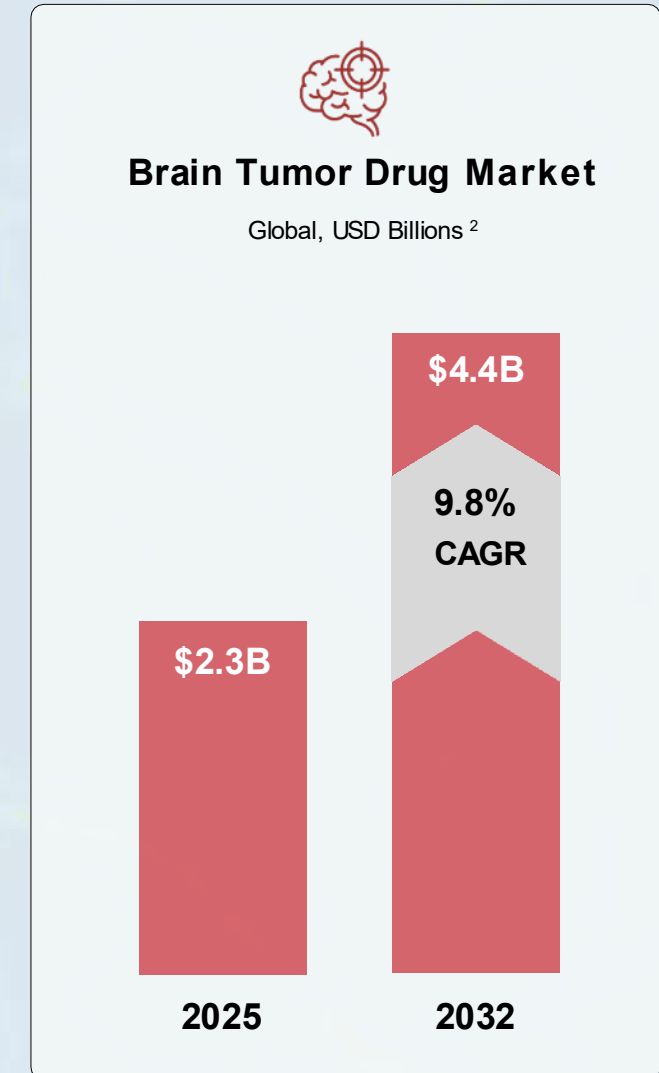
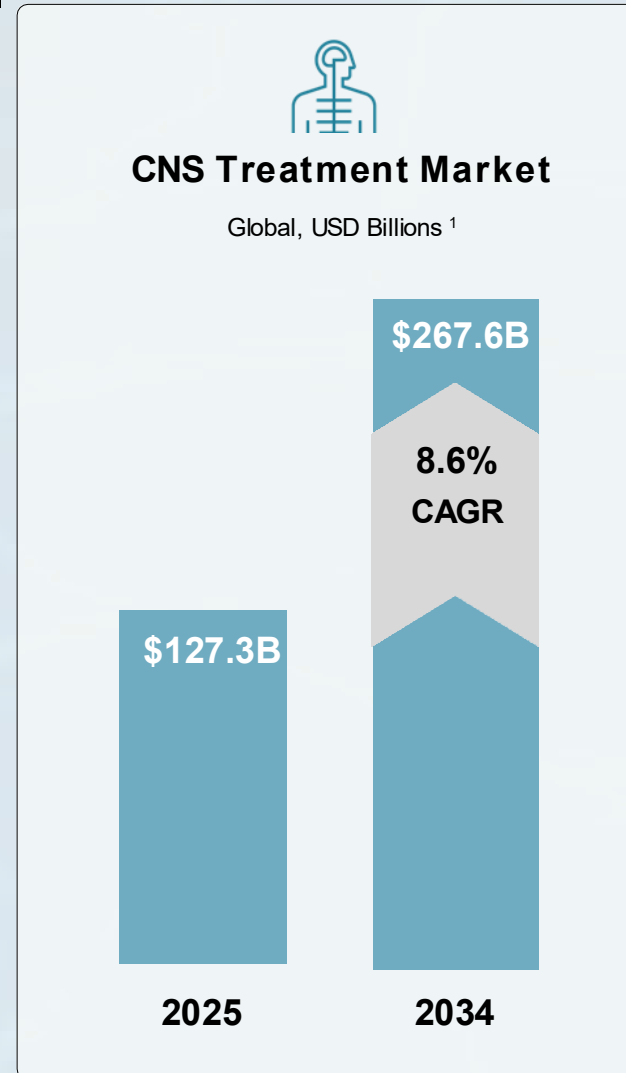
# We are focused on delivery of therapeutic innovations aligned with rapidly expanding global market opportunities.

## Global Market Outlook & Drivers

- **Global CNS treatment market** is projected to grow at a **8.6% CAGR**, reaching **\$267.6 billion by 2034**<sup>1</sup>
- **Global brain tumor drug market** is expected to grow at a **9.8% CAGR**, reaching **\$4.4 billion by 2032**<sup>2</sup>

## Major Market Drivers

- Rising incidence of CNS disorders driven by an **aging global population**
- **Increased FDA approvals** for novel and combination therapies
- **Radiation therapy** currently dominates (**38%** of brain cancer treatment market), while drug therapy remains secondary due to **poor drug delivery across the BBB**<sup>3</sup>



1) [Precedence Research](#), January 2025  
 2) [Fortune Business Insights](#) April 2025  
 3) [Grand View Research Report](#)

# Our Expanding IP Portfolio of Global Patents Creates Competitive Advantages



## U.S. Patents

32 Patents Issued

19 Patents Pending



## International Patents

97 Patents Issued

31 Patents Pending



## NEO™ is a First-of-its-kind Platform Protected By Patents in the U.S., Canada, China, UK & EU

- **Patents cover agent composition & methods of use**, including enhanced methods designed to deliver pharma-based therapeutics to the brain.
- **Patents secured under exclusive global licensing agreement with USC.** USC/NeOnc license is considered USC's largest IP license for commercialization of chemotherapies related to brain & CNS diseases.<sup>1</sup>
- **Biotechnology breakthroughs** based on research and development at USC led by NeOnc CEO, Dr. Chen.
- **Platform technology has produced an IP portfolio of novel drug candidates**, including conjugates and formulations of FDA-approved drugs, with patents extending to 2031-2038.

## Composition & Method Claims

Issued & Pending Patent Applications

**NEO100 Ultrapure POH** – Issued patents expiring in 2031: U.S., Canada, UK, EU and China.

**POH Conjugates such as Temozolomide NEO212 or Rolipram NEO214** – Issued patents expiring in 2031: U.S., UK, EU and Japan.

**NEO400 POH conjugated to linoleic acid** – Anticipated expiration of pending applications in 2031 U.S., EU and China.

**NEO412 POH conjugates with fatty acid and a compound such as Temozolomide / Rolipram** – Issued patents expiring in 2036: U.S., UK, EU, China, Japan and Australia.

**NEO218 POH conjugated to bromopyruvate** – Issued U.S. patent expiring in 2037; Anticipate same expiration for pending applications in China, EU and Japan.

**NEO216 POH conjugated to Valproic Acid** – Anticipate expiration of pending applications in 2038: U.S., EU, and China.