Tubulis Receives FDA Fast Track Designation for Antibody-Drug Conjugate Candidate TUB-040 in Platinum-resistant Ovarian Cancer

- *TUB-040 is a next-generation NaPi2b-targeting Exatecan ADC based on the company's proprietary P5 technology, currently being evaluated in a multicenter Phase I/IIa study NAPISTAR 1-01*
- *Designation for TUB-040 in platinum-resistant ovarian cancer is based on preclinical data in a range of models, demonstrating superior biophysical properties with effective and durable responses*
- *Fast Track status allows for increased interaction with the U.S. Food and Drug Administration ("FDA") to support the development of TUB-040 to expedite regulatory review*
- *Ovarian cancer (OC) is the leading cause of death among women diagnosed with gynecological cancers[1], with platinum-resistant OC being associated with especially poor disease outcomes*

MUNICH, GERMANY, June 27, 2024 – Tubulis announced today that the U.S. Food and Drug Administration ("FDA") has granted Fast Track designation to its lead antibody-drug conjugate (ADC) TUB-040 for the treatment of patients with platinum-resistant ovarian cancer. TUB-040 is a next-generation NaPi2b-targeting Exatecan ADC based on Tubulis' proprietary P5 technology with superior biophysical properties that demonstrated effective and durable responses in a range of preclinical models, including ovarian cancer. The candidate is currently being evaluated in a multicenter Phase I/IIa study (NAPISTAR 1-01, NCT06303505) in patients with platinum-resistant high-grade ovarian cancer (PROC) or relapsed/refractory adenocarcinoma non-small cell lung cancer (NSCLC), who have exhausted other available treatment options.

„Almost all patients with ovarian cancer who are not cured by initial therapy will develop resistance to platinum-based therapy over time. Once platinum-resistant, therapeutic options for these patients are poor with highly unsatisfactory outcomes. The FDA´s Fast Track designation of TUB-040 is an important step in the development of TUB-040 to provide these women with urgently needed new therapeutic options," said Günter Fingerle-Rowson, MD, PhD, Chief Medical Officer of Tubulis. "The FDA decision brings us one step closer to our goal of delivering the true value of ADCs to patients in need, and we are grateful for the agency's support on this path to develop TUB-040 fast and efficiently.

The Fast Track status granted by the FDA is designed to facilitate the development and expedite the review of new therapies that are intended to treat serious conditions and have the potential to address an unmet medical need. Programs granted Fast Track designation are subject to more frequent interactions with the FDA during clinical development and may be eligible for accelerated approval and/or priority review if certain criteria are met.

TUB-040 is currently being evaluated in a multicenter, first-in-human, dose-escalation and optimization Phase I/IIa study. The trial is designed to evaluate the safety, tolerability, pharmacokinetics, and efficacy of TUB-040 as monotherapy and is being conducted in the US, UK, Spain, Belgium and Germany. Phase Ia includes dose escalation and will determine the safety and the maximum tolerated dose or identified dose for optimization, while Phase IIa will focus on dose optimization, safety, and preliminary efficacy of TUB-040.

About Platinum-resistant Ovarian Cancer

Ovarian cancer (OC) is the leading cause of death among women diagnosed with gynecological cancers. While early-stage disease has a high survival rate, OC is often diagnosed at later stages due to its non-

[1] https://pubmed.ncbi.nlm.nih.gov/33620837/; accessed June 26, 2024

specific clinical symptoms and lack of preventive screening methods.[2] The current standard of care is platinum-based therapy, but approximately 20% of patients are platinum-resistant during each treatment line.[3][4] Platinum-resistant OC is defined as disease recurrence during or within 6 months after completing the platinum-based chemotherapy. Platinum-resistant OC is associated with poor disease outcomes and low response rates to subsequent chemotherapy treatment. The median survival for these patients is 12-16 months, highlighting the high unmet medical need of this patient population. [5][6]

About TUB-040 and the P5 Technology

Tubulis' lead antibody-drug conjugate (ADC) TUB-040 is directed against Napi2b, an antigen highly overexpressed in ovarian cancer and lung adenocarcinoma. It consists of an IgG1 antibody targeting Napi2b connected to the Topoisomerase I inhibitor Exatecan through a cleavable linker system based on the company's proprietary P5 conjugation technology with a homogeneous DAR of 8. P5 conjugation is a novel chemistry for cysteine-selective conjugation that enables ADC generation with unprecedented linker stability and biophysical properties. It originated from the fundamental work of Prof. Christian Hackenberger at the Leibniz-Forschungsinstitut für Molekulare Pharmakologie im Forschungsverbund Berlin e.V. (FMP), which unlocked the use of phosphorus chemistry for superior bioconjugation. Preclinical pharmacokinetic analysis also demonstrated that TUB-040 efficiently delivers its payload to the tumor while reducing off-site toxicities. The candidate is currently being investigated in a multicenter Phase I/IIa study (NAPISTAR 1-01, NCT06303505) that aims to evaluate the safety, tolerability, pharmacokinetics, and efficacy of TUB-040 as a monotherapy.

About Tubulis

Tubulis' suite of proprietary platform technologies generates uniquely matched antibody-drug conjugates with superior biophysical properties for treating solid tumors. By demonstrating durable on-tumor delivery of the payload and long-lasting anti-tumor activity, we have reached the clinic with our first program, TUB-040, in ovarian and non-small cell lung cancer. The second candidate from our growing pipeline, TUB-030, is set to follow in the near-term. We will solidify our leadership position by continuing to innovate on all aspects of ADC design to expand their therapeutic potential for our pipeline, our partners and for patients. Visit www.tubulis.com or follow us on LinkedIn.

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[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9358431/#:~:text=Platinum%20resistant%20ovarian%20cancer%20is,et%20al.%2C%202021); accessed June 26, 2024