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Global Coalition for Adaptive Research
Eisai Co., Ltd.

REMAP-CAP TO PARTNER WITH EISAI ON INNOVATIVE TRIAL TO COMBAT COVID

GCAR, EISAI AND UPMC, ON BEHALF OF REMAP-CAP INVESTIGATOR NETWORK, ANNOUNCE ERITORAN'S INCLUSION IN REMAP-COVID, AN ADAPTIVE CLINICAL TRIAL TO TEST INTERVENTIONS FOR PATIENTS WITH MODERATE AND SEVERE COVID INFECTION

EISAI'S ERITORAN SELECTED AS THE FIRST INVESTIGATIONAL IMMUNE MODULATION THERAPY TO BE EVALUATED ACROSS MULTIPLE INTERNATIONAL TRIAL SITES

Global Coalition for Adaptive Research (LOS ANGELES, CA) and Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai"), July 1, 2020 /PRNewswire/ --. The Global Coalition for Adaptive Research (GCAR), in collaboration with UPMC (University of Pittsburgh Medical Center), and Eisai announced today that Eisai will join REMAP-COVID, a substudy of REMAP-CAP (A Randomized, EEmbedded, Multifactorial, Addaptive Platform trial for Community-Acquired Pneumonia) that tests multiple interventions for the treatment of patients hospitalized with COVID-19.

Eritoran, an investigational TLR4 antagonist discovered and developed by Eisai, has been selected as the first investigational immune modulation therapy to be evaluated in the moderate patient group of REMAP-COVID. The trial will be conducted in the multi-hospital UPMC health system along with other medical centers in the United States. Additional global sites across the trial network, including Japan, will follow. Previously observed to be safe in a large Phase 3 randomized trial in sepsis, *eritoran* is designed to suppress the over-production and release of various pro-inflammatory mediators ("cytokine storm") with the aim to protect against damage in COVID-19 patients' lungs and other organs.

"We are excited to initiate our partnership with Eisai and to test this promising intervention in the trial," stated Christopher Seymour, M.D, MSC, Associate Professor, Department of Critical Care Medicine at the University of Pittsburgh and UPMC, and U.S. principal investigator of the REMAP-CAP:COVID study. "By utilizing an adaptive design rather than using a traditional trial approach, we are more likely to get to answers faster, while keeping our patients as safe as possible. REMAP-COVID is an optimal study to identify potential treatments for COVID-19 as safely, quickly, and effectively as possible."

"Eisai is proud to be part of this collaborative initiative to fight the unprecedented COVID-19 pandemic. We are pleased that our investigational immune modulation therapeutic TLR4 antagonist, *eritoran*, will be studied alone and in combination with other drugs to evaluate the effectiveness in COVID-19 hospitalized patients," said Lynn Kramer, M.D, Chief Clinical Officer, Neurology Business Group, Eisai. "As part of our human health care mission, we are committed to making a difference for patients, their families, and health care professionals across the globe."

REMAP-CAP was designed to find optimal treatments for severe pneumonia both in non-pandemic and pandemic settings. When COVID-19 began, REMAP-CAP rapidly pivoted to its pandemic mode (the REMAP-COVID substudy), as per its original intent, to incorporate additional potential treatment regimens specifically targeting COVID-19 and to expand enrollment to COVID-19 patients. This trial is a multicenter, randomized, standard of care vs. multi-active comparators platform study. The primary endpoint for the

REMAP-COVID substudy is organ failure free days over a 21 day observational period. *Eritoran* will be evaluated in hospitalized patients in the immune modulation domain of REMAP-COVID.

REMAP-CAP is led by the world's leading critical care trialists and experts in pandemic and infectious disease outbreaks, virology, immunology, emergency medicine, and Bayesian statistics. REMAP-CAP has enrolled over 1100 patients at 218 sites across North America, Europe, Australia and New Zealand. This vital research is being conducted in collaboration with Berry Consultants, leaders in statistical design for adaptive platform trials, and is being supported by governments and non-profits worldwide. Most recently, the Breast Cancer Research Foundation, committed \$1M to help launch U.S. trial sites through the long-established, innovative trial infrastructure of the Translational Breast Cancer Research Consortium.

"The REMAP study strategy for COVID-19 provides a platform on which to build existing relevant knowledge, plus swiftly and simultaneously evaluate the safety and effectiveness of multiple investigational treatments against the virus, thus enabling us to learn as much as possible in COVID-19 clinical trials," explained Mark McClellan, M.D, PhD, Robert J. Margolis Professor of Business, Medicine, and Policy, and founding Director of the Duke-Margolis Center for Health Policy at Duke University.

"GCAR is honored to participate in this global effort and to serve as trial sponsor of REMAP-CAP:COVID in the U.S. alongside the University of Pittsburgh serving as the U.S. Regional Coordinating Center," shared Meredith Buxton, PhD, MPH, CEO of GCAR. "We are pleased to leverage our extensive experience in running platform trials to support this important endeavor. By working with key partners in academia, industry and philanthropy we will strive to identify improved treatment options for patients with COVID-19."

To learn more about REMAP-CAP and the REMAP-COVID substudy, please visit www.remapcap.org and follow [@remap_cap](https://twitter.com/remap_cap)

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[Notes to editors]

About Global Coalition for Adaptive Research (GCAR)

The Global Coalition for Adaptive Research (GCAR) is a 501(c)(3) nonprofit organization uniting physicians, clinical researchers, advocacy and philanthropic organizations, biopharma, health authorities, and other key stakeholders in healthcare to expedite the discovery and development of treatments for patients with rare and deadly diseases by serving as Sponsor of innovative and complex trials including master protocols and platform trials. As its first major effort, GCAR sponsors GBM AGILE, an international adaptive platform trial for patients with glioblastoma (GBM) – the most common and deadliest of malignant primary brain tumors.

GCAR has expanded to support other innovative collaborations to benefit patients, including most recently those hospitalized with COVID-19. In this effort, GCAR is serving as U.S. Trial Sponsor of REMAP-COVID, a COVID-specific component of the REMAP-CAP adaptive platform trial (www.remapcap.org), designed to determine optimal treatments for pandemic pneumonia.

To learn more about GCAR, visit our website at: www.gcaresearch.org and join us by following us: [@GCARResearch](https://twitter.com/GCARResearch) and www.facebook.com/GCARResearch

About Eisai Co., Ltd.

Eisai Co., Ltd. is a leading global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as "giving first thought to patients and their families and to increasing the benefits health care provides," which we call our *human health care (hhc)* philosophy. With approximately 10,000 employees working across our global network of R&D facilities, manufacturing sites and marketing subsidiaries, we strive to realize our *hhc* philosophy by delivering innovative products to address unmet medical needs, with a particular focus in our strategic areas of Neurology and Oncology. As a global pharmaceutical company, our mission extends to patients around the world through our investment and participation in partnership-based initiatives to improve access to medicines in developing and emerging countries. For more information about Eisai Co., Ltd., please visit www.eisai.com.

About UPMC (University of Pittsburgh Medical Center)

A \$21 billion health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. The largest nongovernmental employer in Pennsylvania, UPMC integrates more than 90,000 employees, 40 hospitals, 700 doctors' offices and outpatient sites, and a 3.8 million-member Insurance Services Division, the largest medical insurer in western Pennsylvania. In the most recent fiscal year, UPMC contributed \$1.2 billion in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution, and paid \$587 million in federal, state and local taxes. Working in close collaboration with the [University of Pittsburgh Schools of the Health Sciences](#), UPMC shares its clinical, managerial and technological skills worldwide through its innovation and commercialization arm, UPMC Enterprises, and through UPMC International. *U.S. News & World Report* consistently ranks UPMC Presbyterian Shadyside on its annual Honor Roll of America's Best Hospitals and ranks UPMC Children's Hospital of Pittsburgh on its Honor Roll of America's Best Children's Hospitals. For more information, go to UPMC.com.

About Eritoran (E5564)

Eritoran is Eisai's in-house discovered and developed TLR4 (Toll-Like Receptor 4) antagonist created with natural product organic synthesis technology. It is a structural analogue of Lipid A which is an activator of endotoxins of bacteria. It has been previously observed to be safe in 14 clinical studies including a large Phase 3 randomized trial in severe sepsis. It is expected to suppress inflammation and increasing in severity caused by COVID-19 by inhibiting the activation of TLR4, which is found in the most upstream of various cytokine gene expression signaling that causes the cytokine-storm.