Theseus Pharmaceuticals Announces First Patient Treated with THE-630 in Phase 1/2 Study in Patients with Advanced Gastrointestinal Stromal Tumors (GIST)

CAMBRIDGE, Mass., Jan. 10, 2022 /PRNewswire/ -- Theseus Pharmaceuticals, Inc. (Theseus) (NASDAQ: THRX), a clinical stage biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development and commercialization of transformative targeted therapies, today announced that the first patient has been treated in the Phase 1 portion of Theseus' ongoing Phase 1/2 study to evaluate lead candidate, THE-630, in patients with advanced gastrointestinal stromal tumors (GIST).

THE-630 is a pan-variant inhibitor of the receptor tyrosine kinase KIT. It is designed for patients with advanced GIST whose cancer has developed resistance to earlier lines of therapy by accruing mutations that render those therapies ineffective. In GIST, these mutations occur most often in the KIT protein, where a patient can have multiple KIT mutations simultaneously, leading to complex disease heterogeneity. Pan-variant inhibitors like THE-630 are single therapeutic molecules designed to inhibit all known, clinically relevant mutations of a target protein to address the problem of disease heterogeneity that contributes to treatment resistance. In preclinical studies, THE-630 demonstrated potent in vitro and in vivo activity against all major classes of KIT activating and resistance mutations in GIST. Moreover, THE-630 achieved predicted pan-variant KIT inhibitory blood concentrations at tolerable doses and was associated with significant anti-tumor activity.

"Patients with unresectable or metastatic GIST who have exhausted standard therapies have limited treatment options and poor clinical outcomes. GIST disease progression remains largely KIT-dependent even after multiple lines of therapy, and a significant unmet need remains for these patients," said Suzanne George, M.D., Clinical Director, Center for Sarcoma and Bone Oncology at Dana-Farber Cancer Institute. "I am excited to work with Theseus on this first-in-human trial of THE-630, and I look forward to evaluating its clinical potential to address the needs of patients with advanced GIST."

"The initiation of our Phase 1/2 trial in patients with previously-treated advanced GIST is an important milestone as we begin to characterize THE-630 in the clinic," said David Kerstein, M.D., Chief Medical Officer at Theseus. "We believe THE-630 has a differentiated profile of pan-variant activity against KIT and we look forward to exploring a number of GIST settings where pan-variant inhibition may translate into meaningful clinical benefit—from the fifth-line, where no standard therapies exist, to earlier lines of therapy, such as the second-line, where current standard of care yields less than optimal outcomes."

About the Phase 1/2 study and clinical development plan

Study THE630-21-101 is a Phase 1/2 open label, multicenter, first-in-human dose-escalation and expansion study designed to evaluate the safety, pharmacokinetics, and anti-tumor activity of oral THE-630 (NCT Number: NCT05160168). The study is expected to be conducted in two parts: a dose escalation phase, followed by an expansion phase. The patient population of the initial dose escalation phase (Phase 1) of the trial will include patients with unresectable or metastatic GIST who had disease progression on or are intolerant to imatinib therapy and have also received at least one of the following: sunitinib, regorafenib, ripretinib, or avapritinib. The primary objective of the dose escalation phase is to determine the safety profile of THE-630, including the dose limiting toxicities, maximum tolerated dose, and the recommended Phase 2 dose.

Once a recommended dose has been determined in the escalation phase, the expansion phase (Phase 2) will enroll patients with unresectable or metastatic GIST into cohorts defined by prior therapy from a second-line population to a fifth-line population. The primary objective of the expansion phase is to evaluate the anti-tumor activity of THE-630 in these GIST patient populations.

Data from the Phase 1/2 clinical trial is expected to inform further clinical development of THE-630 including the design of an initial registrational trial in fifth-line GIST, where there is currently no available therapy and therefore a significant unmet need. THE-630 is also expected to be evaluated in second-line GIST, where a pan-KIT inhibitor with activity against all major classes of activating, or cancer-causing, and resistance mutations has the potential to deliver meaningful clinical benefit over the current standard of care.

Initial data from the Phase 1 portion of the clinical trial is expected to be presented at a scientific meeting in the first half of 2023.

About GIST

GIST is the most common sarcoma of the gastrointestinal tract with an estimated 4,000 to 6,000 new cases diagnosed in the United States each year. Approximately eighty percent of GIST cases are driven by mutations that activate the kinase activity of the receptor tyrosine kinase KIT, and up to ninety percent of all relapse cases are driven by secondary resistance mutations in KIT.
**About Theseus Pharmaceuticals, Inc.**
Theseus is a clinical stage biopharmaceutical company focused on improving the lives of cancer patients through the discovery, development and commercialization of transformative targeted therapies. Theseus is working to outsmart cancer resistance by developing pan-variant tyrosine kinase inhibitors (TKIs) to target all known classes of cancer-causing and resistance mutations that lead to variants in a particular protein in a given type of cancer. Theseus' lead product candidate, THE-630, is a pan-variant KIT inhibitor for the treatment of patients with advanced gastrointestinal stromal tumors (GIST), whose cancer has developed resistance to earlier lines of kinase inhibitor therapy. Theseus is also developing a fourth-generation, selective epidermal growth factor receptor (EGFR) inhibitor for C797S-mediated resistance to first- or later-line osimertinib treatment in patients with non-small cell lung cancer (NSCLC). For more information, visit [www.theseusrx.com](http://www.theseusrx.com).

**Cautionary Statement Regarding Forward Looking Statements**
Certain statements included in this press release are not historical facts but are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook," and similar expressions that predict or indicate future events or trends or that are not statements of historical matters, but the absence of these words does not mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements regarding Theseus' strategy, future operations, prospects and plans, the structure and timing of its planned and ongoing clinical trials and future registrational trials, expected milestones, market opportunity and sizing and objectives of management, including in relation to THE-630 and the Phase 1/2 does escalation and expansion clinical trial and its EGFR and other programs.

Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, such as those described from time to time in the reports Theseus files with the Securities and Exchange Commission (SEC), including Theseus' Form 10-Q for the quarter ended September 30, 2021 filed with the SEC on November 15, 2021. However, new risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. Any forward-looking statements contained in this press release are based on the current expectations of Theseus' management team and speak only as of the date hereof, and Theseus specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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