TRIAL/PROGRAM STATUSES – 10th November 2021

Ph 2 KEAPSAKE clinical trial to be terminated based on a lack of clinica benefit observed in patients treated with telaglenastat in an interim analysis

“We are disappointed in this outcome for the KEAPSAKE trial, but it was a well-run study with an interim analysis that gave us an answer to an important clinical question. We also want to express our sincere gratitude to the patients who participated in the trial and their families, as well as the physicians who served as investigators for the trial and their site staff,” said Susan Molineaux, PhD, chief executive officer of Calithera. “We remain committed to patients with difficult-to-treat cancers and will continue to advance our investigational targeted therapies for biomarker-specific patient populations. Our near-term clinical development plans include leveraging our clinical and biomarker expertise in the KEAP1/NRF2 pathway in the development of our mTORC1/2 inhibitor sapanisertib in squamous non-small cell lung cancer, as well as advancing the development of our SYK inhibitor mivavotinib in specific biomarker-defined populations of diffuse large B-cell lymphoma. In addition, we are continuing the development of our arginase inhibitor CB-280 for the treatment of cystic fibrosis.”

First Patient Dosed in Global Ph 2 ACE-Breast-03 Clinical Study of ARX788 for the Treatment of HER2-Positive Metastatic Breast Cancer

“Dosing the first patient in this Phase 2 study of ARX788 in patients with HER2-positive metastatic breast cancer marks an important milestone for Ambrx,” said Feng Tian, Ph.D., Chairman of the Board, President, and CEO of Ambrx. “We have made excellent progress with our clinical development pipeline over the last few months, highlighted by our positive data of ARX788 for HER2-positive gastric cancer, as well as the dosing of the first patient in a Phase 1 trial of ARX517 for PSMA expressing tumors. Our growing clinical programs, coupled with an influx of capital from our IPO in June 2021, leaves Ambrx well-positioned to potentially attain several near-term clinical and corporate milestones.”

First Patient Dosed in Ph 1/2 Trial of Bicycle® Tumor-targeted Immune Cell Agonist™ BT7480 in Patients with Advanced Solid Tumors Associated with Nectin-4 Expression

“BT7480 is our first Bicycle TICA to enter the clinic and is one of a new class of tumor-targeting agents,” said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. “Overexpression of Nectin-4, a well-validated tumor antigen, has been observed in several common tumor types and is associated with poor disease prognosis. Activation of CD137, a co-stimulatory receptor expressed on multiple components of the immune system, can drive anti-tumor immunity, but activation outside of the tumor may give rise to toxicity. Preclinical studies have shown encouraging results, and we look forward to studying the safety and efficacy of this unique asset as we begin the dose escalation portion of the trial.”

First patient dosed in Ph 1/2 GOBLET Study of Pelareorep-anti-PD-L1 Combination Therapies in Gastrointestinal Cancers

"Fewer than half of gastrointestinal (GI) cancer patients respond to immune checkpoint inhibitor (ICI) monotherapy, creating a pressing unmet need for techniques to enhance the efficacy of

these agents," said Dirk Arnold M.D., Ph.D., Director of Asklepios Tumorzentrum Hamburg, and primary investigator of the GOBLET trial. "We believe that pelareorep can address this need and increase the proportion of GI cancer patients responding to ICIs, as clinical studies have shown that it reverses the immunosuppressive tumor microenvironments underlying checkpoint inhibitor resistance. Dosing the first patient in GOBLET represents a crucial step towards the evaluation of this hypothesis, and we look forward to the trial's continued advancement."

Updated provided on Timing for Upcoming Trials of NOX-A12 in Pancreatic and Brain Cancer

Aram Mangasarian, CEO of NOXXON commented: "The effects of the COVID-19 pandemic continue to impact the healthcare industry in many areas, including the most essential ones like manufacturing supply chains. The NOX-A12 studies in pancreatic and brain cancer are our key clinical programs; the pancreas cancer trial is our second collaboration with MSD, a global leader in the immuno-oncology space, and the pivotal brain cancer trial is expected to deliver the data base for our first marketing authorization. We have worked with our contract manufacturer to overcome the unexpected shortages of what are usually easily sourced chemical reagents affecting these batches of NOX-A12 and are doing everything to ensure these batches will be released as soon as possible with the usual high standards of quality. We look forward to getting the trials underway and examining the potential clinical benefits of NOX-A12 in combination with Keytruda or radiotherapy for patients suffering from highly aggressive cancers."

SAMETA Global Ph 3 Trial of Savolitinib in Combination with PD-L1 Inhibitor IMFINZI® initiated in Patients with MET-Driven Advanced Papillary RCC

- SAMETA global Ph 3 study of savolitinib (ORPATHYS® in China), an oral, potent, and highly selective small molecule inhibitor of MET, a receptor tyrosine kinase, in combination with IMFINZI® (durvalumab) in patients with MET-driven advanced papillary renal cell carcinoma (“PRCC”).
- The first patient received their first dose on October 28, 2021.
- The Phase III trial is an open-label, randomized, controlled study in treatment-naïve patients with MET-driven, unresectable and locally advanced or metastatic PRCC, to evaluate the efficacy and safety of savolitinib in combination with IMFINZI®, compared to single agent IMFINZI® or single agent SUTENT® (sunitinib), an oral multi-kinase inhibitor considered the standard-of-care treatment option in PRCC. The primary endpoint of the study is median progression free survival (“PFS”). Other endpoints include median overall survival (“OS”), objective response rate (“ORR”), duration of response (“DoR”), 6-months and 12-months disease control rate (“DCR”), time to second progression (PFS2), safety, pharmacokinetics (“PK”) and quality of life.
- Additional details may be found at clinicaltrials.gov, using identifier NCT05043090.

First Patient Dosed in a Ph 1b/2 Study of Novel PARP Inhibitor (RP12146) in Patients With Advanced Solid Tumors

“PARP inhibitors are a great success story in the DNA damage response area, but they are not without safety concerns that have limited realization of their full potential. Although our novel PARP inhibitor is competing in a crowded space, we expect its superior preclinical safety to translate into the clinic which will differentiate our program and allow us to extend its application beyond the current landscape of approved indications and combinations”, said Swaroop Vakkalanka, Founder & CEO of Rhizen Pharma. Swaroop also added that “Our PARP program is foundational for our DDR platform efforts and will be the backbone for several novel proprietary combinations that we hope to bring into development going forward.”