NeOnc Technologies Reports Phase 1 Dose-Escalation Results for Dosing and Toxicity and Determination of Recommended Phase 2 Dose for Oral NEO212; Management to Host KOL Conference Call Today at 9 a.m. ET

March 4, 2026

CALABASAS, Calif., March 04, 2026 (GLOBE NEWSWIRE) -- NeOnc Technologies Holdings, Inc. (Nasdaq: NTHI) ("NeOnc" or the "Company"), a multi-Phase 2 clinical-stage biopharmaceutical company developing novel therapies for central nervous system (CNS) cancers, today announced data from the dose-escalation portion of its Phase 1/2 clinical trial for NEO212, the Company's novel oral bio-conjugated therapy and will host a conference call to discuss the data today at 9:00am ET.

NeOnc has formally notified the FDA that the Phase 1 dose-escalation portion of the NEO212-01 Phase 1/2 clinical trial has reached Maximum Tolerated Dose (MTD) at Cohort 5 (810 mg, Days 1–5, 28-day cycle) following a second Dose-Limiting Toxicity. In accordance with protocol-defined stopping rules, dose escalation has been halted, no further patients will be enrolled at 810 mg, and the Recommended Phase 2 Dose (RP2D) has been set at 610 mg (Cohort 4). For the Phase 2a metastasis cohort, the starting dose will be 400 mg (Cohort 3).

Notably, although Phase 1 was mainly designed to assess safety, tolerability, and identify the MTD, promising signs of clinical efficacy appeared during this phase of the study. These efficacy signs—including indications of lasting disease control in heavily pretreated patients with recurrent GBM and brain metastases—were observed within the dose-escalation groups.

The emergence of measurable anti-tumor activity in Phase 1 offers early clinical confirmation of NEO212's therapeutic potential and supports the Company's progress into the Phase 2 segment of the trial.

"These early efficacy signals, observed even within a dose-escalation safety study, provide meaningful clinical validation of NEO212's therapeutic potential," said Amir Heshmatpour, Chairman and CEO of NTHI. "With RP2D now established, we believe NeOnc is entering Phase 2 with positive clinical momentum and a clear development pathway."

The transition into Phase 2 will focus on further assessing efficacy at the RP2D in specific expansion cohorts, aiming to generate strong clinical data to support potential accelerated development pathways in recurrent CNS cancers.

Importantly, this represents the first clinical readout of NeOnc's bioconjugated temozolomide (TMZ) platform in an oral formulation, demonstrating NeOnc's drug-engineering capabilities beyond its established intranasal delivery platform. The data validate the Company's ability to optimize CNS penetration and therapeutic exposure across both intranasal and oral modalities. NeOnc intends to request a Type B (End-of-Phase 1) FDA meeting to review safety, PK/PD, preliminary efficacy, RP2D justification, Phase 2 design modifications, and a potential Accelerated Approval pathway. Supporting regulatory materials, including MedWatch Form FDA 3500A and Form FDA 1571, have been submitted via eCTD, ensuring regulatory transparency and alignment as the program transitions into Phase 2 development.

Mr. Heshmatpour, continued:

"This clinical data readout represents a meaningful advancement relative to the historical standard of care in brain cancer, temozolomide (TMZ), originally developed by Merck (NYSE: MRK). Importantly, we have successfully engineered and clinically evaluated a bio-conjugated oral formulation of TMZ, NEO212, and have established the Recommended Phase 2 Dose (RP2D). Achieving dose confirmation is a critical milestone that substantially de-risks the program and positions us for the next stage of development.

We believe NEO212 has the potential to meaningfully improve upon conventional TMZ by enhancing therapeutic performance while maintaining the practicality of oral administration. With this milestone achieved, we are preparing to engage the U.S. Food and Drug Administration to align on the design of what we anticipate will be a pivotal, registrational Phase 2 study, subject to FDA feedback and approval.

If successful, this program could redefine the treatment paradigm for glioblastoma, astrocytoma, and other aggressive CNS malignancies."

NEO212 is specifically designed to overcome a key biological limitation of TMZ: MGMT-mediated resistance. Preclinical studies have shown that NEO212 effectively inactivates and promotes the degradation of O6-methylguanine-DNA methyltransferase (MGMT), a crucial DNA repair enzyme that causes TMZ resistance. Standard TMZ treatment does not significantly lower MGMT levels and remains vulnerable to MGMT-driven DNA repair in brain tumors. This mechanistic difference may be especially

important for TMZ-resistant and MGMT-high recurrent glioblastoma patients, offering a strong biological reason to advance NEO212 into Phase 2 development in the post-TMZ setting.

Mr. Heshmatpour added:

"This marks our first clinical readout of a bio-conjugated oral oncology asset and validates the broader scientific foundation of our platform. Supported by approximately ten issued patents and patent applications across the NEO212 and NEO100 programs, we believe our intellectual property portfolio provides meaningful long-term strategic protection.

Our immediate priority is regulatory engagement and disciplined execution toward a pivotal registrational pathway. We remain focused on advancing differentiated CNS therapies that can create durable clinical value for patients and sustainable long-term value for shareholders."

Founder, Dr. Thomas Chen, Vice-Chairman and Chief Medical Officer noted that, "The determination of the RP2D at 610 mg is a scientifically significant achievement. It confirms that our bio-conjugation technology allows for high-dose delivery of therapeutic agents with a manageable toxicity profile. We are now positioned to explore the efficacy of this optimized dose in our upcoming Phase 2 expansion."

Dr. Henry Friedman of Duke University emphasized the importance of this milestone, stating, "Establishing a safe and tolerable dose is the foundation of any successful oncology program. The identification of the RP2D for NEO212 allows NeOnc to proceed with confidence into efficacy studies for a patient population in desperate need of new oral therapies."

NEO212 is NeOnc's first oral chemical conjugated chemotherapy drug, uniquely combining Temozolomide (TMZ), the current standard of care for glioblastoma and other brain cancers (marketed as Temodar®), with NEO100 (a proprietary form of perillyl alcohol (POH), which is owned and patented by NeOnc). This proprietary conjugation is designed to overcome the limitations of TMZ, including resistance and limited efficacy, by enhancing blood-brain barrier penetration and antitumor activity.

Conference Call Details:

- **Date:** March 4, 2026
- **Time:** 6:00 a.m. PT / 9:00 a.m. ET
- **Webcast:** A live webcast can be accessed at: https://www.webcaster5.com/Webcast/Page/3151/53708 or by visiting https://investors.neonc.com

ABOUT NEONC TECHNOLOGIES HOLDINGS, INC.

NeOnc Technologies Holdings, Inc. is a clinical-stage life sciences company focused on the development and commercialization of central nervous system therapeutics that are designed to address the persistent challenges in overcoming the blood-brain barrier. The company's NEO™ drug development platform has produced a portfolio of novel drug candidates and delivery methods with patent protections extending to 2038. These proprietary chemotherapy agents have demonstrated positive effects in laboratory tests on various types of cancers and in clinical trials treating malignant gliomas. NeOnc's NEO100™ and NEO212™ therapeutics are in Phase II human clinical trials and are advancing under FDA Fast-Track and Investigational New Drug (IND) status. The company has exclusively licensed an extensive worldwide patent portfolio from the University of Southern California consisting of issued patents and pending applications related to NEO100, NEO212, and other products from the NeOnc patent family for multiple uses, including oncological and neurological conditions.

For more about NeOnc and its pioneering technology, visit https://neonc.com

Important Cautions Regarding Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements can be identified by terminology such as "may," "will," "should," "intend," "expect," "plan," "budget," "forecast," "anticipate," "believe," "estimate," "predict," "potential," "continue," "evaluating," or similar words. Statements that contain these words should be read carefully, as they discuss our future expectations, projections of future results of operations or financial condition, or other forward-looking information.

Examples of forward-looking statements include, among others, statements regarding whether the data validates the Company's ability to optimize CNS penetration and therapeutic exposure across both intranasal and oral modalities and whether NEO212 has the potential to replace TMZ as the future standard of care for all brain cancers. These statements reflect our current expectations and beliefs based on information available at this time, but future events may differ materially from those anticipated.

The "Risk Factors" section of our Quarterly Report on Form 10-Q for the three months ended March 31, 2025 as filed with the Securities and Exchange Commission, along with other cautionary language in that report and risk factors and other cautionary language in our subsequent filings with the Securities and Exchange Commission, outlines important risks and uncertainties. These may cause our actual results to differ materially from the forward-looking statements herein, including but not limited to the

fact that results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials, announced or published data from our clinical trials may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data and our product candidates are in preclinical and clinical stages of development, are not approved for commercial sale and might never receive regulatory approval or become commercially viable.

We assume no obligation to revise or update any forward-looking statements, whether as a result of new information, future developments, or otherwise, except as required by applicable securities laws and regulations.

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