PRESS RELEASE

DEBIOPHARM LAUNCHES PHASE 1/2 COMBINATION TRIAL INVESTIGATING BRAIN-PENETRANT SELECTIVE WEE1 INHIBITOR FOR BRAIN CANCER PATIENTS

- *Glioblastomas (GBM) are among the most aggressive and lethal tumors of the central nervous system with a 5-year survival rate of only 6.8%.*
- *Debiopharm is combining its potent, brain penetrant WEE1 inhibitor Debio 0123 with standard of care (SOC) therapy. Debio 0123 hopes to hinder DNA damage repair (DDR) and reverse the poor prognosis for patients with GBM.*
- *This multicenter clinical trial launched in the US, Spain and Switzerland is following the preclinical GBM data presented at the annual American Association for Cancer Research 2023 meeting (AACR 2023: Abstract #6185) in Orlando, Florida.*

Lausanne, Switzerland – May 17th, 2023 – Debiopharm (www.debiopharm.com), a privately-owned, Swiss-based biopharmaceutical company aiming to establish tomorrow's standards of care to cure cancer and infectious diseases, today announced the start of its open-label Phase 1/2 study evaluating Debio 0123, a brain-penetrant and highly selective WEE1 inhibitor, in combination with temozolomide (TMZ) in patients with recurrent or progressive glioblastoma and in combination with TMZ/RT (SOC) in newly diagnosed patients. The initial phase of this study aims to define the recommended phase 2 doses of Debio 0123.

GBM is among the most aggressive and common lethal tumors of the central nervous system. This disease represents a major cause of morbidity and mortality affecting more than 13,000 Americans and causing the death of about 10,000 patients in 2022 [1]. If left untreated, in some cases GBM can lead to the patient's death in approximately 3 months. This type of cancer tends to occur more often in adults between 65-75 years of age. Throughout the continuum of this devastating disease, patients face serious quality of life issues including motor deficits, personality changes, cognitive deficits, language disorders (aphasia) or visual field defects. The disease's poor prognosis constitutes a serious public health concern.

With its Debio 0123 WEE1 inhibitor, Debiopharm is seeking to meet the urgent need for novel treatment interventions to improve clinical outcomes and quality of life for patients suffering from newly diagnosed or recurrent GBM. In cancer cells, DDR pathways are often upregulated due to genomic instability, elevating the chances of resistance to DNA-damaging therapies. Therefore, blocking DNA repair pathways through inhibition of essential kinases such as WEE1 might contribute to increase the cancer's vulnerability to standard of care therapies. Moreover, preclinical results presented at AACR 2023 have shown that Debio 0123 successfully crosses the blood brain barrier and inhibits tumor growth. Furthermore, the *in vivo* combination of Debio 0123 with TMZ demonstrated significantly increased antitumor activity.

"I am very excited to witness the development of a new generation of brain penetrant drugs. Having drugs like this allows us to explore novel treatments for brain tumors, which remains an ongoing challenge." **Dr. Jordi Rodon Ahnert, MD, PhD, MD Anderson Cancer Center, Houston, Texas**.

"The combination of Debio 0123 with temozolomide is promising. Treatment with Debio 0123 to inhibit WEE1 has the advantage of selectively impacting tumor cells, which, due to the increasing replication stress during the S-phase, become more reliant on the proper functioning of the G2-M checkpoint. Debio 0123 acting at both S-phase and G2-M checkpoint can thus make GBM cells more vulnerable to DNA-damaging agents like temozolomide" expressed **Dr. Victor Rodriguez-**

Freixinos, Associate Medical Direction in Oncology at Debiopharm.

"Due to its physiological and structural properties, the blood brain barrier represents a unique challenge for drug delivery and a massive obstacle to patient's care. Thus, Debio 0123 brain permeability represents an important source of hope to patients suffering from brain cancers" stated **Dr. Patrick Roth, University Hospital Zürich**.

About Glioblastoma

Glioblastomas are fast-growing and aggressive brain tumors that can arise *de novo* or evolve from lower grade gliomas. GBM may be asymptomatic until it reaches a significant size. Aside from diagnostic challenges, nearly all GBM recur, and effective treatment options are limited. The widely accepted SOC for patients with newly diagnosed GBMs consists of surgical resection, followed by radiation therapy with concurrent TMZ. Despite treatment, nearly all GBM recur, the 5-year survival rate is still only 6.8% [1] and treatment options are very limited.

About Debio 0123

Debio 0123 is a brain-penetrant, highly selective WEE1 kinase inhibitor. WEE1 is a key regulator of the G2/M and S phase checkpoints, activated in response to DNA damage, allowing cells to repair their DNA before resuming their cell cycle. WEE1 inhibition, particularly in combination with DNA damaging agents, induces an overload of DNA breaks. In conjunction with abrogation of other checkpoints such as G1, the compound pushes the cells through cycle without DNA repair, promoting mitotic catastrophe and inducing apoptosis of cancer cells. Currently in research for solid tumors in monotherapy and combination, Debio 0123 is being developed to respond to high unmet needs of patients living with the burden of difficult-to-treat cancers.

About DNA-Damage Repair (DDR)

When cells have damaged DNA, they need to undergo a repair process called DDR to be able to survive. Cancer cells use their hyperactive DDR response to divide and grow uncontrollably, which promotes cancer expansion. Inhibition of DDR, particularly in combination with other anticancer agents, induces an overall arrest in the uncontrollable cancer cell cycle. This ultimately activates a self-destruction program in cancer cells. DDR inhibitors such as Debiopharm's WEE1 and USP1 inhibitors, are being tested in clinical and preclinical studies.

Debiopharm's commitment to patients

Debiopharm aims to develop innovative therapies that target high unmet medical needs in oncology and bacterial infections. Bridging the gap between disruptive discovery products and real-world patient reach, we identify high-potential compounds and technologies for in-licensing, clinically demonstrate their safety and efficacy, and then hands stewardship to large pharmaceutical commercialization partners to maximize patient access globally.

For more information, please visit www.debiopharm.com

We are on Twitter. Follow us @DebiopharmNews at http://twitter.com/DebiopharmNews

Debiopharm Contact
Dawn Bonine
Head of Communications
dawn.bonine@debiopharm.com
Tel: +41 (0)21 321 01 11

References

[1] National Brain Tumor Society. About Glioblastoma. https://doi.org/10.1038/s41419-022-05271-0