Momotaro-Gene Inc.
桃太郎源株式会社

News Release

2019 年 9 月 13 日

各　　位

桃太郎源株式会社
代表取締役社長　塩見　均

悪性胸膜中皮腫に対する臨床第 II 相試験に関する
米国でのプレスリリース実施のお知らせ

当社が開発を進めております Ad-SGE-REIC 製剤と抗 PD-1 抗体薬であるオプジーボを併用した悪性胸膜中皮腫に対する臨床第 II 相試験（以下、臨床試験）に関し、ベイラー医科大学（米国テキサス州）で最初の患者への投与を開始したことを、9 月 11 日に米国にてプレスリリースを実施しましたのでお知らせいたします。

同プレスリリースは、Clinical Leader.com、Yahoo! Finance.com（米国）など、多くの現地メディアに取り上げられました。
（参考 URL）https://finance.yahoo.com/news/momotaro-gene-announces-first-patient-113000091.html

以下に、プレスリリースの概要を記載いたします。

桃太郎源株式会社は、2019 年 9 月 11 日、Ad-SGE-REIC 製剤と抗 PD-1 抗体薬の併用療法による臨床第 II 相試験の最初の患者への投与を開始したことを発表しました。

桃太郎源株式会社　CEO 塩見 均は以下のように述べています。
「この臨床第 II 相試験の開始は、Ad-SGE-REIC 製剤の進行中の開発プログラムにおいて重要なマイルストーンであります。私たちは今後もベイラー医科大学との協力関係を継続し、様々ながんに苦しむ患者の治療薬として、Ad-SGE-REIC 製剤の開発を進めていくことを楽しみにしています。」

ベイラー医科大学　ブライアン・バート医師は以下のように述べています。
「私のチームが行った Ad-SGE-REIC 製剤と抗 PD-1 抗体薬の併用法の前臨床研究の結果から、この治療法は有望であると信じています。ベイラー医科大学でこのエキサイティングな研究を実施できることを喜んでおり、試験の結果を楽しみにしています。」

プレスリリース（原文）は、次のページの通りです。

（プレスリリース原文）

Momotaro-Gene Announces First Patient Dosed in Phase 2 Clinical Trial of MTG201 in Combination with Nivolumab in Patients with Relapsed Malignant Pleural Mesothelioma

Combination of Novel Gene Therapy and Immunotherapy Being Evaluated for Synergistic Anti-Tumor Activity in Patients with Cancer with Limited Treatment Options

OKAYAMA, Japan, Sept. 11, 2019 (GLOBE NEWSWIRE) -- Momotaro-Gene, a clinical-stage biotherapeutics company developing novel gene therapies for the treatment of cancer, today announced the dosing of the first patient in a Phase 2 clinical trial combining MTG201, the company's lead therapeutic candidate, with the PD-1 inhibitor nivolumab (Opdivo®) in patients with relapsed malignant pleural mesothelioma. The combination of MTG201 and a PD-1 inhibitor has demonstrated a robust synergistic anti-tumor effect in a preclinical model of malignant mesothelioma.

MTG201 is a novel investigational gene therapy with unique dual mechanisms of action capable of addressing a range of cancers. The drug candidate leverages the company's proprietary adenoviral vector technology platform to deliver the Reduced Expression in Immortalized Cells/Dickkopf-3 gene (REIC/Dkk-3 gene) into cancer cells, where the expression of the gene has been shown to be markedly downregulated. The resulting increase in REIC/Dkk-3 gene expression in cancer cells triggers immunogenic cell death selectively in cancer cells. At the same time, increased expression of REIC/Dkk-3 gene in normal cell components in tumor tissue promotes anti-tumor immunity by activating dendritic cells and natural killer (NK) cells while suppressing immune suppressive regulatory T cells (Tregs) and myeloid derived suppressor cells (MDSC). Based on these novel dual mechanisms, MTG201 is believed to be well positioned to work synergistically with checkpoint inhibitors such as nivolumab.

The Phase 2 trial (NCT04013334), which is being conducted at the Baylor College of Medicine in Houston, Texas, is an open-label, single-arm study designed to assess the efficacy, safety and tolerability of intratumoral administration of MTG201 in combination with nivolumab. The trial will enroll up to twelve patients with malignant mesothelioma who have failed front-line systemic platin-based chemotherapy. The primary objective of the study is to assess efficacy of the treatment combination with the primary endpoint being objective response rate (ORR). Secondary efficacy endpoints will include disease stabilization, duration of response, progression-free survival and overall survival. Investigators will also evaluate traditional safety measures, exploratory biomarkers of activity and the immunogenicity of MTG201.

"The initiation of this Phase 2 clinical trial represents a key milestone in the ongoing development program for MTG201 as it will allow us to build upon the promising results achieved in our two Phase 1 trials of the treatment. Importantly, this study will provide us the very first human data highlighting the therapeutic potential of combining MTG201 with a checkpoint inhibitor, a combination which we believe has significant promise based on preclinical studies," said Hitoshi Shiomi, chief executive officer of

Momotaro-Gene Inc. "We look forward to working with our collaborators at the Baylor College of Medicine on this important study and continuing to advance MTG201 as a potential treatment for patients suffering with a range of cancers."

"Mesothelioma represents an aggressive cancer for which new treatment options are desperately needed. This is especially true for relapsed forms of the disease, for which there are currently no approved therapies," said Bryan Burt, M.D., associate professor of surgery at Baylor College of Medicine and the principal investigator for the study. "Based on preclinical research that my team has conducted on the combination of MTG201 and an anti-PD-1 checkpoint inhibitor, we believe that the synergistic combination of these two therapies may hold promise in this patient population. We are pleased to have the opportunity to conduct this exciting study at the Baylor College of Medicine and look forward to the results of the trial."

Momotaro-Gene has completed two Phase 1 trials of MTG201, demonstrating encouraging safety and tolerability in patients with malignant mesothelioma and localized prostate cancer. In a Phase 1 study conducted with relapsed malignant pleural mesothelioma patients in Japan by Kyorin Pharmaceuticals, a partner of Momotaro-Gene, MTG201 demonstrated promising efficacy by inducing durable disease stabilization.

About Mesothelioma

Mesothelioma is a cancer that occurs in the mesothelium, the thin layer of tissue that covers the lungs and other organs. Mesothelioma is associated with exposure to asbestos in most cases. According to the World Health Organization, there are a total of 59,000 cases of mesothelioma worldwide each year. Most mesotheliomas begin as one or more nodules that progressively grow to form a solid coating of tumor surrounding the lung leading to eventual suffocation and death. There is currently only one approved treatment for mesothelioma and there are no approved therapies for relapsed forms of the cancer. Relapsed mesothelioma is highly aggressive with a median time to disease progression of only six weeks.

About Momotaro-Gene Inc.

Momotaro-Gene is a private, clinical-stage biotherapeutics company developing novel gene therapies for the treatment of cancer. The company has developed Ad-REIC, a proprietary adenoviral vector technology capable of delivery of the Reduced Expression in Immortalized Cells/Dickkopf-3 gene (REIC/Dkk-3 gene). Expression of the REIC/Dkk-3 gene is markedly downregulated in a broad range of human cancer cells. Momotaro-Gene has demonstrated that forced expression of REIC/Dkk-3 gene in tumor tissue induces immunogenic cell death of cancer cells and augmentation of anti-tumor immunity. In addition to the Phase 2 study with malignant pleural mesothelioma in combination with nivolumab, MTG201 is currently being investigated in patients with malignant pleural mesothelioma, hepatocellular carcinoma and glioblastoma multiforme in Japan.

Ad-SGE-REIC 製剤は、これまでの基礎研究と臨床試験により、がん細胞に対する直接効果（がん細胞のみを選択的に死滅させる効果）と抗がん免疫の賦活化による間接効果（全身効果）が実証されるとともに、ヒトへの高い安全性が確認されています。さらにはマウスの悪性中皮腫モデルを使った非臨床試験において、抗 PD-1 抗体薬との併用で顕著な有効性が確認されたことにより、臨床試験の開始に至ったものです。

（ご参考）

ベイラー医科大学：米国テキサス州ヒューストンにある私立医科大学で、US News & World Report による Best Medical Schools ランキング（2019）において、研究部門で全米 16 位、プライマリーケア部門では全米 5 位にランクされています。2014 年には、米国における悪性胸膜中皮腫治療の第一人者である Dr. Sugarbaker（2018 年 8 月 29 日没）が着任し、中皮腫治療センターを立ち上げるなど、悪性胸膜中皮腫治療に関しては、全米トップクラスの実績を誇っています。

抗 PD-1 抗体薬：抗 PD-1 抗体薬は、活性化した T 細胞上の PD-1 に結合して、PD-1 と PD-L1/PD-L2 の結合を阻害することにより、抑制シグナルの伝達をブロックして T 細胞の活性化を維持し、抗腫瘍効果を回復させます。本試験においては、京都大学の本庶佑特別教授と小野薬品との共同研究により開発されたオプジーボ（ニボルマブ）を使用する予定です。

桃太郎源株式会社の概要

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U R L	https://www.mt-gene.com/

（本件に関する照会先：管理本部 伊達 尚範　E-Mail：date@mt-gene.com）

以上