COVER STORY

NeOnc

A NOVEL APPROACH TO TREATING BRAIN CANCER

ONE OF THE ADVANTAGES OF OUR APPROACH IS THAT IT ALLOWS CHILDREN TO INHALE THE MEDICATION DIRECTLY. THIS REDUCES THE PHYSICAL AND EMOTIONAL BURDEN OF IV CHEMOTHERAPY WHILE ENHANCING TREATMENT EFFECTIVENESS

By Stacey Smith

Glioblastoma is recognized as the most aggressive form of brain cancer in adults, with an approximate survival duration of 15 to 18 months, even with the best available treatment. The critical hurdle hindering most medication from reaching the desired site of action is the blood-brain barrier (BBB). Highly selective, the BBB prevents harmful substances from entering delicate cranial tissues. Unfortunately, this protective aspect also hinders many therapeutic drugs from reaching the brain in sufficient concentrations to be effective against tumors.

NeOnc Technologies is shifting this paradigm by pioneering first-of-its-kind methods to enhance drug delivery across the BBB. Led by Thomas Chen MD, PhD, a board-certified neurosurgeon and the director of surgical neuro-oncology at the University of Southern California, the company has formulated novel delivery methodologies and therapeutic formulations for cancers of that affect the central nervous system (CNS).

Advancing Drug Delivery for Improved Cancer Treatment

NeOnc's drug delivery platform, NEO100, is a purified form of perillyl alcohol (POH) with proven efficacy in helping cancer treatment drugs bypass the BBB. Piggybacking on the first (olfactory) and fifth cranial nerves, its small

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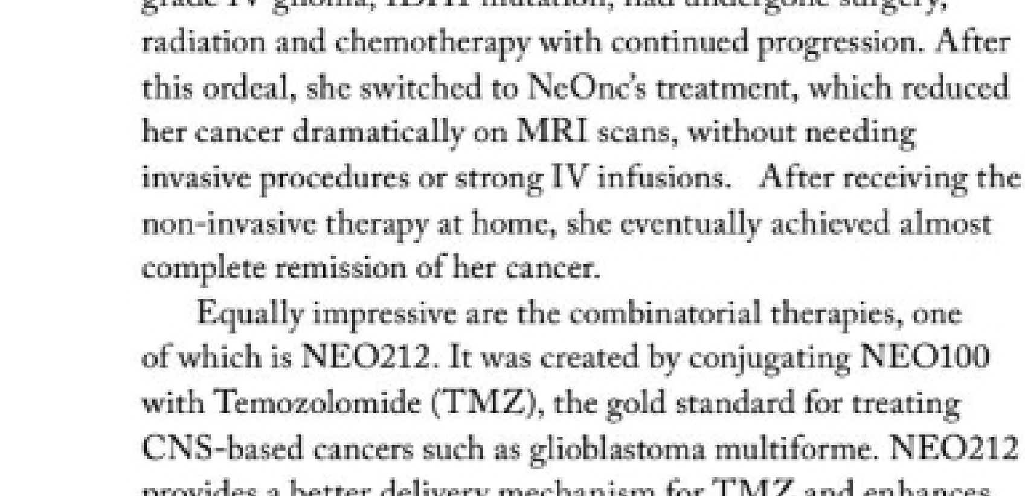
Keithly A. Garnett, Chief Financial Officer | Amir F Heshmatpour, Executive Chairman | Thomas Chen, Founder, CEO, CSO and Board Director | Patrick Walters, Chief Operations Officer

lipophilic molecular size easily permeates the BBB. It allows delivery of itself or a combinatorial therapeutic directly to a tumor site.

Currently in the phase 1/2A trial, NEO100 shows promise and has gained a new chemical entity designation, with the FDA granting it orphan drug status. The drug's impact on patients with recurrent glioma has been extraordinary, as it showcases a significant increase in median survival times, from that typical 15 to 18 months to up to four years. NEO100 demonstrated tumor shrinkage in MRI scans, suggesting effective drug delivery to the desired site of action. It showcased particularly favorable responses in patients with IDH1 and IDH2 mutations.

In the ongoing Phase IIa study, NeOnc's nasal therapies demonstrated remarkable effects. One cancer patient with a grade IV glioma, IDH1 mutation, had undergone surgery, radiation and chemotherapy with continued progression. After this ordeal, she switched to NeOnc's treatment, which reduced her cancer dramatically on MRI scans, without needing invasive procedures or strong IV infusions. After receiving the non-invasive therapy at home, she eventually achieved almost complete remission of her cancer.

Equally impressive are the combinatorial therapies, one of which is NEO212. It was created by conjugating NEO100 with Temozolomide (TMZ), the gold standard for treating CNS-based cancers such as glioblastoma multiforme. NEO212 provides a better delivery mechanism for TMZ and enhances its ability to cross the BBB by increasing its lipophilicity.



"TMZ often fails to reach the brain tumor due to its nature as a prodrug, which is easily broken down in the bloodstream." Says Dr. Chen, founder, CEO and CSO. "By combining TMZ with NEO100, we have created a stable, non-prodrug compound that efficiently crosses the BBB and delivers the required concentration of an active compound at the required site of action."

Designed to reach the tumor intact, NEO212 is broken down into active components within the tumor cell, enhancing its cytotoxic effects. NEO212 crosses the BBB five times more effectively and exhibits ten times the cancer cell-killing activity compared to TMZ alone.

BY COMBINING TMZ WITH NEO100, WE HAVE CREATED A STABLE, NON-PRODRUG COMPOUND THAT EFFICIENTLY CROSSES THE BBB AND DELIVERS THE REQUIRED CONCENTRATION OF AN ACTIVE COMPOUND AT THE REQUIRED SITE OF ACTION

The first two cohorts of NEO212's phase I trial have been completed, and the third cohort is now underway. Overall, the studies are progressing well, indicating good tolerability and promising activity.

A Better Way to Treat Pediatric Brain Tumors

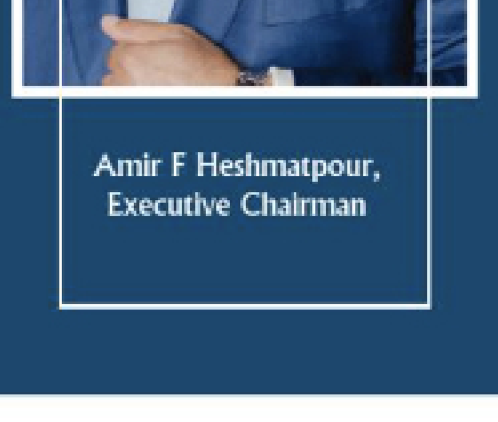
NeOnc's offerings are set to revolutionize the treatment landscape for pediatric brain tumors, particularly gliomas located in sensitive areas like the brainstem and thalamus. Existing treatments for children with these tumors typically involve invasive procedures such as biopsy surgery, followed by aggressive chemotherapy and radiation therapy. These methods often have harsh side effects and result in diminished quality of life for young patients.

NeOnc's innovation flips this script by targeting the trigeminal nerve, which originates from the brainstem—a common location for pediatric gliomas. Using this pathway and intranasal delivery, the company aims to precisely and effectively deliver its therapeutic agents to the tumor site. The potential benefits of NeOnc's intranasal delivery method include enhanced efficacy compared to traditional treatments and significantly improved quality of life for children undergoing therapy.

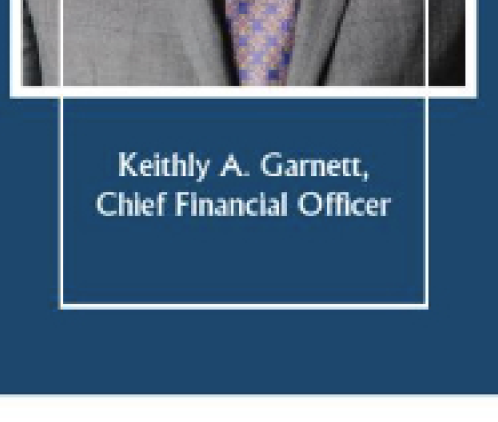
"One of the advantages of our approach is that it allows children to inhale the medication. This reduces the physical and emotional burden of IV chemotherapy while enhancing treatment effectiveness," says Dr. Chen.

NeOnc is also collaborating with the Pediatric Neuro-Oncology Consortium, a network of 60 pediatric neuro-oncology sites across the country, to advance treatment options for pediatric brain tumors through rigorous clinical trials.

Thomas Chen, Founder, CEO, CSO and Board Director



Amir F Heshmatpour, Executive Chairman



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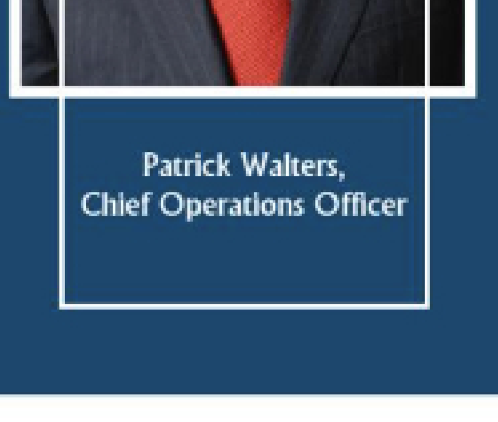

Patrick Walters, Chief Operations Officer

Harnessing the expertise and infrastructure of the medical conglomerate, NeOnc aims to accelerate the evaluation and potential approval of its innovative treatment methodology.

NeOnc's mission is to bring hope and improved outcomes to pediatric patients and their families facing the psychological and physical implications of pediatric brain tumors.

Strategic Collaborations to Advance Neuro-Oncology

At the heart of NeOnc's trailblazing roadmap is a dedicated and multidisciplinary team that spans scientific research, clinical development and strategic advisory roles. Collectively, they are pivotal to its goal of advancing brain cancer treatments.

"Our research efforts are driven by a seasoned translational team based at USC comprising scientists with over two decades of experience running investigational studies on gliomas. These scientists conduct fundamental bench work. For instance, they are involved in performing experiments to assess the efficacy of NeOnc's drugs on tumor cells in vitro and small animal models," says Dr. Chen.

Their insights and findings form the foundational data required for accelerating clinical trials.

Another cornerstone of support for NeOnc's journey through the complex regulatory landscape, particularly with the FDA, is its collaboration with ANOVA Enterprises. This partnership supports the Investigational New Drug (IND) application process to pursue a pediatric indication for NEO100. The combined competencies of NeOnc and ANOVA also boost trial protocol development, FDA submissions, patient recruitment and clinical trial monitoring. Above all, their expertise ensures compliance with rigorous regulatory standards and facilitates the smooth progression of clinical trials.

NeOnc also benefits from its Scientific Advisory Board (SAB), with its diverse group of specialists in neuro-oncology, neurosurgery and pediatrics from around the world. Their collective knowledge spans preclinical research to clinical trial oversight, and the invaluable guidance they provide enhances NeOnc's strategic decision-making and ensures alignment with global standards of care and research excellence.

Building a Future of Impactful CNS Disease Therapies

Post-trial, NeOnc plans to explore new avenues to treat CNS diseases. To support these ambitions, the company is evaluating financing options to secure funding for ongoing and future clinical trials. This seed will enable the company to boost its pipeline and expand the impact of NEO100 and its conjugation therapeutics in neuro-oncology and the broader CNS therapeutic domains.

Bolstered by a powerful team and strategic partnerships, NeOnc's commitment to innovation positions it at the forefront of transforming brain cancer and CNS treatment paradigms. As the company navigates through clinical trials and regulatory milestones, it remains focused on delivering promising therapeutic solutions that enhance patient outcomes and quality of life for patients worldwide.