Tubulis Doses First Patient in Phase I/IIa Trial Investigating ADC Candidate TUB-040 in Ovarian Cancer and Lung Adenocarcinoma

- *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*
- *The clinical trial will enroll up to 140 patients with platinum-resistant high-grade ovarian cancer or relapsed/refractory adenocarcinoma non-small cell lung cancer in the US, the UK and Europe*

MUNICH, GERMANY, June 20, 2024 – Tubulis announced today that the first patient has been treated in its first Phase I/IIa trial (NAPISTAR 1-01, NCT06303505). The study is evaluating Tubulis' next-generation antibody-drug conjugate (ADC) TUB-040 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. TUB-040 targets NaPi2b, a highly overexpressed antigen in ovarian cancer and lung adenocarcinoma. The candidate is the first to enter the clinic from the company's growing pipeline and represents one of Tubulis' two lead candidates developed using its proprietary suite of platform technologies, which enable the creation of uniquely matched ADCs with superior biophysical properties.

The multicenter, first-in-human, dose escalation and optimization Phase I/IIa study aims to investigate the safety, tolerability, pharmacokinetics, and efficacy of TUB-040 as a monotherapy. The trial will be conducted in the US as well as the UK, Spain, Belgium, and Germany. Phase Ia comprises the dose escalation and will determine safety and the maximum tolerated dose or the identified dose for optimization, whereas Phase IIa will focus on dose optimization, safety, and preliminary efficacy of TUB-040. The first patient has been dosed in the US following IND approval by the FDA.

"ADCs are beginning to show their potential as a core treatment modality replacing conventional chemotherapy for several solid tumor indications. Based on our preclinical data we are convinced that TUB-040 can represent a new option for the effective treatment of NSCLC and ovarian cancer patients," said Günter Fingerle-Rowson, MD, PhD, Chief Medical Officer at Tubulis. "The novel P5 technology we use in TUB-040 improves upon current limitations due to off-target toxicity and restricted durability, the main challenges of current ADC treatments. By achieving reduced non-target toxicity together with a more specific, more powerful, and continued on-tumor delivery of the payload, we aim to improve long-term anti-tumor responses and, ultimately, clinical outcomes for patients."

"Initiating our first clinical trial represents an important milestone for the entire Tubulis team and underscores our vision to innovate on all fronts of the ADC design for patient benefit," said Dominik Schumacher, PhD, Chief Executive Officer and Co-founder of Tubulis. "Our objective is to achieve clinical proof-of-concept for our lead candidate, TUB-040, and validate our differentiated platform approach to ADC development."

TUB-040 consists of a humanized, target-specific, Fc-silenced IgG1 antibody equipped with Tubulis' proprietary Tubutecan linker-payload technology, which is based on P5 conjugation chemistry and the topoisomerase-1 inhibitor Exatecan. Tubulis recently presented a comprehensive preclinical data set at AACR, demonstrating the superior stability and minimal loss of linker-payload conjugation for their lead candidate. In a range of preclinical models, Tubulis was also able to show high and long-lasting anti-tumor responses, even at lower expression levels of NaPi2b, with an excellent safety and tolerability profile.

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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